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Polymer Micelles with Hydrophobic Core and Ionic Amphiphilic Corona. 1. Statistical Distribution of Charged and Nonpolar Units in Corona

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Supporting Information

ABSTRACT: Polymer micelles with hydrophobic polystyrene (PS) core and ionic amphiphilic corona from charged *N*-ethyl-4-vinylpyridinium bromide (EVP) and uncharged 4-vinylpyridine (4VP) units spontaneously self-assembled from PS*block*-poly(4VP-*stat*-EVP) macromolecules in mixed dimethylformamide/methanol/water solvent. The fraction of statistically distributed EVP units in corona-forming block is $\beta =$ [EVP]/([EVP]+[4VP]) = 0.3–1. Micelles were transferred into water via dialysis technique, and pH was adjusted to 9, where 4VP is insoluble. Structural characteristics of micelles



were investigated both experimentally and theoretically as a function of corona composition β . Methods of dynamic and static light scattering, electrophoretic mobility measurements, sedimentation velocity, transmission electron microscopy, and UV spectrophotometry were applied. All micelles possessed spherical morphology. The aggregation number, structure, and electrophoretic mobility of micelles changed in a jumplike manner near $\beta \sim 0.6-0.75$. Below and above this region, micelle characteristics were constant or insignificantly changed upon β . Theoretical dependencies for micelle aggregation number, corona dimensions, and fraction of small counterions outside corona versus β were derived via minimization the micelle free energy, taking into account surface, volume, electrostatic, and elastic contributions of chain units and translational entropy of mobile counterions. Theoretical estimations also point onto a sharp structural transition at a certain corona composition. The abrupt reorganization of micelle structure at $\beta \sim 0.6-0.75$ entails dramatic changes in micelle dispersion stability in the presence of NaCl or in the presence of oppositely charged polymeric (sodium polymethacrylate) or amphiphilic (sodium dodecyl sulfate) complexing agents.

1. INTRODUCTION

Self-assembly of ionic amphiphilic block copolymers into micelles with an insoluble hydrophobic core and ionic corona in aqueous media has attracted considerable attention during past two decades.^{1–5} Such micelles are able to solubilize nonpolar substances into their core^{6,7} and bind oppositely charged macromolecules,^{1,2,8} metal ions,⁸ or amphiphilic species^{9,10} into their corona. These properties along with the ability of block copolymers to form diverse spectrum of morphologies^{3,11,12} outline fields of their potential applications as nanocontainers for gene and drug delivery, nanoreactors for synthesis and stabilization of metal and semiconductor nanoparticles, constituents for pH and thermosensitive gels, polyelectrolyte nanolayers, and so forth.^{1,7,8,12}

Until the late 1990s, scientific attention was preferentially focused on AB diblock copolymers, which form structures with chemically homogeneous A core and chemically homogeneous B corona.^{1–5,8} However, solubilization of low-polar substances into the core or binding oppositely charged ionic species into the corona usually deteriorates colloidal stability of micelles. The functionality of micelles is limited by properties of A and B blocks. Significant expansion of micelle properties can be expected for polymer nanostructures with chemically heterogeneous (i.e., composed from two or more types of units) core or corona. These micelles will roughly mimic protein globules, composed of various subdomains and, thus, often combining several different properties, environments, and functions in close proximity. They may be used for simultaneous loading of different incompatible substances into single container, giving rise to a new generation of delivery systems.^{12,13}

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How can one create micelles with a heterogeneous core or corona? One way is to "attach" a third block C to an AB macromolecule.^{12–18} If C block is soluble, micelles with homogeneous A core and mixed B–C corona usually self-assemble. If C block is insoluble, the formation of micelles with multicompartment A–C core and homogeneous B corona is expected. Solubilization of hydrocarbon and fluorinated dyes into different compartments of the core has been described, justifying the availability of heterogeneous micelles as multistorage nanocontainers.^{13,18}

Micelles with heterogeneous corona can self-assemble via hybridization (comicellization) of a pair of diblock copolymers with identical hydrophobic block, for example, A-*b*-B and A-*b*-C, where A is insoluble, B and C are soluble or conditionally soluble (i.e., their solubility depends upon pH, ionic strength, temperature, etc.) blocks.⁷ This approach was proposed first by Stepanek et al.,¹⁹ who reported the formation of hybrid micelles from polystyrene-*b*-poly(methacrylic acid) (PS-*b*-PMAA) and PS-*b*-poly(ethylene oxide) (PS-*b*-PEO) diblock copolymers with a joint PS core and mixed PEO/PMAA corona. Thermodynamic possibility of formation of hybrid micelles was considered in a theoretical paper by Palyulin and Potemkin.²⁰ Subsequent publications in this field focused on design of hybrid micelles with an environmentally sensitive corona for advanced drug delivery applications.^{7,21}

Heterogeneous micelles can be generated from diblock copolymers with one of blocks consisting from statistically distributed polar and nonpolar units. Bendejacq et al. studied micellization of poly(styrene-*st*-acrylic acid)-*b*-poly(acrylic acid) P(S/AA)-*b*-PAA in aqueous media.^{22,23} They found that the content of AA units in the amphiphilic block and their ionization and ionic strength influenced the micelle morphology and equilibrium of micelle formation. When the fraction of AA units in the core exceeded 0.5, micelles did not form at all. Ionization of the hydrophobic core may lead to micelle disintegration when the ionization degree is as low as 0.2.²⁴ In the presence of inorganic counterions with high affinity for ionic units, micelles with so-called ionomer-like, quasi-neutral core may emerge.²⁵

