

Noncovalently Connected Polymeric Micelles in Aqueous Medium

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Differing from the conventional micelles made of block or graft copolymers, in which the core and corona are connected by covalent bonding, the micelles reported in this paper are composed of a polymer pair and the core and corona are connected by hydrogen bonding. Poly(styrene-*co*-methacrylic acid) (SMAA) and poly(vinylpyrrolidone) (PVPo) self-assembled into spherical micelles with hydrodynamic radii around 100 nm in aqueous medium. These stable micelles are composed of the core of collapsed SMAA chains and the corona of solvated PVPo chains. The hydrogen bonding between methacrylic acid and PVPo units and the difference in the solubility in water between SMAA and PVPo are the main factors responsible for the micelle formation. Using dynamic light scattering, it was found that the hydrodynamic radius of the micelles significantly increases with increasing initial concentrations of both SMAA and PVPo. The micelle size does not depend on the MAA content (3.55–13.1 mol %) in SMAA monotonically, which can be rationalized by the coexistence of different stabilization mechanisms. Transmission electronic microscopy (TEM) was used to observe morphologies of the micelles. The core–shell structure of the micelles became visualized only when adequate staining of the TEM specimens was employed.

Introduction

In the past decade, chemists have shown great interest in constructing nanostructures with a variety of morphologies and functions based on self-assembly. Among the different approaches to self-assembly of macromolecules, micellization of block copolymers and graft copolymers in selective solvents is the most common one and has been investigated extensively.^{1,2} Self-assembly of amphiphilic diblock copolymers in selective solvents generally results in aggregates with core–shell structure. In aqueous solution, the hydrophobic blocks compose the core and the hydrophilic blocks the corona. Such micelles in aqueous solutions are of special interest due to the preferential solubility of hydrophobic species in the micelle core which consequently benefits applications of the micelles in many aspects such as controlling drug release³ and preventing water pollution, etc.^{1,4,5}

In all the micelles reported based on block copolymers or graft copolymers, the core and corona are connected by chemical bonds. Recently, on the basis of our long-term research on interpolymer complexation due to hydrogen bonding,⁶ we proposed a new approach to micellization via self-assembly of polymer blends in solution.^{7–10} The

principle is as follows. Suppose we have polymers A and B, which are able to interact on each other via hydrogen bonding, in a solvent that is a precipitant for A but good solvent for B, A chains aggregate but macroscopic precipitation can be prevented by the soluble B chains. Thus, micelle-like particles with a compact A core surrounded by B corona are formed. In such micelles, specific interaction instead of covalent bonding exists between the components A and B.

In this paper, this new approach was employed to prepare micelle-like particles in aqueous medium. Poly(styrene-*co*-methacrylic acid) (SMAA) with a small content of MAA units (3.55–13.1 mol %), which was insoluble in water, served as polymer A and water-soluble poly(vinylpyrrolidone) (PVPo) as polymer B. Hydrogen bonding between methacrylic acid unit and pyrrolidone unit is expected to connect the core and corona, and consequently, the core of SMAA is stabilized by the solvated PVPo. Compared with the amphiphilic block copolymers, homopolymers or random copolymers needed in this approach can usually be prepared in much simpler procedures; thus, it makes this new approach more practical for its potential applications. It is worth mentioning that in recent years there has been a series of reports on so-called “onion micelles”.^{11–16} It contains two block copolymers: the blocks in the first copolymer form the inner core and outer core

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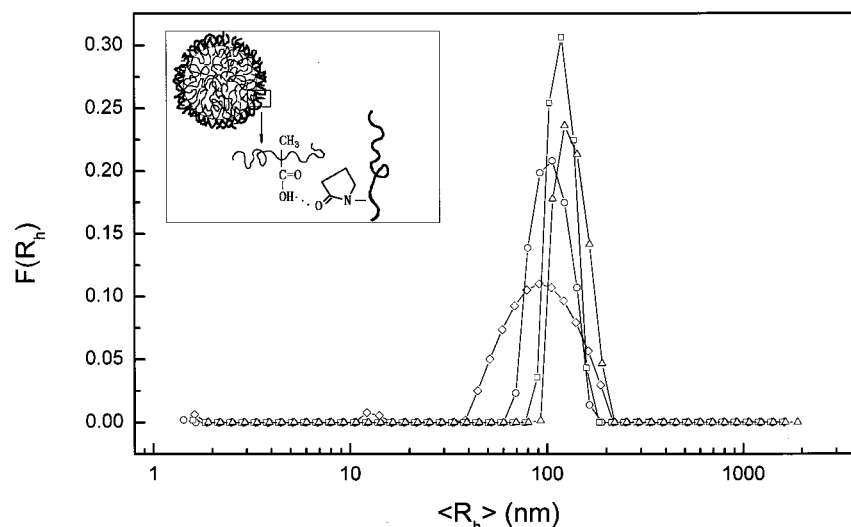


