Communications

UCST Wetting Transitions of Polyzwitterionic Brushes Driven by Self-Association**

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The chemical modification of solid substrates with zwitterionic functionalities has been the subject of intensive research in industry and in academia. The main reason for this interest lies in the potential technological applications of these systems. For example, self-assembled monolayers bearing zwitterionic terminal groups are currently used for designing efficient protein-resistant substrates,[1,2] and surface-immobilized polymers containing zwitterionic side-groups[3,4] have proved to be beneficial in the creation of biocompatible surfaces,[5,6] in providing control over electro-osmotic flow in

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microfluidics,[7] and as the stationary phase in electrostatic ion chromatography.[8] The extremely high dipole moment of zwitterionic groups (around 23 D in the case of sulfobetaines[9,10]) gives rise to a range of unique properties as a consequence of strong inter- and intramolecular dipolar interactions that lead to (reversible) self-association of the polymer chains.[11] Experimentally, a reversible self-association is observed in certain polyzwitterionic hydrogels that display an upper critical solubility temperature (UCST),[12] that is, only at sufficiently high temperatures are the dipolar interactions broken to yield isolated polymer chains that are completely solvated.

Despite many detailed studies on the properties of zwitterionic polymers in solution or bulk,[13–24] it is not well understood how dense layers of these polymers behave on surfaces. Herein, we present a study of the fundamental processes that occur when polyzwitterionic brushes are grown from solid surfaces. We observe the generation of an ionically cross-linked, superdense conformation driven by an avalanche-type self-association process. This conformation, known as the supercollapsed state, and its formation have been predicted in theoretical studies.[25] Consequently, these studies are a crucial step toward the translation of polyzwitterionic solution behavior to surfaces to exploit their diverse properties in the development of new, smart, responsive coatings.

We have synthesized homogeneous and patterned brushes from [2-(methacryloyloxy)ethyl]dimethyl(3-sulfopropyl)ammonium hydroxide (MEDSAH). The synthetic route to these brushes involves the surface-initiated, atom-transfer radical polymerization (ATRP) of MEDSAH on silicon and gold surfaces (Figure 1), adapted from a system previously reported by our group for growing polymer brushes.[26] Emphasis is placed on elucidating the properties of these brushes, and particularly the association states of the zwitterionic side-groups,[27,28] that is, non-associated, interchain associated, or intrachain associated (into a supercollapsed state). We interpreted the results and concluded that all the unique properties ascribed to these zwitterionic brushes arise from these association states and further show that they can be exploited to create "smart" surfaces.

The first and obvious parameter to vary is the thickness (h) of the polymer-brush layers and hence the molecular weight of the polymers. It is well known from bulk or solution behavior that the magnitude and characteristics of the interactions leading to a self-associated state are dependent on the nature of the electrostatic environment and the molecular weight of the polyzwitterionic chains.[18,20,21]

