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# A Zwitterionic ABC Triblock Copolymer That Forms a “Trinity” of Micellar Aggregates in Aqueous Solution

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ABSTRACT: A PEO-based macroinitiator was used to first polymerize 2-(diethylamino)ethyl methacrylate (DEA) and then 2-hydroxyethyl methacrylate (HEMA) in a one-pot synthesis via ATRP in methanol at 20 °C. The resulting PEO−PDEA−PHEMA triblock copolymer precursors were successfully converted into the corresponding PEO−PDEA−PSEMA zwitterionic triblock copolymers by esterification of the hydroxy groups on the HEMA block using excess succinic anhydride in pyridine under mild conditions. A “trinity” of micellar aggregates was formed by these PEO−PDEA−PSEMA triblock copolymers in aqueous solution simply by adjusting the solution pH at ambient temperature. The driving forces for forming these three types of micelles were hydrogen-bonding, interpolyelectrolyte complexation, and hydrophobic interactions, respectively. The hydrogen-bonded PSEMA/PEO-core micelles that were formed at low pH were disrupted at higher temperatures or by addition of methanol, leading to PSEMA-core aggregates. The PSEMA/PDEA interpolyelectrolyte micelles formed at around the IEP were very sensitive to the ionic strength of the aqueous solution. Dilution of these solutions resulted in swollen micelles, and eventually dissociation occurred. As far as we are aware, the rich aqueous solution behavior of this new class of ABC triblock copolymers is unprecedented since, for the first time, three types of micelles are formed in aqueous solution by a single-component system.

## Introduction

Recently, a new class of so-called “schizophrenic” AB diblock copolymers has been reported, primarily by our research group[1] but also by others.[2] These diblock copolymers are designed such that both the A and the B blocks have tunable hydrophilic/hydrophobic character. Hence, this new class of polymeric surfactants can undergo micellar self-assembly to form either A-core micelles or B-core micelles in aqueous solution in response to external stimuli such as pH, temperature, or ionic strength.[1,2] Hydrophobic interactions are most commonly used to produce block copolymer micelles. However, this is not the only approach: an alternative strategy involves interpolyelectrolyte complexation. Thus, two oppositely charged polyelectrolyte chains can form a robust electrostatic complex due to the increased entropy of the released small anions and cations.[3] A third mechanism for achieving attractive interactions between polymer chains in aqueous solution is hydrogen bonding.[4] Recently, Gohy and co-workers[5] reported the pH-dependent micellization of a binary mixture of poly(2-vinylpyridine)-*b*-poly(ethylene oxide) [P2VP−PEO] and poly(methacrylic acid)-*b*-poly(ethylene oxide) [PMAA−PEO] diblock copolymers. At high pH, the P2VP−PEO diblock formed P2VP-core micelles, with the PMAA−PEO remaining molecularly dissolved. At intermediate pH interpolyelectrolyte complex micelles were formed that comprised charge-compensated P2VP and PMAA cores. At low pH, PMAA−PEO blocks formed micelles due to *intrachain* hydrogen bonding between the PMAA and PEO blocks. Similarly, complex micellization behavior was also observed by our research group[6] when studying a binary mixture of a poly(ethylene oxide)-*b*-poly[2-(diethylamino)ethyl methacrylate] [PEO−PDEA] diblock copolymer and a PMAA homopolymer. This second example of a “trinity” of micelles comprised hydrophobic PDEA cores at high pH (with the PMAA homopolymer acting as a spectator), interpolyelectrolyte complexation between the cationic diblock copolymer and the anionic homopolymer at intermediate pH, and *interchain* hydrogen bonding between the PMAA and the PEO block at low pH.

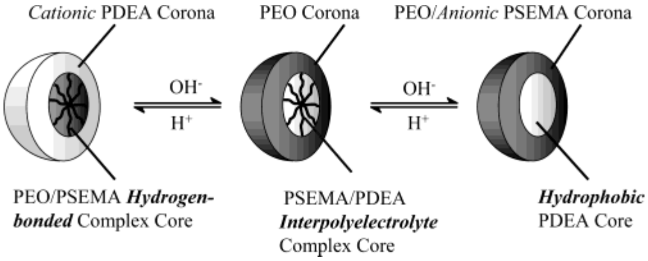

**Figure 1.** The three types of micellar aggregates formed by the zwitterionic PEO−PDEA−PSEMA triblock copolymers in aqueous solution simply by adjusting the solution pH at ambient temperature.

Herein we describe a new class of ABC triblock copolymers that can form a “trinity” of micelles in aqueous solution *with no second component being required*. This micellar self-assembly is reversible and occurs at ambient temperature simply by adjusting the solution pH. Our strategy involved the synthesis of a triblock copolymer comprising of a hydrophilic PEO block, a weak polybase (PDEA), and a weak polyacid block based on poly(2-succinyloxyethyl methacrylate) (PSEMA), as shown in Figure 1. As far as we are aware, the formation of a “trinity” of micelles by a single-component system is unprecedented.

