# Coating of Surfaces with Stabilized Reactive Micelles from Poly(ethylene glycol)−Poly(DL-lactic acid) Block Copolymer

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Reactive micelle was prepared from an end-derivatized block copolymer, acetal−poly(ethylene glycol)−poly(DL-lactic acid)−methacrylate (PEG-PLA). The block copolymer of PEG-PLA formed a micelle with a diameter of approximately 30 nm determined from dynamic light scattering. The glass and Si wafer surfaces coated with 3-aminopropyltriethoxysilane and poly(dimethylsiloxane) (PDMS) treated with $N_2 + H_2$ plasma were coated with the micelle, and the coating was characterized by $\zeta$-potential profile, dynamic contact angle, and atomic force microscopy. The micelle with polymerized core maintained its structure on the surface while the nonpolymerized micelle was disrupted upon attachment. Compared with PEG coatings, micelle coating has higher advancing angle, and larger hysteresis, resulting from the conformational difference of PEG between the homopolymer and the micelle, and the micelle-induced surface topography. The $\zeta$-potential of glass surface coated with the micelle is similar to that with PEG despite the larger dimension of the micelle. However, plasma-treated PDMS showed appreciable magnitude of $\zeta$-potential even PEG was coated, while micelle-coated PDMS showed similar $\zeta$-potential to the glass coated with the micelle. The coatings with PEG−PLA micelles can be applied to the design of nonfouling surfaces and medical implants.

## Introduction

Modification of surfaces with polymers has been investigated to alter the surface property without changing bulk property. This is especially important for biological and biomedical applications. These coatings prevent nonspecific interaction of biopolymers such as plasma proteins and nucleic acids with surfaces, which results in the fouling of materials and reducing the resolution of analysis.[1,2] Coating hydrophilic polymers such as poly-(ethylene glycol) (PEG) can minimize these effects. PEG coatings extremely reduced protein adsorption, resulting from the increased wettability, masked surface charge, and increased osmotic effect by the coated polymer.[1−4] These properties can be applied to biomaterials, electrophoresis, chromatography, and biosensors.[1−9] PEG coating can be performed in a variety of methods such as side-on adsorption of PEG, physical adsorption of block copolymer of PEG with hydrophobic polymer segments, covalent grafting by the interaction of reactive PEG end group and

the surface, self-assembly of PEG−alkanethiol on Au, etc.[1−9]

We are interested in coating polymeric micelles prepared from block copolymer containing poly(ethylene glycol) (PEG). The block copolymer with narrow distribution can be prepared in one-pot anionic polymerization.[10−14] A block copolymer consisting of both hydrophilic and hydrophobic segments can form a micelle with hydrophobic core and hydrophilic corona in an aqueous solution. An optimum preparation allows a narrow distribution of micelle size without aggregation. Attaching micelles to the surfaces has been investigated by several researchers.[15−18] Most of them are physical adsorption of micelle to the surface,[15,16] while Webber et al. chemically coated by the reaction of side groups of polystyrene−polyacid block copolymer micelle with amino group on the surface.[17,18] The disruption of micelle often accompanies the attachment to the surface.[16] Although the polymeric micelles are more stable than surfactant micelles, they still deform under a certain condition. Below the critical micelle concentration (cmc), the block polymer dissolves in an aqueous solution, and the presence of surfactant forces the block copolymer to

† Science University of Tokyo.
‡ The University of Tokyo.
(1) Gölander, C.-G.; Herron, J.; Lim, K.; Claesson, P.; Stenius, P.; Andrade, J. D. In *Poly(ethylene glycol) Chemistry: Biotechnical and Biomedical Applications*; Harris, J. M., Ed.; Plenum Press: New York, 1992; pp 221−246.
(2) Österberg, E.; Bergström, K.; Holmberg, K.; Schuman, T. P.; Riggs, J. A.; Burns, N. L.; Van Alstine, J. M.; Harris, J. M. *J. Biomed. Mater. Res.* **1995,** *29,* 741−747.
(3) Herron, B. J.; Shafer, S. G.; Van ALstine, J. M.; Harris, J. M.; Snyder, R. S. *J. Colloid Interface Sci.* **1987,** *115,* 46−55.
(4) Emoto, K.; Harris, J. M.; Van Alstine, J. M. *Anal. Chem.* **1996,** *68,* 3751−3757.
(5) O'Neill, K.; Shao, X.; Zhao, Z.; Malik, A.; Lee, M. L. *Anal. Biochem.* **1994,** *222,* 185−189.
(6) Preisler, J.; Yeung, E. S. *Anal. Chem.* **1996,** *68,* 2885−2889.
(7) Torres, J. L.; Guzman, R.; Carbonell, R. G.; Kilpatrick, P. K. *Anal. Biochem.* **1988,** *171,* 411−418.
(8) Sigal, G. B.; Bandad, C.; Barberis, A.; Strominger, J.; Whitesides, G. M. *Anal. Chem.* **1996,** *68,* 490−497.
(9) Huang, S.-C.; Caldwell, K. C.; Lin, J.-N.; Wang, H.-K.; Herron, J. N. *Langmuir* **1996,** *12,* 4292−4298.

