

Polyion Complex Nanomaterials from Block Polyelectrolyte Micelles and Linear Polyelectrolytes of Opposite Charge: 1. Solution Behavior[†]

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The present study investigates whether block polyelectrolyte micelles can form soluble complexes upon interaction with oppositely charged linear polyelectrolytes. The phase behavior and molecular characteristics of the complexes were examined by turbidimetry, phase analysis, dynamic light scattering, and sedimentation velocity techniques. At an excess of polyelectrolyte micelles, soluble complexes were formed either independently on the route of preparation or, for select linear polyelectrolytes, through routes that avoided macrophase separation. Such soluble complexes are in a thermodynamic equilibrium state for all polyion pairs. The hydrodynamic sizes and sedimentation coefficients did not depend on the chemical nature of the linear polyelectrolyte, but were determined by the charge ratios and the hydrodynamic properties of the initial micelles. At an excess of linear polyelectrolyte, complex solubility and molecular characteristics depended on the chemical nature of the linear polyelectrolyte. In this region, linear polyelectrolytes formed soluble complexes with micelles if soluble complexes could be formed with the corresponding linear analogues of the block polyelectrolyte.

Introduction

Block ionomer complexes (BIC) represent a special class of polymeric compounds that are products of interaction of ionic block copolymers with oppositely charged species of different chemical nature: low-molecular-mass amphiphilic surfactants, synthetic polyelectrolytes, and biopolymers. This class of compounds has emerged in response to a need to develop novel nanomaterials for biomedical applications.¹ The initial motivation of these works was to create hybrid materials displaying environmental sensitivity of ordinary interpolyelectrolyte complexes (IPECs)^{2–4} and core–shell architecture of block copolymer micelles.⁵ This allowed expanding application of BIC in delivery of DNA and drugs,⁶ where the ordinary IPEC⁷ and polymer micelles⁸ were used already.

One promising type of BIC is based on amphiphilic block copolymers containing a nonionic hydrophobic block and a polyelectrolyte block. In selective solvents, such as water, these polymers spontaneously form micelles with a core–shell structure. In such micelles, the nonionic blocks segregate into a hydrophobic core, whereas polyelectrolyte blocks form a charged corona, providing the micelle solubility in aqueous media (i.e., “dispersion stability”).^{5,9} Interaction of these micelles with oppositely charged surfactants results in formation of nearly stoichiometric water-insoluble complexes.¹⁰ However, interac-

tion of the micelles with oppositely charged linear polyelectrolytes can generally lead to the formation of water-soluble nanosized complexes.^{11–14} Such complexes are believed to have multilayer structure with the hydrophobic nonionic core, intermediate water-insoluble polyelectrolyte complex layer, and surrounding hydrophilic corona from the excessive polyelectrolyte. Due to multilayer structure, these complexes combine hydrophobic nonpolar domains (core) with polar domains, which are either weakly hydrated (polyelectrolyte complex layer) or highly hydrated (ionic corona).

The dispersion stability of these complexes in aqueous media is essential for their use in biomedical applications; however, their solution behavior is poorly understood. Theoretical predictions suggest that such complexes are insoluble,¹¹ yet experimental work shows that, depending on the system, they can have one solubility region at an excess of linear polyelectrolyte¹² or excess of block polyelectrolyte micelles¹³ or two solubility regions at an excess of polyelectrolyte or micelles.¹⁴ Previous reports used block polyelectrolytes with different hydrophobic blocks, which affected the size and structure of the micelles and, perhaps indirectly, the composition and solubility of the BIC. In some cases, there are also concerns regarding the equilibrium nature of soluble complexes.¹² As a result, it is difficult to formulate general criteria for the soluble complex formation on the basis of the current literature data.

To address this problem, the present work investigates BIC formed by linear polyelectrolytes of different chemical nature and anionic or cationic block polyelectrolyte micelles having the same polystyrene core-forming block. To elucidate the contribution of the chemical nature of interacting polymers and their charge ratio, all environmental parameters (pH, ionic