## Experimental Section

**Materials.** 2-Hydroxyethyl methacrylate (HEMA) was kindly donated by Cognis Performrmance Chemicals (Hythe, UK). Monohydroxy-capped PEO ($PEO_{45}$-OH; mean degree of polymerization = 45 and $M_w/M_n = 1.07$), DEA monomer, and other

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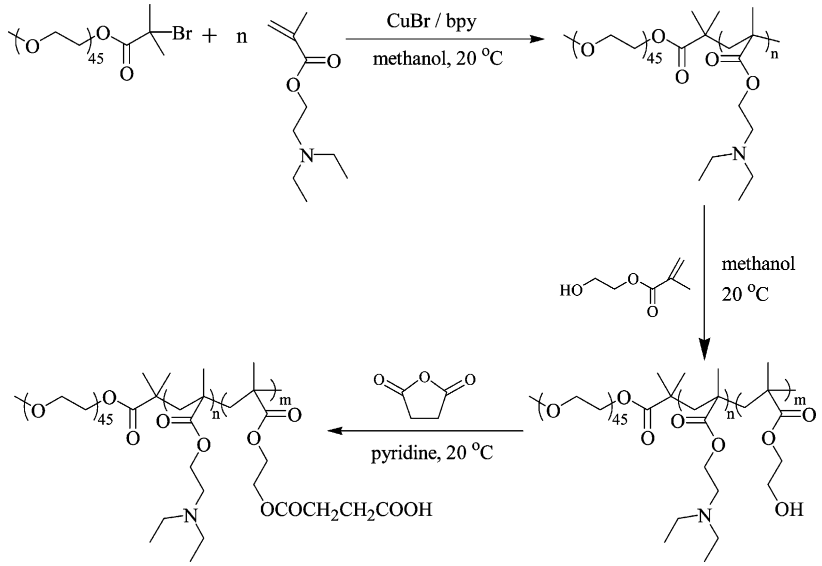

**Figure 2.** Synthesis route for the zwitterionic PEO−PDEA−PSEMA triblock copolymers.

chemicals were purchased from Aldrich. All monomers were passed through silica columns prior to polymerization. Other chemicals were used without further purification. The PEO-based macroinitiator ($PEO_{45}$-Br) was synthesized by esterification of hydroxyl end groups of $PEO_{45}$-OH using 2-bromoisobutyric acid in the presence of 1,3-dicyclohexylcarbodiimide (DCC) and 4-(dimethylamino)pyridine (4-DMAP) as described in the literature.[7] $^1$H NMR studies [in $CDCl_3$: $\delta$ 4.3 (2H, $COOCH_2$), $\delta$ 3.1−3.8 (183H, $OCH_2CH_2O$), $\delta$ 1.9 (6H, $C(CH_3)_2$-Br)] indicated that the degree of esterification of the $PEO_{45}$-OH precursor was essentially 100%.

**ATRP Protocol.** $PEO_{45}$-Br (2.00 g, 0.93 mmol) and DEA (4.30 g, 23.2 mmol, target DP of 25) were dissolved in methanol (8 mL). After purging with nitrogen for 30 min, Cu(I)Br (66.0 mg, 0.46 mmol) and bpy (147.0 mg, 0.94 mmol) were added. The reaction mixture immediately became dark brown and progressively more viscous, indicating the onset of polymerization. After 5 h, $^1$H NMR analysis indicated that 93% DEA had been polymerized. A 50 wt % methanolic solution of HEMA monomer (3.03 g, 23.3 mmol, target DP = 25; previously purged with nitrogen gas for 30 min) was then added to this reaction solution. The reaction mixture was maintained under dry nitrogen for the duration of the second-stage polymerization. After 15 h, the vinyl double bonds at $\delta$ 5.5−6.0 were no longer detected by $^1$H NMR, indicating very high conversion (>99%). The reaction solution turned blue on exposure to air, indicating aerial oxidation of the Cu(I) catalyst. The resulting copolymer was diluted with methanol and passed through a silica column to remove the spent ATRP catalyst. Any unreacted PEO macroinitiator and prematurely-terminated PEO−PDEA diblock copolymer impurities were removed by precipitation into excess *n*-hexane (three times). The final PEO−PDEA−PHEMA triblock copolymer precursor was dried under vacuum overnight to obtain a white product (7.6 g, yield 82%).

**Esterification of the HEMA Block.** The hydroxy groups of the HEMA residues of the triblock copolymer were reacted using succinic anhydride (SA) in anhydrous pyridine at a triblock copolymer concentration of 25% (w/v) and a SA/HEMA molar ratio of 2.0. $^1$H NMR studies indicated that complete esterification was achieved within 24 h at 20 °C. A 5-fold molar excess of methanol (relative to the unreacted SA) was added to consume the unreacted SA, followed by precipitation into excess 2:1 diethyl ether/*n*-hexane to remove the small molecule impurities. The final zwitterionic PEO−PDEA−PSEMA triblock copolymer was dried under vacuum overnight to obtain a white product in 86% yield.

**Copolymer Characterization.** $^1$H NMR spectra were recorded using a Bruker Avance DPX 300 MHz spectrometer. The molecular weights and polydispersities of the $PEO_{45}$-Br macroinitiator and the two PEO−PDEA−PHEMA triblock copolymers were assessed using DMF GPC. The setup comprised a Polymer Laboratories PL gel 5 $\mu$m mixed-B column, a refractive index detector, and DMF eluent that contained 0.01 M LiBr. All measurements were conducted at 70 °C at a flow rate of 1.0 mL $min^{-1}$ using a series of near-monodisperse poly(methyl methacrylate) calibration standards.

