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Hydrogen-Bonding Layer-by-Layer-Assembled Biodegradable Polymeric Micelles as Drug Delivery Vehicles from Surfaces

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ABSTRACT We present the integration of amphiphilic block copolymer micelles as nanometer-sized vehicles for hydrophobic drugs within layer-by-layer (LbL) films using alternating hydrogen bond interactions as the driving force for assembly for the first time, thus enabling the incorporation of drugs and pH-sensitive release. The film was constructed based on the hydrogen bonding between poly(acrylic acid) (PAA) as an H-bond donor and biodegradable poly(ethylene oxide)-*block*-poly(ϵ-caprolactone) (PEO-*b*-PCL) micelles as the H-bond acceptor when assembled under acidic conditions. By taking advantage of the weak interactions of the hydrogen-bonded film on hydrophobic surfaces, it is possible to generate flexible free-standing films of these materials. A free-standing micelle LbL film of $(PEO\text{-}b\text{-}PCL/PAA)_{60}$ with a thickness of 3.1 μm was isolated, allowing further characterization of the bulk film properties, including morphology and phase transitions, using transmission electron microscopy and differential scanning calorimetry. Because of the sensitive nature of the hydrogen bonding employed to build the multilayers, the film can be rapidly deconstructed to release micelles upon exposure to physiological conditions. However, we could also successfully control the rate of film deconstruction by cross-linking carboxylic acid groups in PAA through thermally induced anhydride linkages, which retard the drug release to the surrounding medium to enable sustained release over multiple days. To demonstrate efficacy in delivering active therapeutics, *in vitro* Kirby—Bauer assays against *Staphylococcus aureus* were used to illustrate that the drug-loaded micelle LbL film can release significant amounts of an active antibacterial drug, triclosan, to inhibit the growth of bacteria. Because the micellar encapsulation of hydrophobic therapeutics does not require specific chemical interactions, we believe this noncovalent approach provides a new route to integrating active small, uncharged, and hydrophobic therapeutics into LbL thin films for biological and biomedical coatings.

KEYWORDS: layer-by-layer · drug delivery · block copolymer micelle · hydrogen bond · polymer assembly · biodegradable

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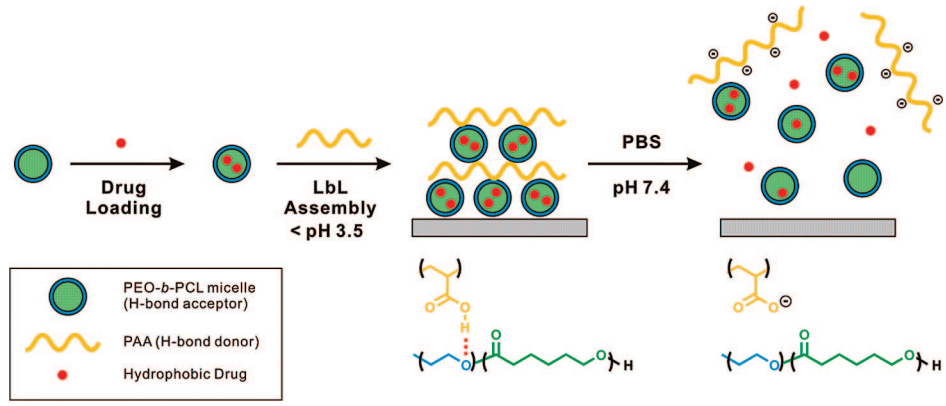
Layer-by-layer (LbL) assembly has been widely used as a versatile method for fabricating multilayer thin films with controlled structure and composition.[1,2] It is typically based on sequential adsorption of materials with complementary functional groups employing electrostatic interactions, hydrogen bonding, or covalent interactions. Due to their facile, inexpensive, and environmentally friendly nature, LbL-assembled multilayer thin films find broad applications ranging from energy and electrochemical devices to biological materials. In particular, recent advances in LbL-based drug delivery include direct integration of polyionic drugs into multilayers,[3] encapsulation within a polyelectrolyte template,[4] use of polymer-bound prodrugs,[5] and incorporation of drugs into porous multilayers.[6] However, it has been challenging to directly incorporate small, uncharged, and hydrophobic therapeutics–which comprises about 40% of FDA-approved drugs–into multilayer thin films due to the lack of general functionality.