A-b-(A-st-B) or A-b-(B-st-C) copolymers (A,C, hydrophobic units; B, ionic units) with amphiphilic corona-forming block were regarded.²⁶⁻²⁸ The formation of micelles with hydrophobic core and amphiphilic corona for the first time was experimentally described by Bhatia et al. for diblock copolymers from PS and partially hydrolyzed poly(ethyl acrylate), containing statistically distributed ethyl acrylate and acrylic acid units.^{26,27} The hydrophobic interaction of ethyl acrylate units in corona manifested itself in intermicellar attraction and formation of gels in semidilute solutions. Theoretically, the structure of micelles with hydrophobic core and amphiphilic corona with high fraction of ionogenic units (0.8 or more) was considered by Uhlik et al., using copolymer from PS and a block of styrene and methacrylic acid P(S/MAA).²⁹ The authors supposed the core had the same dimensions as in pure PS-b-PMAA micelles. Monte Carlo simulations showed the formation of hydrophobic associates of styrene units in corona and at the core-corona interface in the case of microblock distribution of styrene in P(S/MAA) block. When distribution of styrene in P(S/MAA) was even, no hydrophobic association was observed.

The present two papers investigate self-assembly of micelles with hydrophobic PS core and amphiphilic corona from charged *N*-ethyl-4-vinylpyridinium bromide units (EVP) and hydrophobic 4-vinylpyridine units (4VP), pH 9. Such micelles can be obtained via self-assembly of PS-*b*-P(4VP-*st*-EVP) or comicellization of PS-*b*-PEVP and PS-*b*-P4VP copolymers. In the first case discussed below, we have statistical distribution of charged and hydrophobic units within the corona. In the second case, we receive starlike distribution of charged and hydrophobic blocks; this will be the subject of our subsequent publication.

In both cases, we exploit the question of how the fraction of charged units $\beta = [EVP]/([EVP]+[4VP])$ and their distribution pattern influence dispersion stability, molecular mass and structure of polymer micelles. To answer this question, dependencies of micelle characteristics (molecular mass, core, and corona radii) as function of β have been obtained experimentally and analyzed theoretically. Further, we tried to find correlations between micelle composition and micelle ability to respond to external impact. For this purpose, we exploited the micelle's ability to oppose aggregation upon addition of NaCl or oppositely charged polymeric (PMAA) or amphiphilic (sodium dodecylsulfate) complexing agents.

The main phenomenon described in the present paper is the existence of a narrow composition region within $\beta \sim 0.6-0.75$, where micelle structural characteristics change abruptly, while below or above this region micelle parameters are rather constant or change insignificantly. The break in micelle structure entails abrupt variations in a number of properties. Theoretical estimations indicate this phenomenon must be rather general and is inherent to polymer micelles with statistical distribution of charged and hydrophobic units in amphiphilic corona.

2. EXPERIMENTAL SECTION

2.1. Materials. Block copolymer of PS and poly(4-vinylpyridine) (P4VP), PS-*b*-P4VP, was synthesized by sequential anionic polymerization and characterized by gel permeation chromatography, as described.³⁰ The lengths of both blocks equal 100 units; the polydispersity index is 1.12.

Block copolymers of PS and statistical block of 4VP and EVP (PS-b- $P(4VP/EVP-\beta)$ were synthesized through quaternization of PS-b-P4VP by 5-fold excess of ethyl bromide. The reaction was carried out in a mixed methanol/THF solvent (65/35, v/v), T = 60 °C, and concentration of PS-b-P4VP = 4.7%, w/w. Portions of reaction mixture were successively removed from reaction vessel first every 30 min and then every hour and precipitated into dry diethyl ether. The precipitate was washed several times with fresh portions of diethyl ether and dried in a vacuum oven at 60 $^\circ C$ for 48 h. The degree of quaternization of P4VP block was determined by IR spectroscopy using characteristic bands of absorption of EVP units at 1640 cm⁻¹, and 4VP units at 1600 and 1415 cm⁻¹.³¹ Block copolymers with $\beta = 0.15$, 0.3, 0.4, 0.5, 0.55, 0.6, and 0.75 were synthesized. The experimental dependence of ln(1- β) vs time was linear.³¹ The linearity points onto pseudo-first-order of alkylation reaction and indicates no influence of EVP units on 4VP reactivity. The last implies the statistical distribution of EVP and 4VP units in pyridine block. The exhaustively quaternized by ethyl bromide PS-b-P4VP with $\beta \sim 1$ was synthesized as described.

Poly(methacrylic acid) (PMAA) was synthesized in a sealed ampule under argon atmosphere via radical polymerization in 25% w/w solution of methacrylic acid in methanol for 30 h, using dinitrile of azobisisobutyric acid as initiator (0.5% w/w from monomer weight), T = 60 °C. Polymer was precipitated into dry diethyl ether, washed several times by diethyl ether, and dried in vacuum oven for 24 h at 60 °C. Fractionation of PMAA was performed by fractional precipitation from 2% w/w methanol solution by ethyl acetate. In the present investigation, we use PMAA fraction with weight average polymerization degree of 1700 units ($M_w = 146000$, determined by static light scattering). PMAA was dissolved in water and neutralized by equivalent amount of NaOH to get sodium polymethacrylate (PMANa).

Sodium dodecyl sulfate (SDS), sodium chloride (NaCl), dimethylformamide (DMF), methanol, ethyl bromide, tris-(hydroxyethyl)aminomethane (TRIS), and sodium hydroxide (NaOH) (all purchased from Sigma-Aldrich) and doubly distilled water were used. Chemical structures of investigated materials are presented in Chart 1.





