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Programmed Degradation of DNA Multilayer Films**

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We report the design and assembly of DNA multilayer films with programmable degradation properties. The nanostructured DNA films are assembled through the layer-by-layer (LbL) assembly technique and can be programmed to degrade by subsequently introducing DNA strands of specific sequences. The strands preferentially hybridize to the building blocks that stabilize the film structure, causing the film to rearrange and degrade. The rate of degradation is influenced by both the availability and accessibility of the complementary DNA binding sites within the film, as well as the degree of crosslinking within the film. Similar results are obtained for DNA multilayer films assembled on planar and particle supports. This approach offers an avenue to tailor degradability features into DNA-based materials that may find application in the biosciences, in areas such as biosensing and drug delivery.

1. Introduction

Research into the next generation of smart materials, defined by their ability to respond to specific stimuli triggers, has received considerable interest in recent years. There are numerous approaches reported in the literature, focusing on “intelligent” features incorporated into materials, primarily through the use of responsive polymers that undergo physical and

chemical changes in response to a physical (e.g., temperature, light, electrical or magnetic field), chemical (e.g., redox, pH, glucose), or biological (e.g., enzymes) stimuli.^[1] Such features are especially desirable in applications where the controlled degradability of materials is required; for example, to enable the release of encapsulated cargo in therapeutic delivery.^[1c,d,2]

Deoxyribonucleic acid (DNA) is a naturally occurring, stimuli-responsive biopolymer that remains stable under most conditions, yet experiences dramatic changes once exposed to the specific stimuli and conditions.^[3] It is also known for its unique characteristic to undergo highly specific and precise base pairing interactions,^[4] thus making it an attractive building block for engineering materials with molecularly designed architectures and responsive behavior.^[5] Films designed solely using DNA can be engineered to be biocompatible, biodegradable, and with different film architectures. Multilayered DNA films can be prepared using the layer-by-layer (LbL) approach,⁵⁻¹⁰ a widely known versatile technique for constructing thin films of varying composition on supports of different shapes and sizes.^[6] Multiple building blocks such as polymers, particles^[6b] liposomes,^[6c] micelles,^[6c] and/or quantum dots^[6d] have been used to assemble LbL films through the selection of appropriate interactions (e.g., electrostatics,^[6a] hydrogen bonding,^[7] and covalent linkages^[8]) required to assemble and stabilize the films. DNA multilayer films are assembled and stabilized by the hybridization forces between the complementary interactions in alternating layers of DNA “diblocks”.^[5b,9] We have previously shown that the properties of DNA are highly dependent on the DNA sequences used for assembly and the solution assembly conditions.^[10] For example, we reported that DNA building blocks that are short (less than 10 bases) or long (more than 60 bases) do not promote efficient film growth.^[10b,10d] This is due to the formation of hairpins in short sequences (10 bases long) and interstrand bridges with adjacent DNA strands in long sequences (60 bases long), both of which prevent efficient hybridization and

film growth.^[10b,10d] The presence of salt is also important in forming and stabilizing DNA multilayer films, and at high salt concentrations (2 M NaCl), the formation of T·A*T triplexes results in a denser film structure.^[10a] DNA multilayer films can also be stabilized by crosslinking the film by hybridization with a specific crosslinking oligonucleotide, thus ensuring the film is still solely composed of DNA.^[11] DNA films, including those that are stabilized, can be enzymatically degraded using restriction enzymes by engineering restriction cut-sites within the DNA sequences used to assemble the films.^[12]

An important characteristic of DNA multilayer films is its dynamic nature.^[13] In a recent study, we reported that such films undergo rearrangement both during new layer formation through hybridization and spontaneously when left over time.^[13] Hence, by understanding the factors that influence the rearrangement and movement of DNA strands within these films, we expect to be able to engineer DNA films with adaptable properties. In drug delivery, for example, rearrangement within the film could be useful in triggering therapeutic delivery for cargo release, whereas in biosensing, rearrangement could lead to responses related to biological events.

