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Nucleotide-Responsive Wettability on a Smart Polymer Surface

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Responsive materials have been an increasing focus for chemists.[1] Smart-surface materials, in which the surface properties are capable of responding to subtle changes in the surrounding environment, are especially interesting because of their great advantages in applications and have been realized by various methods, including temperature, light, pH, solvent treatment, etc.[2] In view of their great significance in biochemical applications, one interesting but challenging topic is to develop smart surfaces that are sensitive to biomolecule species in solution; these have seldom been reported.

Nucleotides are molecules that constitute the structural units of nucleic acids (e.g., DNA and RNA) and play central roles in many biochemical processes.[3] Here we report smart copolymer films that are responsive to nucleotide molecules in solution. With two adenosine phosphates (ADP and AMP) and the adenosine as examples, we show that the wettability of the film can change significantly and reversibly [with contact angle (CA) decreases of up to ~52° on a flat substrate] upon the nucleotide solution treatment and that reversible switching between superhydrophobicity (CA > 150°) and superhydrophilicity (CA ≈ 0°) can be realized on a structured substrate. An obvious selectivity in responsiveness was also observed for nucleotides that differ in numbers of phosphate units (ADP > AMP > adenosine). This effect was accompanied by a dramatic reversible phase change and a corresponding volume change of the copolymer film upon nucleotide binding and release. These properties may find potential applications in biomolecule recognition and manipulation[4a] and related fields, including nanomedicine,[4b] biochips, microfluidic devices,[4c] etc.

A nucleotide is composed of two main parts: negatively charged phosphate units and a nucleoside unit. In order to realize nucleotide recognition and wettability switching, a tricomponent poly(*N*-isopropylacrylamide) (PNIPAAm)-based[5] random copolymer system [see the Supporting Information (SI)] containing phenylthiourea and phenylboronic acid (PBA) units was designed. As a strong hydrogen-bonding donor that is widely used in anion receptors,[6] phenylthiourea was introduced here to combine the phosphate units of the nucleotides; PBA is famous for its ability to combine with diols,[7] which was used here to bind the pentose ring of the nucleoside unit. Specially, a $-CF_3$ group was introduced into the phenylthiourea units because of its electron-withdrawing property, which may enhance the hydrogen-bond-donating ability of thiourea and the contribution to hydrophobicity, which may enlarge the extent of the wettability switching. On the basis of this design, three copolymers with different $-CF_3$ substitution positions, named PNI-PBA-TF(*p*), PNI-PBA-TF(*o*), and PNI-PBA-TF(*m*), were synthesized and evaluated.

Surface-initiated atom-transfer radical polymerization was used to graft the copolymers onto the flat silicon wafer.[8] The PNI-PBA-TF(*p*), PNI-PBA-TF(*o*), and PNI-PBA-TF(*m*) films showed original CAs (unless otherwise specified, the CA values all refer to static CAs) of 86 ± 1, 82 ± 2, and 100 ± 2°, respectively. They were then treated for ~10 min with nucleotide solutions having different concentrations. After removal of the excess nucleotide solution remaining on them and a subsequent drying process by a N_2 flow, the CAs were measured again to evaluate the nucleotide-responsive wettability. As shown with ADP as an example (Figure 1A), the films became more hydrophilic after the treatment, and a linear relationship between the CA decrease and the logarithm of the nucleotide concentration (log *C*) was observed for all of the films. The CAs changed back to the original values after further treatment with pure water for ~5 min, indicating good reversibility of the nucleotide-responsive wettability. However, control experiments on a pure PNIPAAm film did not show any distinct CA change (<2°), indicating that the excellent nucleotide-responsive wettability of the copolymer films was not induced by physical adsorption or the residue of nucleotides on them.