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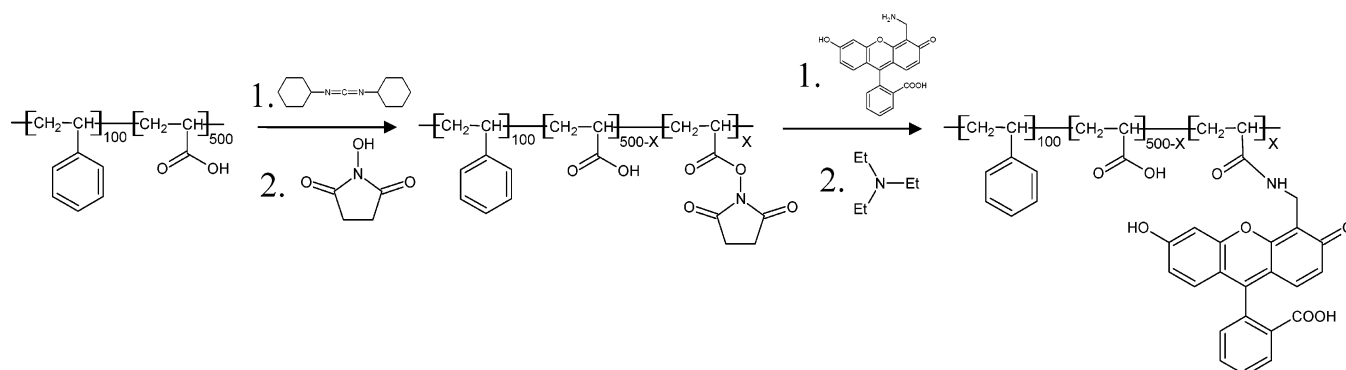
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SCHEME 2: Labeling of Carboxylic Groups of PS(100)-*b*-PAA(500) with AMF

PS(100)-*b*-PAA(500) samples were tagged with a fluorescent label (4'-(aminomethyl)fluorescein hydrochloride (AMF), Molecular Probes, Eugene, OR) using a modified procedure (Scheme 2).¹⁷ Briefly, 0.198 g (2.14 mmol carboxylic groups) of PS(100)-*b*-PAA(500) dissolved in 4 mL of DMF was treated overnight with *N*-hydroxysuccinimide (0.61 mg, $5.35 \cdot 10^{-6}$ mol; Sigma Chemical Co, St. Louis, MO) and 1,3-dicyclohexylcarbodiimide (1.1 mg, $5.34 \cdot 10^{-6}$ mol; Acros Organics, NJ) at room temperature and with constant stirring. After that, the mixture was treated with AMF (2.1 mg, $5.34 \cdot 10^{-6}$ mol) and triethylamine (3.6 mg, $3.56 \cdot 10^{-5}$ mol; Fisher Chemicals, NJ) for 1 day, and the labeled block copolymer was dialyzed against water as described above. PS(70)-*b*-PMAA(150) was labeled using the same procedure. Labeling density measured by combination of potentiometric titration, and UV spectrophotometry was 1 label per 5100 carboxylic groups in the case of PS(100)-*b*-PAA(500) and 1 label per 3700 carboxylic groups in the case of PS(70)-*b*-PMAA(150) (here and below, labeled polymers are designated by the asterisk (*) symbol).

Linear Polyelectrolytes. Poly(acrylic acid, sodium salts) (PANa) of different polymerization degrees ($DP_w = 160, 370, 740, 1000, \text{ and } 2700$) with narrow polydispersity indices were purchased from Polysciences, Inc. (Warrington, PA). Poly(methacrylic acids) (PMAA) of different polymerization degrees ($DP_w = 1740, 2150, 2300$) were synthesized via radical polymerization and fractionated as described previously.^{14a} The shorter PMAA samples ($DP_w = 90 \text{ and } 140$) were purchased from Scientific Polymer Products, Inc. (Ontario, NY). Sodium poly(methacrylic acid, sodium salts) (PMANa) were obtained by neutralization of aqueous PMAA solutions by NaOH. Poly(ethylacrylic acid) (PEAA, $DP_w = 3000, M_w/M_n = 1.5$) was purchased from Polymer Source, Inc. (Montreal, Canada). Poly(ethylacrylic acid, sodium salt) (PEANa) was obtained by dissolution of PEAA in aqueous solution of NaOH. Poly(aspartic acid, sodium salt) (P(Asp)Na, $DP_w = 25$) was purchased from Aldrich Chemical Co., Inc. (Milwaukee, WI).

