Journal of Applied Polymer Science

REVIEW

Dynamically Bonded Layer-by-Layer Films: Dynamic Properties and Applications

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ABSTRACT: Layer-by-layer (LBL) assembly, a simple but versatile method for thin film fabrication, has been widely employed to fabricate nanoengineered films with controlled composition and thickness. Dynamically bonded LBL films are films fabricated using dynamic bonds, that is, chemical bonds which can undergo reversible breaking and reformation usually under equilibrium conditions, as driving forces. Because of the reversible, dynamic nature of the dynamic bonds, these films exhibit various dynamic properties, ranging from a small scale movement of the polymer chains within the films (chain rearrangement), to a large scale movement of the chains, which results in film disintegration. Usually an external stimulus is used to trigger the response of a dynamic film. Novel applications have been proposed by exploiting the dynamic properties of these films. © 2014 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2014**, *131*, 40918.

KEYWORDS: coatings; drug delivery systems; films

Received 12 March 2014; accepted 28 April 2014

DOI: 10.1002/app.40918

INTRODUCTION

The last two decades have witnessed a tremendous advance in layer-by-layer (LBL) assembly, a thin film fabrication method, which was originally developed by Decher et al. in early 1990s.[1–3] In this method, two polymers with complementary functional groups are deposited alternately onto a substrate in a LBL fashion (Figure 1).[4,5] This method offers many advantages over other methods. It does not require any special equipment. Films can be assembled on not only planar substrates, but also those having complex shapes and irregular topographies. More importantly, it allows precision control over the compositions and thicknesses of the resulting films.[4,5] Today LBL assembly has been developed as a highly versatile platform for the synthesis of nanoengineered, functional composite films.

In the early days many efforts were devoted to the development of durable films with high mechanical stability, which is a prerequisite for their use as passive coatings. To improve film stability, the film structures were usually locked via covalent crosslinking.[6–13] Besides passive coatings, however, LBL films have found many other applications, such as drug delivery, biosensing, and bioreactors.[14–16] In many of these applications, the films are required to change their composition, structure and properties in response to a certain external stimulus. In this context, LBL films with smart and dynamic properties are attracting more and more attentions in recent years.

A novel way to design smart LBL films is the use of dynamic bonds as the driving forces for their fabrication. Previously, Lehn et al.[17,18] proposed that smart polymers can be designed by introducing dynamic bonds into polymer structure. Dynamic bonds are chemical bonds that can selectively undergo reversible breaking and reformation, usually under equilibrium conditions. There are two categories of dynamic bonds: noncovalent and covalent ones.[18] Noncovalent dynamic bonds are supramolecular interactions, such as π–π stacking, hydrogen bonding, and so on, while dynamic covalent bonds are covalent bonds that can break and reform under appropriate conditions without irreversible side reactions. Polymers with dynamic bonds in their structure were named as "dynamers" or dynamic polymers.[17–19] These polymers display dynamic properties such as a changeable and tunable constitution even after polymerization, which are originated from the dynamic nature of the dynamic bonds.

In fact, LBL films have been fabricated using various interactions as the driving forces, including electrostatic interactions, covalent bonding, hydrogen bonding,[20–23] metal ion coordination,[24] charge transfer interaction,[12,25] biological affinity,[26–29]

Dedicated to Professor Weixiao Cao, Peking University, China, for his 80th birthday in November 2014.

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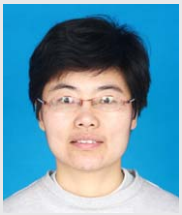

Yongjun Zhang earned his BS from Wuhan University in 1992, MS from Institute of Photographic Chemistry, CAS, in 1995, and PhD from Peking University in 2001. From 2001 to 2003, he worked at Institute of Chemistry, CAS, then he conducted his postdoctrol study at Oklahoma State University and City University of New York. He joined Nankai University in 2006 as a professor.

and so on. Most of these interactions are reversible and can be regarded as dynamic bonds. These dynamically bonded LBL films, like dynamic polymers, also show dynamic properties, and therefore can be called "dynamic LBL films".[30] This review summarizes the dynamic properties of dynamic LBL films reported in the literature and their applications based on their dynamic properties.

DYNAMIC PROPERTIES OF DYNAMIC LBL FILMS

The literature has reported various dynamic properties of the dynamic LBL films, ranging from chain rearrangement in the film to film disintegration due to the breakage of these bonds, all of which are originated from the dynamic nature of the dynamic bonds.

Chain Rearrangement Within the Films

Unlike the films crosslinked with irreversible covalent bands, in dynamic LBL films, the reversible nature of the crosslinks enables the rearrangement of polymer chains in the film. Because hydrogen bonding is relatively weak, in hydrogen-bonded LBL films the chain mobility is high and chain rearrangement is easy to occur. For example, when soaking the hydrogen-bonded poly(vinyl pyrrolidone) (PVPON)/poly(acrylic acid) (PAA) films in water, the defects in the films can be healed via chain rearrangement. As a result, the films become more transparent.[31,32] In addition the film surface becomes smoother[31] (Figure 2). Very recently it was found that compressive stress within the PVPON/PAA film can be relieved via chain rearrangement; therefore, swelling-induced wrinkling pattern on the film surface can be self-healed.[33] It is noteworthy that chain rearrangement can only occur in wet films, not in dry films.[31]

Chain rearrangement is difficult to occur in electrostatic LBL films because of the strong electrostatic interaction among the polymer chains. Even so chain arrangement has long been observed in electrostatic LBL films, particularly during the film buildup.[5] The reorganization of polymer chains in the films is considered to be the physical origin of the nonlinear growth of some polyelectrolyte multilayers.[34,35] In addition, one can weaken the electrostatic interaction by adding salt, and thus significantly enhance the chain mobility. It was found electrostatic LBL films can be smoothed via a brief annealing in high salt concentration solutions.[36,37] Besides ionic strength, chain mobility in electrostatic LBL films may also be affected by solution pH,[38] type of salt,[39] temperature,[39,40] charge density,[41] and molecular weight of the polyelectrolytes.[42] Rubner et al.[43–46] found a brief immersion of PAA/poly(allylamine) (PAH) films in acidic solution results in a substantial and irreversible transformation of the film morphology. The resulting porous films can be used as antireflection coatings[43] and many other applications.[45] Recently, it was found that severe damage on some electrostatic LBL films can self-heal when exposing to water.[47,48] The ability to self-heal was attributed to the reversible nature of electrostatic interaction and the chain mobility in the films.

Tunable Swelling Degree

The LBL films are crosslinked networks of polymer chains, therefore can be regarded as a special type of hydrogels.[49] Like ordinary hydrogels, LBL films swell in water and other solvents.[33,36,37,50–53] It is highly desirable if a film can alter its swelling degree in response to external stimuli.[49] In dynamic LBL films, the polymer chains are crosslinked with dynamic, reversible bonds. Their equilibrium of breaking and reformation can be shifted by many external stimuli, resulting in a changed crosslink density of the film, and, in turn, a changed swelling degree.