2.2. Sample Preparation. Polymer dispersions in water were prepared using the dialysis technique. Initially, 0.25 g of PS-b-P(4VP/ EVP- β) was dissolved in 5 mL of mixed DMF/methanol (80/20 v/v) solvent and stirred for 1 day. After that 2.5 mL of water was added with the speed 10 μ L per minute under vigorous stirring. The mixture was left for 1 day to reach equilibrium. At this water content (33 vol %), micelles are under thermodynamic control. The supporting experiment was the following. Briefly mixing individual PS-b-PEVP and PS-b-P4VP micelles is accompanied by spontaneous formation of joint micelles, containing both block copolymers.³² This means the copolymer chains are mobile and can freely move to reorganize the micelle structure. Further 7.5 mL of water was added in the same manner. The mixture was stirred additionally for 1 day. Finally, the water-organic mixture was dialyzed against pure water during 1 week using membrane tubing (molecular weight cutoff is 12-14 kDa) to remove organic solvents. The concentration of PS-*b*-P(4VP/EVP- β) in aqueous dispersions after dialysis was calculated from UV spectrophotometry measurements at 257 nm with molar absorption coefficients 3900 L mol⁻¹ cm⁻¹ for EVP, 1600 L mol⁻¹ cm⁻¹ for 4VP, and 300 L mol⁻¹ cm⁻¹ for styrene units. Because of high dilutions used and relatively small particle dimensions (see below), the possible effect of micelle light scattering on UV measurements was ignored. Concentration of polymers after dialysis was 3-5 g/L. According to

literature 33 and our own findings (see below), the obtained micelles had a kinetically frozen PS core.

All investigations were conducted at room temperature (25 °C) in TRIS buffer solution (0.01 M, pH 9) to keep 4VP completely uncharged. To evaluate aggregation stability of micelles in the presence of NaCl, PMANa or SDS micelle dispersions were mixed with aqueous solutions of corresponding compounds and vigorously stirred for 1 day. In the case of precipitation, the insoluble phase was separated from supernatant via preparative ultracentrifugation using Eppendorf centrifuge during 15 min at $\omega = 13\,000$ rpm. Block copolymer concentration in supernatant was determined by UV spectrophotometry technique as described above.

2.3. Measurements. UV spectra (230-300 nm) were recorded on a UV-vis spectrophotometer, Lambda-25 (Perkin-Elmer), in 10 mm quartz cells. Static (SLS) and dynamic (DLS) light scattering (LS) measurements were carried out with a Photocor spectrometer. A 25 mW He-Ne laser operating at 630 nm wavelength was used as a light source. LS angles were 90° for DLS and varied within $30-150^{\circ}$ with an increment of 5° for SLS studies; polymer concentrations fit the interval 0.05-1 g/L. Supporting NaCl concentration was 0.05 M. Refractive index increments were measured via a KMX-16 differential refractometer (Milton Roy) with a 2 mW He-Ne laser as the light source, $\lambda = 630$ nm. Prior to light scattering measurements, all solutions were filtered two to three times through Millipore GS 0.45 µm filters. SLS data were treated by the Zimm method. Weightaverage micelle aggregation numbers (number of macromolecules per micelle) $m_{\rm w}$ were calculated as the ratio $M_{\rm w}/M_0$, where $M_{\rm w}$ and M_0 are molecular masses of micelle and single macromolecule, respectively. Diffusion coefficients D_z were calculated from DLS data by cumulant analysis of an autocorrelation function of scattered light intensity fluctuations. Effective hydrodynamic radii $(R_h)_0$ of individual micelles were calculated from extrapolated to zero concentration diffusion coefficients $(D_z)_0$ using the Stokes equation. Primary SLS and DLS data are summarized in Table S1 in the Supporting Information.

Electrophoretic mobility measurements were performed on a ZetaPlus analyzer (Brookhaven Instruments) with 30 mW solid-state laser operated at a laser wavelength of 635 nm. Supporting NaCl concentration was 0.005 M, [EVP] + [4VP] = 3×10^{-5} base mol/L. ζ -Potentials were calculated from electrophoretic mobility values, using the Smoluchowski equation.

The negative staining technique was used for transmission electron microscopy (TEM) studies. An amount of 2 μ L of sample solution with polymer concentration 0.26 g/L was allowed to settle on a Formvar-coated copper grid for 1 min, the excess of sample was removed, and the grid was exposed to 1% uranyl acetate for 20 s. The samples were air-dried and studied with use of a Hitachi H-7000 microscope.

Sedimentation velocity measurements were performed with a Beckman model E analytical ultracentrifuge equipped with schlieren



Figure 1. TEM microphotographs of (a) PS-*b*-P(4VP/EVP-0.15), (b) PS-*b*-P(4VP/EVP-0.5), and (c) PS-*b*-PEVP. Two types of micelle aggregates are highlighted by dashed circles: large (1) and small (2) micelles; R_{TEM} are 13 ± 1 and 8 ± 2 nm (a), 9 ± 1 and 5 ± 1 nm (b), and 7.5 ± 0.5 and 4.0 ± 0.6 nm (c).



Figure 2. (a) Distribution of normalized intensity of scattered light upon particle dimensions for PS-b-P(4VP/EVP-0.5); (b) Zimm plot for PS-b-P(4VP/EVP-0.5) in aqueous dispersion; [NaCl] = 0.05 M.

optical system and an absorption optical detector at ω = 40 000 rpm at room temperature. The cuvette volume was 0.5 mL.

3. RESULTS AND DISCUSSION

The purpose of the current investigation is to find correlations between micelle composition, micelle structure, and micelle properties (e.g., aggregation stability in aqueous media). To follow this goal, this section is divided into three subsections. First, experimentally found dependencies of micelle morphology, molecular mass, electrophoretic mobility, and dimensions versus β will be discussed. Second, scaling model of β influence on micelle structure will be elaborated and compared to experimental data. Third, the impact of β on micelle stability in the presence of inorganic salt (NaCl) or oppositely charged polymeric (PMANa) or amphiphilic (SDS) complexing agents will be regarded. The significance of the obtained results will be discussed in concluding section.