Figure 1. Hydrodynamic radius distributions of the micelles prepared by adding 1 mL of SMAA2/THF with different concentrations (\diamond , 0.1; \circ , 0.5; \square , 1.0; \triangle , 1.5 mg/mL) into 20 mL of PVPo/water with a concentration of 0.1 mg/mL (test group 2 in Table 2). The inset is a schematic illustration of SMAA/PVPo micelles.

Table 1. Characterization Data of SMAA Samples

sample code	M_n (g/mol)/ 10^4	$d = M_w/M_n$	MMA content	
			wt %	mol %
SMAA-1	4.6	1.64	2.99	3.55
SMAA-2	3.5	1.79	8.58	10.1
SMAA-3	3	1.75	11.2	13.1

while the second copolymer composes the outer core and shell. The complex micelle is stabilized by the solvated blocks in the second copolymer. Obviously, there are chemical bonds between the inner and outer core as well as between the outer core and shell. However, no chemical bonds exist between the two block copolymers. This, to some extent, resembles the present micelles which contain two parts without chemical bonds between them.

Experimental Part

Materials. Copolymers of SMAA were synthesized by free-radical polymerization of purified styrene and methacrylic acid. The copolymerization was stopped at a conversion about 10 wt %. MAA contents in the products were adjusted by changing the feed composition. Molecular weight and polydispersity (M_w/M_n) were determined by size exclusive chromatography using monodispersed polystyrene as standard. The MAA contents in the copolymers were determined by titration. The characterization results of SMAA are summarized in Table 1. PVPo with a weight-average molecular weight of 3.6×10^5 was purchased from Aldrich and used as received.

Micelle Preparation. SMAA/PVPo micelle solutions were prepared by adding 1 mL of SMAA/THF solution into 20 mL of PVPo/water solution dropwise under ultrasonic. The resultant solutions were transparent and bluish. For different purposes, SMAA/THF with concentrations ranging from 0.1 to 1.5 mg/mL and PVPo/H₂O from 0.01 to 1.0 mg/mL was used. The final compositions of the micelle solutions ranged from 0.05/1 to 5/1 (SMAA/PVPo, w/w).

Dynamic Light Scattering. DLS was employed to characterize the hydrodynamic size of the SMAA/PVPo micelles in water. The solution was clarified by filtering through a $0.5 \mu\text{m}$ Millipore filter directly into a scattering cell. The measurements were performed in a modified commercial LLS spectrometer (ALV/SP-125) equipped with a multi- τ digital time correlator (ALV-5000e) and a solid-state laser (ADLAS DPY42 II, output power

≈ 50 mW, at $\lambda_0 = 532$ nm). All the DLS were measured at 25.0 ± 0.1 °C and at a scattering angle of 30°. The translational diffusion coefficient D_T and the hydrodynamic radius R_h were obtained from the average decay rate Γ using $D_T = \Gamma/q^2$ and Stokes–Einstein formula, $R_h = kT/6\pi\eta D_T$, where the scattering vector $q = 4\pi n/\lambda \sin(\theta/2)$ and θ , λ , k , T , η , and n are the scattering angle, the incident wavelength in a vacuum, Boltzmann constants, temperature, solvent viscosity, and solvent refractive index, respectively.

Transmission Electron Microscopy. TEM observations were conducted on a Philips CM120 transmission electron microscope at an accelerating voltage of 80 kV. The specimens were prepared by spraying a drop of the micelle solution on a carbon-coated copper grid followed by water evaporation. Staining of the specimens with the vapor of 1% (w/w) of RuO₄ solution in water was performed in a closed vessel for a desired period.