One approach that would enable incorporation of hydrophobic drugs involves the integration of amphiphilic block copolymer micelles, which can serve as vehicles for drugs to be incorporated in LbL films. Similar to other means of embedding hydrophobic drugs within multilayer thin films such as cyclodextrins,[7] amphiphilic polysaccharides,[8] and liposomes,[9] this micellar encapsulation method would provide a general approach, because amphiphilic block copolymers can spontaneously self-assemble in water to encapsulate hydrophobic drugs. These polymeric micelles have been extensively utilized to provide a highly versatile nanometer-sized delivery platform for drugs, proteins, DNA, and personal care products.[10,11] The integration of block copolymer micelles into LbL films has been previously reported, relying either on covalent linkages or on the electrostatic interactions between the polyelectrolyte and the micellar corona block.[12–16] Herein, we present the first example of polymeric micelles incorporated into LbL films based on hydrogen bonding, without the use of charged polyelectrolyte. Specifically, we

have constructed LbL films employing the hydrogen bonding between biologically compatible poly(acrylic acid) (PAA) and a biodegradable block copolymer micelle of poly(ethylene oxide)-*block*-poly(ε-caprolactone) (PEO-*b*-PCL). We demonstrate that the resulting films can be easily disrupted to release drug-loaded micelles into the surrounding medium under physiological conditions due to the very sensitive nature of hydrogen bonding employed to assemble the film (Scheme 1).



Scheme 1. Schmatic representation of hydrogen-bonding layer-by-layer assembly of block copolymer micelles for hydrophobic drug delivery vehicles from surfaces.

Furthermore, we demonstrate the construction of polymeric micelle-containing films on hydrophobic surfaces to obtain free-standing thin films that can carry active therapeutics while providing additional flexibility in handling. Since micelle encapsulation and LbL assembly into thin films does not require specific chemical interactions between the copolymer and the drugs in the core, we argue that this method is particularly well-suited to protecting and assembling hydrophobic therapeutics into LbL thin films for various biological and biomedical coatings.

Block copolymer micelles of PEO-*b*-PCL have been widely explored for biocompatible and biodegradable drug delivery systems.[11,17,18] In this study, PEO-*b*-PCL was chosen on the following basis: the biocompatible, hydrophilic PEO block stabilizes the micellar structure in water and forms a hydrogen-bonding network with PAA, as we and others have previously demonstrated with linear polymeric PEO/PAA multilayer systems,[19–23] whereas the biodegradable, hydrophobic PCL block accommodates hydrophobic drugs and provides the ability to tailor loading efficiency and the release profile of drugs as a function of molecular weight.

According to the protocol established by Eisenberg and co-workers, we prepared PEO-*b*-PCL micelles by initially dissolving the block copolymer in tetrahydrofuran (THF) and induced micellization with a dropwise addition of water followed by dialysis.[17] The size and shape of micelles prepared were determined by transmission electron microscopy (TEM, Figure 1a) and atomic force microscopy (AFM), which indicate spherical micelles with an average diameter of 55 ± 12 nm. Dynamic light scattering (DLS) also supports that the hydrodynamic diameter of the micelles in solution was approximately 71 nm.

Utilizing the corona of the PEO-*b*-PCL block copolymer micelles as a hydrogen bond acceptor and PAA as a donor, multilayer thin films were assembled by repeatedly layering PEO-*b*-PCL micelles and PAA under acidic conditions (pH 2.5) to ensure close to full protonation of PAA ($pK_a \approx 5.5–6.5$). It should be noted that the concentration of micelles used in the film build-up was about 300 times higher than the known critical micelle concentration (1.2×10^{-3} mg/mL),[24] ensuring that the polymers existed predominantly in the micellar form rather than as dissociated free polymer chains.