The solution pH was monitored using a HI 8424 microcomputer pH meter comprising a HI 1230B combination, double junction, gel pH electrode, and a HI 7669AW temperature probe. Calibration was carried out using pH 4, pH 7, and pH 10 buffer solutions.

Dynamic light scattering (DLS) measurements were carried out using a Brookhaven BI-200SM goniometer equipped with a BI-9000AT digital correlator and a solid-state laser (125 mW, $\lambda = 532$ nm). Except where otherwise mentioned, 1.0% (w/v) copolymer aqueous solutions at 20 °C were used for all measurements. The intensity-average hydrodynamic diameter ($\langle D_h \rangle$) and polydispersity index ($\mu_2/\Gamma^2$) were evaluated from cumulant analyses.

Aqueous electrophoresis measurements were carried out on 0.10% copolymer solutions at 20 °C using a Malvern Instruments Zetamaster S instrument. The solution pH was adjusted as required using NaOH and HCl. The zeta potential, $\xi$, was calculated from the electrophoretic mobility ($u$) using the Smoluchowski relationship, $\xi = \eta u/\epsilon$, where it is assumed that $\kappa\alpha \gg 1$ (here $\eta$ is the solution viscosity, $\epsilon$ is the dielectric constant of the medium, and $\kappa$ and $\alpha$ are the Debye−Hückel parameter and particle radius, respectively).

## Results and Discussion

**Synthesis of the PEO−PDEA−PHEMA Triblock Copolymers.** The ABC triblock copolymers were synthesized by sequential monomer addition using atom transfer radical polymerization (ATRP). First, DEA was polymerized using a PEO-based macroinitiator ($PEO_{45}$-Br) in methanol at 20 °C, and then HEMA was added to this polymerizing solution after a high DEA conversion had been achieved, as shown in Figure 2. Thus, the possibility of unwanted statistical copolymerization of DEA with HEMA in the second-stage polymerization was minimized. According to $^1$H NMR analyses in $CDCl_3$, the DEA conversion was more than 92% prior to the addition of the HEMA monomer in all cases [the integrated peak at $\delta$ 4.16 (assigned to the $COOCH_2$ protons of DEA monomer) was compared to that at $\delta$ 3.92 (assigned to the $COOCH_2$ protons of the polymerized DEA units)]. Moreover, no vinyl signals were

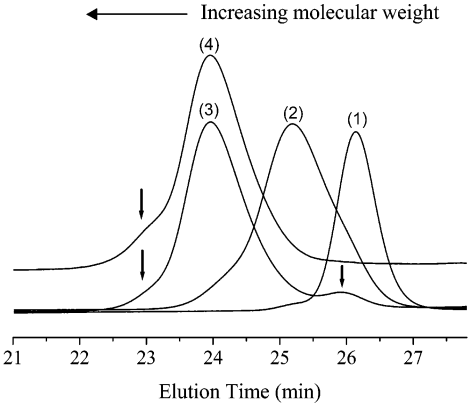

**Figure 3.** DMF GPC traces (vs PMMA standards) for (1) the $PEO_{45}$-Br macroinitiator ($M_n$ = 3900, $M_w/M_n$ = 1.05), (2) the corresponding chain-extended PEO−PDEA just before the addition of HEMA monomer (DEA conversion is 93%, $M_n$ = 7000, $M_w/M_n$ = 1.19), (3) the final reaction mixture after HEMA monomer has been polymerized for 15 h (>99% conversion), and (4) the $PEO_{45}$−$PDEA_{26}$−$PHEMA_{31}$ triblock copolymer after purification ($M_n$ = 15 100, $M_w/M_n$ = 1.20).

detected at $\delta$ 5.50−5.90 after 15 h, indicating that the polymerization of both DEA and HEMA was essentially complete (>99%).

Figure 3 shows the typical evolution of the GPC chromatograms during the syntheses of PEO−PDEA−PHEMA triblock copolymers using the $PEO_{45}$-Br macroinitiator. The target degrees of polymerization ($DP_n$) were 25 for both the DEA and the HEMA blocks. Chromatogram 2 shows the GPC trace of the PEO−PDEA diblock copolymer just before the addition of HEMA monomer; at this point the conversion of DEA monomer was 93%. The monomodal GPC peak ($M_n$ = 7000 and $M_w/M_n$ = 1.19) indicates that the ATRP of DEA was well-controlled, as expected. Chromatogram 3 shows the GPC trace of the reaction mixture after the HEMA monomer had been polymerized for 15 h. $^1$H NMR studies indicated that essentially all of the HEMA (and DEA) had polymerized. A shoulder corresponding to the unreacted PEO macroinitiator and prematurely terminated PEO−PDEA diblock copolymer is evident. The resulting PEO macroinitiator and PEO−PDEA diblock copolymer impurities were removed by precipitation into excess *n*-hexane (see Figure 3). DMF GPC studies (vs PMMA standards) indicated an $M_n$ of 15 100 and an $M_w/M_n$ of 1.20 for this triblock copolymer. A slight shoulder at high molecular weight, which is less obvious in the GPC trace of the crude reaction mixture, can be detected after purification. This is attributed to unwanted termination by combination under monomer-starved conditions. The mean composition of this triblock was calculated to be approximately $PEO_{45}$−$PDEA_{26}$−$PHEMA_{31}$ by the integral analysis of the $^1$H NMR spectrum, using the PEO block as an end group. The slightly HEMA-rich composition of this triblock indicates that some premature termination occurs during the first-stage DEA polymerization. A higher molecular weight triblock copolymer ($PEO_{45}$−$PDEA_{42}$−$PHEMA_{51}$ based on $^1$H NMR studies) was also synthesized for comparison. DMF GPC studies indicated an $M_n$ of 22 200 and an $M_w/M_n$ of 1.15 for this second triblock copolymer.

