Balance of Hydrophobic and Electrostatic Forces in the pH Response of Weak Polyelectrolyte Capsules

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A detailed study of the role of solution pH and ionic strength on the swelling behavior of capsules composed of the weak polyelectrolytes poly(4-vinylpyridine) (P4VP) and poly(methacrylic acid) (PMA) with different numbers of layers was carried out. The polyelectrolyte layers were assembled onto silicon oxide particles and multilayer formation was followed by ζ-potential measurements. Hollow capsules were investigated by scanning electron microscopy and atomic force microscopy. The pH-dependent behavior of P4VP/PMA capsules was probed in aqueous media using confocal laser scanning microscopy. All systems exhibited a pronounced swelling at the edges of stability, at pHs of 2 and 8.1. The swelling degree increased when more polymer material was adsorbed. The swollen state can be attributed to uncompensated positive and negative charges within the multilayers, and it is stabilized by counteracting hydrophobic interactions. The swelling was related to the electrostatic interactions by infrared spectroscopy and ζ-potential measurements. The stability of the capsules as well as the swelling degree at a given pH could be tuned, when the ionic strength of the medium was altered.

Introduction

Polyelectrolyte microcapsules are interesting systems with many potential applications ranging from biomedical devices to microsensing and drug delivery. They are fabricated via the layer-by-layer (LbL) approach developed by Decher et al. for flat substrates in the early nineties.[1] To obtain hollow capsules the polyelectrolytes are adsorbed onto colloidal templates, which can be removed after deposition of the multilayers.[2,3] The properties of these membranes can be tuned by the polymers that are adsorbed onto the colloids.[4,5] For many future applications of such capsules, including controlled delivery of materials, it is desirable to regulate the multilayer wall in response to various external stimuli. Examples of such stimuli are temperature, pH, ionic strength, light, and magnetic field.[6–8]

In this study we will concentrate on pH-responsive systems, which can be obtained by the incorporation of polyelectrolytes with weak acid and base functionalities into the polymeric shells of the capsules. Multilayers with pH-sensitive characteristics have attracted considerable interest, because the average charge per repeat unit can easily be controlled by the acidity and the ionic strength of the surrounding solution, thus providing the possibility to tune the interactions between the charged polymers.[9–14] The intrinsic property of multilayers composed of weak polyelectrolyte complexes is that they can be destroyed at extreme pH conditions, as the pH induced imbalance of charges overcompensates the attractive polymer–polymer ionic binding.

A well-described weak polyelectrolyte pair in the literature is that of poly(acrylic acid) (PAA) and poly(allylamine hydro-chloride) (PAH). This polymer combination was studied in detail on flat substrates and examples of properties that change with pH are surface wettability and roughness, film morphology, layer thickness, pH triggered microporosity, as well as discontinuous swelling/deswelling transitions.[15–18]

PAH and PAA have also been used for the assembly of multilayers on colloidal particles and for the preparation of hollow capsules.[19–23] If multilayers are made of weak poly-electrolytes, the resulting capsules have a stability that is dependent on the pH. We have previously reported about capsules composed of PAH and poly(methacrylic acid) (PMA) on various cores that are stable over a wide pH range.[24,25]

In addition to electrostatic stabilization of weak polyelectro-lyte layers there can also occur hydrogen bonding between uncharged carboxylic acids, amino functions, and hydroxyl groups. Hydrogen bonding self-assembly was first introduced by Stockton and Rubner in 1997.[26] Since then several pairs of polymers have been successfully used in the self-assembly process.[27–29]

Sukhishvili and co-workers studied the assembly of the weakly charged polyacids PAA and PMA with uncharged polymers capable of undergoing hydrogen bond interactions, e.g., poly(ethylenoxide) (PEO) and poly(N-vinylpyrrolidone). With these polymer combinations stable multilayers can be obtained in the acidic pH range and the resulting structures are sensitive to pH changes due to the generation of electrostatic repulsion between the layers within the films.[30,31]

Some recent publications report on hydrogen-bonded hollow capsules[32–34] that were prepared from polymer combinations of PMA with poly(N-vinylpyrrolidone) and PEO by templating them on silica, AgCl, and CdCO$_3$ particles. Cross-linking of the PMA layers with ethylenediamine and exposure to high pH

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Balance of Hydrophobic and Electrostatic Forces

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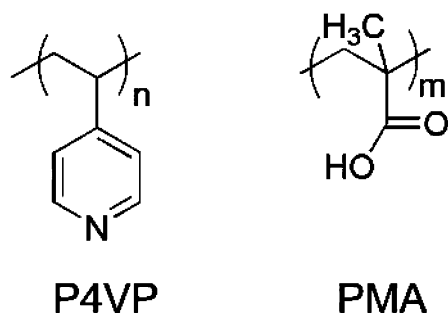
Figure 1. Structures of the polyelectrolytes used in this study.

solutions resulted in hollow hydrogel capsules composed only of PMA.[35] Zhang et al. used poly(N-vinylpyrrolidone) and *m*-methylphenol-formaldehyde resin on silica templates to generate hydrogen-bonded hollow capsules.[36] Rubner and co-workers prepared microcapsules based on hydrogen-bonded multilayers of PAA and poly(acrylamide) that were subsequently cross-linked.[37]

When polyelectrolyte multilayers are assembled of two weakly charged polymers with pK_as that are sufficiently close, one also has to consider H-bonding for the stabilization of the layers in addition to electrostatic interactions. An example of such a system is the polymer combination of poly(4-vinylpyridine) (P4VP) and PAA. This system was first studied on flat substrates by Wang et al. who reported on the stabilization by H-bonding when PAA is adsorbed at low pH and P4VP in ethanol or when both polymers are adsorbed in methanol.[27,38] In addition, P4VP/PAA layers were incorporated in strongly charged flat multilayers. In this case, the H-bonded layers were sandwiched between the electrostatically stabilized ones, and thereby they converted largely pH resistant films into erasable multilayer films with adjustable deconstruction kinetics.[39]

Sukhishvili and co-workers studied the interplay between electrostatic and hydrogen-bond interactions with partially quarternized poly(4-vinylpyridine) (QP4VP) with different alkylation degrees ranging from 12 to 98% and PMA for the generation of stable multilayered films.[40] The stability of multilayers of QP4VP and PMA in salt solution was investigated with different ionization degrees of QP4VP, ranging from 50 to 84% and the multilayer growth was also correlated with phase separation in solution.[41,42] Kharlampieva et al. stabilized hydrogen-bonded films at neutral pH in combining centers for electrostatic and hydrogen bonding in one molecule by copolymerization of acrylamide and dimethyldiallylammonium chloride and layering it with PMA.[43]

In this publication we provide a detailed investigation of the pH-dependent properties of microcapsules composed of the weakly charged polyacid PMA and the weakly charged polybase P4VP. The structures of these polyelectrolytes are shown in Figure 1. The multilayers were templated on silicon oxide particles, as this core material can be removed without affecting the chemical composition of the capsule shell.[25] In the intermediate pH range the multilayers are stabilized by H-bonding and electrostatic interactions, whereas hydrophobic interactions in combination with electrostatic repulsion lead to an interesting stability profile as a function of pH. In addition to the effect of pH we also report results on the stability and the swelling behavior of this system when the ionic strength and the adsorbed polymer amount are increased.