For this study, Poly-MEDSAH (PMEDSAH) brushes with thicknesses between 5 and 200 nm were synthesized and analyzed. Figure 2 shows the dependence of the advancing water contact angle (θ_{AW}) on h. Clearly, the presence of two well-defined regimes can be observed. Thin brushes ($h <$
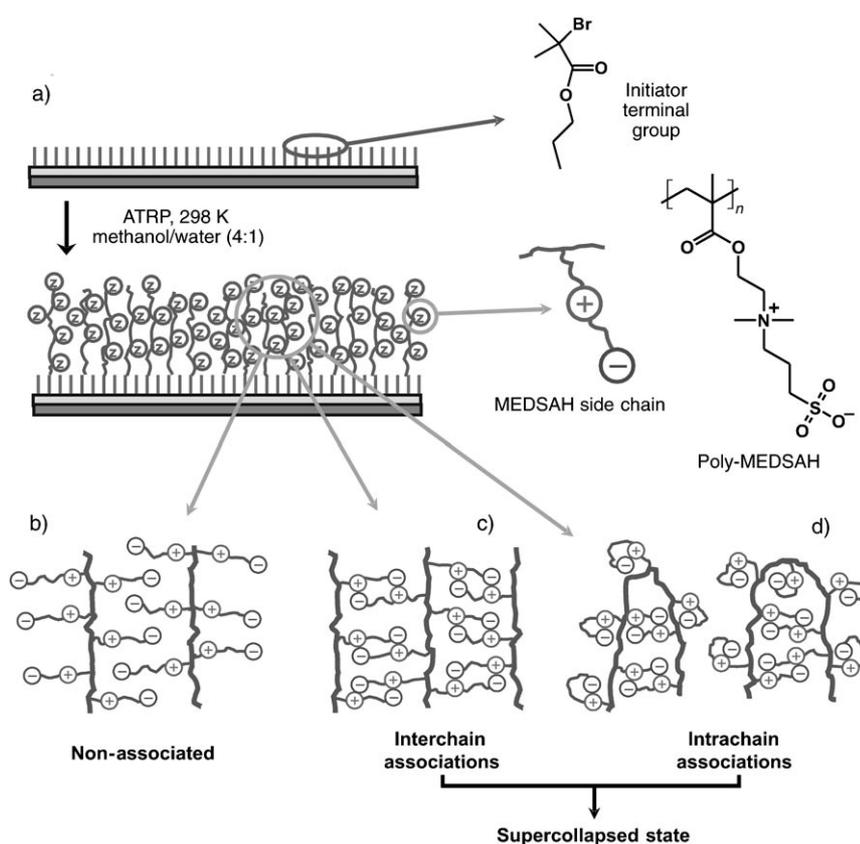
Figure 1. Synthesis of the polyzwitterionic brushes (a) and their different possible conformational states: b) non-associated, c) interchain associations, and d) intrachain associations.
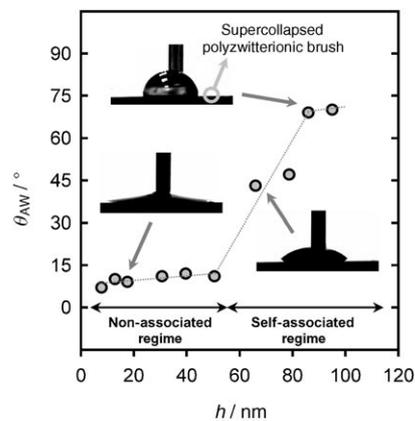
Figure 2. Representation of the advancing water contact angle (θ_{AW}) as a function of polyzwitterionic brush thickness (h). The non-associated and self-associated regimes are indicated by arrows. The insets correspond to pictures showing the water contact angles of PMEDSAH brushes in the different regimes. Dotted gray lines are incorporated as a guide for the eye.

50 nm) display a very hydrophilic surface with a nearly constant θ_{AW} of about 12°. Thicker brushes (h up to 100 nm) show a surprising and more or less linear increase in hydrophobicity with increase in brush thickness. We will refer to the first and second regimes as the "non-associated regime" and the "self-associated regime", respectively.

It is reasonable to suppose that grafted polymer chains bearing high-dipole-moment side-groups will permanently exist in a self-associated conformation. Electrostatic considerations would suggest that opposite charges would be as close as possible to each other, leading to interchain and/or intrachain ionic crosslinks and loops, respectively.[29] However, in water, solvation counteracts the electrostatic effect and forces the anionic and cationic moieties further apart. In addition, electrostatic interactions are dominated by the dielectric characteristics of the medium. In the presence of a solvent of high dielectric constant (ε), like water ($\varepsilon \approx 80$), the electrostatic attraction between the opposite charges should be reduced even more.[30] Lastly, the hydration layer around the charges increases excluded-volume effects, leading to swelling of the brushes. Ion-pairing and self-association would require water to be removed from the charges and will only occur when the electrostatic energy is larger than the energy required for dehydration.[31] To investigate this trade-off between hydration and swelling versus self-association and dehydration, we studied the brushes under water by tapping-mode atomic force microscopy (AFM). Figure 3a shows a 50-nm-thick patterned PMEDSAH brush in air. Under water (Figure 3b), the brushes swell significantly to a thickness of about 150 nm. This swelling is in accordance with the hydrophilic characteristics previously observed by contact-angle goniometry of the homogeneous PMEDSAH-modified substrates. In contrast, Figures 3c and 3d clearly show that thicker PMEDSAH brushes ($h = 90$ nm in air) essentially do not swell under water ($h = 96$ nm). Although PMEDSAH brushes in the hydrophilic, non-associated regime experience a 200% increase in h when

placed in water, the corresponding brushes in the hydrophobic, self-associated regime only experience a 7% increase under similar conditions.