Results and Discussion

Size Dependence of Micelles on Initial Concentrations. It has been known for a long time that the proton donating groups in poly(methacrylic acid) or poly(acrylic acid) may form hydrogen bonding with proton acceptor in PVPo, leading to interpolymer complexes in their common solvent.^{6,17} In this study, we found that when SMAA/THF solution was added dropwise into excessive PVPo/H₂O solution, due to the hydrogen bonding between SMAA and solvated PVPo chains, the aggregates made of the collapsed SMAA chains did not precipitate further but formed particles stabilized by the solvated PVPo chains. Therefore, the two polymers finally constructed micelles composed of a core of collapsed SMAA chains and a corona of solvated PVPo chains. The core and corona are connected by hydrogen bonding (see inset in Figure 1).

DLS was used to measure hydrodynamic radius distributions of the micelles produced in different conditions. The results are summarized in Table 2. There are four test groups. The test groups of 1, 2, and 3 are for the solutions containing PVPo and its counterparts of SMAA1, SMAA2, and SMAA3, respectively. In each group, the concentration of SMAA varied while that of PVPo kept constant. In test group 4 for PVPo/SMAA1, instead, the concentration of PVPo varied, but that of SMAA1 did not change. The resultant R_h distribution curves of test group 2, as an example, are shown in Figure 1. It can be seen that all the solutions display unimodal distributions, and

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Table 2. Characterization Data and Preparation Conditions of Micelles^a

group no.	sample no.	C (mg/mL) [PVPo/H ₂ O]	C (mg/mL) [SMAA/THF]	composition $w_{\text{SMAA}}/w_{\text{PVPo}}$	R_h (nm)
1 PVPo/SMAA1	1-1	0.1	0.1	0.05/1	99.6
	1-2	0.1	0.5	0.25/1	108.1
	1-3	0.1	1.0	0.5/1	138.8
	1-4	0.1	1.5	0.75/1	161.8
4 PVPo/SMAA1	4-1	0.01	1.0	5/1	120.9
	4-2	0.05	1.0	1/1	128.5
	4-3	0.1	1.0	0.5/1	138.8
	4-4	0.5	1.0	0.1/1	171.8
	4-5	1.0	1.0	0.05/1	233.6

^a For simplicity, data for test groups 2 and 3 are not listed. In test groups 2 and 3, SMAA2 and SMAA3 replaced SMAA1, respectively, and the initial concentrations of SMAA were the same as those in group 1. For example, in test 3-2, the concentrations of PVPo and SMAA3 are 0.1 and 0.5 mg/mL, respectively.

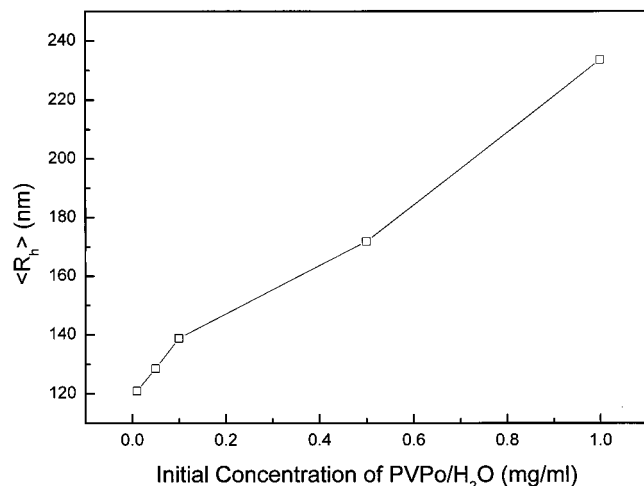


Figure 2. Hydrodynamic radius of particles as a function of the initial concentration of PVPo/H₂O. The solution was prepared by adding 1 mL of SMAA1/THF (0.1 mg/mL) into 20 mL of PVPo/H₂O.

both peak position and the distribution width vary with SMAA2 concentration; i.e., the larger the concentration, the larger the average hydrodynamic radius ($\langle R_h \rangle$) and the narrower the distribution. As evidenced by the data of groups 1, 2, and 3 in Table 2, the three SMAA samples present a similar trend of the change in the micelle size; i.e., $\langle R_h \rangle$ increases with SMAA concentration over the range 0.1–1.5 mg/mL when PVPo concentration remains unchanged. It can be imagined that as the SMAA/THF solution was added into water solutions containing PVPo, the local environment of the hydrophobic SMAA chains worsened rapidly so that the individual SMAA chains quickly collapsed and aggregated. At the same time, due to the favorable enthalpy associated with hydrogen bonding, the PVPo chains moved to and concentrated around the collapsed SMAA chains, resulting in micelle formation. Therefore, the final size of the formed micelles depends on the relative rates of the processes including intrachain and interchain aggregation of SMAA chains and gathering of PVPo chains. Obviously, the concentration increase of SMAA favors interpolymer aggregation and consequently causes larger micelles.