In a previous paper,[8] we reported the unexpected propensity for tertiary amine methacrylates to undergo transesterification during methanolic ATRP conducted under mild conditions. This leads to the formation of undesired *statistical copolymers* of tertiary amine methacrylate and methyl methacrylate (MMA), which can be detected by $^1$H NMR (signal at $\delta$ 3.6−3.7 due to the $COOCH_3$ group of the polymerized MMA units). Fortunately, this side reaction was much slower than the methanolic ATRP of DEA under the conditions used in the present study. There is little evidence for an additional peak due to polymerized MMA units at $\delta$ 3.6−3.7 in Figure 4 (see middle spectrum). Close inspection of the vinyl signals during polymerization suggested that less than 3% of DEA was converted into MMA units, which is expected to have little or no effect on the aqueous solution properties of the final triblock copolymer.

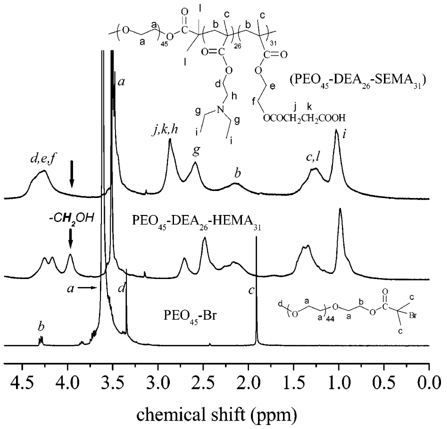

**Figure 4.** $^1$H NMR spectra recorded for the $PEO_{45}$-Br macroinitiator (in $CDCl_3$), the $PEO_{45}$−$PDEA_{26}$−$PHEMA_{31}$ triblock precursor (in $d_5$-pyridine), and the final zwitterionic $PEO_{45}$−$PDEA_{26}$−$PSEMA_{31}$ triblock copolymer (in $d_5$-pyridine).

These two PEO−PDEA−PHEMA triblock precursors were converted into the final PEO−PDEA−PSEMA triblock copolymers by esterification of the hydroxy groups on the HEMA blocks with succinic anhydride in anhydrous pyridine at 20 °C.[9] After 24 h, HEMA signals were no longer detected at $\delta$ 3.9 by $^1$H NMR (see upper spectrum in Figure 4), indicating very high degrees of esterification. Given the mild reaction conditions employed for this esterification, it is reasonable to assume that the relatively narrow molecular weight distributions of the triblock precursors should be retained in the final zwitterionic triblock copolymers.

**Micelles with Hydrogen-Bonded PSEMA/PEO Cores Formed at Low pH.** We have previously established that PSEMA homopolymer precipitates from aqueous solution at low pH,[10] so it is tempting to suggest that PSEMA-core micelles are formed at low pH, with the neutral PEO and cationic PDEA blocks forming the micelle coronas (protonation of the tertiary amine groups of the PDEA block is essentially complete below pH 4). Indeed, the signals due to the PSEMA blocks at $\delta$ 2.9 cannot be detected in the $^1$H NMR spectrum (see Figure 5, lower spectrum) recorded for the $PEO_{45}$−$PDEA_{42}$−$PSEMA_{51}$ triblock copolymer in $DCl/D_2O$ solution at pH 2.5. However, the concomitant suppression of the PEO signal at $\delta$ 3.7 suggests the formation of hydrogen-bonded PEO/PSEMA complexes.[4a,11] Thus, it appears that “flowerlike” micelles comprising hydrogen-bonded PSEMA/PEO complex cores and cationic PDEA coronas are formed.

The angular dependences of the hydrodynamic diameter, polydispersity, and light scattering intensity from DLS measurements of a 1.0 wt % aqueous solution of the $PEO_{45}$−$PDEA_{42}$−$PSEMA_{51}$ triblock copolymer at pH

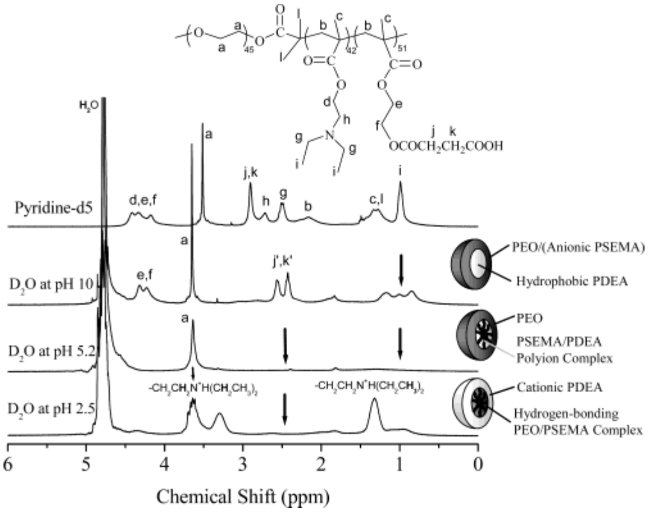

**Figure 5.** $^1$H NMR spectra recorded for the $PEO_{45}$−$PDEA_{42}$−$PSEMA_{51}$ triblock copolymer in either $d_5$-pyridine or $D_2O$ (at pH 10, pH 5.2, and pH 2.5; 1.0 M NaOD or DCl was used for adjusting the solution pH).