(10) Scholtz, C.; Iijima, M.; Nagasaki, Y.; Kataoka, K. *Macromolecules* **1995,** *28,* 7295−7297.
(11) Nagasaki, Y.; Okada, T.; Scholz, C.; Iijima, M.; Kato, M.; Kataoka, K. *Macromolecules* **1998,** *31,* 1473−1479.
(12) Nagasaki, Y.; Kataoka, K. In *Materials for Controlled Release Applications*; McCullough, I., Shalaby, S., Eds.; ACS Symp. Ser.; American Chemical Society: Washington, DC, 1998; pp 105−116.
(13) Iijima, M.; Okada, T.; Nagasaki, Y.; Kato, M.; Kataoka, K. *Macromolecules* **1999,** *32,* 1140−1146.
(14) Kim, J.-H.; Iijima, M.; Emoto, K.; Nagasaki, Y.; Kataoka, K. Accepted for publication in *Polym. Adv. Technol.*
(15) Meiners, J. C.; Quintel-Ritzi, A.; Mlynek, J.; Elbs, H.; Kraisch, G. *Macromolecules* **1997,** *30,* 4945−4951.
(16) Farinha, J. P. S.; d'Oliveira, J. M. R.; Martinoho, J. M.; Xu, R.; Winnik, M. A. *Langmuir* **1998,** *14,* 2291−2296.
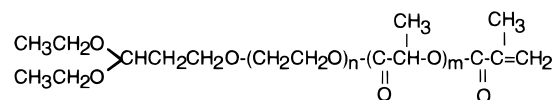(17) Webber, S. E. *J. Phys. Chem. B* **1998,** *102,* 2618−2626.
(18) Karymov, M. A.; Procházka, K.; Mendenhall, J. M.; Martin, T. J.; Munk, P.; Webber, S. E. *Langmuir* **1996,** *12,* 4748−4753.

dissolve.[12–14,19] We have synthesized a block copolymer of PEG (molecular weight ~5000) and poly(DL-lactic acid) (PLA, molecular weight ~5000) bearing an acetal group at the PEG end and methacryloyl at the PLA end. The resultant micelle of ca. 30 nm in diameter was reactive and stable after the hydrolysis of acetal into aldehyde and polymerization, respectively.[10–14] The stabilized micelle is expected to maintain its structure even after the attachment to the surface. It occupies approximately 700 nm$^2$ of the surface. Since the association number of the micelle is approximately 300, the area covered with the micelle is expected to be comparable to the attachment of 0.2 molecule of PEG per nm$^2$. This density is high enough to prevent the adsorption of proteins and adhesion of cells. The micelle coating is not only a substitute for the PEG coating. The surface-attached micelle is also expected to hold drugs. The drug in the micelle on the surface may be released in a controlled manner and can be used as a microreservoir for sustained release systems.

The property of the micelle-coated surface is also of interest. The micelle structure as well as the conformation of polymer may affect the wettability of surface to solution, especially water. Since the micelle is larger in size than linear PEG and consists of water-swellable corona and hydrophobic core, the electrostatic property and wettability of the micelle-coated surface will be different from the linear PEG coating. These properties may be important for the biomedical applications. Sofia et al. coated surfaces with chemically reactive PEG star polymer and compared the effectiveness of the protein rejection with the PEG coating.[20,21] Although they correlate the protein adsorption to the presence of the cavity as a result of the coating of relatively large particles, surface wettability may also contribute to the protein adsorption phenomenon as the star polymer of PEG is reported to be less soluble in water.[22]

The aims of this study are to see (1) whether the micelle is coated without altering its structure, (2) how the surface properties of such micelle coating are different from the less stable micelle and PEG coatings, and (3) whether the micelle can be coated on a variety of surfaces with high density. The surfaces for this study are aminated glass, Si wafer, and poly(dimethylsiloxane) (PDMS). Glass and Si wafers were chosen because these surfaces have been well characterized and are most suitable as model surfaces to coat with polymers and characterize the surface properties. PDMS is used for medical applications, but its surface property leads to an adsorption of proteins that subsequently alters its conformation.[23] PDMS is chosen as a model polymeric biomaterial surface for this reason. A polymeric micelle was prepared from the block copolymer of acetal−PEG−PLA−methacryloyl as shown in Scheme 1. After the formation of the micelle, the acetal group was hydrolyzed into aldehyde, and the methacryloyl group was polymerized. The micelle was coated on aminated surfaces and characterized by atomic force microscopy (AFM), dynamic contact angle, and ζ-potential measurements.

(19) Hagan, S. A.; Coombes, A. G. A.; Garnet, M. C.; Dunn, S. E.; Davis, M. C.; Illum, L.; Davis, S. S.; Harding, S. E.; Purkiss, S.; Gellert, P. R. *Langmuir* **1996**, *12*, 2153−2161.
(20) Sofia, S. J.; Merrill, E. W. In *Poly(ethylene glycol); Chemistry and Biological Applications*; Harris, J. M., Zalipsky, S., Eds.; American Chemical Society: Washington, DC, 1997; pp 342−360.
(21) Sofia, S. J.; Premnath, V.; Merrill, E. W. *Macromolecules* **1998**, *31*, 5059−5070.
(22) Zhou, G.; Chen, X.; Smid, J. In *Hydrophilic Polymers: performance with environmental acceptance*; Glass, J. E., Ed.; American Chemical Society: Washington, DC, 1996; pp 31−47.
(23) Tzannis, S. T.; Hrushesky, W. J.; Wood, P. A.; Przybycien, T. M. *J. Colloid Interface Sci.* **1997**, *189*, 216−228.