Experimental Methods

Materials. ZnSe substrates for IR-measurements were purchased from Korth Kristalle GmbH (Kiel, Germany). P4VP (M_w

= 60 000 g/mol), PMA (M_w = 75 100 g/mol), methanol, NaCl, HF, NH_4F, H_2O_2, NH_4OH, 1-ethyl-3-(3-(dimethylamino)-propyl) carbodiimide (EDC), N-hydroxysulfosuccinimide sodium salt (sulfo-NHS), and rhodamine B amine were obtained from Sigma Aldrich. HCl and NaOH were purchased from Merck. Silica particles with mean diameters of 881 nm and 4.48 ± 0.26 μm were obtained from Microparticles GmbH (Berlin, Germany). All chemicals were used as received. The water used in all experiments was prepared in a three-stage Millipore Milli-Q Plus 185 purification system and had a resistivity higher than 18.2 MΩ·cm.

Capsule Preparation. Multilayers were assembled on the templates by the LbL technique as described previously.[3,44] The polyelectrolytes were prepared as 2 mg/mL solutions in a 1:1 mixture of 0.2 M NaCl and methanol. The pH of all solutions was adjusted to 5. The solvent combination was chosen to ensure solubility of P4VP at this pH.[39] Prior to the polyelectrolyte adsorption the silica particles were exposed to a mixture of 5:1:1 H_2O:NH_4OH (25%):H_2O_2 (30%) for 20 min, followed by multiple water washing steps to yield neutral pH. Multilayers were then assembled by consecutively immersing the SiO_2 particles into the respective polyelectrolyte solutions for 15 min, followed by centrifugation (1400 g, 2 min) and three washing cycles with a mixture of H_2O: methanol (1:1, pH 5). After the assembly of the multilayers, the core was dissolved by treatment with a buffer solution of 0.2 M NH_4F and HF at pH 3.5, followed by five centrifugation/water washing steps. The details of the dissolution protocol are described elsewhere.[25]

Electrophoretic Mobility Measurements. Electrophoretic mobilities of coated silica particles with a mean diameter of 881 nm were measured with a Malvern Zetasizer Nano-Z (Malvern Instruments, UK). The electrophoretic mobility was converted into the ζ-potential with the Smoluchowski relation, using an average mobility value based on 30 measurements. The pH was adjusted with addition of HCl and NaOH. All ζ-potential measurements were performed without additional electrolyte.

Confocal Laser Scanning Microscopy (CLSM). Confocal micrographs of polyelectrolyte capsules were taken with a Leica TCS SP confocal laser scanning microscope from Leica (Germany) equipped with a 100×/1.4−0.7 oil immersion objective. Fluorescent labeling of the capsules was achieved by incorporating one layer of fluorescently labeled PMA during the capsule preparation. Labeling of PMA with rhodamine B amine was realized with the EDC/sulfo-NHS coupling system adapted from ref 44. All experiments were conducted in a sealed chamber to ensure constant pH and ionic strength. For the determination of the capsule diameter, the fluorescence profiles of at least 20 capsules were analyzed with the Leica confocal software (LCS, Version: 2.5) and their diameters were averaged. The error bars correspond to the standard deviation of the averaging. All measured diameters represented an equilibrium state and did not change within several hours.

pH Measurements. The pH of all capsule solutions was adjusted with 0.1 M HCl and 0.1 M NaOH. All measurements were performed with a calibrated microprocessor pH-meter WTW pH 539 (WTW, Germany) using a combined glass/ reference electrode.

Infrared Microscopy. ZnSe slides were used as substrates for the deposition of the capsules. Ten microliters of capsule suspension at a certain pH was placed on the substrate and dried in air. Experiments were conducted on a Bruker Hyperion 2000 IR microscope equipped with a 15× IR-objective and a MCT detector. Data were acquired in transmittance, with a spectral
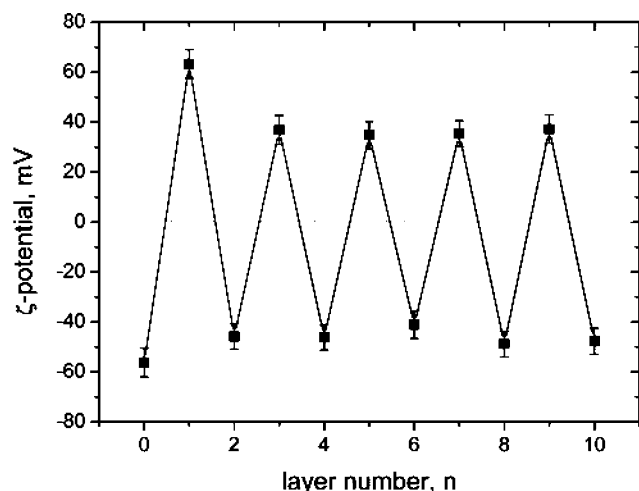
Figure 2. ζ-potential of P4VP/PMA-coated silica particles with a diameter of 881 nm as a function of the number of deposited layers. Odd layer numbers correspond to the deposition of P4VP; even layer number represent the deposition of PMA. All measurements were performed in deionized water at pH 5.

Figure 3. ζ-potential titration curves of coated silica particles with a diameter of 881 nm: (P4VP/PMA)$_4$ (filled squares), (P4VP/PMA)$_4$P4VP (open circles). The solid lines serve as visual guides.

resolution of 4 cm^{-1} and 128 averaged scans. To obtain the absorbance spectra analyzed below, each interferogram was divided by the corresponding background of the ZnSe substrate. Infrared microscopy is well suited for the evaluation of the ionization degree of polyelectrolytes within multilayers, as it combines the advantages of infrared spectroscopy with the possibility to probe small amounts of capsules.

Scanning Electron Microscopy (SEM). SEM measurements were conducted with a Gemini Leo 1550 instrument at an operation voltage of 3 keV. A drop of the sample solution was placed onto a glass slide, dried in air, and sputtered with gold.