In this manuscript, we report the design and assembly of DNA films with programmable features that endow the materials with degradation characteristics. Degradation is achieved through interaction of the DNA films with subsequently added specific DNA sequences (**Figure 1** and **Table 1**). The films are assembled by depositing alternating layers of polyA₁₅X₁₅G₁₅ and polyT₁₅X₁₅C₁₅ onto a polyT₃₀ priming layer.^[11,12] DNA layers form because the outer homopolymeric block (polyA₁₅, polyG₁₅, polyT₁₅ or polyC₁₅) of the triblock strands hybridize to the complementary homopolymeric block of the previously adsorbed layer (polyT₁₅, polyC₁₅, polyA₁₅ or polyG₁₅, respectively), ensuring film buildup. The middle block (polyX₁₅) remains single-stranded throughout the assembly and contains a random sequence. To crosslink and stabilize the films, DNA strands containing a complementary

sequence to the single-stranded middle block (either polyX₁₅ or polyX'₁₅X'₁₅X'₁₅) are introduced. These strands crosslink the film when multiple polyX'₁₅ strands hybridize to the same polyX₁₅ region in the film, or when polyX'₁₅X'₁₅X'₁₅ strands hybridize across multiple polyX₁₅ regions, thus bridging layers within the film.^[11] As shown in Figure 1, DNA strands of specific sequences are introduced to the film to trigger degradation. These include strands that are entirely complementary to the triblock strands used to assemble the film (i.e., polyC₁₅X'₁₅T₁₅ or polyG₁₅X'₁₅A₁₅) or partially complementary (i.e., polyG₁₅X'₁₅, polyX'₁₅A₁₅, polyC₁₅X'₁₅, or polyX'₁₅T₁₅). PolyG₁₅X'₁₅A₁₅ and polyC₁₅X'₁₅T₁₅ were first introduced to uncrosslinked, polyX'₁₅ crosslinked, and polyX'₁₅X'₁₅X'₁₅ crosslinked films to demonstrate the concept of degradation through competitive hybridization. Then, to further investigate whether degradation can be influenced through preferential binding between specific base pairs, the partially complementary diblocks are introduced to the uncrosslinked film.

2. Results and Discussion

2.1. Film Assembly

The assembly of the DNA films was monitored using a quartz crystal microbalance with dissipation monitoring (QCM-D), which provides information on the mass and viscoelasticity of films. A decrease in frequency with deposition of each layer corresponds to an increase in film mass, indicating regular film growth (**Figure 2**). The formation of each polyT₁₅X₁₅C₁₅ layer showed a smaller increase in dissipation compared to each polyA₁₅X₁₅G₁₅ layer (Figure 2). The polyT₁₅X₁₅C₁₅ layer hybridizes to the previously adsorbed layer with the C and G bases binding via three hydrogen bonds, in contrast to the polyA₁₅X₁₅G₁₅ layer, which hybridizes to the adsorbed layer through weaker T=A bonds containing two hydrogen bonds. Thus, there is a smaller increase in the viscoelasticity of the film when the polyT₁₅X₁₅C₁₅ layer forms compared to the polyA₁₅X₁₅G₁₅ layer. Crosslinking the film with polyX'₁₅ led to a

decrease in frequency (23%), the magnitude of which is slightly lower than that expected (33%) if all of the polyX₁₅ sites in the film were crosslinked according to a 1:1 hybridization ratio. Further, an increase in dissipation (215%) was observed upon crosslinking, suggesting that formation of the more rigid dsDNA results in an ‘extended’ structure containing more water. In contrast, crosslinking with polyX’₁₅X’₁₅X’₁₅ resulted in a smaller decrease in frequency (1%) than theoretically expected (33%), suggesting that not all of the polyX₁₅ sites were crosslinked to form dsDNA. Correspondingly, the increase in dissipation (36%) on crosslinking was not as high compared to the polyX’₁₅ crosslinked film (215%), which is likely due to a less swollen structure.