**Scheme 1**



## Experimental Section

The detailed discussion of the one-pot synthesis and the characterization of acetal−PEG−PLA and acetal−PEG−PLA−methacrylate is presented elsewhere.[10–14] Brief explanation of the synthesis of the block copolymer is presented here.

**Synthesis of Functionalized PEG−PLA Block Copolymer.** All the reagents used for the synthesis were purified by distillation before use. The 2 mmol of 3-diethoxypropanol, 2 mmol of potassium naphthalene, and subsequently 227 mmol of chilled ethylene oxide were added to the dry tetrahydrofuran (THF). The solution was stirred at 22 °C for 2 days. The molecular weight (MW) of the obtained PEG estimated by gel permeation chromatography (GPC) and NMR was 4500.

Followed by the PEG polymerization, DL-lactide was polymerized. After the addition of some potassium naphthalene, 83 mmol of DL-lactide was added and stirred for 2 h at 22 °C. The living polymerization was terminated by the addition of 30 mmol of methacrylic anhydride stirring for 3 days. The block copolymer was purified by precipitation in chilled 2-propanol and freeze-dried with benzene. The estimated MW of PLA by NMR was 3500. The peak integration of NMR revealed the same molecular ratio of acetal group as methacryloyl group indicative of the presence of both groups in a polymer molecule.

**Preparation of Polymerized PEG−PLA Micelle.** Micelles were prepared by dialyzing the PEG−PLA block copolymer in dimethylacetamide (DMAc) against deionized water. 280 mg of block copolymer was dissolved in 40 mL of DMAc, and the solution was dialyzed against distilled water with membrane tube with cutoff MW of 12 000−14 000 (Spectra/Pro) for 24 h. The pH of the solution was shifted from 5.8 to 2 with HCl and stirred for 2 h in order to hydrolyze acetal group at the PEG end to aldehyde group. The pH was readjusted to 6 and dialyzed against water for 24 h to remove salts from the micelle solution. The diameter of the micelle at this state was ca. 30 nm from the dynamic light scattering (DLS).[11–14]

After the second dialysis, the core of the micelle was stabilized by polymerizing the methacryloyl group at the end of the PLA segment. The 0.3% (w/w) of $K_2S_2O_8$ was added to the micelle solution as an initiator and purged of air with Ar. The solution was stirred for 24 h at 50−55 °C. The DLS indicated that the size of the core-polymerized micelle was about 30 nm, which is comparable to the micelle without core-polymerization.

**Amination of Substrate Surfaces.** Glass and Si wafers were cleaned by Piranah method.[24] Glass plates for ζ-potential (approximately 15 × 30 × 1 mm) and contact angle measurement (18 × 18 × 0.5 mm) and Si wafers were soaked in the boiling solution of sulfuric acid and hydrogen peroxide (50:50 by volume) for 1 h and rinsed with water exhaustively and dried in a vacuum for 12 h. The samples were then immersed into a 1% (v/v) solution of 3-aminopropyltriethoxysilane (APTS) (Aldrich, Milwaukee, WI) in toluene for 4 h. After rinsing in toluene to remove excess APTS, the APTS-coated substrates were cured at 160 °C in the vacuum for 20 h. The samples were stored in the vacuum until use.

The commercial PDMS samples were dried under vacuum for 12 h. They are treated with rf plasma composed of $N_2$ and $H_2$ in a plasma chamber (Samco, Tokyo, Japan). The pressure of the chamber was reduced below 3 mTorr before the treatment. The pressure was adjusted to 1.5 Torr by $N_2$ and $H_2$ with flow rates of 20 and 40 mL/min, respectively, and then 95 W rf electric field was applied. These plasma-treated PDMS films were stored in water. However, the coating of micelle was performed within 2 h.

**Coating of Aminated Surfaces with PEG−Aldehyde and Reactive PEG−PLA Micelle.** The aminated glass, Si wafer, and PDMS substrates were coated with aldehyde-derivatized PEG (MW 5000) and aldehyde-bearing PEG−PLA micelle.

(24) Bearinger, J. P.; Castner, D. G.; Golledge, S. L.; Rezania, A.; Hubchak, S.; Healy, K. E. *Langmuir* **1997**, *13*, 5175−5183.

Monomethoxy–PEG–adehyde was coated under an optimal condition.[1,4,25] The aminated substrates were immersed in the 5% (w/v) solution of PEG–aldehyde in 0.5 M $Na_2SO_4$ containing 0.25% (w/v) $NaCNBH_3$ and 0.01 M $NaH_2PO_4$, pH 5.5. After the substrate in the PEG solution was heated to 80 °C for 2 h, it was rinsed with water repeatedly and stored in deionized water until use.

For the coating of reactive PEG–PLA micelle, $Na_2SO_4$ was not added because of the precipitation of micelle.[19] The aminated substrates were immersed in an approximately 1 mg/mL micelle solution in 0.01 M $NaH_2PO_4$ containing 0.25% (w/v) $NaCNBH_3$. The coating temperatures were 25, 45, or 80 °C for 2 h. After the coating, the samples were rinsed with distilled and deionized water repeatedly and stored in water until characterization. The samples were characterized within 2 days after the preparation.