Poly(styrenesulfonic acid, sodium salt) (PSSNa, $DP_w = 340 \text{ and } 2400$) was purchased from Polysciences, Inc. (Warrington, PA). Poly(vinylsulfonic acid, sodium salt) (PVSNa, $DP_w = 30$) was purchased from Aldrich Chemical Co., Inc. (Milwaukee, WI). Poly(phosphoric acid, sodium salt) (PPNa) was synthesized as follows:¹⁸ First, poly(phosphoric acid, potassium salt) was synthesized via polycondensation of KH_2PO_4 at $\sim 800^\circ\text{C}$ for 10 h, followed by rapid cooling in liquid nitrogen. Second, potassium ion was substituted by sodium via repeated dissolution of the polymer in 0.1 M NaCl, followed by precipitation in 2 M NaCl. The polymerization degree of PPNa (measured by viscometry¹⁸) was 2100.

PVP samples ($DP_w = 500, 1900$; Polysciences, Inc., Warrington, PA) were exhaustively modified by ethyl bromide to

obtain poly(*N*-ethyl-4-vinylpyridinium bromide) (PEVP)^{10c}. The modification degree was 90%. Poly(diallyldimethylammonium chloride) (PDADMAC, $DP_w = 2800$) was purchased from CPS Chemical Company, Inc. (Old Bridge, NJ). Poly(*N,N*-dimethyl-*N*-ethyl-*N*-methacryloyloethylammonium bromide) (PDMAE-MA(EtBr)) was obtained by exhaustive quaternization of poly(*N,N*-dimethylaminoethylmethacrylate) (PDMAEMA).

Turbidimetry. Turbidity measurements were performed on a UV/vis spectrophotometer, Lambda-25, (Perkin-Elmer, U.S.A.) in 10 mm quartz cells at 500 nm to exclude intrinsic absorbance of polymeric components in solution (PS, PEVP, PMANa*) in the UV region. Turbidity was calculated as $\tau = (100 - T)/100$, where T is transmittance. All the data were expressed in coordinates τ vs ν , where ν is a molar portion of ionic repeating units (r.u.) of a linear polyelectrolyte.

$$\nu = \frac{[\text{linear polyelectrolyte, r.u.}]}{[\text{block copolymer, r.u.}] + [\text{linear polyelectrolyte, r.u.}]}$$

UV Measurements. Insoluble complexes were separated by sedimentation using a preparative microcentrifuge (Eppendorf, model 5415 D, Germany, 15 min at 13 200 rpm). The supernatants were used to determine the relative amounts of PEVP that remained in the solution by UV as well as particle effective size and sedimentation coefficient measurements, described below. UV spectra were recorded on a UV/vis spectrophotometer, Lambda-25, (Perkin-Elmer, Wellesley, MA) in 10 mm quartz cells. The wavelength range available was from 200 to 900 nm.

Dynamic Light Scattering. Dynamic light scattering (DLS) experiments were performed on a FotoKorr-M 72-channel correlator. Diffusion coefficients (D_z) were calculated by a cumulant analysis of an autocorrelation function of scattered light intensity fluctuations. Effective hydrodynamic radii (R_h) were calculated from diffusion coefficients using the Stokes equation,

$$D = \frac{k_B T}{6\pi\eta R_h}$$

where k_B is Boltzmann constant, T is absolute temperature, and η is the intrinsic viscosity of a solvent. Prior to light scattering, the samples were filtered at least two times through Millipore 0.45 μm filters. For all measurements of the diffusion coefficients, the experimental error did not exceed 5%.

Sedimentation. Sedimentation velocity measurements were performed with a Beckman model E analytical ultracentrifuge (Fullerton, CA) equipped with an absorption optical detector at $\omega = 40\,000$ rpm at room temperature.

Fluorescence Measurements. Fluorescence spectra were recorded using a Cary Eclipse fluorescence spectrophotometer (Varian, Inc., Palo Alto, CA) at $\lambda_{\text{EX}} = 490$ nm and $\lambda_{\text{EM}} = 520$ nm with a bandwidth of 2.5 nm for excitation and 5 nm for emission. All measurements were performed on solutions 1–2 days after preparation at room temperature and processed using software provided by the manufacturer.

Results and Discussion

The present study investigates whether block polyelectrolyte micelles can form soluble complexes upon interaction with oppositely charged linear polyelectrolytes. For quantitative characterization of such dispersions, we also measured some of their important hydrodynamic characteristics, such as hydrodynamic sizes and sedimentation coefficients, as functions of the polyelectrolyte chemical nature and mixture composition. Three polystyrene-based block polyelectrolytes with different corona-forming blocks and similar core-forming blocks were chosen as examples: PS-*b*-PEVP, PS-*b*-PMANa and PS-*b*-PANa. The linear polyanion counterparts were also varied: sodium polycarboxylates, polysulfonates, and polyphosphate for PS-*b*-PEVP; and aromatic, aliphatic, and alicyclic quaternized polyamines for PS-*b*-PMANa and PS-*b*-PANa. Chemical structures of all polymers are shown in Scheme 1.