The growth of hydrogen-bonded film was shown to be linear with respect to the number of bilayers deposited after an initial induction period, in which the initial deposition of polymer layers is strongly influenced by the underlying substrate. The average thickness of one bilayer–one PEO-*b*-PCL micelle layer and one PAA layer–corresponds to 54 nm when averaged over 20 bilayers of growth (Figure 1b). Although it does not necessarily reflect the internal structure of thin film, it is interesting to observe that the average bilayer thickness is in close agreement with the dimension of micelles used. Similarly, it is reported that phospholipid vesicles incorporated within polyelectrolyte films exhibit a film thickness which is very close to the diameter of the vesicles in solution.[9]

As we have previously demonstrated for other hydrogen-bonded PEO/PAA systems, we were able to isolate free-standing thin films after deposition by tak-

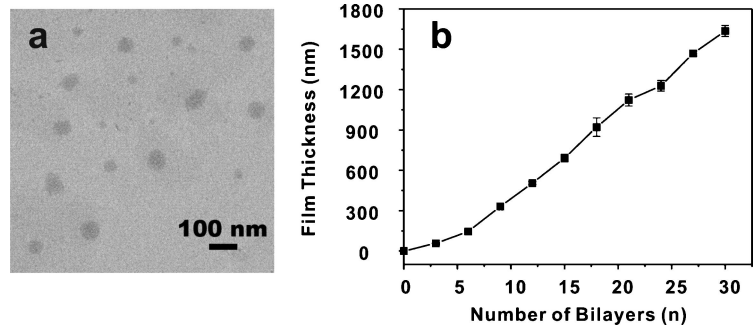


Figure 1. (a) TEM image of PEO-*b*-PCL micelles. (b) Growth curve of hydrogen-bonded (PEO-*b*-PCL/PAA)$_n$ film measured by profilometry in the dried state. Average diameter of micelles by TEM is 52 ± 16 nm.

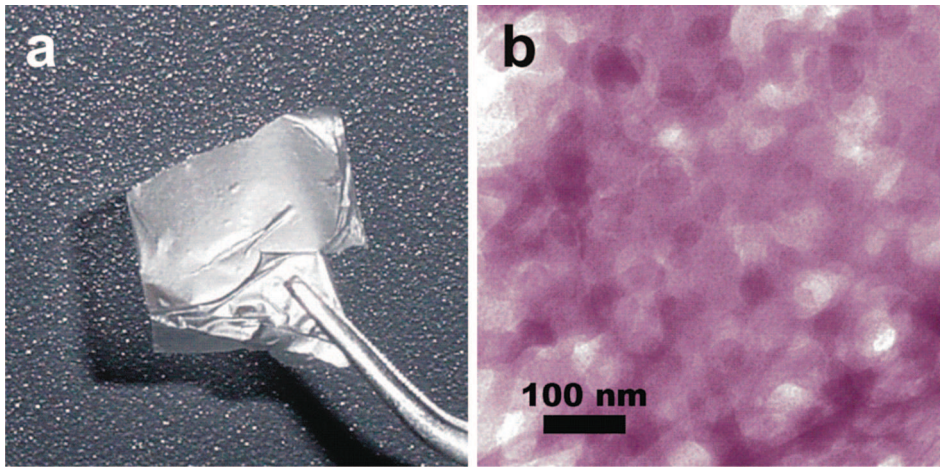


Figure 2. (a) Photograph image and (b) TEM micrograph of a cross-section of free-standing (PEO-*b*-PCL/PAA)$_{60}$ film. Epoxy-embedded free-standing thin film was cryo-microtomed for cross-section TEM. (See Supporting Information for a magnified TEM image.)

ing advantage of weak adhesive interactions of the hydrogen-bonded film on smooth hydrophobic surfaces such as polypropylene and Teflon.[19,21] This offers an advantage in the characterization of the bulk film that would otherwise be hard to access when films are confined on the substrate. This ability is in clear contrast to that of other approaches that require a sacrificial layer[25] or dissolution of the substrate[26] to isolate free-standing thin films. For example, a free-standing thin film of (PEO-*b*-PCL/PAA)$_{60}$ could be easily peeled off from the polypropylene substrate with an average thickness of 3.1 μm and a root-mean-square (rms) roughness of 64 nm, as measured by profilometry (Figure 2a). Due to the versatility of LbL assembly, there should be no restriction to obtaining free-standing films of any size and shape. In addition, isolated hydrogen-bonded films allowed us to further confirm the presence of micelles. As shown in Figure 2b, we were able to observe the incorporated micellar structures by taking a TEM image of a cross-section of the (PEO-*b*-PCL/PAA)$_{60}$ film, finding that the micelle structures are indeed incorporated within the film without significant structural deformation. Additionally, micelles within the films are closely located, and they formed a network structure with the PAA matrix within the LbL polymer film.