**Table 1. Angular Dependence of the Hydrodynamic Diameter ($\langle D_h \rangle$), Polydispersity Index ($\mu_2/\Gamma^2$), and Light Scattering Intensity from Dynamic Light Scattering Studies of a 1.0 wt % Aqueous Solution of the $PEO_{45}$−$PDEA_{42}$−$PSEMA_{51}$ Triblock Copolymer at pH 3.6 and pH 11.3, Respectively**

| angle (deg) | 30 | 60 | 90 | 120 |
|---|---|---|---|---|
| | | pH 3.6 | | |
| $\langle D_h \rangle$ (nm) | 24 | 25 | 25 | 25 |
| $\mu_2/\Gamma^2$ | 0.14 | 0.06 | 0.05 | 0.05 |
| $I$ (kcps) | 83 | 49 | 40 | 47 |
| | | pH 11.3 | | |
| $\langle D_h \rangle$ (nm) | 28 | 31 | 31 | 32 |
| $\mu_2/\Gamma^2$ | 0.16 | 0.12 | 0.09 | 0.08 |
| $I$ (kcps) | 38 | 20 | 16 | 20 |

3.6 and pH 11.3 are summarized in Table 1. The weak angular dependence and narrow micelle size distributions suggest that spherical micelles are formed under these conditions. In the following discussion, only the DLS results obtained at a scattering angle 90° are cited. The light scattering intensity decreased from pH 4 to pH 2, but the $\langle D_h \rangle$ of these micelles remained essentially constant at around 28 nm with relatively low polydispersities being observed (see Figure 6a).

In contrast, the $PEO_{45}$−$PDEA_{26}$−$PSEMA_{31}$ triblock copolymer showed qualitatively different aggregation behavior in acidic solution. DLS studies of the $PEO_{45}$−$PDEA_{26}$−$PSEMA_{31}$ triblock copolymer (see Figure 6b) indicated the formation of micelles with a mean diameter ($\langle D_h \rangle$) of 20 nm ($\mu_2/\Gamma^2 = 0.12$) at pH 4. Below pH 3, the light scattering intensity is reduced, and $\langle D_h \rangle$ increases dramatically, reaching 68 nm (with a relatively high polydispersity of 0.25) at pH 2. Thus, ill-defined, polydisperse aggregates are formed by this zwitterionic triblock copolymer at low pH, rather than well-defined micelles. Strong signals due to PEO and protonated DEA residues are detected in its $^1$H NMR spectrum recorded at pH 2.5 (see Figure S1 in Supporting Information) while the SEMA signals are essentially suppressed; this indicates the formation of purely hydrophobic PSEMA-core micelles, rather than hydrogen-bonded micelle cores due to PEO/PSEMA complexation. Thus, it appears that the hydrogen-bonding interaction between the PSEMA and PEO blocks that is observed at low pH for the $PEO_{45}$−$PDEA_{42}$−$PSEMA_{51}$ zwitterionic triblock copolymer only occurs if the PSEMA block is sufficiently long to interact effectively with the PEO block.

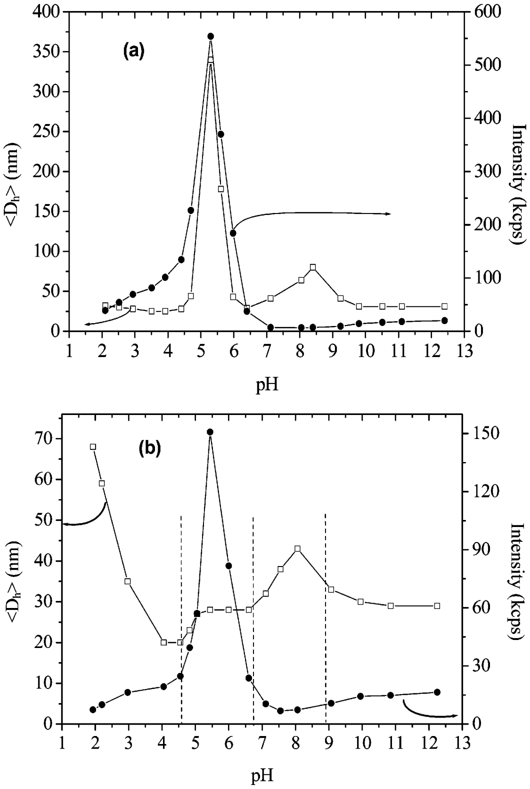

**Figure 6.** Effect of varying the solution pH on the mean hydrodynamic diameter $\langle D_h \rangle$ and light scattering intensity for 1.0 wt % aqueous solutions of (a) the $PEO_{45}$−$PDEA_{42}$−$PSEMA_{51}$ triblock copolymer and (b) the $PEO_{45}$−$PDEA_{26}$−$PSEMA_{31}$ triblock copolymer at 20 °C.