Dispersion Stability of the Complexes. BIC were obtained using three different methods:³ (a) direct mixing, (b) preparation using low pH, and (c) preparation using high ionic strength. The first method involved direct mixing of fully charged polyanion components using conditions favoring polyanion coupling: (i) pH 10.0 (polycarboxylates, 0.01 M TRIS) or pH 7.0 (all other polyanions), and (ii) 0.1 M NaCl. The second method, applied to polycarboxylate-based systems, involved mixing of components at pH ≤ 2.0 to prevent polyanion coupling, followed by a gradual pH increase to pH 10.0 to form complexes. The third method involved mixing of components at a high ionic strength to prevent polyanion coupling, followed by dilution to a lower ionic strength to form complexes. Specifically, complexes disintegrated at 0.5 M $< [\text{NaCl}] \leq 1.0$ M and reassembled at $[\text{NaCl}] = 0.1$ M (except for PSSNa, for which $[\text{NaBr}] > 3.0$ M and $[\text{NaBr}] = 0.3$ M was used for disintegration and reassembly).

The dispersion stability of the complexes was evaluated by measuring (a) solution turbidity and (b) block copolymer concentration in a solute phase. All measurements were carried out 24 h after solution preparation. Examples of solubility diagrams for mixtures of PS-*b*-PEVP micelles and sodium polycarboxylates are presented in Figure 1. This figure shows dependencies of solution turbidity (τ) or relative block copolymer concentration in solute phase ($[\text{Py}^+]/[\text{Py}^+]_0$) as functions of the molar portion of carboxylate units in the system (ν). The complexes were considered soluble if solutions were transparent ($\tau \approx 0$) and no precipitation of polymer components was observed ($[\text{Py}^+]/[\text{Py}^+]_0 \approx 1$). Comparison of Figure 1a and 1b suggested that these two requirements were consistent with each other. Soluble BIC were obtained in selected cases and only at sufficient excess of one of the components: either micelles over linear polyelectrolytes or, vice versa, linear polyelectrolytes over micelles. In the composition regions approximating the charge stoichiometry ($\nu \sim 0.5$), the complexes were insoluble. The regions of solubility were different for each complex. Some complexes, such as PS-*b*-PEVP/PANa(2700) were soluble at an excess of block copolymer micelles ($\nu < 0.2$) but insoluble at any excess of the linear polyelectrolyte ($0.5 < \nu < 1$). Notably, in their regions of solubility, BIC remained stable, revealing no increase in turbidity or polymer precipitation for