An FTIR-ATR spectrum of a free-standing thin film (shown in the Supporting Information) indicates the presence of each layer component, both PAA and the PEO-*b*-PCL block copolymer within the film, but the PCL block was not clearly discernible in the spectrum due to the large overlap of peaks. FTIR also indicated that hydrogen bonding is responsible for the film formation; all the carboxylic acid groups of PAA were fully protonated (1700 cm^{-1}), without any carboxylate anion peak (1570 cm^{-1}) visible.[27]

Previously, it has been shown that PEO-*b*-PCL micelles spontaneously undergo degradation due to chain-end hydrolysis of the PCL block, depending on the pH and temperature.[28] Because assembly of a hydrogen-bonded film between PAA and PEO-*b*-PCL micelles requires an acidic condition (pH 2.5),[23] we have monitored the potential degradation of the PCL core during the LbL assembly process. Using gel permeation chromatography measurements, we found that approximately 5% hydrolysis of the PCL block occurs after 5 days of storage at the assembly conditions–PEO$_{114}$-*b*-PCL$_{60}$ was shortened on average to PEO$_{114}$-*b*-PCL$_{57}$; however, the shape and the size of the micelles did not change significantly with core block degradation, as proven by AFM. Therefore, we have limited the use of the micelle solutions in sample preparation processes to no longer than 5 days to prevent substantive degradation of the micelle core.

The thermal properties of the isolated (PEO-*b*-PCL/PAA)$_{60}$ free-standing film were characterized with differential scanning calorimetry (DSC). Interestingly, the assembled thin film exhibits one melting peak (T_m) and two glass transition temperatures (T_g and T_g*) (Figure 3a). This is in clear contrast to our previous result for pure PEO/PAA films assembled under identical conditions, which exhibited no melting temperature due to the complete suppression of PEO crystallization when hydrogen-bonded to PAA and an averaged T_g representative of the two miscible components.[19] After a careful comparison with each polymer component, it was determined that the melting peak at 49.9 °C corresponds to the crystalline PCL micelle core that does not participate in the hydrogen bonding with PAA (Figure 3b).

We also observed that the T_g of the PCL core (T_g = −69 °C) is also retained within the multilayer film together with the T_g of the fully miscible, hydrogen-bonded blend of PEO and PAA (T_g* = −32 °C), located between the T_g values of pure PEO (−50 °C) and PAA (99 °C). These results further support the structure presented in the cross-sectional TEM image of a homogeneous fully blended PEO/PAA matrix containing dense numbers of randomly oriented isolated crystalline PCL cores. Based on the values obtained from DSC, we employed the Fox equation to account for the composition of the multilayer film, as was done in previous work on PEO/PAA multilayers,[19] yielding about 90 wt % PEO-*b*-PCL and 10 wt % PAA within the film (81:19 wt % of PEO:PAA). This result suggests the potential for high drug loading within the film. For reference, (PEO/PAA)$_{100}$ bilayer films assembled under analogous assembly condi-