**Characterization of Samples Coated with PEG and Micelles.** The samples were characterized with $\zeta$-potential and dynamic contact angle measurements, and an atomic force microscopy (AFM). The $\zeta$-potential over a pH range of 2–11 at 25 °C was measured by LEZA-600 (Otsuka Electric Co., Osaka, Japan) in 7.5 mM NaCl solution, and the pH was adjusted with 7.5 mM HCl or NaOH. A plate or a film of a sample was placed on a groove (10 × 25 × 2 mm) of a quartz cell equipped with medium injector and Pt electrodes. The mobility of the medium particles under an electric field of 21 V/cm was detected along the vertical direction to the center of the sample by the Doppler shift of the laser. Since the cell was coated with polyacrylamide, and the width of the groove was large enough compared with the distance between the cell wall and the sample, one could neglect the effect of the groove wall on the mobility of the particle. The $\zeta$-potential was obtained from the plots of the mobility of the particle versus the distance from the sample that can be fitted to a second-order parabola.

The dynamic contact angle was measured in Wilhelmy Method by Cahn DCA-315 (Madison, WI). A sample was dipped into and pulled out of Mili-Q (>18 MΩ, 72.08 dyn·cm⁻¹) at 22 °C by the rate of 0.1 mm·s⁻¹. The detected force $f$ is the combination of surface tension of water $\gamma$ along the meniscus $l$ with gravitational force $mg$ and the buoyancy $f_b$:

$$f = \gamma l \cos\theta + mg - f_b \tag{1}$$

For each treatment or coating, 9–10 samples were prepared, and the average of each measurement was regarded as the contact angle of each treatment discussed above.

The tapping mode AFM images of micelle-coated Si wafers were obtained by Bioscope (Digital Instruments, Santa Barbara, CA) modulated by Olympus Co. (Tokyo, Japan). For the images in water, the samples were immersed in Mili-Q water until use. They were attached to a Petri dish and filled with Mili-Q. The 1 × 1 $\mu$m image was captured with contact mode cantilever with force constants of 0.09 N/m. For the ambient images, the samples were dried in a desiccator until use. The wafers were attached to a glass slide and deionized. The tapping mode probe with force constant of 20 N/m was scanned over 1 × 1 $\mu$m of the sample.

## Results and Discussion

**The $\zeta$-Potential of Micelle- and PEG-Coated Glass.** Figure 1 shows the alteration of $\zeta$-potential versus pH profile of clean, APTS-treated, PEG-coated, and micelle-coated glass surfaces. The cleaned glass surface is full of silanol groups.[26–28] The p$K$ of the silanol group depends on its environment but usually moderately to weakly acidic.[26,28] The $\zeta$-potential of glass surface is highly negative above pH 5. Although the $\zeta$-potential at lower pH (<p$K$) was expected to be negligible due to the lack of
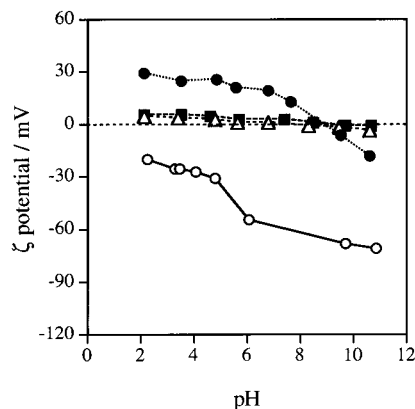
(25) Emoto, K. Ph.D. Thesis, University of Alabama, Huntsville, AL, 1997.

(26) Eremenko, B. V.; Platonov, B. É.; Uskov, I. A.; Lyubchenko, I. N. *Kolloid. Zh.* **1974**, *36*, 240–244.

(27) Scales, P. J.; Greiser, F.; Healy, T. W.; White, L. R.; Chan, D. Y. *Langmuir* **1992**, *8*, 965–974.

(28) Burns, N. L.; Van Alstine, J. M.; Harris, J. M. *Langmuir* **1995**, *11*, 2768–2776.



**Figure 1.** Plot of $\zeta$-potential vs pH of (○) cleaned, (●) APTS-coated, (△) PEG-coated, and (■) PEG–PLA micelle-coated glass surfaces. The core of the micelle was polymerized prior to the coating.
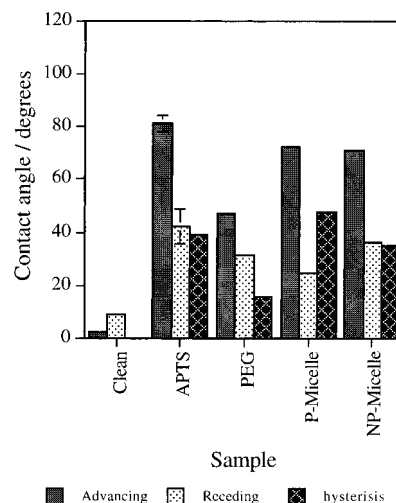


**Figure 2.** Dynamic contact angles of cleaned, APTS-coated, PEG-coated, and micelle-coated glass surfaces. P- and NP-Micelle represent core-polymerized and nonpolymerized micelles, respectively.

siloxy group, it is appreciably negative (<−20 mV). Since the surface is highly wettable as seen in Figure 2 indicative of little contaminants, this negative surface charge at low pH is probably due to the elements doped into the glass, such as $B_2O_3$ and metal oxides. By treating the glass with APTS, the surface has basic amino and acidic silanol groups resulting in a remarkable alteration of surface charge.[4,28]

When APTS-glass was coated with PEG and micelle, $\zeta$-potential over the pH range of 2–11 was significantly reduced. The $\zeta$-potential is an electrostatic potential on the plane of shear.[29] The distance between the charged surface and the plane of shear varies depending on the extent of the interaction of solvent molecule with the charged surface. For a bare glass surface, the interaction with water extends up to a few layers of water molecules, and the $\zeta$-potential is the potential approximately 1 nm away from the surface.[28] In the presence of neutral PEG on the surface, the mobility of water molecule is restricted by the interaction of water molecules with the hydrophilic polymer chain. This extends the distance between the charged substrate and the plane of shear. Since the electrostatic potential decreases nearly exponentially,

(29) Hunter, R. J. *Zeta Potential in Colloid Science—Princeples and Applications*; Academic Press: New York, 1981.

increased distance of the plane of shear results in the decrease in the $\zeta$-potential.[4,28,29] This will also be true for the micelle-coated surface, i.e., neutral micelle coating extended the plane of shear distance resulting in the decrease in the $\zeta$-potential.