2.2. Programmable Film Degradation

Degradation of the uncrosslinked, and polyX’₁₅ and polyX’₁₅X’₁₅X’₁₅ crosslinked films, was achieved by exposing the films to polyG₁₅X’₁₅A₁₅ sequences (**Figure 3a**). These sequences are complementary to the polyT₁₅X₁₅C₁₅ layer used to assemble the films. There was a decrease in film frequency when the complementary strands were first introduced, indicative of adsorption of the complementary strands to the film (inset in Figure 3a). The initial adsorption of both polyG₁₅X’₁₅A₁₅ strands was higher for the uncrosslinked film compared to the crosslinked films, out of which, the polyX’₁₅ crosslinked film showed the least adsorption. This suggests that there are more binding polyX₁₅ sites in the polyX’₁₅X’₁₅X’₁₅ crosslinked film than the polyX’₁₅ crosslinked film, and is consistent with the data in Figure 2, which show that the polyX’₁₅ crosslinked film is more effectively crosslinked than the polyX’₁₅X’₁₅X’₁₅ crosslinked film. The adsorbed amount is thus dependent on the availability of single-stranded polyX₁₅ sites within the film. A similar trend was observed when the films were treated with polyC₁₅X’₁₅T₁₅ strands (Figure 3b).

After the initial adsorption, the degradation rate of the films was determined by the rate at which the frequency of the film increased, indicating a loss of mass. As expected, exposure of the uncrosslinked film to polyG₁₅X'₁₅A₁₅ resulted in a steep increase in frequency, indicating rapid film loss. Within 100 min of exposure to polyG₁₅X'₁₅A₁₅, less than 10% of the film mass remained (Figure 3a). The rate of degradation was slower for the polyX'₁₅ crosslinked films, requiring more than 460 min of exposure to polyG₁₅X'₁₅A₁₅ to reach the same level of degradation as for the polyX'₁₅ crosslinked film. The polyX'₁₅X'₁₅X'₁₅ crosslinked films took the longest to degrade, taking 770 min to degrade 90% of the film after treatment to polyG₁₅X'₁₅A₁₅. A similar degradation trend in the order of uncrosslinked > polyX'₁₅ > polyX'₁₅X'₁₅X'₁₅ was observed when the films were treated with polyC₁₅X'₁₅T₁₅ (Figure 3b). It took longer to degrade 90% of the uncrosslinked (530 min) and polyX'₁₅ crosslinked (650 min) films. However, the polyX'₁₅X'₁₅X'₁₅ crosslinked film degraded faster when treated with polyC₁₅X'₁₅T₁₅ (710 min) than polyG₁₅X'₁₅A₁₅ (770 min). This could be attributed to the way polyG₁₅X'₁₅A₁₅ and polyC₁₅X'₁₅T₁₅ strands interact with the film. The presence of quadruplexes in consecutive G runs^[10a] could affect how the degradation sequences are able to hybridize to the film. It is likely that once polyG₁₅X'₁₅A₁₅ strands are able to successively enter the film, degradation occurs rapidly due to the bulkier nature, which facilitates greater movement within the film compared to the polyC₁₅X'₁₅T₁₅ strands, which do not contain secondary structures. However, once the film is extensively crosslinked over multiple layers, as in the case of the polyX'₁₅X'₁₅X'₁₅ crosslinked films, the polyG₁₅X'₁₅A₁₅ strands might not pass through the film as effectively, and thus the polyC₁₅X'₁₅T₁₅ strands are able to degrade the film at a faster rate.

Degradation is triggered when hybridization with an incoming DNA strand competes for and displaces the base pairs holding the film together. When present within the film, each polyA₁₅X₁₅G₁₅ or polyT₁₅X₁₅C₁₅ strand binds to two polyT₁₅X₁₅C₁₅ or polyA₁₅X₁₅G₁₅ strands