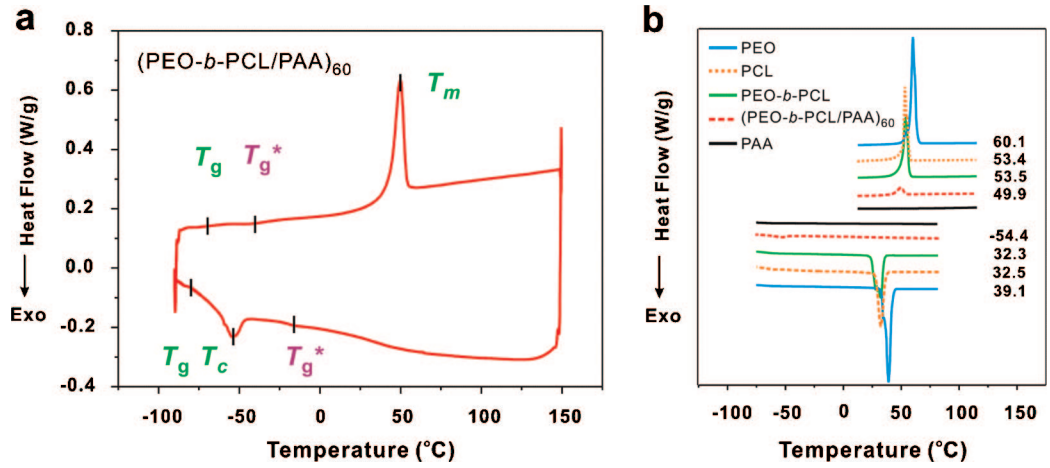


Figure 3. (a) Differential scanning calorimetry graphs of free-standing (PEO-*b*-PCL/PAA)$_{60}$ film. (b) Comparison with pure components of the film. The number beside each graph indicates the peak position in °C. Note that the molecular weights of polymers in comparison are in very close range to each other, and the second scan is used throughout the experiment. All samples were equilibrated at 150 °C for 15 min before the temperature was ramped up at a rate of 10 °C/min under nitrogen.

tions yielded a film with a fraction of PEO reaching about 29 wt %, as determined by DSC.[19] The ratio between the block copolymer micelle and PAA can also be modulated by the assembly pH; for example, increasing assembly pH results in the ionization of the PAA block, which decreases both acid–acid dimerization between PAA acid groups and interaction with the PEO group through hydrogen bonding, thereby enriching PEO-*b*-PCL micelles within the film, as was similarly demonstrated with our previous (PEO/PAA) multilayer.[19] It should be noted, however, that the Fox equation is a simple model operating only for non-interacting polymer blends.[29] Although mechanical characterization of the micelle-containing films was not undertaken, the (PEO-*b*-PCL/PAA)$_{60}$ film exhibited softer, more elastomeric behavior upon handling compared to (PEO/PAA)$_{100}$ films, indicating the higher percentage of rubbery, low-T_g PEO in the film. Moreover, it is found that the recrystallization temperature (T_c = −54.4 °C) of (PEO-*b*-PCL/PAA)$_{60}$ film is much lower than the T_m of any of its components in the cooling cycle (Figure 3b). We postulate that the fully hydrogen-bonded network between the PEO corona and PAA retards the crystallization of the PCL core of the micelle within the film during the cooling process. Previous reports on the crystallization of PCL similarly supported that the spontaneous formation of folded chains within a lattice structure is restricted by covalent bonds to other copolymer blocks.[30] It is also known that confinement within the block domain can decrease the melting point of the crystalline block.[31]

Hydrogen-bonded LbL films are of great interest, as they exhibit the unique feature of film disintegration upon external pH changes.[19,22,32,33] For example, the carboxylic acid group on PAA used to assemble the film as a hydrogen bond donor is deprotonated above a critical pH, thereby breaking the hydrogen-bonded network with PEO to deconstruct the film. In order to evaluate the disassembly of the hydrogen-bonded film under physiological conditions, we exposed a film deposited on a silicon wafer to phosphate-buffered saline (PBS) at pH 7.4. As illustrated in Figure 4a, as soon as the film is exposed to PBS, the deconstruction of the film proceeds through rapid bulk disintegration rather than gradual surface erosion, as the originally smooth

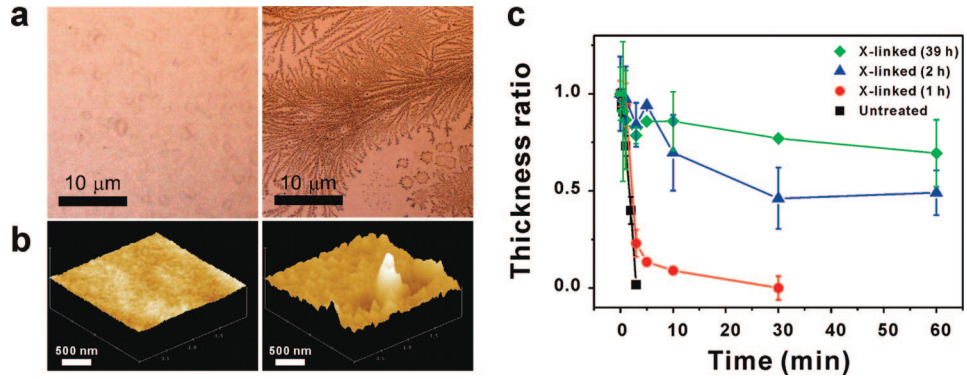


Figure 4. Deconstruction of a hydrogen-bonded (PEO-*b*-PCL/PAA)$_{30}$ film in PBS buffer at pH 7.4. (a) Optical microscope and (b) AFM images of the film surface (left) before and (right) after incubation in PBS buffer for 2 min. (c) Change of film thickness as measured by profilometry. The thickness of the as-prepared film rapidly decreases and the surface becomes rougher upon introduction to PBS buffer, whereas the cross-linked films do not undergo immediate film deconstruction. Note that the *Z*-scale in the AFM image (left) is 25 nm, whereas that on the right is 100 nm. Error bars represent the average standard deviation of measured thickness values from five different locations on the film.