The profiles for both coatings were almost identical despite the remarkable difference in dimension, i.e., 3 nm for PEG with MW of 5000 and 30 nm for the micelle in this study.[11–13,30] Polymers densely grafted on a surface are elongated due to the osmotic effect by the neighboring polymer molecules and due to the solubility of polymer in a good solvent, and the thickness of the polymer layer on a surface is substantially larger than the dimension of polymer in a solution.[31–33] The ellipsometry study suggests over 15 nm thickness of a layer of PEG–alkylate of similar MW on methylated Si wafer, which agrees fairly well with electrophoretic result of PEG–aldehyde grafted on aminated glass surface.[25,34] The glass and Si wafer surfaces coated with PEG–aldehyde under the similar condition reject plasma proteins.[25,34,35] For the micelle coating, the $\zeta$-potential profile is almost identical to that of PEG-coated surface. The core of the micelle is not highly wet by water, and the micelle layer is expected to have smaller permittivity than the PEG layer. The lower permittivity renders less screening of electrostatic potential, resulting in the similar $\zeta$-potential. Although the thickness of micelle coating is much larger than PEG, it is little seen by the $\zeta$-potential. Varying coating temperature (25–80 °C) did not alter the $\zeta$-potential, although the AFM images showed topographical difference as shown in Figure 3. It is important to note that the $\zeta$-potential of micelle coating without NaCNBH$_3$ was not as low as that with NaCNBH$_3$. This indicates that the micelle can be removed from the surface if it is not stably attached to the surface.

**Dynamic Contact Angle of Micelle- and PEG-Coated Glass.** Figure 2 shows the advancing and receding contact angles of clean, APTS-treated, PEG-coated, and micelle-coated glass samples. The standard deviation of contact angles for each sample was small. The glass cleaned by the Piranah method showed almost zero contact angle with little hysteresis. The similar advancing and receding angles and small deviation of angles among samples indicate that the surface of the cleaned glass contained little organic contamination. When APTS was treated, the surface became appreciably hydrophobic, and large hysteresis was seen. The hysteresis of dynamic contact angle probably originates from heterogeneity (presence of high- and low-energy domains), and the roughness generated by the deposition of silane.[36] Advancing angle reflects the low-energy propyl and siloxy groups, and the receding angle is affected by the high-energy polar groups. Roughness is another factor to generate hysteresis. The APTS deposition results in a less smooth surface.

PEG coating facilitated the wettability and reduced the contact angles and hysteresis. The advancing and receding contact angles of aminated glass surface coated with PEG were reduced to 50° and 30° in water, respectively. Lin et

al. also reported a similar contact angle with appreciable hysteresis.[37] For the polymerized micelle-coated glass, the advancing angle is higher and the hysteresis is remarkably larger than the PEG coatings. As a comparison, the contact angles of glass coated with nonpolymerized micelle are also shown in Figure 2. While the advancing angle is similar to the polymerized micelle coating, the receding angle is appreciably higher. The different contact angle profile of the coating of core-polymerized micelle from that of the nonpolymerized indicates that the surface structure is different between these samples.

The high advancing angle and large hysteresis are due to the combination of several factors such as the topography of the surface, amphiphilic behavior of PEG, swelling and shrinking of micelle, and viscoelastic nature of polymers on the surface. The profile of dynamic contact angle for the PEG coating is affected by the topography of the surface and the amphiphilicity of PEG. Sanderson et al. showed the presence of dense and less dense domains of PEG-coated surface.[38] The presence of such domains affected the dynamic contact angle. PEG also takes both hydrophilic and hydrophobic conformations responding to the environment. This may be another reason for the hysteresis. It affected the micelle coating more significantly than the PEG. The solubility of PEG–PLA micelle is lower than PEG, and precipitates even at the room temperature in the presence of sulfate salt, such as Na$_2$SO$_4$.[19] Ahlnäs et al. showed a hydrophobic trans conformation around the C–C bond of the PEG segment in the micelle at a slightly elevated temperature by $^{13}$C NMR.[39] The PEG segment in the micelle may have altered its conformation when the surface was immersed into or withdrawn from water, resulting in high advancing and low receding angles. The swelling behavior of micelle also affects the hysteresis of the dynamic contact angle. The polymerized micelle maintains its structure both in water and in air, while its water content must be altered. Since PEG takes either polar or nonpolar conformation depending on the environment, it swells in water and shrinks in air. Since PLA segment also contains some water, the core of the micelle may also swell and shrink upon immersion into and withdrawal from the water.[40] Such swelling behavior of micelle on the surface also affects the contact angle. Recent report pointed out the viscoelasticity of polymer surface was also a cause of the hysteresis.[41] When in contact with water, the meniscus is under stress rendered by the surface tension of liquid, which is dissipated by the conformational change of polymer. Such conformational alteration with time results in an amplified hysteresis. Surface roughness is another factor to amplify the hysteresis.[36] While nonpolymerized micelle disrupts upon the attachment and the surface gets smoother compared with APTS-glass surface, polymerized micelle is coated with its structure maintained. The surface is covered with lumps of ca. 30 nm. This resultant roughness may affect the contact angle. This will be discussed with AFM images in the next section.