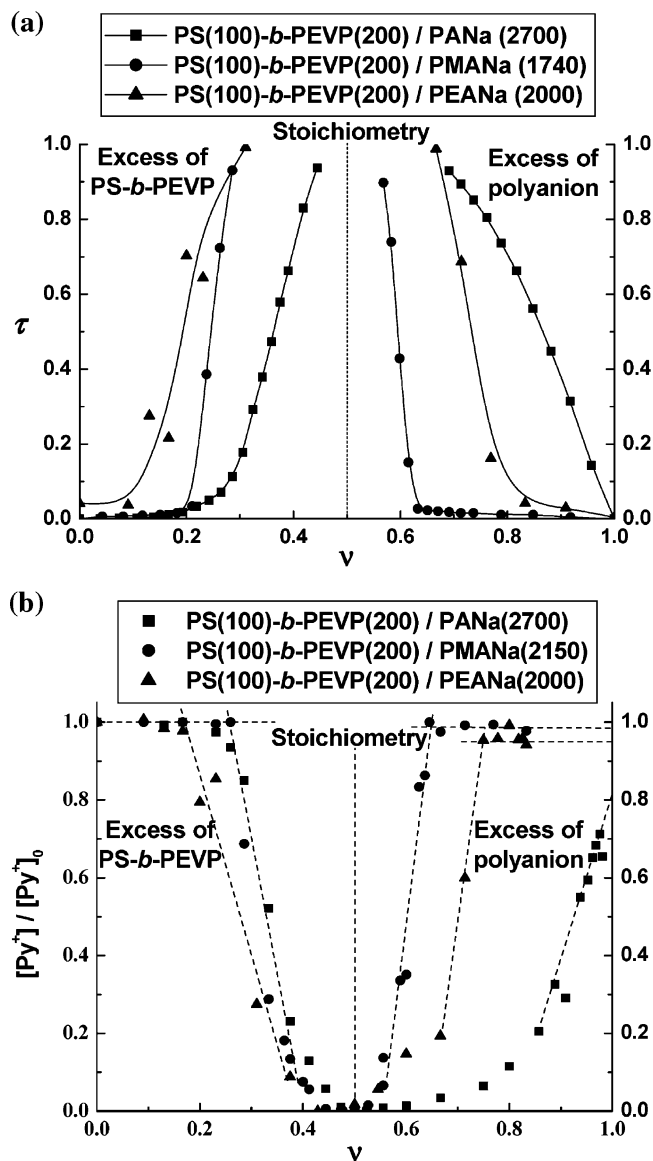


Figure 1. (a) Solution turbidity, τ , and (b) relative concentration of the polyanion in solution, $[\text{Py}^+]/[\text{Py}^+]_0$ as functions of the mixture composition, ν for complexes of PS(100)-*b*-PEVP(200) micelles with PANa(2700), PMANa(1740), PMANa(2150), and PEANa(2000). $[\text{Py}^+]_0$ and $[\text{Py}^+]$ are PS(100)-*b*-PEVP(200) net concentration in the system and its equilibrium concentration in solution, respectively. $[\text{NaCl}] = 0.1$ M; $[\text{TRIS}] = 0.01$ M (pH = 10.0); $[\text{PEVP}] = 5 \cdot 10^{-3}$ M ($0 \leq \nu \leq 0.5$); $[\text{COONa}] = 5 \cdot 10^{-3}$ M ($0.5 \leq \nu \leq 1$).

at least 2 months. The data on the dispersion stability of the BIC and IPEC for the entire set of the block polyelectrolyte micelles and linear polyelectrolytes are summarized in Table 1. The following discusses separately the BIC formed (1) at an excess of block polyelectrolyte micelles and (2) at an excess of linear polyelectrolytes.

Excess of Block Polyelectrolyte Micelles. In this composition region, all micelle and linear polyelectrolyte mixtures were able to form soluble BIC (transparent stable dispersions). For the majority of systems, soluble BIC were formed at $\nu < 0.25$ – 0.35 , which corresponds to an at least 3- to 4-fold excess of block polyelectrolytes. For several systems, the solubility regions were more narrow, such as $\nu < 0.10$ for PS-*b*-PANa/PDMAEMA(EtBr) and $\nu < 0.15$ for PS-*b*-PANa/PDMAEMA(EtBr) and PS-*b*-PEVP/PEANa. Notably, soluble BIC formed even in cases when the corresponding linear analogues of

TABLE 1: Solubility of the BIC and IPEC

block polyelectrolyte or linear analogue	linear polyelectrolyte ^b	solubility ^a	
		excess of block polyelectrolyte	excess of linear polyelectrolyte
PS(100)- <i>b</i> -PEVP(200) or PEVP(500)	polycarboxylates	P(Asp)Na(25)	+ (−)
		PANa(160, 370, 740, 2700)	+ (−)
		PMANa(90, 140, 1740, 2300)	+ (−)
		PEANa(2000)	+ (−)
	polysulfonates	PVSNa(30)	+ (+)
		PSSNa(340, 2400)	± (−)
PS(70)- <i>b</i> -PMANa(150) or PMANa(2150)	polyphosphates	PPNa(2100)	± (−)
		PDADMAC(2800)	+ (+)
		PEVP(500)	+ (+)
		PEVP(1900)	± (+)
		PDMAEMA(EtBr)	± (−)
		PEVP(500)	± (−)
PS(100)- <i>b</i> -PANa(500) or PANa(2700)		PDADMAC(2800)	± (−)
		PDMAEMA(EtBr)	± (−)
		PEVP(500)	± (−)
		PDADMAC(2800)	± (−)

^a Symbol keys: (+) soluble independently on the preparation route; (±) insoluble at direct mixing, but forms stable transparent dispersions upon preparation using high ionic strength (see text for preparation details); (−) insoluble independently on the preparation route. The first symbol denotes solubility of the mixture of a block polyelectrolyte and an oppositely charged linear polyelectrolyte; the symbol in parentheses denotes solubility of the mixture of a linear analogue of the block polyelectrolyte and an oppositely charged linear polyelectrolyte. ^b Numbers in parentheses correspond to weight-average polymerization degrees of polymers or polymer blocks; several numbers in parentheses listed for the same polyion mean that specific solubility behavior was observed for each polyion of different length.

micellar polyelectrolytes did not form soluble IPEC (also reported earlier for PS-*b*-PEVP/PMANa mixtures¹⁴).