Dubas and Schlenoff[36] measured the swelling degree of several electrostatic LBL films in salt solutions by *in situ* atomic force microscopy. These films were found to swell to a different degree, depending on the polyelectrolyte pair constituting the films. Generally the films swell to a larger degree with increasing NaCl concentration, because the reaction equilibrium in the multilayer films can be shifted by the salt:

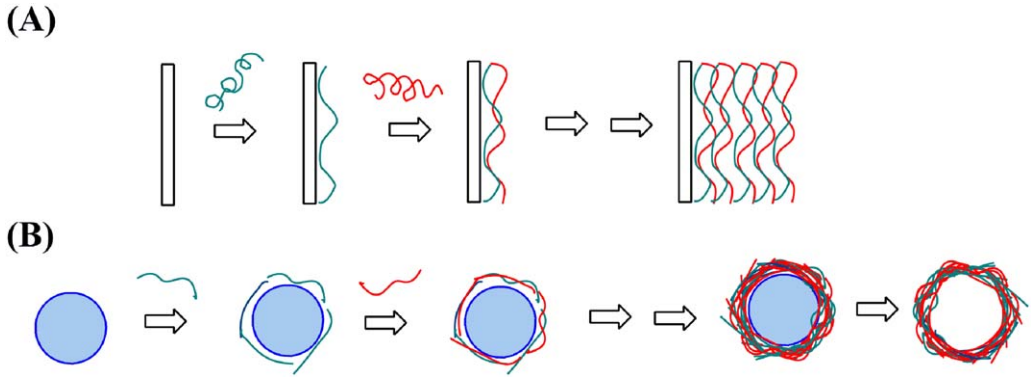

Figure 1. Fabrication of LBL films on planar substrates (A) and on the surface of colloidal particles (B). In the later case, removal of the colloidal template affords hollow LBL capsules. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

$$\mathrm{pol}^{\oplus}\mathrm{pol}^{\ominus}{}_{m}+\mathrm{Na}^{\oplus}_{aq}+\mathrm{Cl}^{\ominus}_{aq}\rightleftharpoons\mathrm{pol}^{\oplus}\mathrm{Cl}^{\ominus}_{m}+\mathrm{pol}^{\ominus}\mathrm{Na}^{\oplus}_{m}$$

where "m" refers to the multilayer film, and "aq" the aqueous solution.

Another example is the increasing swelling of poly[acrylamide-*co*−3-(acrylamido)-phenylboronic acid (P(AAm-AAPBA))/poly(vinyl alcohol) (PVA) film with increasing glucose concentration.[50] In P(AAm-AAPBA)/PVA film the polymers bind together via phenylboronate ester bond, a reversible covalent bond. Because glucose can compete with PVA for the phenylboronic acid (PBA) binding sites, addition of glucose can reduce the cross-link density of the film, thus increase its swelling degree (Figure 3). Glucose may also bind with the free PBA groups and convert them from a neutral, hydrophobic form to a negatively charged, hydrophilic form.[54–56] The increased charge density of the P(AAm-AAPBA) polymer is also favorable for film swelling.

Gradual Disintegration Under Conditions of Equilibrium Control

The dynamic nature of dynamic LBL films is also reflected in that they disintegrate under certain conditions. A unique property of dynamic LBL films is that they may disintegrate gradually under conditions of equilibrium control, that is, just immersing in water.

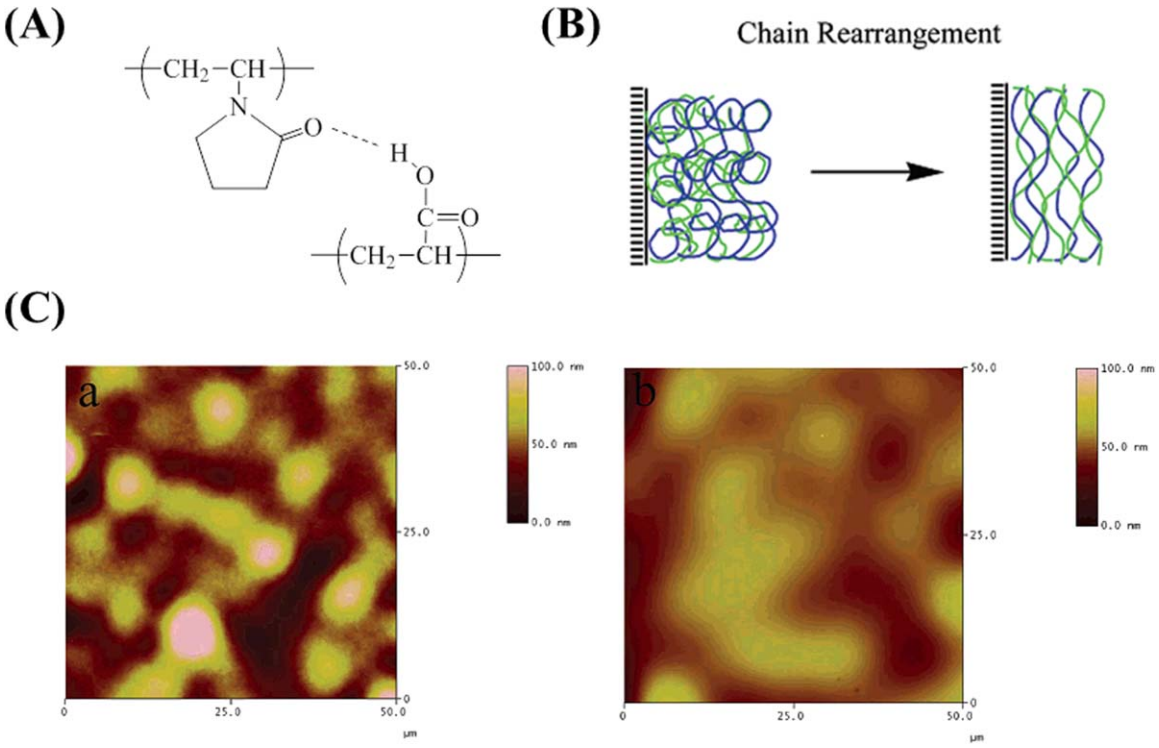

Figure 2. (A) Reversible hydrogen bonding between PVPON and PAA in PVPON/PAA films. (B) A schematic illustration of the chain rearrangement in PVPON/PAA films. (C) Surface morphology of a PVPON/PAA film before (a) and after (b) annealing in water (Reproduced from Ref. 31, with permission from American Chemical Society). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

For example, when immersing a hydrogen bonded PVPON/PAA film in deionized water, the film thickness decreases gradually with increasing immersion time, indicating the gradual disintegration of the film.[31] The film disassembly is attributed to the shift of equilibrium of the following reaction because of the reversible complexation between PVPON and PAA:

$$\text{PVPON} + \text{PAA} \rightleftharpoons \text{PVPON/PAA (complex)}$$

In most cases, the film thickness decreases linearly with annealing time, suggesting the film is eroded gradually from the top to the bottom. The erosion rate increases with increasing pH because more carboxylic acid group will deprotonate and thus weaken the interaction between PVPON and PAA. Interestingly, addition of NaCl accelerates the film disintegration, because salt enhances the dissociation of PAA and partially breaks the hydrogen bonds in the films.[57] In general, the erosion rate decreases with the increasing polymer Mw.[31]

The gradual disintegration of PVPON/PAA film in deionized water is very different from the pH-induced disintegration of the same film (see below). First, the gradual film erosion occurs even at pHs much lower than the pKa of PAA. At these pHs, the hydrogen bonds between PVPON and PAA remain intact. Therefore, the film disintegration is not caused by the disruption of the hydrogen bonds. Second, the film disintegration is much slower in deionized water than in basic solutions. While pH-induced disintegration always occurs instantly, the disintegration in deionized water takes a much longer time, making this type of disintegration highly desirable for sustained drug release.

Besides PVPON/PAA films, gradual disintegration was also observed from other hydrogen bonded LBL films, such as the LBL hollow capsules using hydroxypropylcellulose (HPC) as hydrogen acceptor and PAA as hydrogen donor.[58] The disintegration rate of the capsule decreases with decreasing pH. Addition of NaCl can slow down the capsule disintegration because the repulsive interaction among the ionized groups can be effectively screened by high ionic strength, however, it cannot totally prevent the capsule wall from disassembling.

When soaked in aqueous solution, P(AAm-AAPBA)/PVA LBL film, which is linked with reversible phenylboronate ester bonds, also disassociates and releases soluble PVA and P(AAm-AAPBA) polymer into the solution.[59] The film disintegration rate can be adjusted by various external stimuli. Increasing pH accelerates it, while increasing ionic strength retards it. Furthermore, the film disintegration rate can be tuned by glucose. Because glucose competes with PVA for PBA groups and weakens the interaction between the two polymers (Figure 3), the film disintegration rate increases with increasing glucose concentration.