via the homopolymeric blocks while the random block remains unbound. Thus when an incoming DNA strand, for example, polyG₁₅X'₁₅A₁₅, is entirely complementary to one of the assembly strands (polyT₁₅X₁₅C₁₅), hybridization between these strands is preferred. Additionally, hybridization of the previous single-stranded random sequences imparts more stability compared to homopolymeric sequences holding the film together, which are easily displaced through slippage. This has been reported in our earlier studies which show that DNA films are dynamic structures and will undergo rearrangement when hybridization to new DNA strands occurs.^[13] Degradation of the uncrosslinked film was most effective as the single-stranded unbound polyX₁₅ sites were easily accessible to the complementary strands and the film was free of any crosslinking. The polyX'₁₅X'₁₅X'₁₅ crosslinked film degraded at a slower rate than the polyX'₁₅ crosslinked film, even though it contained more polyX₁₅ sites, which provide more binding sites for the incoming complementary strands. This suggests that the longer crosslinked polyX'₁₅X'₁₅X'₁₅ strands, which crosslink across multiple layers within the film, are able to bind and hold the film together more effectively and are not easily displaced during hybridization and rearrangement of the film when new strands are introduced. In contrast, the shorter polyX'₁₅ strands are less likely to hybridize across layers and more likely to fall apart as the film rearranges. Thus, degradation is influenced by the availability and accessibility of the polyX₁₅ sites within the film and the degree of crosslinking within the film.

To better understand whether binding to a preferred section of an incoming strand could influence degradation, the uncrosslinked films were treated with polyG₁₅X'₁₅, polyX'₁₅A₁₅, polyC₁₅X'₁₅ and polyX'₁₅T₁₅. We found that no degradation was observed when polyG₁₅X'₁₅ was introduced. It is likely that the incoming homopolymeric G bases exist as stable dimeric chair G quadruplex complexes,^[10a] which could reduce the efficiency of competitive hybridization with the X₁₅C₁₅ portion of the polyT₁₅X₁₅C₁₅ strands on the surface.

Additionally, their bulkier nature could limit access through the film and prevent degradation. As such, the strands are likely to preferentially hybridize to the X bases in the film, leading to overall film growth. Degradation thus relies on the polyX'₁₅A₁₅ end of polyG₁₅X'₁₅A₁₅ strands to enter and competitively bind to the complementary polyC₁₅X₁₅T₁₅ strands within the film. In contrast, C and T bases within polyC₁₅X'₁₅ and polyX'₁₅T₁₅ strands do not form secondary structures, and are likely to access the film more easily. However, as observed in **Figure 4b**, polyC₁₅X'₁₅ strands degrade the film at a slower rate than polyX'₁₅T₁₅. This could be attributed to the C bases, which have to compete for hybridization with G quadruplexes within the film. A strong initial adsorption of polyX'₁₅T₁₅ was also observed and may be due to the formation of T·A*T triplexes that form when the incoming T bases bind to the T=A duplexes present within the film.^[10a] Nonetheless, this does not reduce the efficiency of degradation, as the rate of degradation is fastest when both the C and T bases are present in polyC₁₅X'₁₅T₁₅.

Degradation of the films was also studied on particles by following the change in fluorescence intensity of the films over time after incubation with polyG₁₅X'₁₅A₁₅ and polyC₁₅X'₁₅T₁₅ (**Figure 5**). The polyT₁₅X₁₅C₁₅ layers within the films were labeled with AF488. A similar trend to the films prepared on planar supports was observed, where there was an initial increase in fluorescence intensity in the order of: uncrosslinked > polyX'₁₅X'₁₅X'₁₅ > polyX'₁₅ when the complementary strands were introduced, followed by a decrease in fluorescence intensity, indicating film loss. However, as no fluorescence species was introduced, this increase in fluorescence likely stems from rearrangement within each unique film structure. Thus, although the decrease in fluorescence intensity suggests degradation of the film occurs over time, we cannot accurately compare the degradation rate of the various films (uncrosslinked, polyX'₁₅, and polyX'₁₅X'₁₅X'₁₅). Using fluorescence microscopy, we show qualitatively that DNA capsules, formed by dissolving the silica core coated with the

uncrosslinked film, degrade within minutes upon exposure to polyG₁₅X'₁₅A₁₅ (**Figure 6**). A similar observation was made when the film was degraded using polyC₁₅X'₁₅T₁₅.

