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Stereoselective Interaction between DNA and Chiral Surfaces

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One of life's distinctive biochemical signatures is the high selectivity of chiral molecular species.[1] As a result, many biological events are greatly influenced by the chirality of molecules.[2] A typical example is that, as we[3] and Addadi et al.[4] reported, cells can sense the surface chirality and exhibit much different adhesion and activation behaviors on enantiomorphous surfaces. Although of great significance in biomaterial and the relevant biological studies,[5] this research is only at a starting point and a lot of questions still remain to be answered. Since biomacromolecules, e.g., proteins, DNA, RNA, *etc.*, form the most important species regulating the normal functions of cells, the investigation of their interaction with chiral surfaces not only may help to explain these effects from the chemical or biochemical points of view but also provides useful information to understand the origin of the high chiral preference in nature. Here we report an interesting phenomenon of the stereoselective interaction between DNA and chiral surfaces. On the *N*-isobutyryl-L(D)-cysteine (NIBC) enantiomer modified gold surfaces, DNA molecules have a much stronger interaction with the L surface than the corresponding D surface, which reflects on differences in both the state and morphology of the adsorbed DNA molecules and a distinctively larger adsorption quantity on the surface. Analysis indicates that this effect may be caused by the stereospecific hydrogen bonding (H-bond) interaction between the chiral moieties of the DNA molecules and the surface, which also brings novel insights to understanding the DNA properties and the application in biochemical devices.[6]

Atomic force microscopy (AFM) is a versatile technique to image DNA on surfaces, which has been extensively utilized to study DNA properties under different circumstances and its interaction with other molecules.[7] In this work, a full-sequence single-stranded DNA (ssDNA) specimen from calf thymus was used, which was dissolved in a tris-EDTA buffer at different concentrations from 10 to 75 μg/mL. In AFM experiments, "ultraflat"[8] evaporated gold film on a silicon wafer was used as a substrate to obtain good images of DNA, on which the NIBC enantiomers were coated through the simple self-assembly process of the −SH group. The AFM observation was made after the chiral surface was immersed and incubated in the DNA solution at 25 °C for ∼4 h and a subsequent gentle washing procedure.

During the experiments, we observed diverse morphologies of adsorbed DNA molecules under different concentrations on D and L surfaces and noticed the remarkable difference between them. At low concentration (10 μg/mL), the DNA adsorption on both D and L surfaces is weak, and most of the adsorbed DNA molecules exhibit a particle-like morphology (for the L surface, the relaxed DNA chains can be occasionally found, while, for the D surface, we did not find that in the scanned areas), indicating a folded state of DNA chains. However, at a middle concentration (50 μg/mL),

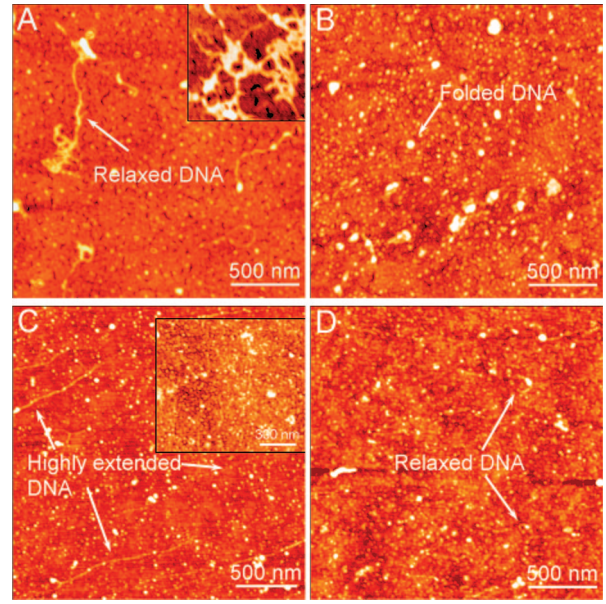

Figure 1. Typical AFM images for DNA adsorption on L- (A, C) and D-NIBC (B, D) modified surface. DNA concentration: (A and B) 50 μg/mL; (B and D) 75 μg/mL. Inset in (A): Entangled DNA in another area. Inset in (C): DNA chains with another orientation and dense arrangement.

as shown in Figure 1A, a considerable number of relaxed DNA chains (Averagely, in every 10 different scanned areas, relaxed chains can be found in more than 8 areas, Figure 1A) appear on the L surface. They distribute randomly on the surface and entangle (inset of Figure 1A) to form the winding or supercoil-like structures. As a comparison, on the D surface, most DNA molecules still display a folded particle-like morphology (relaxed chains could only be found in less than 2 areas for every 10 scanned areas, Figure 1B). The difference is also predominant at a higher DNA concentration (75 μg/mL). On the L surface, The DNA chains show a highly extended state and their density is much higher than the middle concentration, and more interestingly, they show specific orientations in different areas (Figure 1C and the inset), which may be induced by the rinse process. Nevertheless, on the D surface (Figure 1D), although relaxed DNA chains can also be easily observed, the quantity is less and the chains are less relaxed.