The receding angle of micelle-coated sample was lower than even PEG coatings. The static contact angle of air bubble on the micelle-coated glass surface in water was

(30) Thyagarajan, P.; Chaiko, D. J.; Hjelm, R. P., Jr. *Macromolecules* **1995**, *28*, 7730–7736.

(31) de Gennes, P. J. *Macromolecules* **1980**, *13*, 1069–1075.

(32) Milner, S. T. *Science* **1991**, *251*, 905–914.

(33) Zhulina, E. B.; Borisov, O. V.; Priamitsyn, V. A. *J. Colloid Interface Sci.* **1990**, *137*, 495–511.

(34) Malmsten, M.; Van Alstine, J. M. *J. Colloid Interface Sci.* **1996**, *177*, 505–512.

(35) Malmsten, M.; Emoto, K.; Van Alstine, J. M. *J. Colloid Interface Sci.* **1998**, *202*, 507–517.

(36) Andrade, J. D.; Smith, L. M.; Gregois, D. E. In *Surface and Interfacial Aspects of Biomedical Polymers*; Andrade, J. D., Ed.; Plenum Press: New York, 1985; pp 249–292.

(37) Lin, Y. S.; Hlady, V.; Gölander, C. G. *Colloids Surf. B* **1994**, *3*, 49–62.

(38) Sanderson, L. A. W.; Emoto, K.; Van Alstine, J. M.; Weimer, J. J. *J. Colloid Interface Sci.*, in press.

(39) Ahlnäs, T.; Karlström, G.; Lindman, B. *J. Phys. Chem.* **1987**, *91*, 4030–4036.

(40) Goldmints, I.; von Gottberg, F. K.; Smith, K. A.; Hatto, T. A. *Langmuir* **1997**, *13*, 3659–3664.

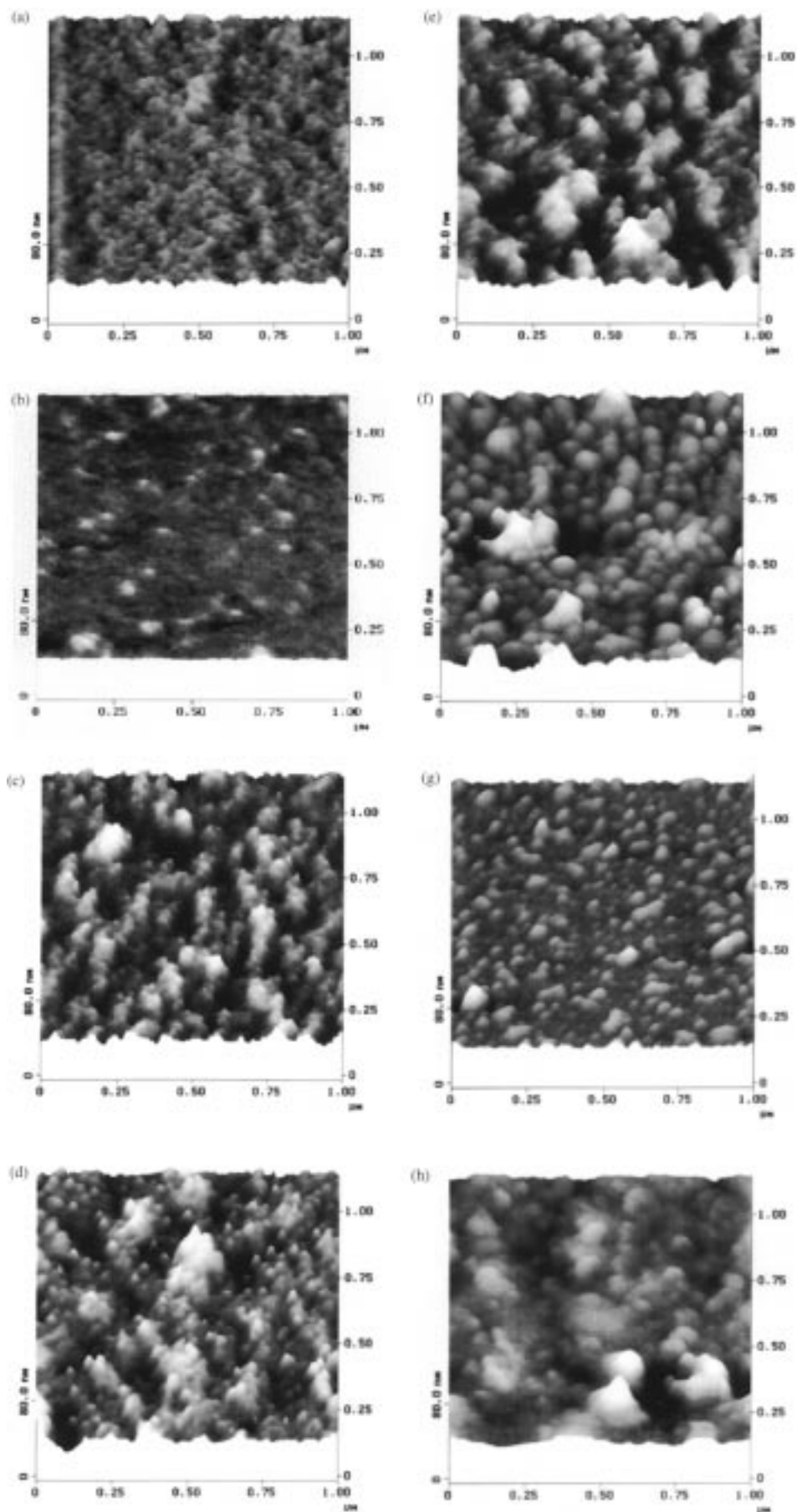(41) Tomasetti, E.; Rouxhet, P. G.; Legras, R. *Langmuir* **1998**, *14*, 3435–3439.