3. Conclusions

We have shown that DNA films can be programmed to degrade by introducing DNA strands to compete and bind to the sequences holding the films together. These strands are designed to be entirely complementary to the building blocks to induce preferential hybridization between them. The rate of degradation is influenced by the availability and accessibility of the polyX₁₅ sites within the film, and the degree of crosslinking within the film. When the complementary strands (polyG₁₅X'₁₅A₁₅ or polyC₁₅X'₁₅T₁₅) are introduced, an initial decrease in frequency corresponding to DNA adsorption is first observed, followed by rapid degradation of the uncrosslinked film, and the polyX'₁₅ and polyX'₁₅X'₁₅X'₁₅ (slowest) crosslinked films. Similar results are obtained on particle supports. The adsorbed amount is directly proportional to the availability of binding polyX₁₅ sites within the film (uncrosslinked > polyX'₁₅X'₁₅X'₁₅ > polyX'₁₅ crosslinked). Even though the polyX'₁₅X'₁₅X'₁₅ crosslinked film has more available binding polyX₁₅ sites than the polyX'₁₅ crosslinked film, it degrades at a slower rate, as the longer polyX'₁₅X'₁₅X'₁₅ strands hybridize across multiple layers within the film and thus hold the film together more effectively during rearrangement when the competing strands are introduced. The uncrosslinked films were also treated with polyG₁₅X'₁₅, polyX'₁₅A₁₅, polyC₁₅X'₁₅ and polyX'₁₅T₁₅ to understand whether preferential hybridization influences degradation rates. Degradation was observed in all sequences except polyG₁₅X'₁₅, possibly due to the stable and bulkier dimeric chair G quadruplex complexes, which do not penetrate the film readily. Thus the polyX'₁₅A₁₅ portion of the polyG₁₅X'₁₅A₁₅ strand is important for initiating degradation. Although polyX'₁₅T₁₅ is likely to form T·A*·T triplexes through hybridization with the polyT=A duplexes in the film, it does not affect the rate of degradation. The ability to tailor degradability features into films offers new opportunities and

we anticipate this approach to be useful in engineering films for various bioscience applications.

4. Experimental Section

Materials. Sodium chloride (NaCl), sodium citrate, and sodium hydroxide were obtained from Sigma-Aldrich and used as received. High purity water of resistivity greater than 18 MΩ cm was obtained from an inline Millipore RiOs/Origin system (Milli-Q water). A stock solution of saline sodium citrate (SSC buffer) was prepared by dissolving 4.8 g of citric acid and 14.6 g of sodium chloride in 500 mL of water to give a final concentration of 500 mM sodium chloride and 50 mM sodium citrate (Na^+ concentration of 650 mM). Using a Mettler-Toledo MP220 pH meter, the pH of the buffer solution was adjusted to pH 6.5 using 1 M sodium hydroxide. The oligonucleotides (polyT₃₀, polyA₁₅X₁₅G₁₅, polyT₁₅X₁₅C₁₅, polyX'₁₅, polyX'₁₅X'₁₅X'₁₅, polyG₁₅X'₁₅A₁₅, polyC₁₅X'₁₅T₁₅, polyG₁₅X'₁₅, polyX'₁₅A₁₅, polyC₁₅X'₁₅, and polyX₁₅T₁₅) used were custom synthesized by Geneworks (Adelaide, Australia). PolyT₁₅X₁₅C₁₅ labeled with Alexa Fluor® 488 (AF488) on the 5' end was synthesized by TriLink BioTechnologies (San Diego, CA, USA). The DNA sequences are shown in Table 1. The lyophilized oligonucleotides were rehydrated in Milli-Q water to give a stock concentration of 150 μM and further diluted in SSC buffer to a final nucleotide concentration of 150 μM for the experiments. 3 μm-diameter aminated silica particles were obtained from Microparticles GmbH (Umwelttechnologie-Zentrum, Germany) and used as received. Standard 5 MHz gold-coated AT-cut quartz crystals (Q-Sense AB, Västra Frölunda, Sweden) were cleaned with Piranha solution (70/30 v/v% sulfuric acid/hydrogen peroxide), washed thoroughly in water and dried under a nitrogen stream. *Caution! Piranha solution is highly corrosive. Extreme care should be taken when handling Piranha solution, and only small quantities should be prepared.* The gold crystals were further treated in a UV-ozone

TipCleaner (Bioforce NanoSciences, Inc.) for 10 min to remove any remaining contaminants prior to the experiments.