This radical change in wettability upon increasing the brush thickness reflects reorganization processes within the macromolecular film. These changes were observed by analysis of the outermost layers of the PMEDSAH brushes by Auger electron spectroscopy (AES). AES is a surface chemical analysis technique that is capable of detecting elements at concentrations above 0.5–1 atom% in the outer region (≈ 2 nm) of the surface layer (Figure 4a).[32] This
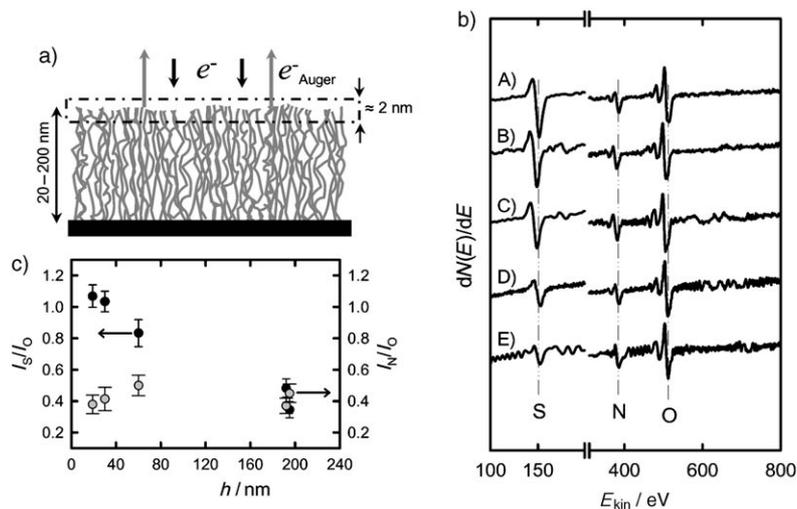
Figure 4. a) Simplified scheme depicting a brush layer bombarded by an electron beam. The Auger electrons generated are collected and measured from the outmost layers. b) Broad AES spectra corresponding to PMEDSAH samples with different thicknesses: A) 19 nm, B) 30 nm, C) 65 nm, D) 192 nm, E) 195 nm. The Auger signals for S (LVV, 152 eV), N (KLL, 380 eV), and O (KLL, 506 eV) are shown. c) Dependence of the Auger signal ratio with thickness for S (I_S/I_O, ●) and N (I_N/I_O, ●). $E_{kin} =$ kinetic energy.

Figure 3. AFM cross-sectional analysis of patterned PMEDSAH brushes: a) 50-nm-thick brushes imaged in air and b) the same brushes imaged under water; c) 90-nm-thick brushes imaged in air and d) the same brushes imaged under water. $L =$ length.

technique is commonly used to probe the surface composition of polymer surfaces[33] and it has recently been successfully employed to elucidate the chemical composition of the topmost layer of polymer brushes.[34] We monitored the elemental composition of S (due to the SO_3^- moieties), N (due to the quaternary ammonium moieties), and O (due to both SO_3^- moieties and COO ester groups; Figure 4b). AES characterization of PMEDSAH films with different thicknesses revealed a quite sensitive decrease in S composition with increasing film thickness, as determined by the decrease in the Auger signal ratio between S and O (I_S/I_O; Figure 4c). However, the N composition remained nearly constant for polymer films of varying thickness ($I_N/I_O \approx 0.4$). This fact could imply a reorganization process leading to a new conformation where the SO_3^- moieties (hydrophilic character) could be preferentially buried in the macromolecular film.