Atomic Force Microscopy (AFM). AFM measurements were performed in air at room temperature using a Nanoscope III Multimode AFM (Digital Instruments Inc., USA) operating in tapping mode. The samples were prepared by placing a drop of the sample solution onto a freshly cleaved mica substrate and drying it at room temperature. To ensure a better attachment of the negatively charged capsules on the surface, the mica was precoated with poly(ethylenimine). The single wall thickness of a capsule was determined as half of the height of the collapsed flat regions of dried shells. At least 20 profiles of different capsules were analyzed, and the mean thickness differences between the mica surface and the lowest region of the shells were averaged.[45]

Results and Discussion

Formation of P4VP/PMA Multilayers on SiO$_2$ Templates. P4VP and PMA were alternately adsorbed onto silicon oxide particles with a mean diameter of 881 nm at pH 5. The adsorption process can be monitored by microelectrophoresis (Figure 2). Bare SiO$_2$ particles at pH 5 display a ζ-potential of -56 mV. Regular alternation of the ζ-potential between ca. $+35$ mV and -47 mV for the P4VP and PMA layers, respectively, was found, suggesting successful deposition of P4VP and PMA. The first P4VP layer displayed a higher ζ-potential of $+63$ mV in comparison to the following odd layers. The higher potential can be rationalized if one takes into account that the weak polybase can adjust its charge depending on the surface layer it adsorbs to.[46] In this case it adsorbs onto the more negatively charged SiO$_2$ in comparison with the following PMA layers. The alternation in the sign of the ζ-potential and therefore of the surface charge of the covered templates occurs with each
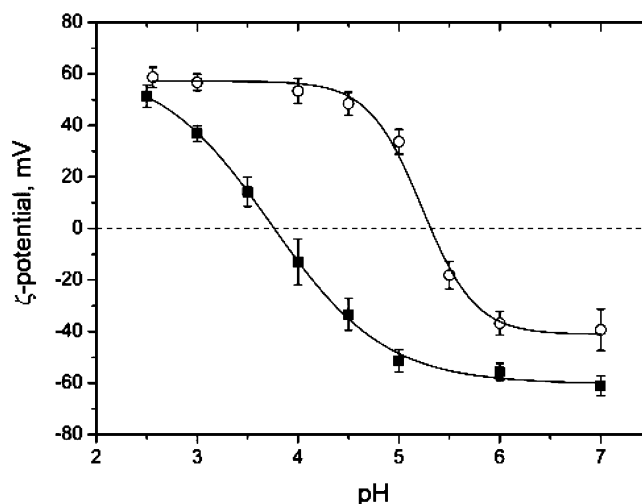
additional layer, indicating the existence of electrostatic interactions for the assembly of the multilayers. Notably the change in the sign of the ζ-potential does not indicate whether adsorption or desorption has occurred with each polyelectrolyte cycle.

As the multilayer is composed of two polyelectrolytes with weak functional acid or base groups, the charge density along the polymer backbone as well as the density of the individual charges within the multilayers should be a function of pH. The surface charge of colloidal particles can be probed with microelectrophoresis, from which the ζ-potential can be calculated. We investigated the electrophoretic mobility of silicon oxide particles (diameter: 881 nm) coated with (P4VP/PMA)$_4$ and with (P4VP/PMA)$_4$P4VP layers as a function of pH of the dispersing medium. The particles coated with eight layers result in an outermost layer consisting of the polyanion PMA while the particles coated with nine layers result in a multilayer that is terminated by the polycation P4VP. The results are shown in Figure 3. Irrespective of the outermost layer the ζ-potential can be reversed from negative to positive by increasing the acidity of the solution. As it is well established that polyelectrolyte multilayers comprise networks of interpenetrated polymer chains, the surface charge is not only due to the last adsorbed layer but the underlying polyanion or polycation layer also has an influence on the surface charge, explaining the observed reversal of the ζ-potential.[47]

The graphs in Figure 3 represent titration curves and can therefore be used to determine the apparent dissociation constants (pK_a) of the acid and base functional groups on the surface.[19] The apparent dissociation constant reflects the overall acid dissociation equilibrium of a polyelectrolyte and is given by the pH at the inflection point of the titration curves.[48] This results in pK_a values of 3.8 and 5.3 for PMA and for protonated P4VP adsorbed onto a multilayer, respectively.

The acid−base equilibria in multilayers deviate from the solution behavior of the corresponding polymers, as they are not only determined by the external pH and ionic strength but also by the local microenvironment including the charge density of an oppositely charged self-assembled polyelectrolyte and the charge of the polymer included in the top layer.[49,50] The electrostatic interaction between polyacid and polybase increases the dissociation in both polymers. The increase in base strength of P4VP from dilute solution (p$K_a = 4.3$)[51] to the adsorbed state may be attributed to the influence of the negatively charged

Balance of Hydrophobic and Electrostatic Forces

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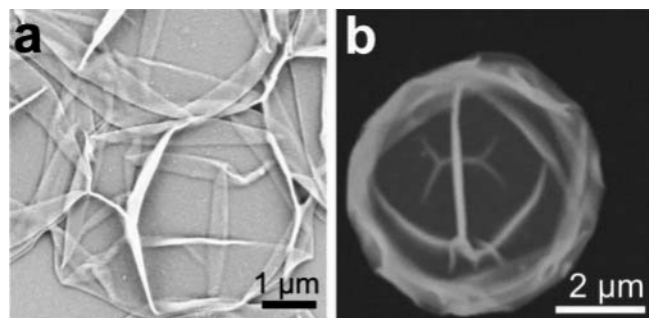
Figure 4. SEM (a) and AFM (b) pictures of dried hollow (P4VP/PMA)$_5$ capsules.

carboxylic groups of the underlying PMA layer in promoting the protonation of the pyridine groups, which is bigger than the resistance to protonation due to electrostatic repulsion of neighboring groups. The same argument can be used for the increased acidity of PMA in the multilayers compared to the solution behavior, as in this case the charge density of the PMA chains decreases with decreasing pH, but at the same time the protonation degree of the P4VP chains from the previously adsorbed layer is increased. The protonated P4VP strongly promotes the dissociation of the COOH groups to neutralize the high residual positive charge obtained with decreasing pH, leading to a decrease in the pK_a of the PMA terminated surface in comparison to the solution pK_a of 6.8.[24]

Formation of Capsules. Silicon oxide particles with a mean diameter of 4.48 μm were used as templates for the deposition of polyelectrolyte multilayers. After the core dissolution with a buffer system composed of ammonium fluoride and hydrofluoric acid hollow capsules could be obtained. SEM and AFM pictures of dried capsules composed of 10 layers are shown in Figure 4. The mean thickness per layer as determined by AFM is 1.8 ± 0.2 nm.

ζ-potential measurements of multilayers adsorbed onto silica particles probe the surface charge and therefore the ionization degree of a polycation or polyanion adsorbed on top of a multilayer. To gain more insight into the interactions present within the layers at different pH and therefore into the stability of the shells, we measured infrared spectra of polyelectrolyte capsules. Infrared spectroscopy measurements were made on capsules dried from suspensions of different pHs, and differences in the IR bands of −COO$^-$ and −COOH of PMA and of pyridine and pyridinium groups of P4VP were investigated. The drying process can have an influence on the exact pH value, but nevertheless the evaluation of IR bands of multilayered shells provides an indication of the interactions present within the layers.[52] The IR spectra of capsules as a function of pH are shown in Figure 5. The individual spectra are overlaid for clarity.