Quartz Crystal Microgravimetry. QCM measurements were carried out on a Q-Sense E4 instrument (Q-Sense AB, Västra Frölunda, Sweden) at a constant temperature of 23.8 °C. All overtones measured (1st, 3rd, 7th, 11th, and 13th) showed the same trend; however, only the fifth overtone frequency and dissipation values are reported. Briefly, the DNA films were assembled by first adsorbing a priming layer of polyT₃₀ (225 µL of a 5 µM solution for 10 min) onto the gold-coated quartz crystal electrodes, followed by alternating layers of polyA₁₅X₁₅G₁₅ (225 µL of a 3.33 µM solution for 20 min) and polyT₁₅X₁₅C₁₅ (225 µL of a 3.33 µM solution for 20 min) to a total of nine layers (including the polyT₃₀ layer). The films were then crosslinked using polyX'₁₅ (225 µL of a 5 µM solution for 20 min) or polyX'₁₅X'₁₅X'₁₅ (225 µL of a 3.33 µM solution for 20 min). Each film was rinsed in 1 mL of SSC buffer after each adsorption step to remove any loosely bound oligonucleotides. All solutions were flowed over the crystal sensor surface at a constant flow rate of 300 µL min⁻¹. The raw data were analyzed using the QTools 3.0.0.175 software.

Layer-by-layer (LbL) Assembly of DNA Films on Silica Particles. The amine-functionalized silica particles (220 µL of a 5 wt % dispersion) were first primed with a polyT₃₀ layer (396 µL of a 5 µM solution). To assemble the layers, alternating layers of polyA₁₅X₁₅G₁₅ (20 min) and polyT₁₅X₁₅C₁₅ (20 min) were deposited to a total of nine layers (including the polyT₃₀ layer), and crosslinked with either polyX'₁₅ (20 min) or polyX'₁₅X'₁₅X'₁₅ (20 min). After deposition of each layer, the particles were washed three times in SSC buffer to remove any excess DNA.

Flow Cytometry. Degradation of the films was carried out by incubating the DNA film-coated particles (0.3 wt%) with polyG₁₅X'₁₅A₁₅ or polyC₁₅X'₁₅T₁₅ (3.33 µM) and measuring the

average fluorescence intensity of the particles over time. The ratio of DNA in solution to surface area of the particles was consistent with the ratio of DNA in solution to the surface area of the QCM crystals. Using a BD LSRFortessa™ flow cytometer with an excitation wavelength of 488 nm, the 3 µm-diameter particles (0.003 wt% suspended in 200 µL of SSC buffer) were analyzed using a 530/30 nm band pass filter (515-545 nm) with a PMT voltage of 440 V. The average fluorescence intensity of 20 000 particles was measured. The signals obtained on different days were normalized by measuring the fluorescence intensity of eight peak Spherotech rainbow calibration particles. Analysis of flow cytometry data was performed using FlowJo software.

Microscopy. Visual observation of capsule degradation was carried out using the 60 X objective on an Olympus IX71 inverted fluorescence microscope. A droplet containing silica particles coated with four bilayers of the uncrosslinked film (0.5 wt%, 4 µL final volume in SSC buffer) was placed on a microscope glass slide. The silica cores were dissolved using ammonium fluoride (2 M) buffered hydrofluoric acid (8 M) at pH 5. *Caution! Hydrofluoric acid is highly toxic and great care must be taken when handling.* Dissolution of the silica cores occurred within 1 min. The capsules were degraded by introducing polyG₁₅X₁₅A₁₅ (3.33 µM, 9 µL) strands.

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Figure 1. Exposure of uncrosslinked DNA multilayer films to various strands that initiate degradation through hybridization. (a) $\text{polyG}_{15}\text{X}'_{15}\text{A}_{15}$, (b) $\text{polyG}_{15}\text{X}'_{15}$, and (c) $\text{polyX}'_{15}\text{A}_{15}$.