The route of preparation was also a factor in forming soluble BIC for some, but not all, polyion mixtures (Table 1). Route-independent behavior was observed for PS-*b*-PEVP/polycarboxylates, PS-*b*-PEVP/PVSNa, PS-*b*-PMANa/PEVP(500), and PS-*b*-PMANa/PDADMAC (Table 1, depicted as “+”). This behavior was similar to that previously reported for polyisobutylene-*b*-PMANa/PEVP(500)¹³ and PS-*b*-PEVP/PMANa.¹⁴ Furthermore, comparison of results for PS-*b*-PMANa/PEVP(500) (Table 1) and polyisobutylene-*b*-PMANa/PEVP(500)¹³ suggests that at an excess of micellar component, soluble BIC can form with copolymers having the same corona-forming block and different core-forming blocks. Another set of systems, PS-*b*-PANa/polycation, PS-*b*-PMANa/PEVP(1900), PS-*b*-PMANa/PDMAEMA(EtBr), PS-*b*-PEVP/PSSNa, and PS-*b*-PEVP/PPNa (Table 1, depicted as “±”), exhibited strong dependence on the preparation route. These systems formed precipitates upon direct mixing or preparation using low pH, whereas preparation using high ionic strength resulted in formation of transparent and stable dispersions that did not precipitate for at least several weeks.

This striking dependence on the preparation route suggested formation of nonequilibrium polyion complexes during mixing. Following initial polyion coupling, soluble complexes equilibrate through consequent polyion exchange reactions.¹⁹ Thus, a route-independent system, PS-*b*-PMANa/PEVP(500), and route-dependent systems, PS-*b*-PMANa/PEVP(2000) and PS-*b*-PANa/PEVP(500), were compared to determine whether the difference in behavior is related to differences in polyion exchange. The exchange reactions were monitored using a fluorescence quenching technique.¹⁹ The polycarboxylate blocks were labeled with AMF that was quenched by PEVP upon formation of the polyion complex. The reactions were studied in two directions (Figure 2). First, addition of labeled block polyelectrolyte micelles to complexes of unlabeled micelles and PEVP resulted in fluorescence quenching due to transfer of PEVP to labeled micelles (filled symbols). Second, addition of unlabeled micelles to complexes of labeled micelles and PEVP resulted in a fluorescence increase due to transfer of PEVP to unlabeled micelles (open symbols). In both cases, the reactions were slow, proceeding over many weeks. For each polyion pair,

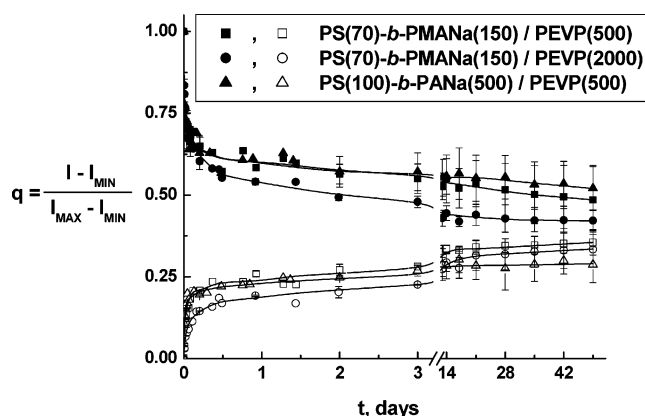


Figure 2. Migration of PEVP chains between labeled and unlabeled block copolymer micelles studied by fluorescence quenching. Pairs of block copolymer/PEVP(X) are as follows: a) PS(70)-*b*-PMANa(150)/PEVP(500) (BIC with route-independent solubility); b) PS(70)-*b*-PMANa(150)/PEVP(2000) and c) PS(100)-*b*-PANa(500)/PEVP(500) (BICs with route-dependent solubility). [NaCl] = 0.1 M; [TRIS] = 0.01 M (pH = 10.0); [COO[−]]^{*} = [COO[−]] = 5·10^{−4} M; [PEVP] = 1.5·10^{−4} M.