To summarize, the difference between thin, hydrophilic, swollen brushes and thick, hydrophobic, collapsed brushes can be explained as follows: The presence of a hydrophilic regime is determined by a number of factors. For instance,

1) the high dipole moment of the bearing groups must be stabilized by a high ε solvent like water, 2) there is a more favorable interaction of the sulfonate groups with water than with the quaternary ammonium groups, and 3) steric factors related to the polymer backbone and the hydrated charged groups hinder the formation of ion pairs.[29–31] When the brushes are considerably thicker, all these factors change. The electrostatic characteristics (and, as a consequence, the number of ion pairs) depend strongly on the value of the dielectric constant ε of the medium. As suggested by various authors working within a theoretical framework, i.e. "theoreticians", the dielectric characteristics of the polymer environment are quite sensitive to the polymer conformation.[35–37] In other words, the effective ε affecting the electrostatic conditions is dependent on the microenvironment of the grafted chains. As a consequence, the inner environment of the brush can suffer a drastic change in ε after changing from a swollen to a collapsed conformation. The polymer volume fraction in the swollen state is low, and ε is close to that corresponding to the pure solvent (in our case water, $\varepsilon \approx 80$). However, in the collapsed state there is a significant increase in the polymer volume fraction, which results in a much smaller value for ε ($\varepsilon \approx 4$ for the dry polymer).[37] Increasing the thickness (i.e. chain length) of the PMEDSAH brushes involves an increase in the number of zwitterionic groups or "stickers" per grafting site.[38] This implies that by increasing h the probability of ion-pairing events or self-association between zwitterionic moieties becomes higher. It must be noted that ion pairing leads to an increase in polymer volume fraction and a decrease in ε. Thus, after reaching a critical h where the first ion-pairing events start, the self-association becomes more favorable and leads to a rapid collapse of the chains. This process has been described theoretically by Khokhlov and co-workers[36,37] as a "supercollapsed state" of charged polymer chains, and corresponds to a very dense conformation where practically all charged functionalities in bearing groups form intra and/or interchain ion pairs.[27,28] The self-associated state of the brush is the first experimental evidence of the supercollapsed state in surface-grafted polymers.

As explained in the introduction, sulfobetaines like MEDSAH exhibit an upper critical solution temperature (UCST).[18] Translating the UCST characteristics of sulfobetaines to our PMEDSAH brushes should allow us to create a thermoresponsive brush with a hydrophobic-to-hydrophilic transition when raising the temperature above the sulfobetaines' UCST (around 30°C). To corroborate this behavior we measured the contact angles of 180-nm-thick, hydrophobic PMEDSAH brushes at room temperature and at 52°C. Figure 5 shows the variation in wetting properties (from $\theta_{AW} \approx 79°$ to $\theta_{AW} \approx 58°$) when the temperature is increased from 22°C to 52°C, thus supporting the predicted thermoresponsive behavior of PMEDSAH brushes. It must be noted that in the case of our polysulfobetaine brushes the UCST is slightly higher (approx. 40–50°C) than other values reported in the literature.[18] This fact could be attributed to the presence of traces of inorganic ions remaining in the brush from the polymerization solution, as described in detail by Laschewsky and co-workers.[39] None of our brushes showed levels of
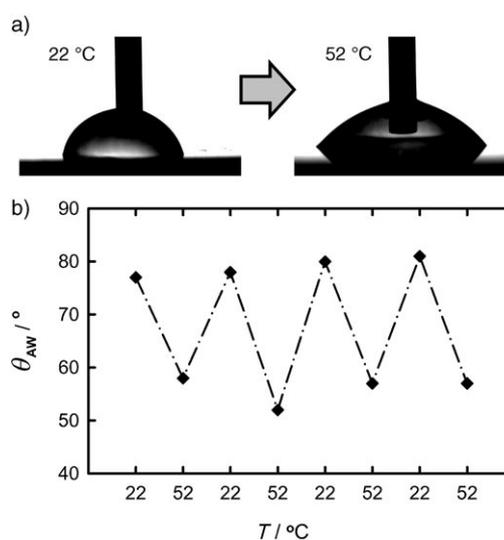
Figure 5. a) Change of the wetting characteristics of thick, supercollapsed PMEDSAH brushes ($h \approx 180$ nm) after increasing the temperature from 22°C to 52°C. b) Representation of the advancing contact angle in water (θ_{AW}) as a function of temperature (T), depicting the reversible thermoresponsive behavior of PMEDSAH brushes after repeated cycles between 22°C and 52°C.

impurities above the detection limit of Auger spectroscopy (0.5 atom%), which indicates that any effect due to these trace metal ions will be similar for every surface.