The absorption band at 1560 cm^{-1} is attributed to the carboxylate (−COO$^-$) asymmetric stretch, whereas the band at 1716 cm^{-1} originates from C=O of the carboxylic groups (−COOH). The peak centered at 1638 cm^{-1} is associated with the in plane stretch of the charged pyridinium ring and the peak centered at 1604 cm^{-1} stems from the neutral ring.[40] Pure PMA exhibits a strong absorption band at 1701 cm^{-1}, which is associated with the stretching of the uncharged dimerized or associated form of carboxylic groups. The shift to higher frequencies compared with pure PMA is an indication that hydrogen bonds among the carboxylic groups of PMA are partly detached and intermolecular hydrogen bonds are formed with P4VP.[34] The relative ratios of −COOH and −COO$^-$ and of unprotonated and protonated P4VP in the capsules were not investigated quantitatively, because of the overlap with bands
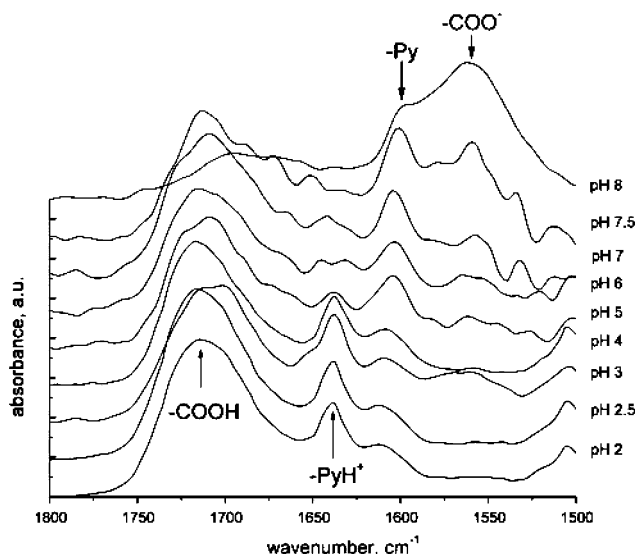
Figure 5. Infrared spectra of (P4VP/PMA)$_5$ capsules as a function of pH. The spectra are overlaid with an arbitrary offset for clarity.
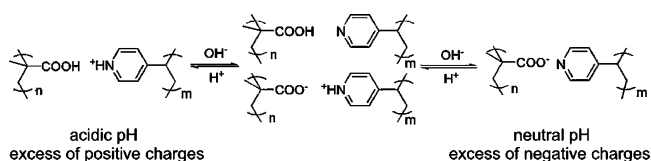

Figure 6. Summary of the interactions present within the multilayer film at different pH.

associated with the in-plane vibration of pyridine groups in the region of 1518−1573 cm^{-1}.[39,40]

The peak at 1716 cm^{-1} that is assigned to the uncharged carboxylic groups is present over most of the pH range investigated and it only vanishes in the pH range from 7.5 to 8. At pH values higher than 6 the intensity of the peak at 1560 cm^{-1} increases. The absorption associated with the protonated pyridinium groups exists till a pH of 5, whereas in the range from pH 5−8 the intensity of the peak centered at 1604 cm^{-1} increases. In the intermediate pH region pyridine as well as pyridinium groups coexist within the multilayer while only a small fraction of the carboxylic groups is deprotonated. A summary of the different interactions within the film as a function of pH is shown in Figure 6.

In the intermediate pH region the stabilization between the layers seems to be due to a combination of hydrogen-bonding and electrostatic interactions. Multilayer films composed of P4VP and PAA that are assembled in pure methanol are stabilized only by hydrogen-bonding interactions.[38] Pure H-bonding interactions were also observed, when PAA was deposited from acidic aqueous solutions and P4VP from ethanol.[27] Abe et al. on the other hand only considered electrostatic interactions between the polyelectrolytes when they discussed the stability of a polyelectrolyte complex of PMA and P4VP in different water:methanol mixtures.[53] Cho et al. considered multilayers formed of P4VP and PAA prepared in a water: methanol mixture at pH 3.5 to be mainly stabilized by hydrogen bonding but also considered electrostatic interactions to be present within the layers.[39] Sukhishvili and co-workers studied the ionization and pH stability of flat multilayers with PMA and QP4VP with different alkylation degrees ranging from 12 to 98%. They found that film growth at pH 5 was primarily controlled by electrostatic interactions.[40]

Whereas in the intermediate pH range the multilayers are stabilized both by hydrogen-bonding and electrostatic interac-
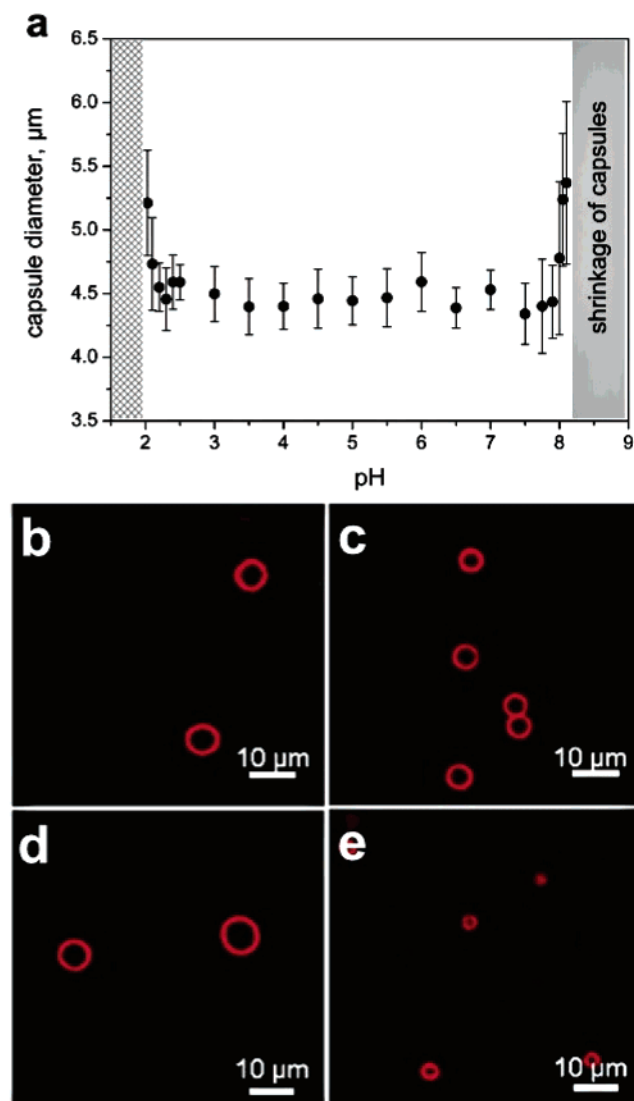
Figure 7. pH-dependent behavior of capsules. Diameter of (P4VP/PMA)$_5$ capsules as a function of pH (a). The average diameter was calculated from 20 individual capsules. The hatched area indicates the region where the capsules are dissolved (pH < 2). At pH > 8.1 the capsules shrink to a particlelike structure. CLSM images of individual capsules at different pH are shown in panels b–e: pH 2 (b, swollen state), pH 5 (c, initial state), pH 8.1 (d, swollen state), pH 9 (e, collapsed state).

tions, higher and lower pH values lead to an excess of negative and positive charges within the film, respectively. Whenever there is an increase of the concentration of one charged group in combination with a decrease of the attractive (electrostatic or H-bond) interactions between different layers, the multilayers will be destabilized.