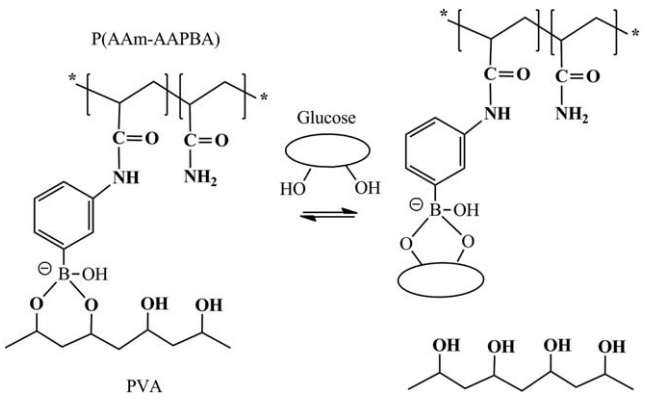

Figure 3. Reaction between P(AAm-AAPBA)/PVA and glucose.

Disintegration by Bond Disruption

Besides the gradual disintegration under conditions of equilibrium control, dynamic LBL films undergo instant disintegration as a result of the disruption of the dynamic bands. This type of disintegration has been reported widely in the literature. It is noteworthy that the disintegration of dynamic LBL films by bond disruption is different from the film disintegration via the chemical degradation of one of the polymer components. In the later case, the films were fabricated from a degradable polymer and a nondegradable polymer. When immersing in aqueous solutions, the degradable component degrades via hydrolysis[60–65] or a reduction reaction in the presence of a reducing agent,[66] resulting in the disintegration of the film. Unlike this kind of film disintegration, both components of the dynamic LBL film remain intact during the film disintegration.

Disintegration of Electrostatic LBL Films. Electrostatic LBL films are usually very stable; however, they can also undergo disintegration when the electrostatic interaction among the polymer chains are effectively weakened.[67–71] Dubas and Schlenoff[72] studied the disintegration of electrostatic LBL films in which a weak polyacid was used as the anionic polyelectrolyte. Two methods were developed to loosen the interactions among the polymer chains. The first one is to raise the ionic strength of the solution. With the competition of the polymer/polymer ion pairs by external salt ions, the films decompose rapidly and completely. This method requires a high NaCl concentration ($>0.6M$). In the second method, the polymer/polymer interactions were loosened by protonating the weak acid. However, lowering pH can only partially disintegrate the films. The incomplete loss of polymer was attributed to additional hydrogen bonding from the protonated polyacid.

When a polyzwitterion is involved in the electrostatic LBL films, the films can be disrupted more easily. Kharlampieva et al.[73] first studied the LBL assembly of polycarboxybetaines, which are zwitterionic at neutral to basic pH values, but become cationic when the carboxylic groups are protonated at low pH. LBL films can be assembled from polycarboxybetaine and a polyanion at a low pH; however, the resulting films dissolve when increasing pH value above a critical value, because polycarboxybetaine becomes polyzwitterion and its interaction with the polycation is reduced. Similarly, Gui et al.[74] assembled films from poly(4-vinylpyridiniomethanecarboxylate) (PVPMC) and PAA. They found the disintegration of PVPMC/PAA films can be controlled by the salt concentration in the aqueous solutions. Particularly the films could be completely disintegrated in 0.9% normal saline solution within 15 min. Later the same group[75] fabricated LBL films using a new polycarboxybetaine incorporated with ester groups. Film disintegration can be further controlled by the hydrolysis of the ester groups.

Alternatively, LBL films can be fabricated from a precursor polyzwitterion. Under proper conditions, the precursor polyzwitterion turns into a real polyzwitterion, and the LBL films fall apart. For example, De Geest et al.[76] synthesized a PBA-containing polycation and used it to assemble LBL hollow capsules. In the presence of glucose, the neutral PBA groups will become negatively charged PBA-glucose complex and the polycation turns into a polyzwitterion, therefore, the capsules dissolve quickly when brought into contact with a glucose-containing medium.

Another type of glucose-disintegrable electrostatic LBL films was developed by Manna and Patil.[77,78] In these films, PVA-borax complex acts as anionic polyelectrolyte and chitosan cationic polyelectrolyte. Because borate ions prefer to form a complex with glucose, therefore addition of glucose can break the bonds between PVA and chitosan, resulting in the disintegration of the LBL films and also hollow capsules.

Disintegration of Hydrogen-Bonded LBL films. Compared to electrostatic LBL films, it is much easier to disintegrate a hydrogen-bonded film, because hydrogen bonding is much weaker. One may break hydrogen bonds in the film and thus disintegrate the film by immersing it in polar solvents such as DMF.[79] A more popular method is to elevate pH, because a weak polyacid is usually used as the hydrogen donor in the film. At elevated pH, the weak polyacid dissociates, resulting in the disruption of the hydrogen bonds and the disintegration of the film.

Polycarboxylic acids, such as PAA or poly(methacrylic acid) (PMAA), are widely used as hydrogen-donor.[80] Sukhishvili and Granick[81,82] first studied the stability of the hydrogen-bonded LBL films consisting polycarboxylic acids. For each film they examined, there is a critical pH value, below which the film is stable while above which it disintegrates sharply. It was thought the critical pH is determined by the tradeoff between the electrostatic repulsions and hydrogen-bonding in the films. Therefore, LBL films in which the polymer pair forms stronger hydrogen bonds can tolerate a higher pH. Films using PMAA usually show a higher pH stability than PAA films, which is attributed to the presence of the methyl groups in PMAA, leading to stronger hydrophobic interactions that stabilize the film.[82,83] Using higher Mw polymer can slightly enhance the stability of the LBL film. However, Lee et al.[83] observed that PVA/PAA films containing PVA chains of different molecular weights exhibit essentially the same critical pH value. High ionic strength screens the electrostatic repulsions among the charged groups, and thus increases the film stability.[82] For films with a neutral, temperature-responsive polymer, such as poly(*N*-isopropylacrylamide) (PNIPAM) as hydrogen acceptor, the critical pH they can tolerate is also temperature-dependent.[84]

Besides polycarboxylic acids, polyphenols[22,85] can also be used as hydrogen donor to assemble LBL films. Similar to films from polycarboxylic acids, films constructed from polyphenols also disintegrate in high pH solutions. However, because their higher p*K*a compared to that of polycarboxylic acids, polyphenol films can tolerate a much higher pH. Their stability at physiological pH makes them suitable for biomedical applications.[86]

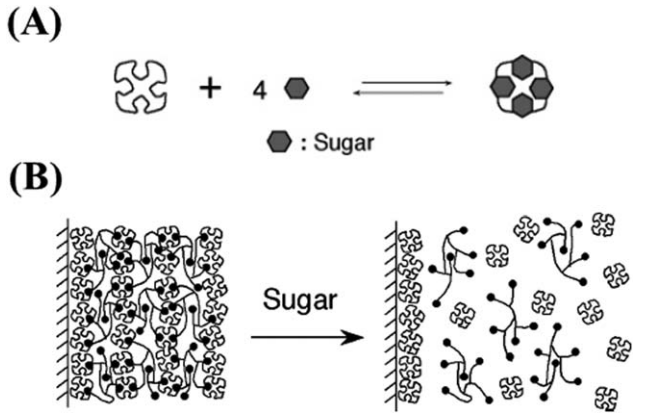

Figure 4. (A) Complexation between Con A and sugar. (B) Sugar-induced disintegration of a Con A/glycogen LBL film (Reproduced from Ref. 26, with permission from American Chemical Society).

Instead of elevating the bulk pH, Schmidt and Hammond[87] developed a method to electrochemically trigger the dissolution of hydrogen-bonded LBL films. When applied a cathodic potential to films fabricated on conductive substrates, the electrochemical reduction of dissolved oxygen generates OH^- ions, resulting in an increase in the local pH and, in turn, the dissolution of the film.