independently of the direction of the reaction, the processes approximated the same equilibrium state that was not accompanied by precipitation. Therefore, soluble BIC formed at an excess of block polyelectrolyte micelles correspond to a thermodynamical equilibrium state for all studied combinations of polyions, both route-dependent and independent. Clearly, due to slow polyion exchange, some soluble BIC may initially be in a nonequilibrium state but are likely to evolve to equilibrium-soluble BIC upon storage. Finally, the observed dependence on the route of preparation is most likely due to formation of nonequilibrium precipitates in some mixtures. Soluble BIC were formed if precipitation was avoided (using high ionic strength or mixing of existing BIC with polyions).²⁰

Excess of a Linear Polyelectrolyte. For each system presented in Table 1, BIC (and IPEC) were either soluble or insoluble, independent of the preparation route. The only system known so far to form soluble BIC at an excess of a linear polyelectrolyte was PS-*b*-PEVP/PMANa.¹⁴ It is interesting to note that IPEC of PMANa with PEVP was also soluble at an excess of PMANa. We identified another poly(alkyl)acrylic acid, PEANa that

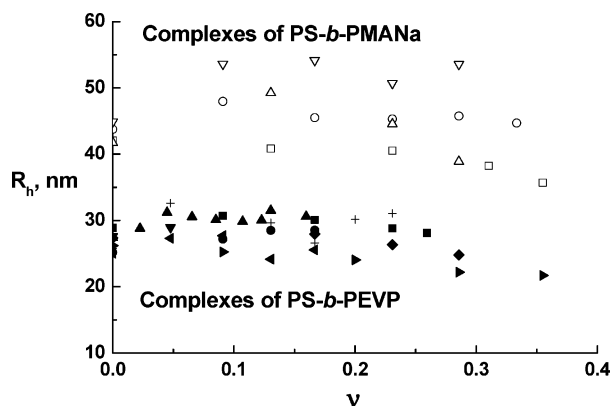


Figure 3. Dependences of hydrodynamic radii of BIC particles on mixture composition for the complexes at an excess of block polyelectrolyte micelles. The complexes of PS(100)-*b*-PEVP(200) with polyanions (filled symbols), prepared through either direct mixing (■ PANa(2700); ● PMANa(90); ▲ PMANa(2300); right-pointing triangle, P(Asp)Na(25); left-pointing triangle, P(VS)Na(25)) or from high ionic strength (▼ PEANa(2000); ◆ PPNa(2100); + PSSNa(2400)). The complexes of PS(70)-*b*-PMANa(150) with polycations (open symbols), prepared through either direct mixing (□ PEVP(500)) or from high ionic strength (○ PEVP(1900); △ PDADMAC(2800); ▽ PDMAEMA-(EtBr)). [NaCl] = 0.1 M; for the systems containing carboxylic polyelectrolytes, [TRIS] = 0.01 M (pH = 10.0).

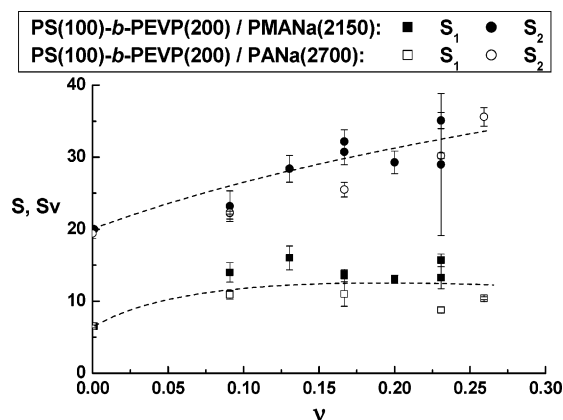


Figure 4. Dependences of sedimentation coefficients on mixture composition for the complexes of PS(100)-*b*-PEVP(200) with PMANa-(2150) and PANa(2700) at an excess of block polyelectrolyte micelles. [NaCl] = 0.1 M; [TRIS] = 0.01 M (pH = 10.0); [PEVP] = $5 \cdot 10^{-3}$ M.

formed soluble complexes with both PS-*b*-PEVP micelles and linear PEVP. Notably, we did not find any other polyelectrolyte that produced soluble complexes with PS-*b*-PEVP, PS-*b*-PMANa, and PS-*b*-PANa or their linear analogues, PEVP, PMANa, and PANa. Thus, we posit that soluble BIC can form at an excess of a linear polyelectrolyte only in the case that the corresponding linear polyelectrolytes form soluble IPEC. These BIC compositions corresponding to solubility regions are $\nu > 0.64$ for PS-*b*-PEVP/PMANa and $\nu > 0.75$ for PS-*b*-PEVP/PEANa. This corresponds to excesses of linear polyelectrolytes of at least 1.78-fold for PMANa and 3-fold for PEANa.