A comparison of the ζ-potential data with the IR-spectra shows a different charge regulation of the functional groups on the surface and within the multilayers. The data suggest that the interactions within the layers are stabilized against pH changes. A similar stabilization of the degree of ionization within a PAH/poly(styrene sulfonate) (PSS) multilayer was reported by Itano et al.[54]

pH-Dependent Behavior of P4VP/PMA Capsules. Capsules composed of 10 layers of P4VP and PMA show pH dependent stability behavior. In Figure 7 the capsule diameter is plotted as a function of pH, and confocal micrographs of individual capsules at different pH are shown. All capsule diameters were measured in equilibrium and did not change for at least several hours. In the intermediate pH range from 2.2 to 7.9 the capsules are stable with a diameter of 4.5 ± 0.3 μm as measured by CLSM, which is determined by the diameter of the template. When the pH is reduced to pH 2 the capsules swell by 16% to a diameter of 5.3 ± 0.4 μm and with further reduction of the pH the multilayers decompose and dissolve. At a pH of 8 a similar phenomenon is observed, here the systems swell to a diameter of 5.4 ± 0.6 μm, which corresponds to a swelling by 20%. When the pH is further increased the capsules shrink, till they reach a globular state with diameters below 2 μm. This complicated pH dependent behavior can be rationalized by the electrostatic interactions within the multilayers in combination with hydrophobic interactions. As can be inferred from the IR-data (see Figure 5) the interactions within the multilayers are stable over a broad pH range, due to charge regulation. At low pH positive pyridinium groups occur within the layers that are not compensated by negatively charged carboxylic groups. Therefore they reduce the possible electrostatic and hydrogen-bonding interactions between PMA and P4VP and destabilize the capsules. Furthermore the excess of positive groups induces electrostatic repulsion between them. To ensure the overall electroneutrality of the system, counterions are accumulated in the vicinity of the shells and/or within the layers. The higher ion concentration as compared to the bulk exerts an osmotic pressure that tends to swell the capsules.

The swollen states are stabilized by hydrophobic interactions within the layers, as both PMA and PVP show hydrophobic stabilization. For PMA in solution, e.g., there is a drastic change of dissociation at low pH, that is due to the conformational change of PMA from a compact structure to a random coil one.[46,55] Furthermore the uncharged carboxylic acid groups can stabilize the system via intramolecular hydrogen bonds that can occur within the same layer as well as between different layers of PMA.[41]

At pH 8 a similar situation occurs. From the infrared data as well as from the ζ-potential it can be inferred that the P4VP is not charged at that pH, whereas the PMA remains in its fully charged state. Therefore interactions between different layers are reduced and the excess of negative carboxylic groups in the multilayers leads to a destabilization of the capsule shells. This electrostatic destabilization is counteracted by hydrophobic interactions of the uncharged P4VP. P4VP is a hydrophobic polymer that is water insoluble when the degree of ionization is less than 35%,[51] and thereby it stabilizes the swollen multilayers. When the pH is increased further, the hydrophobic attraction and surface tension are the most prominent forces leading to shrinkage and an irreversible collapse of the capsules, resulting in particlelike structures, which do not possess the characteristics of capsules anymore.

The presence of hydrophobic stabilization in water is further evidenced in conditions where this hydrophobic stabilization is decreased. In a mixture of 1:1 methanol and water both polymers are soluble over a broad pH range, so that uncharged P4VP is not precipitating and hydrophobic stabilization of PMA at low pH is reduced. Therefore the hydrophobic interaction becomes inoperative.[51,53] When examining the stability of capsules in a solution of 1:1 methanol and water at different pH, we observe stable capsules over the same pH range between pH 2 and 8, but in this case no stable swollen state can be observed and neither any shrinkage of the systems when the pH is increased above 8. At the edges of stability the capsules swell and dissolve within a second.

The large stability range of the capsules correlates with the charge regulation within the multilayers as observed in the IR

spectra. The pH values where the capsules swell and dissolve are different from the solution pK_as of the component polyelectrolytes; the one in the alkaline region is higher than the pK_a of PMA, and the one in the acidic region is lower than the pK_a of P4VP. This suggests, as well as the IR data, that interactions within multilayers are stabilized against pH change. The association of hydrophobic elements of a polymer chain can increase the local density of weak functional groups and/or decrease the local dielectric constant experienced by weak functional groups. In both cases it becomes more difficult to ionize the weak groups due to an unfavorable electric potential. In other words cooperative interactions stabilize the polyelectrolyte layers, and this can also explain the drastic onset of swelling within 0.1 pH unit.

Abe et al. observed plateaus in the potentiometric titration curves of P4VP/PMA complexes in solution in the acidic and basic pH ranges that correspond well to the edges of stability observed for (P4VP/PMA)$_5$ capsules. They also observed dissociation of the complex into the component polyelectrolytes at such pH values.[53] The stability range is also similar to that reported for flat multilayers of 10 layers of P4VP and PAA by Caruso and co-workers, where the films are stable up to pH ≈ 7, after which the desorbed amounts increase in the range from pH 7.5 to 9.[39] Sukhishvili et al. studied the ionization and pH stability of flat multilayers with PMA and QP4VP with different alkylation degrees. They observed dissolution of the multilayers below pH 2, due to protonation of carboxylic groups and disruption of polymer/polymer ionic contacts. The stability of the multilayer in acidic conditions was dependent on the alkylation degree of QP4VP.[40] They attributed the destruction of the multilayers to the protonation of a small <5% residual fraction of carboxylic groups that was included into polymer/polymer ionic pairs and suggested that a cooperative effect in the formation of polymer−polymer ionic pairs might play an additional role in film stability.

The observed stability at neutral pH of P4VP/PMA capsules is much higher than usually observed for purely hydrogen-bond-stabilized multilayers. For such systems the dissolution occurs at pH 6.9 (poly(vinylpyrrolidone)/PMA), pH 4.6 (PEO/PMA), and pH 3.6 (PEO/PAA).[31]

The increased stability of our system in slightly basic medium may be influenced by electrostatic interactions between PMA and P4VP, which are not present in multilayers that are only stabilized by H-bond interactions.[39]

With the adsorption of more polyelectrolyte layers the amount of polymer adsorbed is increased. This results in a higher swelling degree both at low and at high pH. The results are shown in Figure 8.