3.1. Influence of β **on PS-***b***-P(EVP/4VP-** β **) Micelle Structure: Experimental Data.** TEM micrographs for PS-*b*-PEVP, PS-*b*-P(4VP/EVP-0.15), and PS-*b*-P(4VP/EVP-0.5) micelles in water are presented in Figure 1. During sample preparation, the micelle corona dehydrates and after contrasting by uranyl acetate looks like a thin dark rim around the brighter PS core. In all cases, *spherical* aggregates are observed. Two types of micelle species can be distinguished, which we shall refer to as "large" and "small" micelles in accordance with their relative dimensions. Small micelles have radii (R_{TEM}) approximately one-half of those for large ones (Figure 1).

The spherical shape of micelles is an expected result, since this morphology is typical for block copolymers with comparable lengths of core-forming and lyophilizing blocks in selective solvents.¹¹ Detailed discussion of the phenomenon of coexistence of two micelle populations from single diblock copolymer can be found in the Supporting Information and in some other publications.^{34–38}

Experimental dependencies of micelle parameters versus β were obtained from DLS and SLS experiments. Polymers with $\beta = 0.3-1$ were studied. Since there are two micelle populations in dispersion, first we must specify to what type of micelles SLS and DLS data are referred. Essential inequality in micelle dimensions in the dehydrated state (Figure 1) points to significant difference in molecular masses. Sedimentation velocity data (see Supporting Information) indicate approximately 2-fold domination of the large micelles fraction. Since LS intensity is proportional to both molecular mass and concentration, the input of large micelles into light scattering must be overwhelming. In other words, values of molecular masses and hydrodynamic radii, determined by LS, must

correspond to large micelles while small micelles are not detectable.

Figure 2a presents distribution curve of normalized intensity of scattered light upon dimensions for PS-b-P(4VP/EVP-0.5) in dilute dispersions. Only one major peak is observed, indicating particles with average hydrodynamic radius $R_{\rm h} = 21$ nm (the additional peak at $R_{\rm h} > 70$ nm probably corresponds to formation of insignificant quantities of secondary intermicellar aggregates; their fraction is less than 1% and their existence may be ignored). Only one major peak was observed for copolymers with other β (data not shown). The obtained results confirm the supposition about visibility of only large micelles by LS technique.

A typical Zimm plot for PS-*b*-P(4VP/EVP-0.5) is presented in Figure 2b. Values of calculated molecular masses as function of β are shown in the inset of Figure 3. One can see that weight



Figure 3. Dependence of weight average aggregation number m_w of PS-*b*-P(4VP/EVP- β) micelles upon β (dependence of M_w vs β is depicted in the inset); [NaCl] = 0.05 M.

average molecular mass (M_w) slightly increases within the range $\beta = 0.3-0.6$. Such linear increase is caused by growth of EVP fraction in macromolecule; EVP units are twice heavier than 4VP ones. Indeed, if we calculate weight average aggregation number m_w , we will find that $m_w = 180$, and it is constant within the range (Figure 3). When $\beta = 0.75$, molecular mass drops abruptly and further increases slightly within $\beta = 0.75-1$ ($m_w = 100$, Figure 3). The abrupt decrease of M_w may point out structural differences between micelles with $\beta \leq 0.6$ and $\beta \geq 0.75$.

It should be mentioned that aggregation number decrease upon charged units fraction growth is a general trend described for a number of starlike micelles with hydrophilic corona from weak polyelectrolytes.^{39,40} But in contrast to PS-*b*-P(4VP/EVP- β), changes for these micelles have monotonic rather than abrupt character.

To understand the matter of structural differences between micelles, we investigated their electrophoretic and hydrodynamic properties. Figure 4 shows the dependence of micelle ζ -potential upon β . The correlation between ζ -potential and m_w



Figure 4. Dependence of ζ -potential of PS-*b*-P(4VP/EVP- β) micelles upon β ; [NaCl] = 0.005 M.

changes can be easily observed. When $\beta \le 0.6$ or $\beta \ge 0.75$, ζ -potential weakly increases with the growth of β , while within $\beta = 0.6-0.75$ it changes in a jumplike manner.

Figure 5 presents the dependencies of the micelle hydrodynamic radius $(R_h)_{0}$, the radius of the core (R_{core}) , and the



Figure 5. Dependencies of hydrodynamic (\blacksquare), core (\bullet), and corona (\blacktriangle) radii of PS-*b*-(P4VP/EVP- β) micelles upon β ; [NaCl] = 0.05 M. Open circles show radii of dehydrated micelles, R_{TEM} .

radius of the corona (D_{corona}) as a function of β (see also Chart 2). Values of $(R_h)_0$ were taken from DLS data. To calculate R_{core} , we use the following equation:

$$R_{\rm core} \,(\rm nm) = \left(\frac{3M_{\rm PS}P_{\rm PS}m_{\rm w} \times 10^{21}}{4\pi N_{\rm AV}\rho_{\rm PS}}\right)^{1/3} \tag{1}$$

Here $M_{\rm PS} = 104$ g/mol is the molar mass of the PS unit, $P_{\rm PS} = 100$ is the polymerization degree of the PS block, $\rho_{\rm PS} = 1.04$ g/ cm³ is the density of amorphous PS in a solid state (it is supposed that PS core does not contain water^{6,33}), and $N_{\rm AV}$ is Avogadro's number. The radius of the corona was calculated as

$$D_{\rm corona} = (R_{\rm h})_0 - R_{\rm corol}$$

First of all, we would like to point out very good correlation between calculated $R_{\rm core}$ and radii of large micelles, determined from TEM ($R_{\rm TEM}$, open circles in Figure 5). For dehydrated micelles, $R_{\rm TEM}$ must be close to $R_{\rm core}$. Coincidence between $R_{\rm core}$ and $R_{\rm TEM}$ confirms both of our suppositions: one is about LS visibility of only large micelles, and the second is about the density of PS core.