As shown for the test group 4 in Table 2, the initial concentration of PVPo/H₂O also plays a significant role in controlling the micelle size. When SMAA/THF solution with concentration of 1 mg/mL was added into PVPo/H₂O solutions with concentration ranging from 0.01 to 1.0 mg/mL, it was found that the average hydrodynamic radius of the micelles increased from 120.9 to 233.6 nm (Figure 2). This trend is in agreement with that observed for the micelles composed of slightly sulfonated polystyrene (SPS)

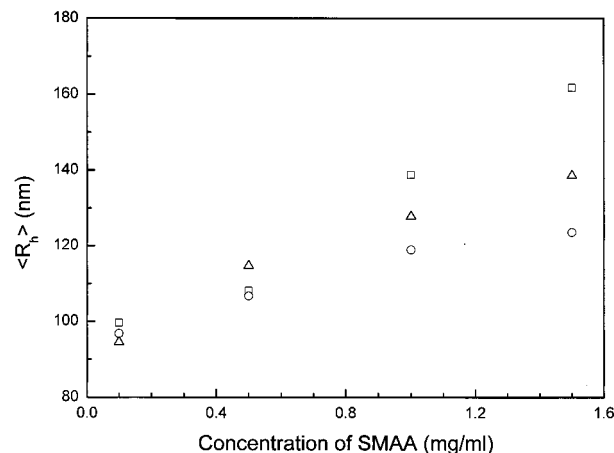


Figure 3. Average hydrodynamic radius of micelles as a function of the initial concentration of SMAA/THF. The solutions were prepared by adding 1 mL of SMAA/THF (□, SMAA1; ○, SMAA2; △, SMAA3) into 20 mL of PVPo/H₂O solution (0.1 mg/mL).

and poly(vinylpyridine) (PVPy) produced in methanol/THF (10/1, v/v), where the SPS aggregates were stabilized by soluble PVPy; namely, the micelle size increases with the concentration of PVPy.⁸ Obviously, the extent of gathering of PVPo chains around the SMAA core depends on PVPo concentration in water. The higher concentration leads to more chains gathering and consequently larger particles. In fact, as the PVPo concentration increases beyond 1 mg/mL, the formed particles became unstable causing gelation in a few hours.

It is interesting to know how the micelle size varies with SMAA composition. Figure 3 compares $\langle R_h \rangle$ of the micelles respectively containing SMAA1, SMAA2, and SMAA3 produced from the same preparation conditions. The micelle size differs a little when the concentration of SMAA is low (0.1 and 0.5 mg/mL). However, as the concentration increases to more than 1.0 mg/mL, the difference in SMAA composition gives rise to a significant difference in micelle size. SMAA 1 with the lowest MAA content (3.6 wt %) corresponds to the largest micelle size while SMAA 2 with the middle content (10.1 wt %) rather than SMAA3 with the highest content (13.1 wt %) presents the lowest size. This implies that the mechanisms of micelle formation are quite complicated.

In recent years, we reported that the water-insoluble ionomers with functional groups in either acid or salt forms may form surfactant-free stable nanoparticles in water.^{18–23}

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For example, stable dispersion of the particles of partially carboxylated polystyrene (CPS) with $\langle R_h \rangle$ of a few tens of nanometers due to the self-stabilization of the carboxyl groups could be obtained by adding dilute CPS/THF solution into an excess of water.¹⁹ In all the cases reported with the particles made of different ionomers and block ionomers, the particle size decreases with increasing the content of the functional groups.^{19–23} For a given ionomer system, it has been speculated that the average surface area occupied and stabilized by each functional group should be a constant.^{19–23}

In the present case, the particle size does not change with the content of the functional groups monotonically. This reflects that both self-stabilization of MAA groups and the stabilization of solvated PVPo chains, which are connected with the SMAA core by hydrogen bonding, play the role. Obviously, increasing the MAA content favors the self-stabilization, leading to smaller size of the core. However, at the same time it strengthens the interaction of the core with PVPo as well. This may cause more PVPo chains to gather around the core, resulting in a larger corona. Therefore, the measured micelle size actually reflects the competition between the two opposite trends.

