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Title(English)	Mechanism underlying anti-biofouling properties of protein- and cell-resistant nonionic and zwitterionic self-assembled monolayers
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（博士課程）
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論 文 要 旨

THESIS SUMMARY

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要旨（英文 800 語程度）
Thesis Summary（approx.800 English Words ）

Surfaces that resist the attachment of biomolecules are desired in biomedical research such as biosensing and cell patterning. For decades, the interfacial interaction responsible for the anti-biofouling property has been investigated to elucidate the mechanism underlying protein and cell resistance of different materials. Thus, model systems of protein- and cell-resistance surfaces are necessary to fully clarify the mechanism underlying the nonfouling behavior and boost the design of anti-biofouling surfaces.

Self-assembled monolayers (SAMs) of alkanethiols are platforms that enable the quantitative investigation of interfacial phenomena because of their well-defined, ordered, and customizable structure. Moreover, they are easy to fabricate. Anti-biofouling SAMs are widely utilized to correlate surface chemical properties with protein adsorption and cell adhesion. Two classes of anti-biofouling SAMs exist: nonionic and zwitterionic. Nonionic SAMs are generally composed of poly(ethylene glycol) (PEG) and oligo(ethylene glycol) (OEG)-terminated alkanethiols on gold substrates. The SAMs of betaine- and phosphorylcholine (PC)-terminated alkanethiol are representative anti-biofouling zwitterionic SAMs. Theoretical and experimental studies of water molecules in the vicinity of the two types of anti-biofouling SAMs have indicated that water plays the role of a physical barrier protecting the SAMs from interacting with proteins and cells. Despite their different chemical structures (and thus hydration mechanisms), the two types of anti-biofouling SAMs exhibit similarly strong anti-biofouling properties.

This work unveils the difference in the mechanism underlying the similar anti-biofouling properties shown by protein- and cell- resistant nonionic- and zwitterionic-terminated SAMs. By examining the water-induced forces with an atomic force microscope (AFM) and the hydrogen-bonding states of vicinal water employing surface-enhanced infrared absorption (SEIRA), I was able to distinguish the difference in hydration states (in terms of SAM-water and water-water interactions) between the anti-biofouling nonionic hydroxy-terminated tri(ethylene glycol) (EG3-OH) SAM and zwitterionic sulfobetaine-terminated (SB) SAMs. My key strategy was the modeling of short- and long-range hydration forces which enabled me to connect the measured water-induced forces at short and long ranges with the state of the hydrogen bonding of water in the SAMs' vicinity. It was found that a 1 nm-thick water barrier on the zwitterionic SB SAMs induces strong short-range repulsion due to the strong interaction between water molecules and the SB groups whereas a weak interaction between water molecules and EG3 groups extends up to 6 nm and causes long-range hydration.

In addition, I successfully identified the dominant water type (in terms of water-SAM interaction, i.e., strongly, or weakly bound water) of several anti-biofouling nonionic and zwitterionic SAMs. My approach consisted of fitting multiple peaks to the measured SEIRA spectrum in the OH stretching mode region of water for each corresponding SAM. Next, the percentage of area occupied by each fitted peak was calculated. Subsequently, the dominant OH stretching vibration mode in each measured spectrum was identified. By combining the results with those from surface force measurements, it was revealed that weakly bound water is the dominant water type in the vicinity of anti-biofouling nonionic and zwitterionic SAMs, but the amount of this water was different for each type (i.e., a greater amount was observed on those of anti-biofouling nonionic SAMs). Finally, Pearson correlation analysis for the peak areas, protein adsorption, and cell adhesion enabled me to show the strong negative relationship between the relative abundance of weakly bound water and protein/cell attachment, suggesting that a thick layer of water weakly binding the SAM is a good indicator of protein and cell resistance.

Based on these findings, the rationale for the alike cell/protein resistance of the two classes of anti-biofouling SAMs was exposed. Although differences in the mechanism underlying their anti-biofouling properties were mainly due to the different SAM-water interactions, the formation of a thick barrier of weakly bound water is generally observed and likely inducing the similar anti-biofouling property of protein- and cell-resistant SAMs.

Previous theoretical calculations revealed the differences in hydration free energy between EG and SB molecules; however, such calculations were limited to the first hydration shell of single molecules. This doctoral work provides experimental evidence of the differences in hydration forces of full systems (i.e., SAMs) beyond the first hydration shell (up to several nm). Moreover, my work's findings connect the hydrogen bonding states of vicinal water molecules with the hydration forces reflected in the surface force measurements. For instance, the low OH-stretching vibrational energy of the interfacial water for SB SAM measured by SEIRAS, revealed the strong interaction between the SB groups and water molecules (water strongly bound to SB groups) which causes strong short-range water-mediated force. Furthermore, the combination of my results with a statistical correlation test revealed that a thick layer of weakly bound water is a good indicator of protein and cell resistance of nonionic and zwitterionic SAMs.

Finally, I expect that this work's findings will expedite the design of anti-biofouling surfaces by presenting the SAM-water interaction responsible for the resistance to protein and cell attachment and acknowledging the hydration capacities of anti-biofouling nonionic- and zwitterionic-terminated SAMs.