Comparing Figures 3–5, one can easily see analogous features in micelle dimensions, m_{w} , and ζ -potential changes. Within the interval of $\beta = 0.3-0.6$, R_{core} is constant, while $(R_{\rm h})_0$ and $D_{\rm corona}$ are slightly increasing. At $\beta = 0.75$, an abrupt decrease of $R_{\rm core}$ and increase of $(R_{\rm h})_0$ and $D_{\rm corona}$ are observed.

Further, within $\beta = 0.75-1$, R_{core} is constant again, while $(R_h)_0$ and D_{corona} are slightly decreasing.

Data describing the influence of charge density of corona block on micelle structure are generalized in Chart 2. When β

Chart 2. Structure of PS-b-P(4VP/EVP- β) Micelles as a Function of β^a



^{*a*}Br⁻ counterions are omitted. Dashed circles, indicating the boundary of the micelle corona, are for eye guide only.

 \leq 0.6, micelles with enlarged PS core (higher aggregation number) and contracted corona do form. When $\beta \geq$ 0.75, micelles with reduced PS core (lower aggregation number) and expanded corona do form. The "transformation" between two structural types occurs in a narrow region of charge density changing ($\Delta\beta \sim$ 0.15). Note that for all $\beta D_{corona} > R_{core}$; that is, in all cases, we deal with "starlike" spherical micelles.³⁸

We believe the reason of structural transformation is the change in balance between nonpolar interactions of 4VP and electrostatic interactions of EVP units in corona. At low β , micelle structure is determined by hydrophobic attraction of excessive 4VP units. Such attraction leads to corona contraction. The increase of micelle aggregation number also facilitates 4PV attraction due to growth of local 4VP concentration. Thus, micelles with enlarged core and contracted corona do form (left micelles in Chart 2). In such corona, Br⁻ counterions are tightly bound with EVP units, and the value of ζ -potential is relatively small, ca. +15 mV.

At high β , the fraction of 4VP units is low and micelle structure is determined by electrostatic repulsion of EVP units. The micelle "tries" to alleviate unfavorable electrostatic repulsion in the corona. This is achieved by unfolding of P(4VP/EVP) chains and by decrease in aggregation number. Thus, micelles with diminished core and extended corona do form (right micelles in Chart 2). In expanded corona, outer EVP units are located more loosely and bind Br⁻ counterions weaker. Hence, the value of ζ -potential jumps up until ca. +50 mV.

Two questions arise about the universality of the found regularities. First, do the same structural reorganizations on β occur in the case of small micelles? The aggregation number of small micelles (*m*) can be approximately estimated from TEM data using eq 1 and assuming $R_{\text{core}} \cong R_{\text{TEM}}$. Then for small micelles with $\beta = 1$, we receive $m_{\text{TEM}} \sim 16$, and for small micelles with $\beta = 0.5$, we get $m_{\text{TEM}} \cong 34$. Here again we see approximately 2-fold increase of aggregation number within $\beta = 0.5-1$. In other words, decrease of β is accompanied by the growth small micelles aggregation number similar to that for large ones. This result allows one to think the influence of β on micelle structure does not depend upon their dimensions.

Second, how much do the experimental regularities reflect the system thermodynamics? We found the PS core is kinetically frozen in water while the corona is not. The following experiment illustrates this statement. If we take PS-*b*- P(4VP/EVP-0.4) at pH 9, we have aggregation number $m_w =$ 180 and $(R_{\rm h})_0 = 21$ nm. If we decrease pH to 2, all 4VP units are protonated $(\beta \rightarrow 1)$, and this copolymer must become similar to PS-b-PEVP with $m_{\rm w} = 100$ and $(R_{\rm h})_0 = 25$ nm. Nevertheless, PS-b-P(4VP/EVP-0.4) at pH 2 still preserves m_w = 180, while its hydrodynamic radius really increases up to 25 nm. The result implies the structure of investigated micelles is subjected to both thermodynamic and kinetic control. Kinetic factors may originate from the electrostatic barrier of the charged corona, the glassy state of the PS core, and the hydrophobic association of 4VP units. All these terms may preclude micelle relaxation.⁴¹ For micelle preparation, we added water very slowly and by tiny portions, thus changing solvent quality very gradually and allowing the system to approach equilibrium as close as possible.⁴¹ Our protocol is essentially different from that used for pure kinetic control micelle preparation.⁴² Still, variation of β may influence both thermodynamic and kinetic factors. Their relative contributions to micelle structure cannot be extracted from experimental data. This task could be at least partially resolved theoretically, using the thermodynamic approach described below.

3.2. Influence of β on PS-*b*-P(EVP/4VP- β) Micelle Structure: Theoretical Approach. Following the experimental system, our theoretical model considers a dilute salt-free aqueous solution of A-*b*-B/C hydrophobic-amphiphilic diblock copolymer with N_A and N_{BC} statistical segments in A and B/C blocks, respectively. Both blocks are flexible chains with statistical segment length *a* which is used as a unit length. Amphiphilic B/C block is moderately insoluble and consists of charged B and neutral hydrophobic C monomer units. Charged units are randomly distributed in the B/C block, their fraction equals β .