The final micelle solutions produced by mixing SMAA/THF and PVPo/H₂O solutions as mentioned above actually contained 5 vol % of THF. Dialysis of some of the micelle solutions against water for a week was performed. It was found that dialysis did not affect the stability of the micelles, but the micelle radius was reduced by about 20%. For example, for the specimens of test 2-3 (Table 2), $\langle R_h \rangle$ values were found to be 119 and 92.3 nm before and after dialysis, respectively. This decrease obviously can be attributed to deswelling of the micelle core as THF was removed.

It is interesting to compare the results of tests 1-1 and 4-5 as they have the same final composition in the blend solutions, i.e., 0.05/1 for SMAA1/PVPo (w/w), but were prepared by solutions with different initial concentrations. In 1-1, both concentrations of PVPo/H₂O and SMAA/THF were 0.1 mg/mL while in 4-5, 10 times concentration, i.e., 1 mg/mL, was used. Strikingly different R_h values, i.e., 99.6 nm in the former and 233.6 nm in the latter, were obtained. This of course reflects the kinetically controlled nature of the micelle formation.

Direct Observations of Core–Shell Structure.

TEM as a good local structural probe presenting a real-space image at high resolution has been the most powerful technique to study morphologies of polymeric microparticles or nanoparticles. However, the TEM image as a two-dimensional project is usually hard to distinguish between core and corona, especially for the case of the corona scattering stronger than the core, unless the natural contrast between the core and shell is strong enough. Recently, Serizawa et al.²⁴ and Li et al.²⁵ observed such core–shell structure by embedding the micelles or microspheres in epoxy resin followed by ultra-microtoming. In this case, the electrons transmit through the same thickness for the core and shell so that the resultant image may reflect the difference in chain density between

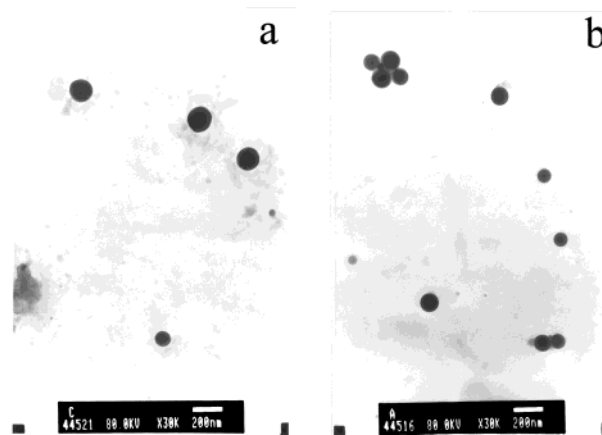


Figure 4. TEM micrographs of micelles of (a) SMAA1/PVPo and (b) SMAA2/PVPo prepared as that for tests 1-3 and 2-3 (see Table 2), respectively.

them. However, microtoming inevitably alters the periphery size and its distribution of the micelles or microspheres. In this section we report our direct observations of TEM exploring the core–shell structure of SMAA/PVPo micelles in water by means of staining techniques.

Figure 4 shows the TEM micrographs for SMAA1/PVPo and SMAA2/PVPo. The observations were performed for the dried particles without staining. Both pictures reveal that the micelles show spherical shape with a sharp boundary. The diameter of single particles is under 100 nm, which is much lower than that observed by light scattering. The possible reasons for this difference are as follows. First, the micelles collapsed and shrank during the process of water evaporation. Second, only the core of the micelles can be observed by TEM as the chain density in the corona is probably not high enough to make visible contrast to the background. Therefore, this observation failed to visualize the complex core–shell microstructure.

As polystyrene unit can be selectively stained by RuO₄, staining of the micelles was performed prior to the TEM observations. Figure 5 demonstrates the importance of using adequate staining conditions. Here, parts a, b, and c of Figure 5 correspond to the SMAA2/PVPo micelles being stained for 45, 60, and 120 min, respectively. For the case of 45 min staining, the picture shows morphologies quite different from the unstained ones. Instead of homogeneous dark spheres, black circles with a diameter around 100 nm, which correspond to shells in three-dimensional space, appeared. The black shells implied that only the surface of the core was stained while the remains were not because the staining time is not long enough to enable RuO₄ vapor to diffuse into the central part of the core. The irregular less dark halos surrounding the black circles can be attributed to the PVPo chains in corona being slightly stained. An extension of the staining to 60 min resulted in a much better image (Figure 5b), in which a homogeneous dark core appeared, and particularly, the core–corona structure was revealed. Further staining of the samples to 120 min gave rise to black particles without internal structure. Obviously, it was overstained.