Zhang et al.[21,23,88–90] fabricated a series of hydrogen-bonded films also using polyacid such as PAA as hydrogen donor, but poly(4-vinylpyridine) (PVP) as hydrogen acceptor. These films also disintegrate at high pHs as a result of the dissociation of polyacids. While the soluble polyacids are released from the film, PVP, which is insoluble in a basic aqueous solution, remains on the substrate. It is interesting that the remaining PVP polymer chains rearrange gradually and finally produce a microporous film.[88–90]

Disintegration of Other Dynamic LBL films. Metal−ligand coordination bands were found to be involved in many LBL films.[91–95] These films can be disintegrated by adding a chelator for the metal ion, which captures the metal ions from the film and disrupts the coordination bands linking the polymer chains. As an example, LBL films were assembled through metal ion coordination from a polymer bearing bipyridine metal ion receptors and a metal salt. These films disassemble instantly when exposing to EDTA, because metal ions are captured by EDTA.[24]

LBL films were also fabricated based on the hydrophobic interaction among the polymer chains. Recently Zhao et al.[96] fabricated LBL films from two temperature-responsive homopolymers, poly(*N*-vinylcaprolactam) (PVCL) and poly(2-hydroxypropyl acrylate (PHPA). The hydrophobic interaction among the polymer chains is temperature-dependent; therefore, when the films are immersed in water at a temperature lower than the assembly temperature, they partially or completely dissolve, depending on the immersion temperatures.

LBL films assembled via phenylboronate ester bond can be disintegrated using pH or glucose as trigger.[97,98] For example, Levy et al.[98] fabricated LBL hollow capsules from mannan, a

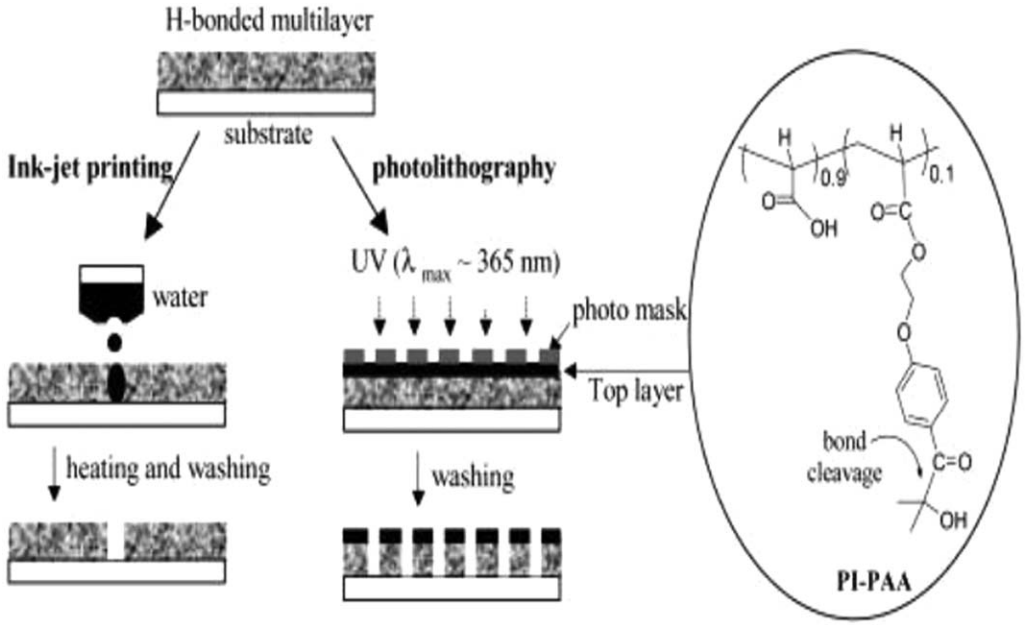

Figure 5. Patterning processes of PAA/PAAm films by ink-jet printing and photolithography (Reproduced from Ref. 7, with permission from American Chemical Society).

polysaccharide, and PAA grafted with PBA moieties (PAA-BOH). The capsules disintegrate when exposing to a low pH, because phenylboronate ester bond only forms at a high pH.[99–101] Also because sugar competes the PBA binding site with mannan, adding sugar rapidly dissolves the capsules. The sensitivity of the capsules to fructose is about one order of magnitude higher than to glucose, galactose, and mannose, because the equilibrium constants for the binding of fructose to PBA are one order of magnitude higher than for galactose, mannose, and glucose.[102,103]

LBL films based on biological affinity[26–29] are highly attractive considering their potential applications in biomedical areas. Concanavalin A (Con A) is a lectin protein containing four identical binding sites to sugars such as mannose and glucose. Exploiting this special interaction, LBL films were fabricated from Con A and glycogen.[26] The binding between Con A and sugar is not a covalent binding but a reversible one. In addition, because glucose can bind to the binding sites of Con A and thus remove the D-glucose residues of glycogen from the binding sites, addition of D-glucose can significantly accelerate the disintegration of Con A/glycogen LBL films (Figure 4). Other sugars, such as D-mannose, can also accelerate the film disintegration. Because D-mannose has a higher affinity to Con A, D-mannose induces the film disintegration more effective than D-glucose. In contrast, addition of D-galactose scarcely facilitates the film disintegration, because D-galactose is known not to bind to Con A.

Another biological affinity used for LBL film fabrication is avidin–biotin interaction.[104–106] Avidin is a glycoprotein found in egg white which contains four binding sites to biotin. This interaction is also reversible, therefore the resulting films can be disintegrated via the loosening of the interaction. Inoue et al.[107,108] found that LBL films from avidin and 2-iminobiotin-labeled poly(ethyleneimine) (ib-PEI) can be disintegrated by adding biotin or its analogs into the solution. The binding of the added biotin competes the binding site of avidin, weakens the interaction among the polymer chains and thus results in the film disintegration. The avidin/ib-PEI assemblies can also be disintegrated by lowering the pH of the solution, because the binding constant of 2-iminobiotin to avidin decreases with decreasing pH. The disintegration of avidin/ib-PEI films was further achieved electrochemically.[29] Upon application of an electric potential, the avidin/ib-PEI film, which was assembled on a Pt-coated quartz resonator, can be decomposed almost completely within a minute, due to a pH change in the vicinity of the electrode surface.

APPLICATIONS BASED ON DYNAMIC PROPERTIES

Surface Patterning

LBL films with a porous morphology can be obtained via a dewetting process, like other polymer thin films, such as polystyrene and poly(methyl methacrylate).[109,110] The dynamic nature of the dynamic LBL films allows for the polymer chains to diffuse within the film, which is a prerequisite for dewetting to occur.[111] Qin et al.[44] obtained a porous poly(sodium 4-styrenesulfonate) (PSS)/ poly(diallyldimethylammonium chloride) (PDDA) film by immersing the films in hot water to allow it to dewet. Other electrostatic LBL films were found to dewet and produce porous films too.[112–115] Hydrogen bonding is weaker than electrostatic interaction, therefore the dewetting of hydrogen bonded films can occur under milder conditions.[57,116]

Porous films can also be produced via the partial disintegration of the films. As mentioned above, the disintegration of PVP/PAA films in a basic solution results in microporous films because of the gradual reconformation of the remaining PVP polymer chains.[88–90] In another example, nanoporous LBL films