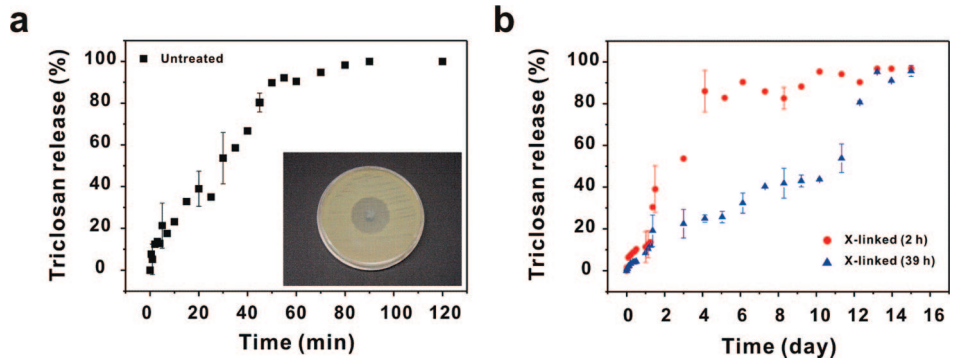


Figure 5. Release profile of triclosan from (PEO-*b*-PCL/PAA)$_{30}$ film in PBS buffer at pH 7.4 (a) Non-cross-linked film. The inset shows a sample set of Kirby−Bauer disk diffusion assay from non-cross-linked film. (b) Cross-linked film with different degrees of linking. All release profiles are normalized with untreated control sample with the same surface area and averaged over two measurements. Kirby−Bauer assay clearly demonstrated the efficacy of triclosan-loaded (PEO-*b*-PCL/PAA)$_{30}$ antimicrobial films deposited on a silicon wafer in inhibiting the growth of *Staphylococcus aureus*. Cross-linking significantly enhanced the duration of triclosan release compared to that of untreated, non-cross-linked sample.

film becomes significantly rougher, nonuniform, and pitted with the progress of film deconstruction (Figure 4b). The thickness of the portions of film remaining on the surface was determined to decrease linearly with respect to time of exposure to PBS over a 3 min time period (Figure 4c). Furthermore, we could also tailor the rate of film deconstruction by introducing cross-linking between carboxylic acid groups in PAA to form anhydride linkages *via* heat treatment,[19] which would resist the film degradation for an extended period of time under the identical condition (Figure 4c). For example, cross-linked films (>2 h) persist even for hours in a swollen state as opposed to the untreated (PEO-*b*-PCL/PAA)$_{30}$ film, which dissolves in PBS buffer within minutes. One-hour cross-linked film, on the other hand, does not enhance the film resistance to the PBS buffer to a large extent, possibly due to the low degree of anhydride linkage formation between PAA.