Figure 6 displays the microstructure of SMAA1/PVPo micelles which were stained for 60 min. Obviously, in addition to the single particles composed of a spherical core and corona with irregular contour, there are many clusters consisting of a few SMAA cores as well. As in the corresponding R_h distribution examined by DLS, no such particles with size up to 400–500 nm were observed; the

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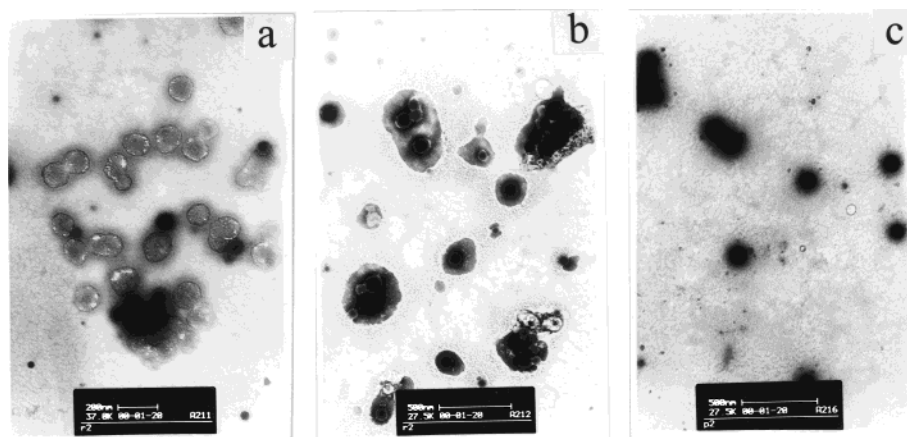


Figure 5. TEM micrographs of micelles of SMAA2/PVPo prepared as that for test 2-3 (see Table 2) and stained with RuO_4 for (a) 45, (b) 60, and (c) 120 min.

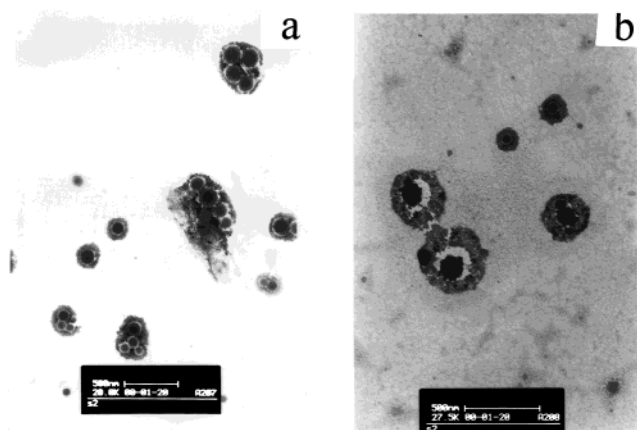


Figure 6. TEM micrographs of micelles of SMAA1/PVPo prepared as that for test 1-3 (see Table 2) and stained with RuO_4 for 60 min.

clusters were believed to be built up by aggregation of single micelles during drying of the micellar solutions on the grid. A close examination reveals that the individual core diameter is around 100 nm, and particularly, the core and corona become distinguishable due to the appearance of a bright ring between them. As MAA units in SMAA is inert to RuO_4 staining, this bright ring is most

probably associated with a MAA-rich shell. The segregation of MAA units is driven by the favorable enthalpy decrease associated with the hydrogen bonding of the MAA units with PVPo, which constructs the corona. Such kind of segregation of the functional groups was reported for the micelles of copolymers of ethylene and methacrylic acid.²⁶

In Figure 6b, two large micelles in which the core and shell are separated by a bright ring with a thickness about 50 nm were observed. This, in our opinion, may not reflect the original morphology of the micelles in solution. Instead, it was probably formed during the process of water evaporation in TEM sample preparation. Both core and shell collapsed and shrunk but possibly in different rate and degree; therefore, separation between the core and corona occurred because of no "permanent connection", i.e., covalent bonds existing between them.

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