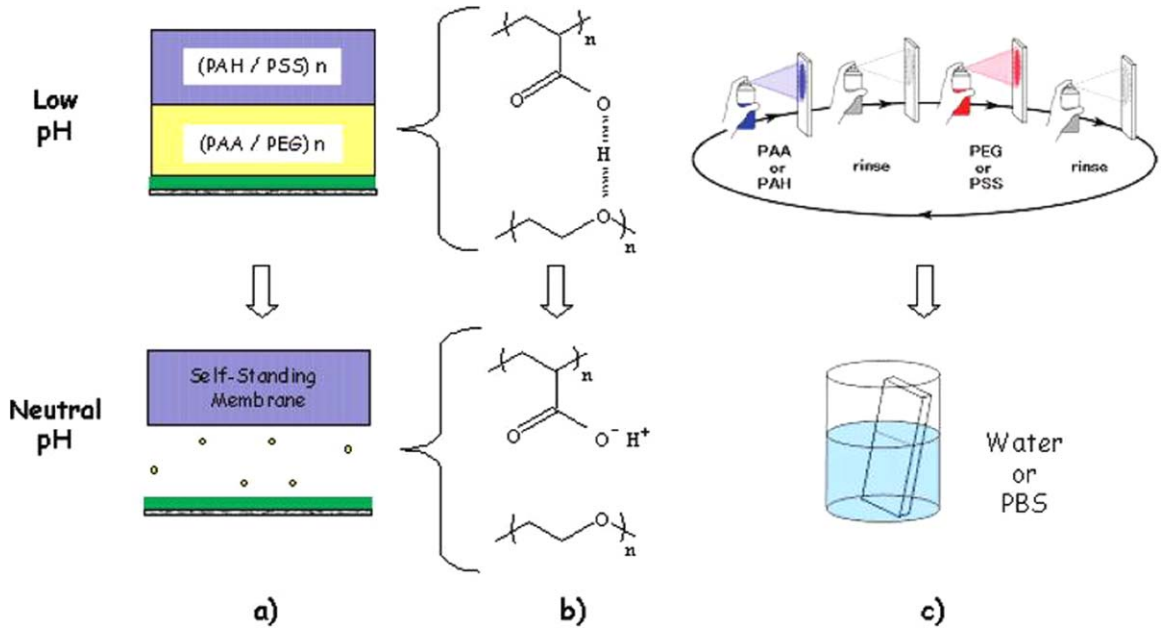

Figure 6. Releasing of self-standing PAH/PSS LBL films by pH-triggered disintegration of hydrogen-bonded PAA/PEG sublayer (Reproduced from Ref. 121, with permission from American Chemical Society). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

were prepared by partly disintegration of (PVPMC + PDDA)/PAA multilayer films in a 0.15*M* NaCl solution, using PVPMC/PAA as sacrificial template.[117]

Besides these spontaneously produced patterns, complex patterns can be obtained from dynamic LBL films via photolithography or other advanced patterning methods.[7,118] The hydrogen-bonded LBL films of PAA and polyacrylamide (PAAm) are stable at low pH but dissolved quickly in neutral pH water. By selective stabilization of the films, micropatterning can be achieved (Figure 5). In an ink-jet printing approach, an ink-jet printer was used to "print" pH 7.0 water onto the multilayer film followed by a thermal treatment at 95°C for 8 h. The regions "printed" with water are rendered noncrosslinkable due to ionization of the acid groups of PAA, and dissolve when rinsing with water, whereas the nonprinted regions become crosslinked by the heat treatment and remain when developing in water. In the case of photolithography, the film was covered with a photomask and irradiated with UV light. Similarly when washing with neutral water, the unirradiated region was removed but the irradiated and crosslinked region left.[7]

Sacrificial Sublayer for the Fabrication of Free-Standing Films

LBL films usually were fabricated on a solid substrate, however, for many potential applications, such as in the fields of thermomechanical sensing, controlled release, optical detection and drug delivery, free-standing films are highly desirable.[119] A general method to produce free-standing films is to use a sacrificial sublayer. The substrate is first coated with a sacrificial sublayer, followed by the deposition of the LBL assemblies (Figure 6). The LBL films are then released from the substrate via the dissolution of the sacrificial sublayer in an appropriate solvent. The erasable properties of dynamic LBL films make them good candidate to be used as sacrificial sublayer to produce free-standing LBL films.

Schlenoff et al.[72,121] first used electrostatic LBL multilayers as sacrificial sublayers to produce free-standing LBL films. Using PAA/PDDA as sacrificial sublayer, the PSS/PDDA upper stratum is quickly released from the substrate upon immersion in 1*M* NaCl. They also used pH-sensitive PSS/PDDA-*co*-PAA as sacrificial sublayer. In this case the upper layers were released by raising pH to >6. Electrostatic LBL films comprising of polyzwitterion are more sensitive than ordinary polyelectrolyte multilayers. For example, PVPMC/PAA can be disintegrated in 0.9% normal saline solution, therefore is a better choice as sacrificial sublayer.[74]

In term of the ability to disintegration, hydrogen bonded layers are superior to electrostatic LBL film. Many hydrogen bonded films can be decomposed under physiological conditions, making them good choice for sacrificial sublayers.[120] Besides free standing electrostatic LBL films, free-standing hydrogen-bonded films with a higher stability can be produced using hydrogen-bonded films more sensitive to pH change as sacrificial sublayers, taking advantages of their different critical pH for disintegration.[122] The hydrogen-bonded sublayers can be dissolved by immersion in a solution with pH higher than their critical pH, or by applying an electric potential, if they are fabricated on a conductive substrate.[87]

Drug Release

LBL films have been widely exploited as drug carriers.[16,123–126] Usually the drugs are loaded in the films and release via diffusion. In this case the LBL films act as diffusion barriers and the drug release rate can be controlled via the tuning of bilayer number of the coatings,[127] ionic strength,[128] pH, temperature,[129] and so on. Dynamic LBL films, however, provide a

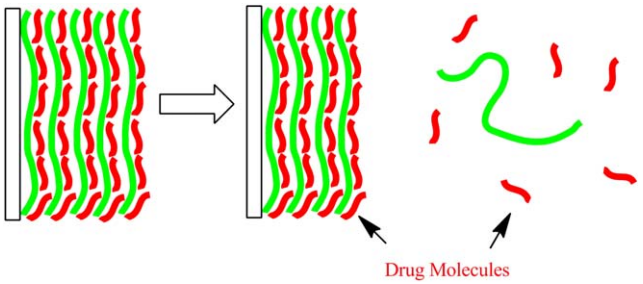

Figure 7. Drug release from dynamic LBL film as a result of the gradual disintegration of the film (Reproduced from Ref. 135, with permission from American Chemical Society). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

different way to release drug from the films, that is, via the disintegration of the films.

The abrupt disintegration of dynamic LBL films in response to an external stimulus has been exploited for instant drug release. Particularly model drugs were incorporated into hydrogen-bonded LBL films. The films disintegrate in response to pH, salt, or temperature change and thus release the drugs instantly.[57,87,130,131] Cao and He[132] synthesized a PVPON-based glucocorticoid prodrug and hydrogen-bonded PAA/prodrug multilayers on the surface of neural electrodes. When the electrodes were implanted into brain tissue, the physiological pH quickly released the film off the electrode surface, leading to an implanted bare electrode in the neural tissue surrounded by molecular components of the disintegrated film. Here the neural electrodes serve as a temporary support for film construction, transport the film to the tissue-electrode interface via implantation and effectively release therapeutics to a local area. At the same time the electrical functionality of the neural electrodes will not be damaged. As hydrogen-bonded films can also be decomposed electrochemically, electrically triggered drug delivery as part of an implantable "pharmacy-on-a-chip" or transdermal device can be designed.[87] For the delivery of hydrophobic drugs, Hammond et al.[133] fabricated hydrogen-bonded LBL films from PAA and amphiphilic block copolymer micelles, the latter of which was used as nanometer-sized vehicles for hydrophobic drugs. The film can be rapidly deconstructed to release the drug-containing micelles upon exposure to physiological conditions.