Finally, to examine the potential of this micelle-containing LbL film as a platform for hydrophobic therapeutic delivery, we encapsulated an antibacterial drug, triclosan, within PEO-*b*-PCL micelles and assembled them into LbL thin films with PAA (as shown in Scheme 1). The drug content in a micelle was evaluated by measuring the absorbance of triclosan (λ_{max} = 276 nm), which corresponds to approximately 25 wt % of PEO-*b*-PCL. Film growth was also followed by the measurement of triclosan incorporated as a function of number of bilayers in the film, indicating a linear growth profile similar to that previously demonstrated without the drug. In order to determine the efficacy of the release of triclosan from the micelle LbL film, we conducted a Kirby−Bauer assay, which is a common antibiotic susceptibility test.[34] For comparison, LbL films of (PEO-*b*-PCL/PAA)$_{30}$ with and without triclosan on a silicon substrate (*ca.* 0.5 × 0.5 cm^2) were assayed against Gram-positive *Staphylococcus aureus*, a bacterial species responsible for many biomedical device infections. As the films are incubated on the bacterial agar plates, the drug diffuses out of the micelles and inhibits the growth of the bacteria, leaving a circular area free of bacteria, called a zone of inhibition (ZOI). The ZOI of the film containing triclosan was around 15.0 ± 0.7 mm, whereas the control film without triclosan did not show any bacterial growth inhibition. No residual film was observed on the substrate after the assay, suggesting that the entire film was deconstructed under physiological conditions to release drug-loaded micelles and, eventually, to allow diffusion of antibacterial triclosan to the surrounding medium to inhibit the bacterial growth. However, thermal cross-linking of the film would provide a tighter mesh-like structure within the film, thereby preventing the micellar structures from releasing into the medium to release the drug. The release kinetics of triclosan were also evaluated by measuring the drug release from LbL films after incubation in PBS buffer. Drug release lasted for 90 min for the untreated, non-cross-linked (PEO-*b*-PCL/PAA)$_{30}$ film, whereas the cross-linked film exhibited a significantly longer release lasting up to 4 days for a 2 h cross-linked film and 13 days for a 39 h cross-linked film (Figure 5). This is a unique feature of the hydrogen-bonded system, for which simple postmodification to introduce internal cross-links within the LbL film enables the control of the release kinetics of active small, hydrophobic therapeutics from 90 min to up to 13 days in duration of drug release. We expect that this fine control over the release profile will be highly advantageous for potential use in biological applications that require a controllable release of active therapeutics with respect to their needs. For example, untreated, non-cross-linked films would be interesting for wound dressings and therapeutic surface coatings, where an immediate delivery of therapeutics is necessary upon contact with the film. In contrast, cross-linked film would be useful as a carrier for active therapeutics on biomaterial surfaces for an extended period of time. Quantitatively, the amount of triclosan released was calculated on the basis of UV–vis measurements to be 45.1 μg/cm^2 for a (PEO-*b*-PCL/PAA)$_{30}$ film (*ca.* 0.5 × 0.5 cm^2), which is well above the known minimal inhibitory concentration of triclosan to *S. aureus* (10 ng/mL).

CONCLUSION

In summary, we have established that incorporated polymeric micelles can be utilized as nanometer-sized vehicles for hydrophobic, neutral therapeutics that

would otherwise be difficult to incorporate within LbL films. The assembly of these LbL films utilized the hydrogen bonding between biodegradable, amphiphilic block copolymer micelles of PEO-*b*-PCL and PAA. Due to the sensitive nature of the hydrogen bond, we were able to demonstrate the disintegration of the LbL film to release micelles under physiological conditions. Moreover, by taking advantage of weak interactions of the film with the hydrophobic substrates, we were able to isolate a free-standing LbL thin film, which may make this approach of interest for a broad range of applications. The ability to obtain free-standing films allowed us to characterize the internal structure by TEM and to determine the composition of the film by DSC. Finally, micelle LbL films loaded with antibacterial triclosan were fully functional in inhibiting the growth of *S. aureus*. We have also established tailoring the rate of film deconstruction and drug release by introducing cross-links between the PAA acid groups within the multilayer film structure. Overall, we anticipate that this hydrogen-bonded micelle LbL approach will provide a general means to deliver active therapeutics in biomedical applications for therapeutic surface coatings with controllable release properties.

METHODS

Materials. Poly(acrylic acid) (PAA, M_w = 90 000, 25% aqueous solution) was obtained from Polysciences Inc. (Warrington, PA). Amphiphilic block copolymer, poly(ethylene oxide)$_{114}$-*block*-poly(ε-caprolactone)$_{60}$ (PEO-*b*-PCL, M_n(PEO) = 5000, M_n(PCL) = 6500, PDI = 1.3) was purchased from Polymer Source (Montreal, Canada). PEO (M_n = 5000) and PCL (M_n = 8000) were used for comparison. All other reagents and solvents were purchased from Aldrich and used as received. Quartz slide, silicon wafer, Teflon, and polypropylene were used as substrates for the LbL assembly and cleaned extensively prior to the deposition.