The increase in swelling degree at pH 8.1 as a function of layer number is much more prominent than at pH 2. For 16 layers, the capsules swell by 70 % in basic medium compared to 23 % at pH 2. An increase in the swelling can be rationalized as more polymeric material leads to an increase in the osmotic pressure induced by the counterions. In addition the capsules, which are swollen to a higher extent, are still stable because of increased entanglement and hydrophobic interactions with additional layers. When capsules in their swollen state at low and at high pH are washed with water at pH 4, and the diameter is determined after 1 h, the swelling is reduced in all cases, from 8 to 16 layers. For capsules swollen at pH 2 real reversibility was achieved for 8 and 10 layers. Capsules composed of 12−16 layers only showed a reduction in size to a diameter of 4.7−5 μm. Capsules swollen at pH 8.1 could be shrunk back to their original size in the whole range from 8 to
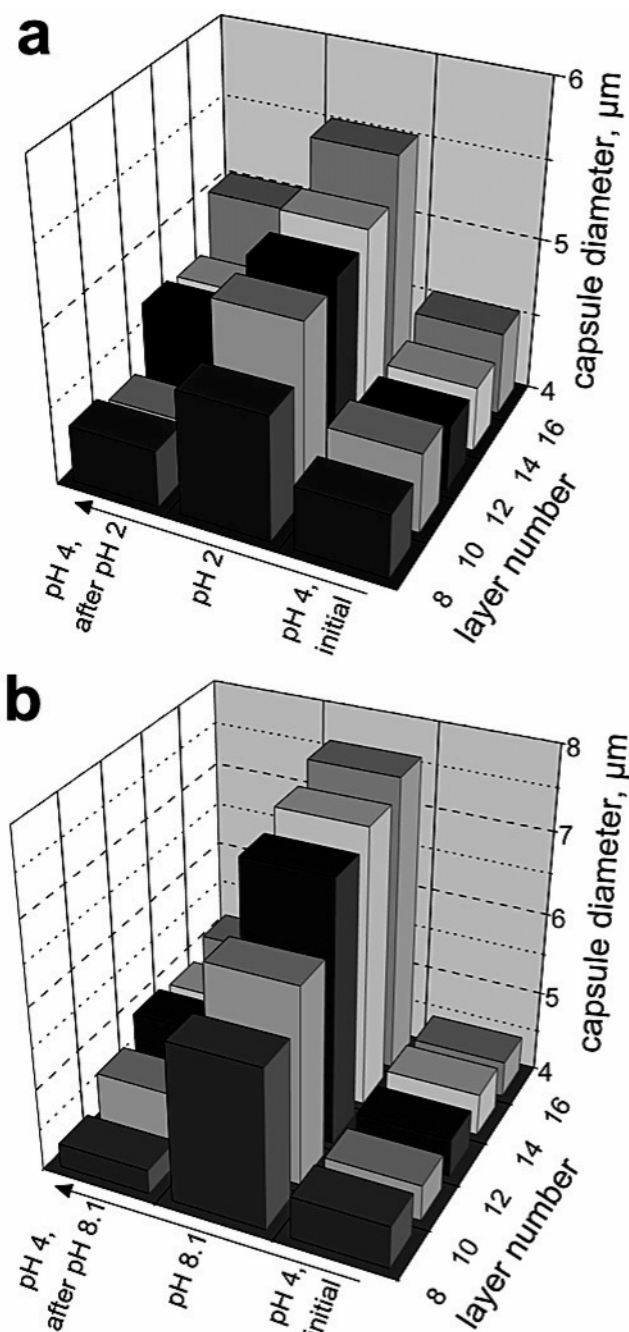

Figure 8. Swelling degree and reversibility as a function of layer number. (a) Swelling at pH 2; (b) swelling at pH 8.1.

16 layers. This reversibility is an important prerequisite for any application involving weak polyelectrolyte capsules, as it opens the possibility for the system to reversibly exist in two different states, a swollen and a shrunk one.

Influence of Ionic Strength on the pH-Dependent Stability. Addition of sodium chloride to the swollen states leads to a destruction of the capsules. At pH 2 capsules dissolve within seconds, whereas at pH 8.1 capsules shrink to particles (data not shown). When the pH dependent stability with increased ionic strength is investigated, the stability of the capsules as well as the swelling behavior are altered. The results are shown in Figure 9. The increase of the ionic strength leads to less stable capsules in the pH regions of 2−3 and 7−8. The stability range is decreased as compared to the situation without added salt. At low pH the swelling sets in at a slightly increased pH value, whereas in basic pH the swelling sets in at a decreased pH value.
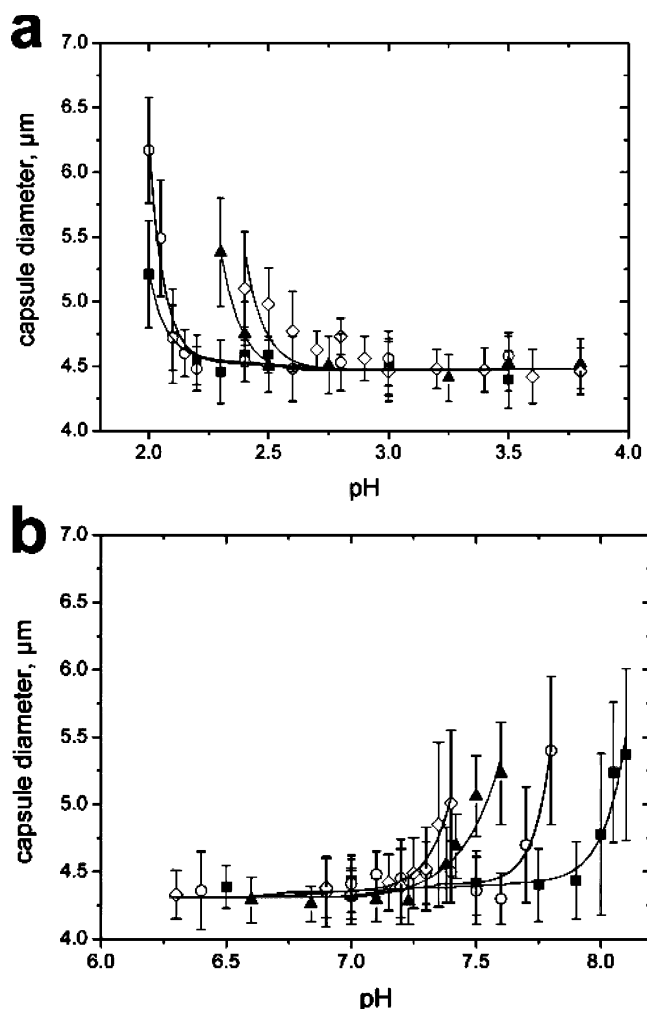
Figure 9. Influence of ionic strength on the pH dependent stability of (P4VP/PMA)₅ capsules. Low-pH region (a): 0 M NaCl (closed squares), 10 mM (open circles), 50 mM (closed triangles), 100 mM (open diamonds). Neutral-pH region (b): 0 M NaCl (closed squares), 5 mM (open circles), 10 mM (closed triangles), 20 mM (open diamonds).