LBL films based on metal ion coordination disintegrate in the presence of a suitable chelator.[24,91] Based on this property, Dong et al.[134] developed a novel gene delivery system. They fabricated LBL films of DNA and zirconium (IV) ion (Zr^{4+}), which disassemble and release the incorporated DNA when incubated in a chelator solution. When plasmid DNA (pDNA) is incorporated, the released pDNA retain its integrity and transcriptional activity, and express enhanced green fluorescent protein (EGFP) after being transfected into HEK 293 cells.

It was known that cancer cells possess high concentration of glucose. Glucose-triggered anticancer drug delivery may be beneficial for cancer treatment. For this purpose, the LBL films of PVA-borate/chitosan were loaded with DOX. It was found more DOX molecules were released at a higher glucose concentration because of the disintegration of the films in the presence of glucose.[78]

The gradual disintegration of dynamic LBL films under conditions of equilibrium control is particularly desirable for sustained drug release (Figure 7). We[135] recently fabricated hydrogen-bonded LBL films from tannic acid (TA), a model polyphenolic drug, and PVPON. Like other hydrogen-bonded films, when soaked in aqueous solutions, the PVPON/TA films disassemble gradually and thus release TA to the media. The release rate of TA increases with increasing pH and temperature but decreases with increasing ionic strength. The released TA can scavenge $ABTS^{+\bullet}$ cation radicals, indicating it retains its antioxidant activity, a major biological activity of polyphenols.

In another example, dynamic LBL films based on phenylboronate ester bond were used to release insulin.[30] The films were fabricated from a insulin–PVA conjugate and P(AAm-AAPBA). Similarly, when immersed in an aqueous solution, the films disintegrate gradually and thus release insulin into the media. Insulin release rate increases with increasing pH and decreasing ionic strength of the media. More importantly, in the presence of glucose the films disintegrate at a faster rate and release insulin faster. This system has potential to be developed as a new self-regulated insulin release system.

Biosensing

One major property of dynamic LBL films is their stimuli-responsivity; therefore, they have potential to be used in biosensing. Using FRET (fluorescence resonance energy transfer) technique, Chinnayelka and McShane[27] designed a glucose sensor based on Con A-dextran LBL films. FRET is the radiationless transfer of energy between two fluorophores with overlapping emission and excitation spectra, which occurs if they are very close to each other (~10 nm). In the LBL films of FITC-dextran and TRITC-Con A, addition of glucose increases the distance between the two fluorophores, resulting in a decrease in FRET. The detection range of this sensor system was reported to be from 0 to 1800 mg/dL and the sensitivity be 4×10^{-4} ratio units/(mg/dL).

Another glucose sensor was developed based on the P(AAm-AAPBA)/PVA film. As mentioned above, the swelling degree of the film increases with increasing glucose concentration.[50] This event can be reported via the shift of Fabry−Perot fringes using the thin film itself as Fabry−Perot cavity. The response of P(AAm-AAPBA)/PVA film to glucose is linear and reversible. More importantly, the response is quite fast, making it possible to be used for continuous glucose monitoring.

CONCLUSIONS

Because of the reversible, dynamic nature of dynamic bonds, LBL films linked with dynamic bonds exhibit various dynamic properties, ranging from the small scale movement of the polymer chains in the films, or, chain arrangement, to a large scale movement of the chains, that is, film disintegrations. Numerous external stimuli, including physical ones such as temperature, pH and ionic strength, and chemical ones such as chelator, glucose and other biologically important molecules may trigger the response of a dynamic LBL film. When developing durable, passive

coatings, these dynamic properties are considered to be disadvantage and should be avoided. However, for the design of functional coating, these properties are highly desirable. Some novel applications exploiting these properties, especially drug delivery, have emerged in the literature. Considering the tremendous strength of LBL assembly, we expect that these nano-sized, intelligent materials will found more applications in the future.

ACKNOWLEDGMENTS

The authors thank financial support for this work from the National Natural Science Foundation of China (Grants Nos 21174070, 21274068, 21228401, and 21374048), Program for New Century Excellent Talents in University (NCET-11–0264), PCSIRT program (IRT1257), and Tianjin Public Health Bureau(13KG110).

REFERENCES

1. Decher, G.; Hong, J. *Makromol. Chem. Macromol. Symp.* **1991**, *46*, 321.
2. Decher, G.; Hong, J. D. *Ber. Bunsen Ges. Phys. Chem.* **1991**, *95*, 1430.
3. Decher, G.; Hong, J. D.; Schmitt, J. *Thin Solid Films* **1992**, 210, 831.
4. Decher, G. *Science* **1997**, *277*, 1232.
5. Bertrand, P.; Jonas, A.; Laschewsky, A.; Legras, R. *Macromol. Rapid Commun.* **2000**, *21*, 319.
6. Yang, S. Y.; Lee, D.; Cohen, R. E.; Rubner, M. F. *Langmuir* **2004**, *20*, 5978.
7. Yang, S. Y.; Rubner, M. F. *J. Am. Chem. Soc.* **2002**, *124*, 2100.
8. Liu, Y.; Bruening, M. L.; Bergbreiter, D. E.; Crooks, R. M. *Angew. Chem. Int. Ed.* **1997**, *36*, 2114.
9. Beyer, D.; Bohanon, T. M.; Knoll, W.; Ringsdorf, H.; Elender, G.; Sackmann, E. *Langmuir* **1996**, *12*, 2514.
10. Harris, J. J.; DeRose, P. M.; Bruening, M. L. *J. Am. Chem. Soc.* **1999**, *121*, 1978.
11. Sun, J.; Wu, T.; Sun, Y.; Wang, Z.; Zhang, X.; Shen, J.; Cao, W. *Chem. Commun.* **1998**, 1853.
12. Zhang, Y. J.; Cao, W. X. *Langmuir* **2001**, *17*, 5021.
13. Zhang, Y. J.; Cao, W. X. *Macromol. Rapid Commun.* **2001**, *22*, 842.
14. Tong, W. J.; Gao, C. Y. *J. Mater. Chem.* **2008**, *18*, 3799.
15. Such, G. K.; Johnston, A.; Caruso, F. *Chem. Soc. Rev.* **2011**, *40*, 19.
16. Tong, W.; Song, X.; Gao, C. *Chem. Soc. Rev.* **2012**, *41*, 6103.
17. Lehn, J. *Prog. Polym. Sci.* **2005**, *30*, 814.
18. Wojtecki, R. J.; Meador, M. A.; Rowan, S. *J. Nat. Mater.* **2011**, *10*, 14.
19. Maeda, T.; Otsuka, H.; Takahara, A. *Prog. Polym. Sci.* **2009**, *34*, 581.
20. Stockton, W. B.; Rubner, M. F. *Macromolecules* **1997**, *30*, 2717.
21. Wang, L.; Wang, Z.; Zhang, X.; Shen, J.; Chi, L.; Fuchs, H. *Macromol. Rapid Commun.* **1997**, *18*, 509.
22. Zhang, Y. J.; Guan, Y.; Yang, S. G.; Xu, J.; Han, C. C. *Adv. Mater.* **2003**, *15*, 832.
23. Wang, L. Y.; Fu, Y.; Wang, Z. Q.; Fan, Y. G.; Zhang, X. *Langmuir* **1999**, *15*, 1360.
24. Krass, H.; Papastavrou, G.; Kurth, D. G. *Chem. Mater.* **2003**, *15*, 196.
25. Shimazaki, Y.; Mitsuishi, M.; Ito, S.; Yamamoto, M. *Langmuir* **1997**, *13*, 1385.
26. Sato, K.; Imoto, Y.; Sugama, J.; Seki, S.; Inoue, H.; Odagiri, T.; Hoshi, T.; Anzai, J. *Langmuir* **2005**, *21*, 797.
27. Chinnayelka, S.; McShane, M. J. *J. Fluoresc.* **2004**, *14*, 585.
28. Lvov, Y.; Ariga, K.; Ichinose, I.; Kunitake, T. *J. Chem. Soc. Chem. Commun.* **1995**, 2313.
29. Sato, K.; Kodama, D.; Naka, Y.; Anzai, J. *Biomacromolecules* **2006**, *7*, 3302.
30. Zhang, X.; Guan, Y.; Zhang, Y. *J. Mater. Chem.* **2012**, *22*, 16299.
31. Guan, Y.; Yang, S. G.; Zhang, Y. J.; Xu, J.; Han, C. C.; Kotov, N. A. *J. Phys. Chem. B* **2006**, *110*, 13484.
32. Yang, S. G.; Zhang, Y. J.; Zhang, X. Y.; Guan, Y.; Xu, J.; Zhang, X. L. *Chemphyschem.* **2007**, *8*, 418.
33. Han, Q.; Li, C.; Guan, Y.; Zhu, X. X.; Zhang, Y. *Polymer* **2014**, *55*, 2197.
34. Guzmán, E.; Ritacco, H.; Ortega, F.; Rubio, R. G. *Colloid Surf. A Physicochem. Eng. Asp.* **2011**, *384*, 274.
35. Guzmán, E.; Ritacco, H. A.; Ortega, F.; Rubio, R. G. *J. Phys. Chem. C* **2012**, *116*, 15474.
36. Dubas, S. T.; Schlenoff, J. B. *Langmuir* **2001**, *17*, 7725.
37. McAloney, R. A.; Dudnik, V.; Goh, M. C. *Langmuir* **2003**, *19*, 3947.
38. Ankner, J. F.; Rubinstein, M.; Sukhishvili, S. A.; Kharlampieva, E. *Phys. Rev. Lett.* **2008**, *100*, 128303.
39. Nazaran, P.; Bosio, V.; Jaeger, W.; Anghel, D. F.; V. Klitzing, R. *J. Phys. Chem. B* **2007**, *111*, 8572.
40. Wong, J. E.; Zastrow, H.; Jaeger, W.; von Klitzing, R. *Langmuir* **2009**, *25*, 14061.
41. Xu, L.; Ankner, J. F.; Sukhishvili, S. A. *Macromolecules* **2011**, *44*, 6518.
42. Xu, L.; Selin, V.; Zhuk, A.; Ankner, J. F.; Sukhishvili, S. A. *ACS Macro Lett.* **2013**, *2*, 865.
43. Hiller, J.; Mendelsohn, J. D.; Rubner, M. F. *Nat. Mater.* **2002**, *1*, 59.
44. Qin, S.; Wei, D. S.; Liao, Q.; Jin, X. G. *Macromol. Rapid Commun.* **2006**, *27*, 11.
45. Zhai, L.; Nolte, A. J.; Cohen, R. E.; Rubner, M. F. *Macromolecules* **2004**, *37*, 6113.
46. Mendelsohn, J. D.; Barrett, C. J.; Chan, V. V.; Pal, A. J.; Mayes, A. M.; Rubner, M. F. *Langmuir* **2000**, *16*, 5017.
47. South, A. B.; Lyon, L. A. *Angew. Chem.* **2010**, *122*, 779.
48. Wang, X.; Liu, F.; Zheng, X.; Sun, J. *Angew. Chem. Int. Ed.* **2011**, *50*, 11378.