Two points can be drawn from the above results: the DNA chains may experience a transformation process[9] from the folded state to the relaxed state with an increase of the DNA concentration, and DNA exhibits different adsorption behaviors on the D and L surfaces. In order to clarify these points, we further used the dynamic light scattering (DLS) experiment to study the DNA properties in solutions. It shows that DNA has a small dynamic radius from tens of nanometer to more than 100 nm at low concentrations, while it increases significantly (up to ∼1500 nm) with the increase of

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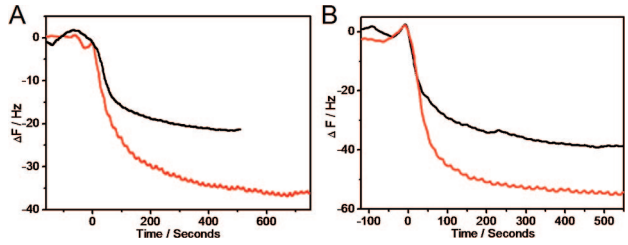

Figure 2. Time dependence of the QCM frequency shift of the D- (black) and L-NIBC (red) modified Au coated quartz-crystal resonator at DNA solutions with different concentrations. (A) 50 μg/mL; (B) 75 μg/mL. Experiment temperature: 25 °C.

concentration, which is accompanied by a wider size distribution and an increment of the large size proportion (see Supporting Information). This result is very consistent with the AFM observation and illustrates that the increment of the relaxed DNA chains on both surfaces is mainly due to the solution property of DNA. Thus, it can be concluded that the relaxed DNA chains have a stronger interaction with the L surface and prefer to adsorb on it, while, on the D surface, it is weaker and the adsorbed DNAs show a less relaxed state.

In order to confirm the above effect, we also investigated the DNA adsorption quantity on the two surfaces using the quartz crystal microbalance (QCM) method, in which the adsorbed mass has a linear relationship with the frequency decrease (ΔF) of the quartz crystal resonator. The Au-coated quartz-crystal resonators were used as the sensors, and the chiral modification was made by the same procedure as above. Figure 2 shows the time dependence of the QCM frequency shift of D- and L-NIBC modified resonators at a flow of DNA solutions with concentrations of 50 μg/mL (Figure 2A) and 75 μg/mL (Figure 2B), respectively. It shows that the L surface displays a much larger frequency shift than the D surface for both concentrations. Since all the experimental conditions are kept the same, it can be concluded that DNA has a larger adsorption quantity on the L surface, and the adsorption differences could be calculated through the relationship between the adsorbed mass and ΔF, which are ~270 ng/cm^2 and ~308 ng/cm^2 for the two concentrations, respectively.

The above results disclose a remarkable stereoselective interaction between DNA and chiral surfaces. We notice that the NIBC enantiomers have a strong capacity to form H-bonds due to the existence of the −COOH, −NH−, and carboxyl groups, while the spatial arrangements of these group are different (Figure 3A and B), which show different orientations for the H-bond environments that are mirror images to each other. For DNA, the H-bond interaction is also one of the most important factors influencing its physical and chemical behaviors and the interaction with other molecules,[10] which shows a specific orientation because of the chain structure and the chirality of D-nucleosides or D-nucleotides that comprise the DNAs. Thus, DNA may have different abilities to form effective H-bonds with the NIBC enantiomers, considering the chirality of NIBC molecules and the differential effects of steric hindrance caused by the large isopropyl side group. That is to say, the L surface may have a stronger H-bond interaction with the DNA, which results in a higher DNA adsorption and a more relaxed state of the DNA chains, while, for the D surface, it is not easy to form effective H-bonds with DNA because of the steric hindrance, thus exhibiting a lower adsorption to DNA, and the DNA prefers to show a more folded or less relaxed state on the surface (Figure 3C).

In conclusion, we report an interesting phenomenon of the very different adsorption behaviors of ssDNA molecules on D- and L-NIBC enantiomer modified surfaces. This effect not only may help to understand the stereospecific cell/substrate interaction and the origin of the chiral preference in nature but also brings novel insights to the study of DNA properties and the application in biochemical devices.

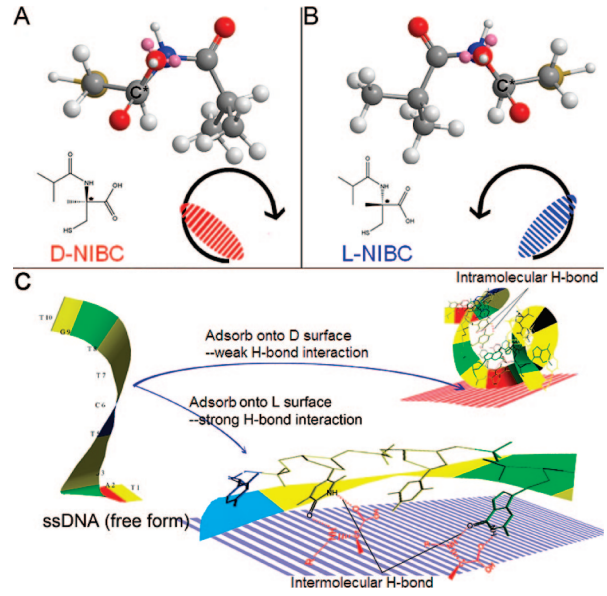

Figure 3. Schematic diagram for the possible mechanism of the stereoselective interaction between ssDNA and the D- and L-NIBC enantiomer modified surfaces. (A, B) Optimized 3-D structures of free D- and L-NIBC molecules, which show different orientations for the H-bond environment that are mirror images to each other, which may have different abilities to form H-bonds with the ssDNA. (C) ssDNA prefers to adsorb onto the L surface with a more relaxed configuration due to the strong H-bond interaction between the L-NIBC and the ssDNA; while on the D surface, ssDNA prefers to show a less relaxed or folded state due to the lack of efficient H-bonds.

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Supporting Information Available: Experimental details, DLS results. This material is available free of charge via the Internet at http://pubs.acs.org.

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