Additionally at a given pH, the capsule diameter is increased when the ionic strength is increased. Figure 9a describes the swelling at low pH with the addition of $10-100$ mM NaCl. The swelling without added NaCl and with 10 mM NaCl sets in at the same pH, but the capsules swell more when 10 mM NaCl is added. This finding can be rationalized, as the ionic strength of an HCl solution at pH 2 is already around 10 mM, therefore the addition of 10 mM NaCl only increases the ionic strength by a factor of 2. For all other salt concentrations investigated at low pH the maximal stable swelling is reduced in size compared to the swelling without added salt. All swollen capsules dissolve when the pH is lowered further. Figure 9b shows the stability of capsules that are exposed to solutions containing $5-20$ mM NaCl in the pH range from 6 to 8. Swollen capsules shrink, once the pH is increased further. Data for the shrunk states are not shown, as the capsule size during the shrinking process is time dependent and the final particle-like state is mainly due to precipitated P4VP. In contrast to the shrinking, the sizes of swollen capsules are stable at least for several hours.

The general expectation would be to observe a decrease in capsule swelling with increasing ionic strength at a given pH, due to a reduction of the difference of ion concentration between the multilayer surface and the bulk. However the experimental results show an increased swelling with increasing ionic strength.

These results can be understood when one considers the local charge distribution near the polymeric shells.

We first concentrate on the low-pH region, where there is an excess of positive charges of P4VP present within the multilayer. If we assume a case without any counterions in the solution, protonation of pyridine groups would be hindered due to the electroneutrality condition. The addition of salt (NaCl) to such a system favors the protonation of pyridine groups, as the resulting positive charges can be compensated by Cl⁻ ions. This results in an increase of the ionization degree of the polymer chains. As a consequence the onset of swelling of weak polyelectrolyte capsules in acidic solutions is shifted to higher pH values, and the swelling at a given pH is increased when the ionic strength of the solution is increased. This shift in the protonation/deprotonation equilibrium is also found in the pH range from 7 to 8, where an increased ionic strength induces the onset of swelling at a decreased pH. Such a behavior is similar to the osmotic brush regime that is well known for polyelectrolyte brushes composed of weak polyacids or polybases.[56-60]

The observed effects of an increase in the ionic strength reported here occur at much lower salt concentrations than the smoothing and shrinking of capsules composed of strong polyelectrolytes. In that case the shrinking was attributed to a rearrangement of polyelectrolyte chains resulting in an energetically more stable shrunk state.[61,62]

Conclusions

We have prepared capsules composed of two weak polyelectrolytes, P4VP and PMA, templated on silica cores. These systems show an interesting pH-dependent behavior, as they are stabilized by hydrogen bonds as well as electrostatic interactions over a broad pH range from pH $2-8$. At the edges of the stability range the pH-induced imbalance of charges reduces the stability between layers and leads to a swelling of the system. The diameters of swollen capsules are stable at least for several hours. Swollen capsules can be stabilized by counteracting hydrophobic as well as hydrogen-bonding interactions at pH 2 and 8. The competition between attractive (hydrophobic or H bonding) and repulsive (electrostatic) interactions is the key element for the creation of multilayers with pH switchable properties. An exchange of the solvent to a mixture of water and methanol reduces hydrophobic stabilization. In this case no stable swollen states are observed. The swelling degree can be increased by additional polyelectrolyte layers. The swelling process is reversible, which is a prerequisite for most of the possible applications of weak polyelectrolyte systems. The reversible swelling in the pH range around 8 makes this type of polyelectrolyte capsules an interesting tool for the encapsulation of biopolymers. Detailed investigations about permeability and encapsulation properties of this system are currently on the way. In addition to pH effects we also probed the influence of ionic strength on the swelling behavior. At low ionic strength the stability range of the capsules is slightly decreased and the observed swelling behavior is another example of the behavior found in the osmotic brush regime of weakly charged polyelectrolyte brushes.

References and Notes

(1) Decher, G.; Hong, J. D.; Schmitt, J. *Thin Solid Films* **1992**, *210*, 831−835.

(2) Donath, E.; Sukhorukov, G. B.; Caruso, F.; Davis, S. A.; Möhwald, H. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2202−2205.

(3) Sukhorukov, G. B.; Donath, E.; Davis, S.; Lichtenfeld, H.; Caruso, F.; Popov, V. I.; Möhwald, H. *Polym. Adv. Technol.* **1998**, *9*, 759−767.

(4) Peyratout, C. S.; Dähne, L. *Angew. Chem., Int. Ed.* **2004**, *43*, 3762−3783.

(5) Antipov, A. A.; Sukhorukov, G. B. *Adv. Colloid Int. Sci.* **2004**, *111*, 49−61.

(6) Déjugnat, C.; Sukhorukov, G. B. *Langmuir* **2004**, *20*, 7265−7269.

(7) Sukhishvili, S. A. *Curr. Opin. Coll. Int. Sci.* **2005**, *10*, 37−44.

(8) Déjugnat, C.; Sukhorukov, G. B. In *Responsive Polymer Materials: Design and Applications*; Minko, S., Ed.; Blackwell Publishing Professional: Ames, IA, 2006.

(9) Richert, L.; Lavalle, P.; Payan, E.; Shu, X. Z.; Prestwich, G. D.; Stoltz, J. F.; Schaaf, P.; Voegel, J. C.; Picart, C. *Langmuir* **2004**, *20*, 448.

(10) Dubas, S. T.; Schlenoff, J. B. *Macromolecules* **2001**, *34*, 3736−3740.

(11) Tong, W. J.; Gao, C. Y.; Möhwald, H. *Macromolecules* **2006**, *39*, 335−340.

(12) Rmaile, H. H.; Schlenoff, J. B. *Langmuir* **2002**, *18*, 8263−8265.

(13) Sui, Z. J.; Schlenoff, J. B. *Langmuir* **2003**, *19*, 7829−7831.

(14) Richert, L.; Boulmedais, F.; Lavalle, P.; Mutterer, J.; Ferreux, E.; Decher, G.; Schaaf, P.; Voegel, J. C.; Picart, C. *Biomacromolecules* **2004**, *5*, 284.

(15) Fery, A.; Schöler, B.; Cassagneau, T.; Caruso, F. *Langmuir* **2001**, *17*, 3779−3783.