The effect of adding a cosolvent on the aggregation behavior of a 1.0 wt % aqueous solution of the $PEO_{45}$−$PDEA_{42}$−$PSEMA_{51}$ triblock copolymer at pH 2.5 was investigated using $^1$H NMR and DLS. On addition of methanol, a strong PEO signal at $\delta$ 3.7 was observed in the $^1$H NMR spectrum (see Figure 7a), indicating that the hydrogen bonding between the PEO and PSEMA blocks was effectively disrupted by addition of a small amount of methanol (<12 wt %); this effect was anticipated on the basis of the literature.[11] On the other hand, only a relatively weak PSEMA signal was detected by $^1$H NMR (see Figure 7a), indicating a relatively low degree of solvation for this acidic block. Thus, the PSEMA block appears to remain essentially hydrophobic and compact PSEMA-core micelles were formed under these conditions, which resulted in a pronounced increase in the scattered light intensity (see Figure S2 in Supporting Information). On further addition of methanol, the hydrophobic PSEMA cores became gradually solvated, and finally micellar dissociation occurred, leading to a reduction in the light scattering intensity (see Figure S2 in Supporting Information).

These hydrogen-bonded micelles were also disrupted at lower temperatures. $^1$H NMR studies of the $PEO_{45}$−$PDEA_{42}$−$PSEMA_{51}$ triblock copolymer at 5 °C in DCl/$D_2O$ (pH 2.5) revealed a strong PEO signal at $\delta$ 3.4 and an attenuated PSEMA signal at $\delta$ 2.4 (see Figure 7d). This indicates the formation of PSEMA-core micelles, rather than the micelles with hydrogen-bonded PSEMA/PEO that were formed at 20 °C (see Figure 7c). DLS studies indicated that relatively compact PSEMA-core

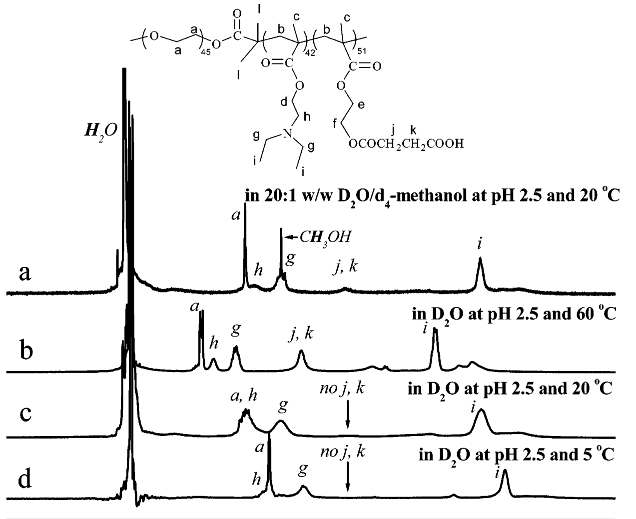

**Figure 7.** $^1$H NMR spectra recorded for the PEO$_{45}$−PDEA$_{42}$−PSEMA$_{51}$ triblock copolymer in (a) 20:1 w/w D$_2$O/$d_4$-methanol at pH 2.5 (1.0 M DCl in D$_2$O was used for adjusting the solution pH) and in DCl/D$_2$O (pH 2.5) at (b) 60 °C, (c) 20 °C, and (d) 5 °C.

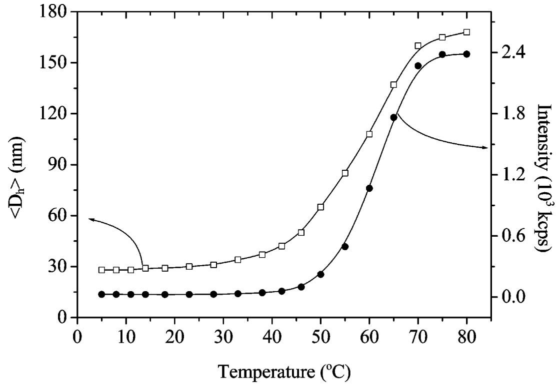

**Figure 8.** Temperature dependence of the light scattering intensity and ⟨$D_h$⟩ for a 1.0 wt % aqueous solution of the PEO$_{45}$−PDEA$_{42}$−PSEMA$_{51}$ triblock copolymer at pH 2.5.

micelles (⟨$D_h$⟩ = 28 nm) were formed from 5 to 11 °C (see Figure 8). Above 45 °C, relatively large micelles were observed. At 60 °C, a strong NMR signal due to the PEO block was detected at $\delta$ 4.2 (see Figure 7b), suggesting disruption of the hydrogen-bonded PSEMA/PEO complex and formation of PSEMA-core aggregates. Similar temperature-dependent dissociation was also reported for the hydrogen-bonded micelles formed by a binary mixture of P2VP−PEO and PMAA−PEO diblock copolymers.[5]