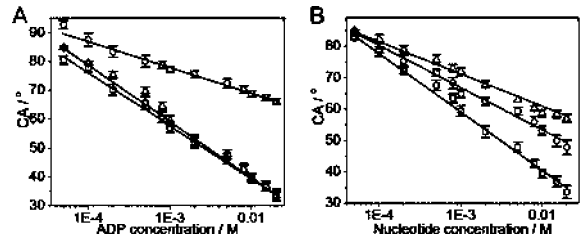

Figure 1. Relationship between CAs on flat copolymer films and the concentration of nucleotide solutions used to treat the films: (A) PNI-PBA-TF(*p*) (□), PNI-PBA-TF(*o*) (Δ), and PNI-PBA-TF(*m*) (○) films treated with ADP solution; (B) PNI-PBA-TF(*p*) film treated with ADP (□), AMP (○), and adenosine (Δ) solutions.

The PNI-PBA-TF(*o*) film behaved similarly to the PNI-PBA-TF(*p*) film upon treatment with the ADP solution with respect to both the extent of CA variation (maximum CA decreases: ~49 and ~52°, respectively) and slope of the CA−log *C* plot [−17.2 and −18.5°/log(10), respectively]. However, for the PNI-PBA-TF(*m*) film, the CA extent switched to a much more hydrophobic range, with a maximum CA decrease of ~35° and a significantly smaller value of about −9.9°/log(10) for the slope of the CA−log *C* curve, indicating an evidently weaker responsiveness to the nucleotides than the other two films. These results agree very well with the different electron-withdrawing abilities of $-CF_3$ at the para, ortho, and meta positions, suggesting that the phenylthiourea unit plays a critical role in the complexation and that the nucleotide-responsive wettability could be conveniently modulated by different $-CF_3$ substitution positions on the benzene ring. Since the PNI-PBA-TF(*p*) film showed the best performance in the responsive wettability, we selected this film for subsequent studies.

Interestingly, a distinct selectivity in responsive wettability was observed on the PNI-PBA-TF(*p*) film for ADP, AMP, and adenosine, although their only difference is the number of phosphate units. As shown in Figure 1B, the slopes of the CA−log *C* curves were about −18.3, −13.5, and −10.3°/log(10), respectively, indicating

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a responsiveness sequence of ADP > AMP > adenosine. In the quartz crystal microbalance (QCM) experiment, these molecules also exhibited corresponding differences in the adsorption quantity on the film (see the SI). This shows that the phosphate units and their numbers can greatly influence the binding and interactions between the nucleotides and the copolymer film.

Biomimetic studies of lotus leaves have revealed that the micro- and nanostructures of the substrate can improve both the hydrophilicity and the hydrophobicity of the surface.[9] In order to obtain better performance of the nucleotide-responsive wettability, we grafted the PNI-PBA-TF(*p*) film onto a structured substrate composed of well-aligned silicon micropillars with further silicon nanofibrous structures on top of them (Figure 2A) and studied the nucleotide-responsive wettability on it. As expected, the film originally was superhydrophobic with a CA of ~156 ± 2° (Figure 2C, left) and switched to superhydrophilic (CA ≈ 0°) after the treatment with 1×10^{-2} M ADP solution. A cycling experiment indicated good reversibility of this property (Figure 2B). However, for AMP and adenosine treatments under same conditions, the film exhibited only weak hydrophilic states with CAs of ~51 ± 2 and ~86 ± 3°, respectively (Figure 2C). Comparison of these results with those for the flat substrate shows that the selectivity for the responsive wettability was also amplified on the structured substrate, which is so predominant that it may have potential for applications including nucleotide discrimination, biochips, etc.