(16) Mendelsohn, J. D.; Barrett, C. J.; Chan, V. V.; Pal, A. J.; Mayes, A. M.; Rubner, M. F. *Langmuir* **2000**, *16*, 5017−5023.

(17) Yoo, D.; Shiratori, S. S.; Rubner, M. F. *Macromolecules* **1998**, *31*, 4309−4318.

(18) Shiratori, S. S.; Rubner, M. F. *Macromolecules* **2000**, *33*, 4213−4219.

(19) Burke, S. E.; Barrett, C. J. *Langmuir* **2003**, *19*, 3297−3303.

(20) Kato, N.; Schuetz, P.; Fery, A.; Caruso, F. *Macromolecules* **2002**, *35*, 9780−9787.

(21) Gao, C. Y.; Möhwald, H.; Shen, J. C. *Adv. Mater.* **2003**, *15*, 930−933.

(22) Schuetz, P.; Caruso, F. *Adv. Funct. Mater.* **2003**, *13*, 929−937.

(23) Petrov, A. I.; Antipov, A. A.; Sukhorukov, G. B. *Macromolecules* **2003**, *36*, 10079−10086.

(24) Mauser, T.; Déjugnat, C.; Sukhorukov, G. B. *Macromol. Rapid Commun.* **2004**, *25*, 1781−1785.

(25) Mauser, T.; Déjugnat, C.; Möhwald, H.; Sukhorukov, G. B. *Langmuir* **2006**, *22*, 5888−5893.

(26) Stockton, W. B.; Rubner, M. F. *Macromolecules* **1997**, *30*, 2717−2725.

(27) Wang, L. Y.; Wang, Z. Q.; Zhang, X.; Shen, J. C.; Chi, L. F.; Fuchs, H. *Macromol. Rapid Commun.* **1997**, *18*, 509−514.

(28) Kharlampieva, E.; Kozlovskaya, V.; Tyutina, J.; Sukhishvili, S. A. *Macromolecules* **2005**, *38*, 10523−10531.

(29) Zhang, H. Y.; Wang, Z. Q.; Zhang, Y. Q.; Zhang, X. *Langmuir* **2004**, *20*, 9366−9370.

(30) Sukhishvili, S. A.; Granick, S. *Macromolecules* **2002**, *35*, 301−310.

(31) Sukhishvili, S. A.; Granick, S. *J. Am. Chem. Soc.* **2000**, *122*, 9550−9551.

(32) Kozlovskaya, V.; Ok, S.; Sousa, A.; Libera, M.; Sukhishvili, S. A. *Macromolecules* **2003**, *36*, 8590−8592.

(33) Kozlovskaya, V.; Yakovlev, S.; Libera, M.; Sukhishvili, S. A. *Macromolecules* **2005**, *38*, 4828−4836.

(34) Yang, S. G.; Zhang, Y. J.; Yuan, G. C.; Zhang, X. L.; Xu, J. A. *Macromolecules* **2004**, *37*, 10059−10062.

(35) Kozlovskaya, V.; Kharlampieva, E.; Mansfield, M. L.; Sukhishvili, S. A. *Chem. Mater.* **2006**, *18*, 328−336.

(36) Zhang, Y. J.; Guan, Y.; Yang, S. G.; Xu, J.; Han, C. C. *Adv. Mater.* **2003**, *15*, 832−835.

(37) Lee, D.; Rubner, M. F.; Cohen, R. E. *Chem. Mater.* **2005**, *17*, 1099−1105.

(38) Wang, L. Y.; Fu, Y.; Wang, Z. Q.; Fan, Y. G.; Zhang, X. *Langmuir* **1999**, *15*, 1360−1363.

(39) Cho, J.; Caruso, F. *Macromolecules* **2003**, *36*, 2845−2851.

(40) Kharlampieva, E.; Sukhishvili, S. A. *Langmuir* **2003**, *19*, 1235−1243.

(41) Izumrudov, V.; Sukhishvili, S. A. *Langmuir* **2003**, *19*, 5188−5191.

(42) Izumrudov, V.; Kharlampieva, E.; Sukhishvili, S. *Macromolecules* **2004**, *37*, 8400−8406.

(43) Kharlampieva, E.; Sukhishvili, S. A. *Macromolecules* **2003**, *36*, 9950−9956.

(44) Déjugnat, C.; Halozan, D.; Sukhorukov, G. B. *Macromol. Rapid Commu.* **2005**, *26*, 961−967.

(45) Leporatti, S.; Voigt, A.; Mitlohner, R.; Sukhorukov, G.; Donath, E.; Möhwald, H. *Langmuir* **2000**, *16*, 4059−4063.

(46) Blaakmeer, J.; Bohmer, M. R.; Stuart, M. A. C.; Fleer, G. J. *Macromolecules* **1990**, *23*, 2301−2309.

(47) Decher, G. *Science* **1997**, *277*, 1232−1237.

(48) Schulz, S. F.; Gisler, T.; Borkovec, M.; Sticher, H. *J. Colloid Int. Sci.* **1994**, *164*, 88−98.

(49) Katchalsky, A.; Spitnik, P. *J. Polym. Sci.* **1947**, *2*, 432−446.

(50) Gregor, H. P.; Frederick, M. *J. Polym. Sci.* **1957**, *13*, 451.

(51) Satoh, M.; Yoda, E.; Hayashi, T.; Komiyama, J. *Macromolecules* **1989**, *22*, 1808−1812.

(52) Choi, J.; Rubner, M. F. *Macromolecules* **2005**, *38*, 116−124.

(53) Abe, K.; Senoh, S. *J. Polym. Sci. Pol. Chem.* **1986**, *24*, 3461−3474.

(54) Itano, K.; Choi, J. Y.; Rubner, M. F. *Macromolecules* **2005**, *38*, 3450−3460.

(55) Tan, J. S.; Gasper, S. P. *Macromolecules* **1973**, *6*, 741−746.

(56) Zhang, H. N.; Ruhe, J. *Macromolecules* **2005**, *38*, 4855−4860.

(57) Wesley, R. D.; Cosgrove, T.; Thompson, L.; Armes, S. P.; Billingham, N. C.; Baines, F. L. *Langmuir* **2000**, *16*, 4467−4469.

(58) Currie, E. P. K.; Sieval, A. B.; Fleer, G. J.; Stuart, M. A. C. *Langmuir* **2000**, *16*, 8324−8333.

(59) Biesalski, M.; Johannsmann, D.; Rühe, J. *J. Chem. Phys.* **2002**, *117*, 4988−4994.

(60) Biesheuvel, P. M. *J. Colloid Int. Sci.* **2004**, *275*, 97−106.

(61) Heuvingh, J.; Zappa, M.; Fery, A. *Langmuir* **2005**, *21*, 3165−3171.

(62) Georgieva, R.; Dimova, R.; Sukhorukov, G.; Ibarz, G.; Möhwald, H. *J. Mater. Chem.* **2005**, *15*, 4301−4310.