**Figure 3.** Tapping mode AFM images of (a) APTS-coated, (b) nonpolymerized micelle-coated and (c)−(g) polymerized-micelle-coated Si wafer. Coating temperature of micelle were 25 °C (c,f), 50 °C (d,g), and 80 °C (e,h). Images (a)−(e) were taken in water, while (f)−(h) were taken in air.

about 140° ± 3°, while that of APTS coating was 102° ± 4°. High contact angle of air bubble and low receding angle for micelle coatings indicate that the micelle coating tends to prevent the surface from dewetting.

**AFM Imaging of Micelle-Coated Surface.** Figure 3 shows the tapping-mode AFM images in water and air of APTS−Si wafers coated with micelle at various temperatures. All coatings with polymerized micelle show the presence of lumps originated from the attached micelle on the surface. By polymerizing the PLA end, the highly entangled structure prohibits the free movement of PLA in the core, and the micelle structure cannot be easily disrupted. Although the degree of polymerization of methacryloyl group at the PLA end could not be determined, polymerization of the core significantly reduces the reptation of polymer chain in the core of the micelle and consequently enhances the stability of the spherical micelle structure. Such topography was not observed for the coating of nonpolymerized micelle as in Figure 3b. The surface was much smoother than the coating of polymerized micelle, indicating that the micelle disrupted upon attachment to the surface. When the surface was exposed to nonpolymerized micelle solution, the surface was covered with block copolymer rather than micelle. The maintained micelle structure is attributed to the enhanced stability by the polymerization of methacryloyl group at the hydrophobic PLA end. On attachment of the PEG end to the surface, polymer molecules in the micelle reduce its conformational freedom. To overcome such restriction, micelles undergo structural alteration, i.e., disruption into either a lamellar structure of micelles or the monolayer of end-on attachment of block copolymers. For the typical polymeric micelle, the deformation or conservation of micelle structure upon attachment to the surface depends on the associative strength of the core, MW ratio of soluble to insoluble segments, and surface topography. Meiners et al. and Webber et al. showed conserved micelle structure of micelle on flat mica and polymer surfaces, while Farrinha et al. showed the disrupted or conserved structure on the various sizes of polystyrene particles.[15−18] The micelle from PEG−PLA in this study does not seem to have strong intermolecular association to maintain its structure upon attachment, unless the core is polymerized.

The size of lumps on the surface depends on the coating temperature. The lobe size decreased when the coating temperature was increased from 25 to 50 °C. However, further increase in temperature to 80 °C resulted in larger lobes. The change in the size of the micelle lumps with coating temperature is due to the decrease in solubility of micelle with temperature as in the case of PEG. When the surface is covered with micelle to some extent, micelles on the surface prevent the bulk micelle particles from further attaching to the surface by repulsive and osmotic interaction between micelles.[16] This repulsive force balances with the affinity of the micelle to the surface. At low temperature, micelles solubilize well in the solution and the affinity with the surface is not high. As the temperature is elevated, the micelle is less soluble and the affinity to the surface is increased. At higher temperature, the intermicelle interaction is significant, and the micelle is not dispersed in the solution. Around 90 °C the micelle precipitates to form a cloudy aggregate.

Such topography affected the contact angle. The micelle-coated surfaces have high contact angle, although the surface is covered with PEG. One reason for that is the hydrophobic conformation of PEG as discussed ear-
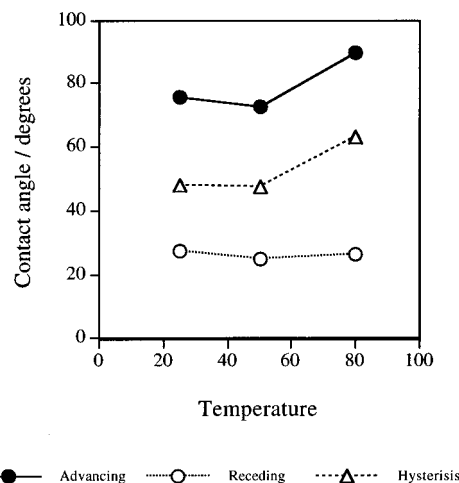


**Figure 4.** Variation of dynamic contact angle with coating temperature of APTS-glass surface with polymerized micelle.
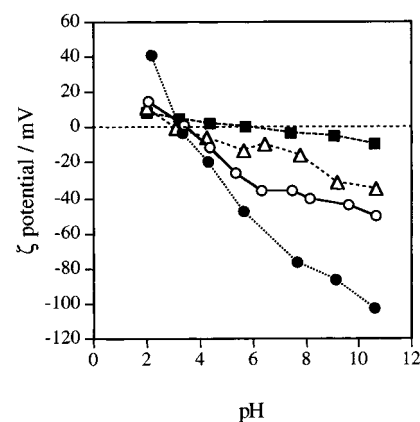