Figure 2. Growth of the triblock multilayer film assembled by depositing four alternating bilayers of polyA₁₅X₁₅G₁₅/polyT₁₅X₁₅C₁₅ on a polyT₃₀ precursor layer. The film was also crosslinked with either polyX'₁₅ or polyX'₁₅X'₁₅X'₁₅. The polyA₁₅X₁₅G₁₅ and polyT₁₅X₁₅C₁₅ layers are represented by the odd and even numbers, respectively.

(a)

(b)

— Uncrosslinked — polyX'_{15} crosslinked — $\text{polyX}'_{15}\text{X}'_{15}\text{X}'_{15}$ crosslinked

Figure 3. Degradation of the uncrosslinked, and polyX'_{15} and $\text{polyX}'_{15}\text{X}'_{15}\text{X}'_{15}$ crosslinked triblock multilayer films with (a) $\text{polyG}_{15}\text{X}'_{15}\text{A}_{15}$ and (b) $\text{polyC}_{15}\text{X}'_{15}\text{T}_{15}$ over time. Inset: Initial change in normalized film frequency from 0 to 9 min.

Figure 4. Degradation of uncrosslinked triblock DNA multilayer films with **(a)** polyG₁₅X'₁₅A₁₅, polyG₁₅X'₁₅ or polyX'₁₅A₁₅, and **(b)** polyC₁₅X'₁₅T₁₅, polyC₁₅X'₁₅ or polyX'₁₅T₁₅. Inset: Initial change in normalized film frequency from 0 to 9 min.

Figure 5. Degradation of triblock DNA multilayer films with (a) polyG₁₅X'₁₅A₁₅ and (b) polyC₁₅X'₁₅T₁₅.

Figure 6. Uncrosslinked 4-bilayer triblock DNA multilayer film **(a)** on 3 μm -diameter silica particles, **(b)** after dissolution of the silica particles, and **(c)** after treatment with polyG₁₅X'₁₅A₁₅.

Table 1. Oligonucleotide sequences used.

Name	Sequence (5' to 3' end)
PolyT ₃₀	TTT TTT TTT TTT TTT TTT TTT TTT TTT TTT
PolyA ₁₅ X ₁₅ G ₁₅	AAA AAA AAA AAA AAA GTC AGG AAT TCT AGC GGG GGG GGG GGG GGG
PolyT ₁₅ X ₁₅ C ₁₅ [a]	TTT TTT TTT TTT TTT GTC AGG AAT TCT AGC CCC CCC CCC CCC CCC
PolyX' ₁₅	GCT AGA ATT CCT GAC
PolyX' ₁₅ X' ₁₅ X' ₁₅	GCT AGA ATT CCT GAC GCT AGA ATT CCT GAC GCT AGA ATT CCT GAC
PolyG ₁₅ X' ₁₅ A ₁₅	GGG GGG GGG GGG GGG GCT AGA ATT CCT GAC AAA AAA AAA AAA AAA
PolyG ₁₅ X' ₁₅	GGG GGG GGG GGG GGG GCT AGA ATT CCT GAC
PolyX' ₁₅ A ₁₅	GCT AGA ATT CCT GAC AAA AAA AAA AAA AAA
PolyC ₁₅ X' ₁₅ T ₁₅	CCC CCC CCC CCC CCC GCT AGA ATT CCT GAC TTT TTT TTT TTT TTT
PolyC ₁₅ X' ₁₅	CCC CCC CCC CCC CCC GCT AGA ATT CCT GAC
PolyX' ₁₅ T ₁₅	GCT AGA ATT CCT GAC TTT TTT TTT TTT TTT
[a] PolyT ₁₅ X ₁₅ C ₁₅ -AF488 contains the same sequence, with the 5' end labeled with Alexa Fluor® 488	

Table of contents entry

Nanostructured DNA multilayer films assembled through the layer-by-layer (LbL) assembly technique can be programmed to degrade by introducing DNA strands of specific sequences which competitively hybridize to the building blocks that stabilize the film structure, causing film rearrangement and degradation.

DNA structures, multilayers, hybridization, biodegradable materials, DNA recognition

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Programmed Degradation of DNA Multilayer Films

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