It is interesting to note that PMANa and PEANa belong to the same homologous series of polyions. We also examined PANa that is more hydrophilic than PMANa and PEANa and could be regarded as a more efficient lyophilizing agent. Surprisingly, this polyion did not form soluble complexes with either PS-*b*-PEVP or PEVP. Thus, we suggest that both PMANa and PEANa chains are retained in the micelle corona due to hydrophobic interactions of methyl or ethyl groups present in their backbones as well electrostatic interactions with PEVP. As a result, an excess of these polyions can bind with

the block polyelectrolyte micelle and stabilize BIC in solution. Similarly, these polyions can bind to and solubilize ordinary IPEC. In fact, such a mechanism of colloidal stabilization was proposed for IPEC formed by plasmid DNA and shorter polycations added in excess.²¹ The PANa chains are, perhaps, too hydrophilic to be retained in the complexes, and therefore, both the BIC and IPEC formed at an excess of this polyion are insoluble. At the same time, compared to PMANa, PEANa is more hydrophobic and, perhaps, a worse lyophilizing agent, which may explain why its greater excess is required to form a soluble complex.

Characterization of Soluble BIC Particles. In this part, we present a more detailed characterization of the influence of the chemical nature of ionic groups of a micellar block polyelectrolyte and a linear polyelectrolyte on the molecular properties of the soluble BIC particles. As in the previous part, we discuss separately the complexes formed at an excess of block polyelectrolyte micelles and at an excess of oppositely charged linear polyelectrolyte.

Excess of Block Polyelectrolyte Micelles. Two examples of soluble BIC formed at an excess of block polyelectrolyte micelles were described in the literature.^{13,14} In both cases, their solubility did not depend on the preparation route. For each of these complexes, a multilayer structure was proposed, assuming that the complex particles include a hydrophobic core of a micelle, an intermediate IPEC layer, and a hydrophilic corona of the polyion chains present in excess. DLS data for soluble complexes formed at an excess of both positively and negatively charged block polyelectrolyte micelles (Figure 3) were consistent with this model. These data show that for each system, the particle dimensions were determined by those of the initial micelles and did not depend on the chemical nature of linear polyelectrolytes or preparation routes. The sedimentation velocity experiments using several soluble BICs (Figure 4) also reinforced such a conclusion: sedimentation coefficients were determined only by the characteristics of the initial micelles and composition of the complex; they did not depend on the nature of the polyelectrolyte.²²

Excess of a Linear Polyelectrolyte. A PS-*b*-PEVP/PMANa system that forms soluble complexes at an excess of a linear polyelectrolyte was described in detail previously.¹⁴ The sizes of the BIC particle formed under these conditions ($R_h = 32$ nm) were only slightly higher than those of initial PS-*b*-PEVP micelles ($R_h = 27$ nm). Contrary to that, soluble complexes formed at an excess of a linear polyion in the PS-*b*-PEVP/PEANa system ($R_h = 53$ nm) were considerably larger than the initial micelles (not shown in figures). A possible explanation of such a difference in the particle size is the bridging of several micelles together by a linear polyelectrolyte. The aggregation of the micelles by a linear polyelectrolyte added in excess was previously shown for the PS-*b*-poly(2-vinylpyridinium hydrochloride)/PSSNa system.¹²

Conclusion

Solubility of BICs formed by amphiphilic block polyelectrolyte micelles and oppositely charged linear polyelectrolytes depends on which component is present in excess. In an excess of block polyelectrolyte, the micelles provide the ability to form soluble complexes. In this case, the chemical nature and length of the linear polyelectrolyte determine whether a soluble BIC can be obtained independently on the preparation route or through route(s) avoiding macroscopic phase separation. Hydrodynamic sizes and sedimentation coefficients of soluble BIC particles are determined by those of the initial micelles. In

contrast, at an excess of a linear polyelectrolyte, the role of the chemical nature of the polyion chains becomes critical. In this case, linear polyelectrolyte can form a soluble BIC only if it forms a soluble IPEC with a corresponding linear analogue of a block polyelectrolyte. Hydrodynamic sizes and sedimentation coefficients of the soluble BIC particles strongly depend on the chemical structure of the linear polyelectrolyte. Altogether, these studies present comprehensive information on the solution behavior of novel polyion complex dispersions that can have useful applications in practical areas, such as nanomedicine and gene delivery.

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