**Interpolyelectrolyte PDEA/PSEMA Micelles Formed at Intermediate pH.** Above approximately pH 4.5, the carboxylic acid groups of PSEMA block become progressively more ionized, while the PDEA blocks begin to lose some of their cationic character. Under these conditions charge-compensated micelles were formed with mixed PSEMA/PDEA cores and PEO coronas. Essentially no PDEA or PSEMA signals were detected by $^1$H NMR studies at pH 5.2 (see Figure 5), which is consistent with interpolyelectrolyte complexation. A 1.0% (w/v) aqueous solution of the PEO$_{45}$−PDEA$_{26}$−PSEMA$_{31}$ triblock copolymer scattered light strongly from pH 5.1 to pH 6.4 (see Figure 6b), indicating the formation of interpolyelectrolyte micelles, as expected. Cumulant analysis indicated an essentially constant ⟨$D_h$⟩ of around 32 nm and polydispersities ranging from 0.06 to 0.08. The scattered light intensity increased dramatically and reached a maximum at approximately pH 5.4, which is in reasonably good agreement with the calculated isoelectric point of 5.48 estimated for this zwitterionic triblock copolymer.[12] In contrast, the aggregation behavior of PEO$_{45}$−PDEA$_{42}$−PSEMA$_{51}$ copolymer is quite different in this solution pH range. Both the scattering intensity and ⟨$D_h$⟩ increased dramatically above pH 4.5, and both reached maximum values at around pH 5.3; the largest aggregates had a ⟨$D_h$⟩ of 340 nm and a polydispersity of 0.38. Somewhat smaller aggregates with much narrower polydispersities were observed by DLS just above and below pH 5.3. It is well-known that zwitterionic *diblock* copolymers usually precipitate from aqueous solution at their isoelectric points.[1a,d,e,10b,12,13] However, in the present study, the nonionic PEO block can act as a steric stabilizer for the interpolyelectrolyte complex, allowing the formation of either stable micelles or micellar aggregates.[14] Thus, the DLS studies suggest a *specific micellization pH* for this zwitterionic *triblock* copolymer, rather than an isoelectric point (at which precipitation occurs) or a critical micelle pH (above or below which micelles are formed).[15] As far as we are aware, this is a new concept in the field of water-soluble block copolymers.

The colloidal stability of these interpolyelectrolyte complexes was very sensitive to the ionic strength of the aqueous solution, as expected. For a 1.0% (w/v) aqueous solution of the PEO$_{45}$−PDEA$_{26}$−PSEMA$_{31}$ triblock copolymer at pH 5.4, DLS studies indicated that micellar dissociation occurred above 0.15 M NaCl due to electrostatic screening (see Figure S3 in Supporting Information).[16] A dramatic decrease in light scattering intensity above pH 6.5 indicated dissociation of the interpolyelectrolyte complexes (see Figure 6b). $^1$H NMR signals due to all three blocks were detected for the PEO$_{45}$−PDEA$_{26}$−PSEMA$_{31}$ triblock copolymer dissolved in D$_2$O at pH 7.5. However, normalization with respect to the PEO signal suggests that only approximately 85% of the PDEA and PSEMA residues were solvated under these conditions, indicating the formation of loose, highly hydrated aggregates rather than true molecular dissolution. DLS studies indicated a very low light scattering intensity (less than 7 kcps) at pH 7.55 (see Figure 6b). Cumulant analysis revealed polydisperse aggregates with a ⟨$D_h$⟩ of 38 nm. On the basis of our previous studies, the p$K_a$ of PDEA homopolymer is around 7.3.[17] Thus, the PDEA blocks should still have significant cationic charge density at pH 7.55, allowing weak electrostatic interactions with the highly anionic PSEMA blocks. Similar observations were made for the PEO$_{45}$−PDEA$_{42}$−PSEMA$_{51}$ zwitterionic triblock copolymer on varying the solution pH from pH 6.5 to pH 9.5. The effect of varying the copolymer concentration on the aggregation behavior of the PEO$_{45}$−PDEA$_{26}$−PSEMA$_{31}$ triblock copolymer at pH 5.4 was investigated using DLS at 20 °C. As shown in Table 2, the hydrodynamic micelle diameters remained almost constant (⟨$D_h$⟩ = 27−28 nm) on diluting from 10.00 to 0.50 g L$^{-1}$. On lowering the copolymer concentration further, the hydrodynamic diameter increased significantly, until finally no aggregates could be detected at 0.02 g L$^{-1}$.

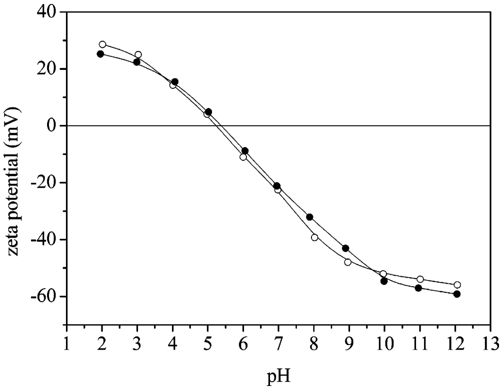

**Figure 9.** Aqueous electrophoresis data for 0.10 wt % aqueous solutions of (●) the $PEO_{45}-PDEA_{26}-PSEMA_{31}$ triblock copolymer and (○) the $PEO_{45}-PDEA_{42}-PSEMA_{51}$ triblock copolymer at 20 °C.