In aqueous solutions, these A-*b*-B/C diblock copolymer chains can self-assemble into micellar aggregates with average aggregation number *m*. The core of micelles consists of insoluble hydrophobic A units, while the corona is formed by B/C block and is amphiphilic. Here, we consider the case of starlike spherical micelles, that is, micelles with the total radius $R_{\rm m}$ much larger than the core radius $R_{\rm core}$, $R_{\rm m} \gg R_{\rm core}$. Hence, the total micelle radius and the corona radius are approximately equal. The radius of the dense core can be calculated as $R_{\rm core} = a(3mN_{\rm A}/4\pi)^{1/3}$.

The total free energy per chain in kT units is the sum of five terms:

$$F_{\text{tot}} = F_{\text{surf}} + F_{\text{el}} + F_{\text{vol}} + F_{\text{el-st}} + F_{\text{ci}}$$
(2)

The first term is the excess free energy of the core–corona interface; it is proportional to interfacial area per block copolymer chain $s = 4\pi R_{core}^2/m$:

$$F_{\rm surf} = \gamma s = G N_{\rm A}^{2/3} m^{-1/3}$$

where $G = (36\pi)^{1/3} \gamma a^2 \approx 5\gamma a^2$ is the dimensionless surface tension coefficient. For simplicity and due to a lack of experimental evidence, we neglect a possible adsorption of the EVP and 4VP units onto the hydrophobic core surface and their effect on the surface tension coefficient. We assume that the value of γ has a fixed value independent of the amphiphilic coronal block composition.

The term $F_{\rm el}$ describes elastic deformation of the corona chain:⁴³

$$F_{\rm el} \cong \frac{3}{2} \left(\frac{R_{\rm m}^2}{N_{\rm BC} a^2} + \frac{N_{\rm BC} a^2}{R_{\rm m}^2} \right)$$

This expression takes into account both stretching and compression of B/C blocks in the corona. It should be noted that the contribution to free energy due to conformational entropy loss in stretched A blocks in the core is negligible for the case of starlike micelles.

The term $F_{\rm vol}$ corresponds to the energy of volume interaction of monomeric links in the corona. In case of low concentration, $n \cong mN_{\rm BC}/R_{\rm m}^{-3}$, of monomer units in the corona, it can be written in the form of the virial expansion:⁴³

$$F_{\rm vol} = N_{\rm BC}({\rm B}n + {\rm C}n^2) \cong N_{\rm BC}\left(\frac{mN_{\rm BC}}{R_{\rm m}^3}a^3\tau + a^6\frac{m^2N_{\rm BC}^2}{R_{\rm m}^6}\right)$$

where τ is the relative temperature deviation from the θ -point for the B/C block. In this expression, the solvent quality is assumed to be the same for the B and C monomeric units and the solvent is poor for the coronal block, so that $\tau < 0$. Indeed, the EVP units modeled by the B monomeric units have a hydrophobic part contributing to attraction in short-range interactions and the 4VP (C monomeric units) are purely hydrophobic. Introduction of only one τ parameter seems to be quite a reasonable first step to describe attractive interactions in the micelle corona.

The micelle solubility is ensured by the presence of charges in B/C coronal blocks. These are last two terms in (2) that take this fact into account. Charges in B/C chains appear in the course of dissociation of polar B groups with release of counterions into solution. Some part of counterions is kept within the corona neutralizing its charge while others leave to the outer solution. Let α be the fraction of counterions moving freely in outer solution, and $(1 - \alpha)$ is the fraction of counterions held inside the corona. Then the total electric charge of the micelle is equal to $Q = e\alpha\beta mN_{\rm BC}$. The electrostatic energy of charged micelle can be estimated as the energy of uniformly charged ball of the radius $R_{\rm m}$:

$$F_{\text{el-st}} \cong \frac{1}{m} \frac{Q^2}{\varepsilon k T R_{\text{m}}} \cong u \frac{(\alpha \beta N_{\text{BC}})^2}{R_{\text{m}}/a} m$$

The dimensionless parameter $u = e^2/\varepsilon akT$ describes the strength of electrostatic interactions. Here ε is the dielectric permeability of the solvent.

The concentrations of mobile counterions inside the corona and in the outer solution are equal to $N_{\rm BC}\beta m(1-\alpha)/R_m^3$ and $\Phi\beta\alpha N_{\rm BC}/((N_{\rm A}+N_{\rm BC})a^3)$ respectively, and Φ denotes the total volume fraction of polymer in solution. The free energy of translational motion of counterions reads:

$$\begin{split} F_{\rm ci} &= N_{\rm BC}\beta(1-\alpha)\ln\!\left(\frac{N_{\rm BC}\beta m(1-\alpha)}{R_{\rm m}^{-3}/a^3}\right) \\ &+ N_{\rm BC}\beta\alpha\ln\!\left(\frac{\Phi\beta\alpha N_{\rm BC}}{N_{\rm A}+N_{\rm BC}}\right) \end{split}$$

Thus, the free energy of micellar solution is completely defined. For $N_{\rm A} = N_{\rm BC} = N$, the total free energy per chain can be written as

$$\begin{split} F_{\text{tot}} &= G N^{2/3} m^{-1/3} + u \frac{(\alpha \beta N)^2}{R_{\text{m}}/a} m + \frac{3}{2} \left(\frac{R_{\text{m}}^2}{Na^2} + \frac{Na^2}{R_{\text{m}}^2} \right) \\ &+ \frac{m N^2}{(R_{\text{m}}/a)^3} \tau + \frac{m^2 N^3}{(R_{\text{m}}/a)^6} + N\beta (1-\alpha) \ln \left(\frac{N\beta m (1-\alpha)}{(R_{\text{m}}/a)^3} \right) \\ &+ N\beta \alpha \ln \left(\frac{\Phi \beta}{2} \alpha \right) \end{split}$$