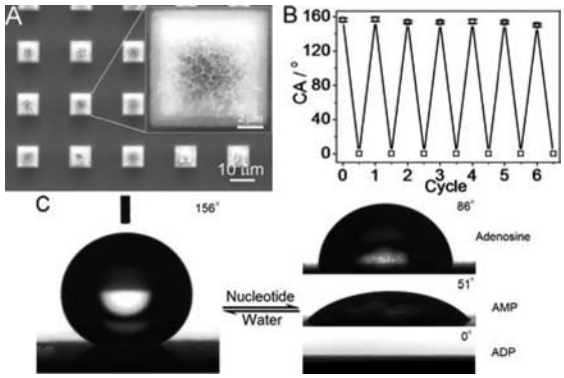

Figure 2. (A) Scanning electron microscope image of the structured silicon substrate. (B) Cycling experiment for the wettability switching between superhydrophobicity and superhydrophilicity on the structured PNI-PBA-TF(*p*) film upon alternate treatments with ADP solution (1×10^{-2} M) and pure water. (C) Water-drop profiles on the structured PNI-PBA-TF(*p*) film (left) before and (right) after treatment with different nucleotide solutions (1×10^{-2} M).

Since dynamic wettability is important in some applications, such as microfluidics,[10] we also evaluated the responsive wettability using dynamic CAs (see the SI for experimental details). The flat PNI-PBA-TF(*p*) film showed original advancing and receding CAs of ~96 ± 3 and ~24 ± 2°, respectively, and these changed to ~39 ± 1 and ~13 ± 3°, respectively, after treatment with 1×10^{-2} M ADP. For the structured film, the corresponding original values were ~164 ± 2 and ~127 ± 2°, respectively, and both changed to 0° after ADP treatment. A similar linear relationship and selectivity as for the static CAs were also observed for the advancing CAs (see Figure S7 in the SI). These data are in good agreement with the static CA results, revealing a good prospect of our film in practical applications.

We further used atomic force microscopy (AFM) to study the PNI-PBA-TF(*p*) film on a flat silicon wafer for more information. The original film exhibited a particle-like morphology (Figure 3A) with feature sizes of tens of nanometers and a film thickness of ~14.5 ± 2.0 nm. The section profile showed fluctuations of ~10−20 nm, and the mean roughness was ~3.1 nm. However, after the ADP solution treatment, as shown in Figure 3B, the particle-like morphology became quite ambiguous and the film was flattened. The section profile showed fluctuations of less than 4 nm, and the mean roughness was only ~1.3 nm, while the film thickness increased remarkably to ~23.0 ± 1.5 nm. These results clearly demonstrate a phase change and swelling[11] of the copolymer upon treatment with the nucleotide solution, which may bring extra benefits in applications. On the basis of these results, a hydrogen-bonding-based molecular mechanism was proposed for the nucleotide responsive wettability (see the SI).

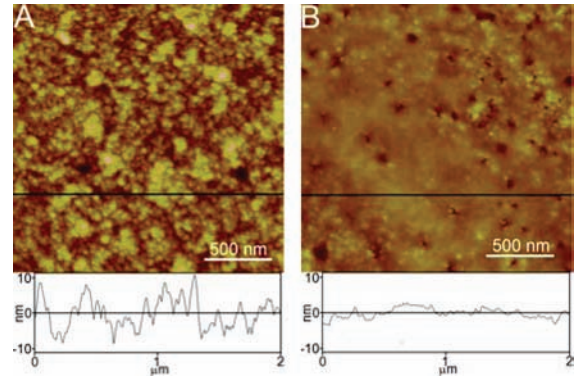

Figure 3. AFM images of the PNI-PBA-TF(*p*) film on a flat silicon wafer (A) before and (B) after treatment with ADP solution (1×10^{-2} M).

In summary, a smart copolymer film that is sensitive to the nucleotide species in solution was developed. The film exhibits an excellent reversible wettability response to nucleotide solutions, which is accompanied by a phase change and corresponding volume change of the copolymer. These properties may find applications in biomolecule recognition and manipulation and other biochemical applications, including controllable drug release, microfluidic devices, biochips, etc.

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Supporting Information Available: Experimental details, QCM measurements, ^{1}H NMR and UV−vis titration studies, and the molecular mechanism for the nucleotide-responsive wettability. This material is available free of charge via the Internet at http://pubs.acs.org.

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