This thermally responsive wettability is completely reversible, as indicated by repeated temperature cycling (Figure 5b). Similar experiments performed after a few months gave identical results, thus confirming the stability of the films and their thermoresponsive characteristics. This system represents, to the best of our knowledge, the first example of a thermoresponsive brush exploiting the UCST properties of the polymer chains. The magnitude of the effect ($\Delta\theta_{AW} \approx 20$–25°) is similar to the well-known polyacrylamide-based brushes[40] and hydrogels,[41] but with an inverse thermoresponsive behavior.

In conclusion, we have found that the bulk or solution behavior of sulfobetaines has its counterpart in the surface domain through the thickness- and temperature-dependent characteristics of the brush-like layer. This dependence is evidenced by a pronounced transition in the wetting characteristics that is related to the polyzwitterionic brush forming a completely collapsed self-associated state, which has a significant impact on the wetting characteristics. After passing through the hydrophilic, non-associated regime with $\theta_{AW} \approx 12°$, the self-associated regime develops hydrophobic surface characteristics until it reaches $\theta_{AW} \approx 75°$, thus indicating that in the collapsed state water becomes a poor solvent (poor wetting). This sharp difference in the interaction between the water and the two states was also observed in the swelling behavior. Finally, we have shown that the self-associated state can be reversed by increasing the temperature, leading to a hydrophobic-to-hydrophilic switch that closely resembles the UCST characteristics observed for the same polyzwitterion in solution. This reversible switching of the brushes is ideally suited for applications in microfluidic devices where control

over liquids wetting or not wetting channels will greatly aid the design of more complex device layouts.

Experimental Section

Patterned gold samples were prepared by microcontact printing (μCP) of a thiol initiator (ω-sulfanylundecylbromobutyrate) onto clean gold substrates. For brushes grown on Si/SiO$_2$, 2-bromo-2-methylpropionic acid 3-trichlorosilanylpropyl ester was used to prepare the initiator-modified substrates. MEDSAH was purchased from Aldrich (97% purity) and was used as received. Analytical Reagent grade methanol (99.99%) was purchased from Fisher Scientific and used as received. Deionized water with a resistance of 18.2 MΩ cm was obtained from a Millipore Simplicity 185 system. The polymerization solution was prepared as follows: MEDSAH (30 g, 107 mmol) was dissolved in Milli-Q water (20 mL) and MeOH (80 mL) at 20 °C and deoxygenated by passing a continuous stream of dry N$_2$ through the solution whilst stirring (20 min). 2,2′-Dipyridyl (840 mg, 5.37 mmol), CuCl (212 mg, 2.15 mmol), and CuCl$_2$ (29 mg, 0.21 mmol) were added to this solution. The mixture was then stirred whilst deoxygenating with a stream of dry N$_2$ (15 min). Initiator-modified samples (≈ 1 cm^2 each) were sealed in Schlenk tubes, deoxygenated (four high-vacuum-pump/N$_2$ refill cycles), and left at 20 °C under N$_2$. The polymerization solution was then transferred into each Schlenk tube by means of a syringe, adding enough solution to submerge each sample completely. After various polymerization times, the samples were removed, washed with warm Milli-Q water (60 °C), and dried under a stream of N$_2$. Contact-angle goniometry was performed by using a homemade stage with a computer-controlled microsyringe and digital camera. Infusion and withdrawal rates of 4 μL min^{-1} were used. Advancing water contact angles (θ_{AW}) were recorded. Surface elemental analyses by AES (INIFTA–La Plata) were carried out by using a single-pass cylindrical mirror analyzer (CMA, Physical Electronics). All spectra were recorded in the differential mode d$N(E)$/dE. Multi-point analysis across each sample was performed in order to obtain an average estimation of surface composition. AFM experiments were carried out in a liquid cell by using a MacMode PicoSPM magnetically driven dynamic force microscope (Molecular Imaging). Images were taken by using commercially available type II MAClevers with a nominal force constant of 2.8 N m^{-1} at a driving frequency of 19 Hz in the liquid environment.

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