Equilibrium values of the aggregation number *m*, radii R_{core} , and R_{m} of core and corona regions as well as equilibrium distribution of counterions in the system are calculated via minimization of the free energy F_{tot} with respect to R_{m} , *m*, α variables:

$$\begin{cases} \frac{\partial F_{\text{tot}}}{\partial R_{\text{m}}} = 0\\ \frac{\partial F_{\text{tot}}}{\partial m} = 0\\ \frac{\partial F_{\text{tot}}}{\partial \alpha} = 0 \end{cases}$$

This system of equations has been solved numerically for N = 25, u = 1, G = 37, $\tau = -1$, and $\Phi = 10^{-5}$, with these values being close to experimental conditions. The calculated dependences of micellar parameters on the fraction β of charges in the coronal block are shown in Figures 6–8. One can see that the micelle structure changes in a jumplike fashion at $\beta = 0.72$.



Figure 6. Dependence of the equilibrium aggregation number m on β .

Our analysis of free energy indicates that at intermediate β the dependence of free energy versus β might exhibit two minima: one corresponding to large micelles with dense corona, and the other corresponding to small micelles with highly swollen corona. When fraction of charged units in corona is less than ca. 0.7, micelles with higher aggregation number are formed. Counterions are preferentially localized within the corona ($\alpha \ll 1$, Figure 8), neutralizing its charge and creating osmotic pressure. Short-range attraction between hydrophobic C units plays an important role in this regime. An increase in fraction of charged monomer units induces a transition, so that at high β small micelles are formed. For these micelles, long-range repulsive Coulomb interactions between coronal blocks and translational entropy of counterions dominate over short-range nonelectrostatic interactions. In a model system at high β and small polymer concentrations, the micelle aggregation number is rather low (about 10) and micelles keep only a small fraction of counterions, entropy dominates, and the major part of counterions leaves for the outer solution.

Comparison Model and Experiment. Experimental data and theoretical estimations give a similar principal result: the existence of a sharp transition near $\beta \sim 0.7$ where micelle parameters change abruptly. One can see that theoretical dependences of micelle dimensions on β (Figure 7) for



Figure 7. Dependences of micelle $R_{\rm m}/a$ (solid line) and core $R_{\rm core}/a$ (dashed line) radii on β .

hypothetical equilibrium micelles qualitatively coincide with experimental observations (Figure 5). The experimental dependence of ζ -potential on β (Figure 4) is akin to that of α versus β (Figure 8). Remarkable differences between theory



Figure 8. Dependence of the fraction of counterions α in outer solution on β .

and experiment are observed for aggregation number dependencies. Experiment shows no dependence of m_w upon β when β = 0.3-0.6 and β = 0.75-1 (Figure 3), while theory predicts monotonous m change before and after the transition point (Figure 6). Overall the model predicts larger changes in *m* than it is observed experimentally. We believe the mismatch should be ascribed to equilibrium factor. As was mentioned above, the model deals with thermodynamically equilibrium micelles, while in experiment micelles are subjected to both kinetic and thermodynamic control. Still the existence of a "jump" for both experimental and theoretical curves gives us a basis to consider it be conditioned by preferentially thermodynamic reasons. For additional support of this statement, we could note that existence of thermodynamically determined jumplike transition coil→globule is described in a number of publications for statistical B/C copolymers^{44,45} as well as for polyelectrolyte gels^{46,47} and microgel particles in dilute solutions.⁴⁸ Such a transition resembles very much the studied contraction/ expansion of chains in micelle corona. But in our system, amphiphilic ionic block is chemically attached to insoluble A block, so the coil \rightarrow globule transition of B/C chain is accompanied by simultaneous reorganization of micelle core. The simultaneous, jumplike reorganization of both corona and core seems to be the main feature of hydrophobic-*block*-amphiphilic ionic copolymers, described in the paper.

3.3. Influence of β **on Properties of PS-b-P(EVP/4VP-\beta) Micelles in Aqueous Media.** Structural changes of PS-*b*-P(4VP/EVP- β) micelles must affect their properties. In the last subsection, we will briefly examine the influence of β onto micelle properties, related to its polyelectrolyte corona.

Influence of β on Aggregation Stability of PS-b-P(4VP/ EVP- β) Micelles in the Presence of NaCl. Figure 9



Figure 9. Diagram of aggregation stability of PS-*b*-P(4VP/EVP- β) micelles in NaCl aqueous solutions. Key: (O) phase separation points and (\bullet) points of quantitative precipitation. [EVP] = 5 × 10⁻⁴ base mol/L.

demonstrates micelle aggregation stability diagram in the presence of NaCl. Below the dashed line (region I) micelles are stable, while above it phase separation is observed (region II). Solid line designates the area of quantitative precipitation. Above this line (region III) all micelles are included into solid phase. As can be seen from Figure 9, the value of threshold salt concentration for micelle salting out monotonously increases with increase of $\beta = 0.15 - 0.6$. Micelles with $\beta \ge 0.75$ do not precipitate even at saturated NaCl concentrations, ca. 5.5 M. Here we can clearly see the correlation between micelle structure and its ability to persist with aggregation. Increasing salt concentration causes screening electrostatic repulsions between EVP units. As a result, intra- and intermicelle attraction of 4VP units is promoted, causing micelle aggregation/precipitation. Nevertheless, if $\beta \ge 0.75$, the association of 4VP units is suppressed and PS-b-P(4VP/EVP- β) micelles preserve their aggregation stability even at high ionic strengths.