49. Kozlovskaya, V.; Kharlampieva, E.; Erel, I.; Sukhishvili, S. A. *Soft Matter* **2009**, *5*, 4077.
50. Zhang, X.; Guan, Y.; Zhang, Y. *Biomacromolecules* **2012**, *13*, 92.
51. Ding, Z. B.; Guan, Y.; Zhang, Y. J.; Zhu, X. X. *Polymer* **2009**, *50*, 4205.
52. Parveen, N.; Schönhoff, M. *Macromolecules* **2013**, *46*, 7880.
53. Guzmán, E.; Ritacco, H.; Rubio, J. E. F.; Rubio, R. G.; Ortega, F. *Soft Matter* **2009**, *5*, 2130.
54. Asher, S. A.; Alexeev, V. L.; Goponenko, A. V.; Sharma, A. C.; Lednev, I. K.; Wilcox, C. S.; Finegold, D. N. *J. Am. Chem. Soc.* **2003**, *125*, 3322.
55. Zhang, Y. J.; Guan, Y.; Zhou, S. Q. *Biomacromolecules* **2006**, *7*, 3196.
56. Kataoka, K.; Miyazaki, H.; Bunya, M.; Okano, T.; Sakurai, Y. *J. Am. Chem. Soc.* **1998**, *120*, 12694.
57. Lin, W.; Guan, Y.; Zhang, Y. J.; Xu, J.; Zhu, X. X. *Soft Matter* **2009**, *5*, 860.
58. Guan, Y.; Zhang, Y. J.; Zhou, T.; Zhou, S. Q. *Soft Matter* **2009**, *5*, 842.
59. Ding, Z. B.; Guan, Y.; Zhang, Y.; Zhu, X. X. *Soft Matter* **2009**, *5*, 2302.
60. Flessner, R. M.; Jewell, C. M.; Anderson, D. G.; Lynn, D. M. *Langmuir* **2011**, *27*, 7868.
61. Fredin, N. J.; Zhang, J. T.; Lynn, D. M. *Langmuir* **2005**, *21*, 5803.
62. Smith, R. C.; Leung, A.; Kim, B. S.; Hammond, P. T. *Chem. Mater.* **2009**, *21*, 1108.
63. Smith, R. C.; Riollano, M.; Leung, A.; Hammond, P. T. *Angew. Chem. Int. Ed.* **2009**, *48*, 8974.
64. Chuang, H. F.; Smith, R. C.; Hammond, P. T. *Biomacromolecules* **2008**, *9*, 1660.
65. Macdonald, M.; Rodriguez, N. M.; Smith, R.; Hammond, P. T. *J. Controlled Release* **2008**, *131*, 228.
66. Blacklock, J.; Handa, H.; Manickam, D. S.; Mao, G.; Mukhopadhyay, A.; Oupicky, D. *Biomaterials* **2007**, *28*, 117.
67. Kovacevic, D.; van der Burgh, S.; de Keizer, A.; Stuart, M. A. C. *Langmuir* **2002**, *18*, 5607.
68. Izumrudov, V.; Sukhishvili, S. A. *Langmuir* **2003**, *19*, 5188.
69. Mawad, D.; Molino, P. J.; Gambhir, S.; Locke, J. M.; Officer, D. L.; Wallace, G. G. *Adv. Funct. Mater.* **2012**, *22*, 5020.
70. Nolte, A. J.; Takane, N.; Hindman, E.; Gaynor, W.; Rubner, M. F.; Cohen, R. E. *Macromolecules* **2007**, *40*, 5479.
71. Schuler, C.; Caruso, F. *Biomacromolecules* **2001**, *2*, 921.
72. Dubas, S. T.; Schlenoff, J. B. *Macromolecules* **2001**, *34*, 3736.
73. Kharlampieva, E.; Izumrudov, V. A.; Sukhishvili, S. A. *Macromolecules* **2007**, *40*, 3663.
74. Gui, Z. L.; Qian, J. W.; An, Q. F.; Zhao, Q.; Jin, H. T.; Du, B. Y. *J. Mater. Chem.* **2010**, *20*, 1467.
75. Gui, Z.; Qian, J.; He, Y.; An, Q.; Wang, X.; Tian, C.; Sun, W. *J. Colloid Interface Sci.* **2011**, *361*, 122.
76. De Geest, B. G.; Jonas, A. M.; Demeester, J.; De Smedt, S. C. *Langmuir* **2006**, *22*, 5070.
77. Manna, U.; Patil, S. *J. Phys. Chem. B* **2009**, *113*, 9137.
78. Manna, U.; Patil, S. *ACS Appl. Mater. Interface* **2010**, *2*, 1521.
79. Zhang, H. Y.; Wang, Z. Q.; Zhang, Y. Q.; Zhang, X. *Langmuir* **2004**, *20*, 9366.
80. Kharlampieva, E.; Kozlovskaya, V.; Sukhishvili, S. A. *Adv. Mater.* **2009**, *21*, 3053.
81. Sukhishvili, S. A.; Granick, S. *J. Am. Chem. Soc.* **2000**, *122*, 9550.
82. Sukhishvili, S. A.; Granick, S. *Macromolecules* **2002**, *35*, 301.
83. Lee, H.; Mensire, R.; Cohen, R. E.; Rubner, M. F. *Macromolecules* **2012**, *45*, 347.
84. Zhuk, A.; Pavlukhina, S.; Sukhishvili, S. A. *Langmuir* **2009**, *25*, 14025.
85. Shutava, T.; Prouty, M.; Kommireddy, D.; Lvov, Y. *Macromolecules* **2005**, *38*, 2850.
86. Erel-Unal, I.; Sukhishvili, S. A. *Macromolecules* **2008**, *41*, 3962.
87. Schmidt, D. J.; Hammond, P. T. *Chem. Commun.* **2010**, *46*, 7358.
88. Fu, Y.; Bai, S.; Cui, S.; Qiu, D.; Wang, Z.; Zhang, X. *Macromolecules* **2002**, *35*, 9451.
89. Zhang, H. Y.; Fu, Y.; Wang, D.; Wang, L. Y.; Wang, Z. Q.; Zhang, X. *Langmuir* **2003**, *19*, 8497.
90. Bai, S. L.; Wang, Z. Q.; Zhang, X.; Wang, B. *Langmuir* **2004**, *20*, 11828.
91. Huang, X.; Schubert, A. B.; Chrisman, J. D.; Zacharia, N. S. *Langmuir* **2013**, *29*, 12959.
92. Zhang, W.; Zhang, A.; Guan, Y.; Zhang, Y.; Zhu, X. X. *J. Mater. Chem.* **2011**, *21*, 548.
93. Kurth, D. G.; Pitarch Lopez, J.; Dong, W. *Chem. Commun.* **2005**, 2119.
94. Zhang, G.; Ruan, Z.; Ji, S.; Liu, Z. *Langmuir* **2009**, *26*, 4782.
95. Zhang, W.; Song, J.; Liao, W.; Guan, Y.; Zhang, Y.; Zhu, X. X. *J. Mater. Chem. C* **2013**, *1*, 2036.
96. Zhao, Z.; Yin, L.; Yuan, G.; Wang, L. *Langmuir* **2012**, *28*, 2704.
97. Wang, B.; Liu, Z.; Xu, Y.; Li, Y.; An, T.; Su, Z.; Peng, B.; Lin, Y.; Wang, Q. *J. Mater. Chem.* **2012**, *22*, 17954.
98. Levy, T.; Dejugnat, C.; Sukhorukov, G. B. *Adv. Funct. Mater.* **2008**, *18*, 1586.
99. Bosch, L. I.; Fyles, T. M.; James, T. D. *Tetrahedron* **2004**, *60*, 11175.
100. Yan, J.; Springsteen, G.; Deeter, S.; Wang, B. *Tetrahedron* **2004**, *60*, 11205.
101. Guan, Y.; Zhang, Y. *Chem. Soci. Rev.* **2013**, *42*, 8106.
102. James, T. D.; Sandanayake, K. R. A. S.; Shinkai, S. *Angew. Chem. Int. Ed.* **1996**, *35*, 1910.
103. Springsteen, G.; Wang, B. H. *Tetrahedron* **2002**, *58*, 5291.