Micelle Formation. Block copolymer micelles of PEO-*b*-PCL were prepared according to a modification of a literature method.[17] Briefly, a stock solution of PEO-*b*-PCL was freshly prepared in tetrahydrofuran (THF) at a concentration of 10 mg/mL. Then, 200 μL of stock solution was placed in a vial with a gentle stirring. To this solution was gradually added 5.0 mL of Millipore water (18 MΩ · cm) with vigorous stirring. After an additional 1 h of stirring, the resulting suspension was subjected to dialysis against Millipore water for over 24 h (Spectra/Por 4 regenerated cellulose membrane, MWCO = 12 000–14 000) to remove any residual solvent. The resulting PEO-*b*-PCL micelle was filtered prior to use. The pH of the resulting micelle suspension was adjusted with 0.10 M HCl solution right before LbL film formation. For triclosan loading, we followed a modification of a literature protocol.[35] Briefly, triclosan solution in CH_2Cl_2 (concentration 1.0 mg/mL) was dropwise added to 5.0 mL of the micelle suspension prepared above (0.40 mg/mL). The emulsion was vigorously stirred overnight with a loose cap to evaporate the organic solvent. The solution obtained was centrifuged (4500 rpm, 10 min) and filtered through a 0.45 μm syringe filter. The drug content in a micelle was evaluated by measuring the characteristic absorbance of triclosan (λ_{max} = 276 nm) in a solvent mixture of MeOH and H_2O (9:1 v/v), employing a calibration curve with a known concentration of triclosan using an Agilent 8453 UV–visible spectrometer.

LbL Film Assembly. All LbL films were assembled with a modified programmable Carl Zeiss HMS slide stainer. Typically, films were constructed on various substrates with approximate size of 1 × 2 in^2. The substrate was first dipped into PEO-*b*-PCL micelle solution (0.40 mg/mL, pH 2.5) for 10 min and rinsed three times with water (pH 2.5) for 1 min each. Subsequently, the substrate was introduced into aqueous solution of PAA (20 mM, concentration of repeating unit, pH 2.5) for 10 min and washed again three times with water (pH 2.5) for 1 min each. This cycle provides one bilayer of PEO-*b*-PCL micelle and PAA polymer, denoted (PEO-*b*-PCL/PAA)$_1$. The dipping process was repeated until the desired number of bilayers was obtained. Similarly, triclosan-loaded micelles were assembled with PAA according to the same protocol.

LbL Film Characterizations. Film thickness was measured with a Tencor P-10 surface profilometer. Epoxy-embedded free-standing thin film was cryo-microtomed for cross-section TEM measurement (JEOL JEM 200CX). A thin slice of carbon-coated thin film was measured by TEM operated under a voltage of 200 kV. The thermal property of free-standing film was characterized on a TA Instruments Q50 thermogravimetric analyzer. The films were equilibrated at 150 °C for 15 min before the temperature was ramped up at a rate of 10 °C/min. A second scan was collected to report. The surface morphology of the LbL film was observed by using a Nanoscope IIIa atomic force microscope (Digital Instruments, Santa Barbara, CA) in tapping mode in air.

pH-Induced Film Deconstruction. Film deconstruction was observed through profilometry measurement of a (PEO-*b*-PCL/PAA)$_{30}$ film built on a silicon substrate. After exposure to PBS buffer (pH 7.4) for a predetermined time, each sample was dried gently with air, and the thickness of the film left on the substrate was measured. These films were also observed with tapping-mode AFM in air.

Drug Release from LbL Film. Drug release from the LbL gilm was followed by measuring UV–vis spectra of released triclosan (λ_{max} = 280 nm) from a (PEO-*b*-PCL/PAA)$_{30}$ film built on a silicon substrate (*ca.* 0.5 × 0.5 cm^2). After incubation of the film in a cuvette containing PBS buffer (pH 7.4, 1 mL) for a predetermined time, each spectrum was collected with using Agilent 8453 UV–visible spectrometer. Cross-linked samples were also measured with the same protocol until no more changes in the UV–vis spectrum were observed. All measurements were conducted in duplicate.

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Supporting Information Available: FTIR-ATR spectrum of (PEO-*b*-PCL/PAA)$_{60}$ free-standing film, magnified TEM image of free-standing (PEO-*b*-PCL/PAA)$_{60}$ film, AFM of PEO-*b*-PCL micelles, model dye loading and release experiments on preassembled (PEO-*b*-PCL/PAA)$_{20}$ film, and FT-IR spectrum of triclosan-loaded (PEO-*b*-PCL/PAA)$_{30}$ film. This material is available free of charge *via* the Internet at http://pubs.acs.org.

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