Influence of β on Aggregation Stability of Complexes between PS-b-P($4VP/EVP-\beta$) Micelles and Oppositely Charged Polyelectrolyte or Surfactant. If one mixes aqueous dispersions of PS-*b*-P(4VP/EVP- β) micelles with aqueous solutions of oppositely charged PMANa or SDS, micelle polyelectrolyte complexes (MPC) do form. As we have shown earlier,^{9,49} the solubility of MPC is defined by the chemical nature of mixing components and their charge ratio Z =[-]/[+] = [MANa]/[EVP] = [SDS]/[EVP], where MANa are sodium methacrylate units. At stoichiometric charge ratio, Z =1, insoluble complexes do form, while at charge excess of one component, Z < 1 or Z > 1, soluble complexes, stabilized by excessive charged units, may form.^{9,49} We have found that at Z = 1, both components quantitatively precipitate for any β . It implies that the β -value does not affect the ability of P(4VP/ EVP) chains to bind oppositely charged species. Nevertheless, β significantly influences the solubility of MPC at $Z \neq 1$.

Figures 10 and 11 present diagrams of aggregation stability of MPC between PS-*b*-P(4VP/EVP- β) micelles and PMANa or SDS molecules, respectively. The shaded field between solid



Figure 10. Diagram of aggregation stability of complexes of PS-*b*-P(4VP/EVP- β) micelles with PMANa. Key: (O) phase separation points and (\bullet) points of quantitative precipitation. [NaCl] = 0.1 M; [EVP] = 1 × 10⁻³ base mol/L ($Z \le 1$) or [MANa] = 1 × 10⁻³ base mol/L ($Z \ge 1$).



Figure 11. Diagram of aggregation stability of complexes PS-*b*-P(4VP/ EVP- β) micelles with SDS. Key: (O) phase separation points and (\bullet) points of quantitative precipitation. [NaCl] = 0.01 M; [SDS] = 8 × 10⁻⁴ M.

curves (region III) corresponds to quantitative precipitation of MPC. Shaded areas between dashed and solid lines (regions II) designate areas of partial precipitation of MPC. The field below the bottom dashed line Z^* (region Ia) corresponds to the formation of positively charged soluble MPC, stabilized by excessive EVP units. The field above the top dashed line Z^{**} (region Ib) designates the formation of negatively charged (overcharged) soluble MPS, stabilized by excessive MANa units or SDS molecules. It can be easily noticed that aggregation stability of MPC is a function of three variables: chemical nature of the complexing agent, *Z*, and β .

Figures 10 and 11 show that all investigated micelles can form soluble complexes when PS-b-P(4VP/EVP- β) is taken in charge excess. The upper boundary of complex solubility $Z^* \approx$ 0.3 (PMANa) or $Z^* \approx 0.5$ (SDS) practically does not depend on β . Such relative independence of Z^* upon β may be qualitatively explained within the onion-type model of MPC structure.^{49,50} According to this model, MPC particle at Z < 1consists of three layers: the insoluble hydrophobic core, the intermediate complex layer of salt bonds from mutually neutralized components, and the outer lyophilizing layer from excessive charged units of block copolymer. If dispersion stability of micelles is provided by the outer, most remote part of the corona, then its state and, hence, the solubility of MPC may be insensitive to complexation until $Z \leq Z^*$. As was shown earlier, the value of Z^* is only weakly dependent upon the nature of complexing agents, both the copolymer block and the second component.⁵¹

Contrary to Z^* , the lower boundary of complex solubility at charge excess of complexing agent Z^{**} is strongly dependent upon β and the correlation with micelle structure is observed.

In the case of PMANa, soluble negatively charged (overcharged) complexes are formed, if $\beta \ge 0.75$. These complexes include ca. 2-fold excess of MANa units (Figure 10). In the case of SDS, the situation is reversed. PS-*b*-PEVP does not form soluble MPC, PS-*b*-P(4VP/EVP-0.75) is stable only at 20-fold or more excess of SDS, while MPC with $\beta \le 0.6$ are stable at only 2-fold excess of SDS (Figure 11).

Such differences can be interpreted by micelle structural transformation at $\beta = 0.6-0.75$. To form overcharged MPC, some excessive (toward stoichiometry) quantity of complexing agent must be included in the corona. Expressed hydrophobic attraction of 4VP units at $\beta \leq 0.6$ precludes the embedding of PMANa into the corona, but promotes the embedding of amphiphilic SDS molecules. Therefore, when $\beta \leq 0.6$, formation of overcharged MPC is possible in the case of SDS and impossible for PMANa. When $\beta \geq 0.75$, association of 4VP units is suppressed. Therefore, overcharging of MPC particles is facilitated for PMANa, but is hindered for SDS (due to significant loss of entropy of surfactant molecules).

4. CONCLUSIONS

In our investigation, we have exploited the question of what would happen if we take AB micelle (A is hydrophobic block and B is ionic block) in aqueous media and start to substitute ionic B units onto hydrophobic C units in a statistical fashion. The answer is the following. Until the fraction of C units reaches 25-40 mol %, micelles will not "feel" such substitution. This fact implies that we can vary corona composition within certain boundaries without any loss of aggregation, molecular mass, and hydrodynamic properties. If we raise the fraction of C units above this limit, we shall get a sharp transition in micelle structure, caused by hydrophobic attraction of C units in corona. The transition in structure is accompanied by a transition in micelle properties, that is, electrophoretic mobility, aggregation stability, and ability to form soluble polyelectrolyte complexes. We believe that the conducted research will assist in construction of a robust physicochemical basis for design of multifunctional polymeric micelles, based on the heterogeneity of their structure.

ASSOCIATED CONTENT

S Supporting Information

Summary of primary data of SLS and DLS experiments; discussion on the origins of formation of two micelle populations for PS-*b*-P(4VP/EVP- β) copolymers in water-organic and aqueous media. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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