104. Anzai, J.; Kobayashi, Y.; Suzuki, Y.; Takeshita, H.; Chen, Q.; Osa, T.; Hoshi, T.; Du, X. *Sensor. Actuat. B Chem.* **1998**, *52*, 3.
105. Anicet, N.; Bourdillon, C.; Moiroux, J.; Savéant, J. *J. Phys. Chem. B* **1998**, *102*, 9844.
106. Takahashi, S.; Sato, K.; Anzai, J. *Anal. Bioanal. Chem.* **2012**, *402*, 1749.
107. Inoue, H.; Sato, K.; Anzai, J. *Biomacromolecules* **2004**, *6*, 27.
108. Inoue, H.; Anzai, J. *Langmuir* **2005**, *21*, 8354.
109. Reiter, G. *Phys. Rev. Lett.* **1992**, *68*, 75.
110. Xue, L.; Han, Y. *Prog. Polym. Sci.* **2011**, *36*, 269.
111. Karapanagiotis, I.; Evans, D. F.; Gerberich, W. W. *Langmuir* **2001**, *17*, 3266.
112. Zhang, J.; Fredin, N. J.; Lynn, D. M. *Langmuir* **2007**, *23*, 11603.
113. Fredin, N. J.; Zhang, J. T.; Lynn, D. M. *Langmuir* **2007**, *23*, 2273.
114. Zhang, L.; Zheng, M.; Liu, X.; Sun, J. *Langmuir* **2011**, *27*, 1346.
115. Lim, S. K.; Perrier, S.; Neto, C. *Soft Matter* **2013**, *9*, 2598.
116. Yang, S.; Li, Y.; Li, X.; Li, Y.; Zhang, X.; Xu, J. *Thin Solid Films* **2009**, *517*, 3024.
117. Gui, Z. L.; Qian, J. W.; Yin, M. J.; An, Q. F.; Gu, B. B.; Zhang, A. *J. Mater. Chem.* **2010**, *20*, 7754.
118. Shi, F.; Dong, B.; Qiu, D.; Sun, J.; Wu, T.; Zhang, X. *Adv. Mater.* **2002**, *14*, 805.
119. Jiang, C.; Tsukruk, V. V. *Adv. Mater.* **2006**, *18*, 829.
120. Ono, S. S.; Decher, G. *Nano Lett.* **2006**, *6*, 592.
121. Dubas, S. T.; Farhat, T. R.; Schlenoff, J. B. *J. Am. Chem. Soc.* **2001**, *123*, 5368.
122. Lee, H.; Sample, C.; Cohen, R. E.; Rubner, M. F. *ACS Macro Lett.* **2013**, *2*, 924.
123. Wohl, B. M.; Engbersen, J. F. J. *J. Controlled Release* **2012**, *158*, 2.
124. De Koker, S.; De Cock, L. J.; Rivera-Gil, P.; Parak, W. J.; Auzély Velty, R.; Vervaet, C.; Remon, J. P.; Grooten, J.; De Geest, B. G. *Adv. Drug Delivery Rev.* **2011**, *63*, 748.
125. Pavlukhina, S.; Sukhishvili, S. *Adv. Drug Delivery Rev.* **2011**, *63*, 822.
126. Zelikin, A. N. *ACS Nano* **2010**, *4*, 2494.
127. Dai, Z. F.; Heilig, A.; Zastrow, H.; Donath, E.; Mohwald, H. *Chem. Euro. J.* **2004**, *10*, 6369.
128. Ibarz, G.; Dahne, L.; Donath, E.; Mohwald, H. *Adv. Mater.* **2001**, *13*, 1324.
129. Peyratout, C. S.; Dahne, L. *Angew. Chem. Int. Ed.* **2004**, *43*, 3762.
130. Quinn, J. F.; Caruso, F. *Langmuir* **2004**, *20*, 20.
131. Kharlampieva, E.; Erel-Unal, I.; Sukhishvili, S. A. *Langmuir* **2007**, *23*, 175.
132. Cao, Y.; He, W. *Biomacromolecules* **2010**, *11*, 1298.
133. Kim, B.; Park, S. W.; Hammond, P. T. *ACS Nano* **2008**, *2*, 386.
134. Wang, F.; Wang, J.; Zhai, Y.; Li, G.; Li, D.; Dong, S. *J. Controlled Release* **2008**, *132*, 65.
135. Zhou, L.; Chen, M.; Tian, L.; Guan, Y.; Zhang, Y. *ACS Appl. Mater. Interface* **2013**, *5*, 3541.