**Table 2. Effect of Copolymer Concentration on the Dynamic Light Scattering Data Obtained for the Polyion Complex Micelles Formed by the $PEO_{45}-PDEA_{26}-PSEMA_{31}$ Triblock Copolymer in Aqueous Solution at pH 5.4 and 20 °C**

| $C_p$ (mg/mL) | 0.02 | 0.05 | 0.10 | 0.20 | 0.50 | 1.00 | 2.00 | 5.00 | 10.00 |
|---|---|---|---|---|---|---|---|---|---|
| $\langle D_h \rangle$ (nm) | | 43 | 35 | 30 | 28 | 27 | 27 | 27 | 28 |
| $\mu_2/\Gamma^2$ | | 0.37 | 0.24 | 0.18 | 0.13 | 0.08 | 0.08 | 0.08 | 0.07 |
| $I$ (kcps) | 0.7 | 1.2 | 1.8 | 2.9 | 6.5 | 13 | 26 | 67 | 138 |

**Hydrophobic PDEA-Core Micelles at High pH.** At pH 9.5, the tertiary amine groups were almost completely deprotonated and the PDEA blocks became hydrophobic. Moreover, the PSEMA residues were completely ionized in their anionic carboxylate form. Inspecting Figure 5, no PDEA signals were detected in the $^1$H NMR spectrum of the $PEO_{45}-PDEA_{42}-PSEMA_{51}$ triblock copolymer at pH 10 (it is noteworthy that the methacrylate backbone signals observed at 0.8−1.2 ppm are due to the PSEMA block, rather than the PDEA block; the j′ and k′ signals simply reflect the chemical shifts of the original j and k signals caused by ionization of the PSEMA block in alkaline media). This indicates the formation of PDEA-core micelles, with the micelle coronas comprising a mixture of anionic PSEMA chains and neutral PEO chains. DLS studies under the same conditions (see Figure 6) indicated $PEO_{45}-PDEA_{26}-PSEMA_{31}$ micelles with a $\langle D_h \rangle$ of 29 nm ($\mu_2/\Gamma^2 = 0.14$) and $PEO_{45}-PDEA_{42}-PSEMA_{51}$ micelles with a $\langle D_h \rangle$ of 31 nm ($\mu_2/\Gamma^2 = 0.11$).

**Aqueous Electrophoresis Studies.** Positive zeta potentials were observed at pH 2 (+25 mV for the $PEO_{45}-PDEA_{26}-PSEMA_{31}$ copolymer and +29 mV for $PEO_{45}-PDEA_{42}-PSEMA_{51}$ copolymer) (see Figure 9). On increasing the solution pH, the degree of protonation of the tertiary amine groups of the PDEA block was reduced and the carboxylic acid groups of the PSEMA block became ionized; thus, the net zeta potentials of both copolymers decreased. Isoelectric points were observed at around pH 5.3 for the $PEO_{45}-PDEA_{42}-PSEMA_{51}$ copolymer and at approximately pH 5.4 for the $PEO_{45}-PDEA_{26}-PSEMA_{31}$ copolymer. The maximum light scattering intensities observed for these two copolymers in the DLS studies also occurred at approximately these isoelectric points, but it is emphasized that no macroscopic precipitation was observed in either case. On further increasing the solution pH, the PDEA block became hydrophobic, whereas the PSEMA residues became highly anionic; hence, negative zeta potentials of approximately −55 mV were observed.

## Conclusions

Two well-defined PEO−PDEA−PHEMA triblock copolymer precursors were synthesized via ATRP using a PEO-based macroinitiator in methanol at 20 °C. Both copolymers were successfully converted into the corresponding PEO−PDEA−PSEMA zwitterionic triblock copolymers by treatment with excess succinic anhydride in pyridine under mild conditions. A “trinity” of micellar aggregates was formed in aqueous solution by these PEO−PDEA−PSEMA triblock copolymers simply by adjusting the solution pH at ambient temperature. The driving force for micellization was via hydrogen-bonding, interpolyelectrolyte complexation, and purely hydrophobic interactions, respectively. The hydrogen-bonded PSEMA/PEO micelles that were formed at low pH were disrupted at higher temperatures, leading to PSEMA-core aggregates. The hydrogen-bonded micelles were also readily destroyed by the addition of methanol, forming more compact PSEMA-core micelles as the PEO chains became solvated. The PSEMA/PDEA interpolyelectrolyte micelles formed at around the IEP were very sensitive to the ionic strength of the aqueous solution. Dilution of these solutions resulted in swollen micelles, and eventually dissociation occurred. As far as we are aware, the rich aqueous solution behavior of this new class of ABC triblock copolymers is unprecedented since, for the first time, three types of micelles are formed by a single-component system.

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**Supporting Information Available:** $^1$H NMR spectrum of the $PEO_{45}-PDEA_{26}-PSEMA_{31}$ triblock copolymer recorded in $DCl/D_2O$ solution at pH 2.5 and 20 °C; effect of addition of methanol on the scattered light intensity for a 1% aqueous solution of the $PEO_{45}-PDEA_{42}-PSEMA_{51}$ triblock copolymer at pH 2.5; and effect of addition of NaCl on the scattered light intensity for a 1% aqueous solution of the $PEO_{45}-PDEA_{26}-PSEMA_{31}$ triblock copolymer at pH 5.4. This material is available free of charge via the Internet at http://pubs.acs.org.

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