**Figure 5.** Plot of $\zeta$-potential vs pH of (○) bare, (●) plasma-treated, (△) PEG-coated, and (■) micelle-coated poly(dimethylsiloxane) (PDMS). The core of the micelle was polymerized prior to the coating.

lier.[39,42,43] The other reason is probably the nanoscopic roughness of surface as described earlier.[36] The size of micelle islands decreased when the coating temperature was moderately high, but close to the cloud point resulted in a less organized arrangement of large islands. Such topography affects the contact angles as shown in Figure 4. Both advancing and receding angles slightly decrease as the coating temperature was increased from 25 to 50 °C. But the advancing angle increases appreciably while the receding angle increases slightly for the 80 °C coating, resulting in a larger hysteresis. The contact angle is affected by the size of islands covering the glass surface, and the surface with large islands of micelles tends to have large hysteresis. However, roughness parameters did not seem to reflect the AFM images. For soft surfaces, roughness parameters do not correlate with the apparent topography and the contact angle.[38]

**Coating of Micelle and PEG on Plasma-Treated PDMS Surface.** As an application for the biomaterial, the micelle was coated on plasma-treated PDMS surface in the same manner as the APTS-glass surface. Figure 5 shows the $\zeta$-potential profile of bare, plasma-treated, PEG-coated, and micelle-coated surfaces. The $\zeta$-potential of untreated PDMS is slightly positive at pH 2, but ap-

(42) Bailly, F. E., Jr.; Callard, R. W. *J. Appl. Polym. Sci.* **1959**, *1*, 56−62.
(43) Karlström, G.; Carlsson, A.; Lindman, B. *J. Phys. Chem.* **1990**, *94*, 5005−5015.

preciably negative above pH 6 ($-50$ to $-60$ mV). Typically, the negative $\zeta$-potential is seen for hydrophobic surfaces possibly due to the adsorption of anions to the surface.[44]

When the film was treated with $N_2 + H_2$ plasma, the $\zeta$-potential at pH 2 increased to over 40 mV indicative of an introduction of amino group on the surface, while it is strongly negative above pH 3. This highly negative surface charge results from the generation of silanol group on a large surface area due to the formation of silanol group by the cleavage of PDMS chain, and possible flip-flop of surface PDMS, increased surface area by the destruction of surface, and the adsorption of anions.

Although the $\zeta$-potential vs pH profile is reduced after the PEG coating, the reduction is not as significant as on glass surface (Figure 1). The $\zeta$-potential of materials with high surface charge is dominantly affected by the plane of shear distance over the surface charge density. Provided that the surface charge of aminated glass is the same as that of aminated PDMS, this difference in $\zeta$-potential is due to the location of the plane of shear. The plane of shear distance of plasma-treated PDMS grafted with PEG is smaller than that of PEG-coated glass surface due to the low polymer density.[4,25] When the density of PEG is low, the polymer takes mushroom-like structure resulting in a small plane of shear distance.[4] Although the coating condition is optimal for the high density, the amino group on the PDMS was not accessible to the aldehyde group of PEG end due to the steric hindrance of PDMS polymer and the flip-flop of reactive groups by high-temperature coating.

The $\zeta$-potential profile of micelle-coated PDMS is as low as that of glass surface coated with PEG and micelle. A single micelle particle occupies approximately 700 nm$^2$ and this area is covered with high density of PEG. Although the accessibility of amino group was low, the micelle was effectively coated on the surface and probably cross-linked the PDMS chains near the surface. For the production of biomaterials, an autoclave treatment is often applied to the product as a sterilization. The coating must

withstand such harsh environment. The $\zeta$-potential profile taken after the 120 °C $\times$ 20 min autoclave was little altered (data not shown). The micelle can be efficiently coated on the surface with low density of reactive group, and covalent linkage stabilized the coating, withstanding hydrothermal treatment.

## Conclusion

In this research, a reactive PEG–PLA micelle with polymerized core was coated on the surface. The AFM images revealed that a stabilized reactive micelle from PEG–PLA diblock polymer was coated on the surface without deformation. When coated on the glass surface, the $\zeta$-potential of the micelle coating was similar to that of PEG coatings despite the tremendous difference in size. However, on plasma-treated PDMS, the micelle-coated surface showed as small $\zeta$-potential as on the glass surface, while PEG coating decreased the $\zeta$-potential less significantly. The advancing contact angles and the hysteresis are much larger for micelle coating than the PEG coating due to the conformational change of PEG in the micelle corona, nanoscopic roughness by the islands of micelles and viscoelasticity of both PEG and PLA segments. We are interested in the in situ monitoring of the micelle attachment to the surface. The interaction of plasma protein with the micelle-coated surface is another interest. These will be presented in a future paper. From the measurement of $\zeta$-potential, micelle coating was found to easy, effective, and applicable to a variety of surfaces. Such micelle coating can be useful as a variety of nonfouling surfaces and a microreservoir for sustained drug release. Although degradable PEG–PLA block copolymer was used in the present study, synthesis of stable polymer is under investigation.

(44) Uchida, E.; Uyama, Y.; Ikada, Y. *Langmuir* **1994**, *10*, 1193–1196.