Mini Accounts

Interfacial Supramolecular Chemistry for Stimuli-Responsive Functional Surfaces

Wan Pengbo[1] *Hill Eric H.*[2] *Zhang Xi*[1]*
(1. Key Lab of Organic Optoelectronics and Molecular Engineering of Ministry of Education, Department of Chemistry, Tsinghua University, Beijing 100084, China;
2. Department of Chemical and Nuclear Engineering, Center for Biomedical Engineering, University of New Mexico, Albuquerque, New Mexico 87131-1341, United States)

Prof. Zhang Xi was born in 1965. He received his B.S. degree (1986), M.Sc. degree (1989) and Ph.D. degree (1992) at Jilin University under supervision of Prof. Shen Jiacong. During his Ph.D. study, he worked at University of Mainz, Germany with Prof. Helmut Ringsdorf. He was lecturer and then promoted as a full professor at Jilin University from 1992 to 1993. He is a professor of chemistry at Tsinghua University since 2004. His research interests include supramolecular chemistry in solution and at interfaces, controlled self-assembly and disassembly, organic molecular films, and single-molecule force spectroscopy of polymers. In 2007, he was elected Academician of Chinese Academy of Sciences. Currently, he serves as a Senior Editor of *Langmuir* and advisory board members of several scientific journals, including Chemical Communications, Polymer Chemistry, Polymer and ACS Applied Materials & Interfaces. He has also served as a Vice President of the Chinese Chemical Society since 2010.

Abstract The combination of supramolecular chemistry with interfaces enhances the development of supramolecular chemistry as well as colloid and interface science. Supramolecular chemistry at interfaces allows for the construction of various smart and soft surfaces that can adapt to environmental changes, such as biomimetic surfaces and self-cleaning surfaces. In this article, we discuss strategies for the transfer of supramolecular complexes of azobenzene and cyclodextrin from solution to surfaces for the fabrication of stimuli-responsive surfaces with novel interfacial functions including tunable surface wettability, reversible protein adsorption and resistance, and photo-switchable bioelectrocatalysis. It is anticipated that these concepts can be extended to other supramolecular systems in order to engineer functional surfaces with designed structures and functions.

Key words interfacial supramolecular assembly; stimuli-responsive biosurface; host-guest interaction; protein immobilization and release; bioelectrocatalysis

Received Aug. 27, 2011
*Corresponding author e-mail: xi@mail.tsinghua.edu.cn

1 Introduction

Supramolecular chemistry refers to the behavior of molecular assemblies formed through noncovalent interactions. In other words, it is an area of chemistry that looks beyond the single molecule, aimed at studying molecular assemblies and revealing the physical interactions behind the formation of these molecular assemblies. As initiated by J. M. Lehn, supramolecular chemistry has led to some unique concepts and systems, resulting in a new subdivision in the family of chemistry. In the meantime, it heralds many promises that range from biomimetics to the engineering of controllable supramolecular soft materials and devices[1].

In nature, many biotransformation, matter transportation, and energy transduction processes begin with interfacial molecular recognition. The understanding of interfacial molecular recognition allows for regulation and control of these processes, leading to the development of new materials and medicines. In addition, the need for improved miniaturization of microelectronics and molecular devices has inspired many investigations into molecular assemblies, and the performance of these devices can be influenced significantly by the composition of the interface.

The combination of supramolecular chemistry with interfaces enhances the development of supramolecular chemistry as well as colloid and interface science. Supramolecular chemistry at interfaces allows for the construction of various smart and soft surfaces that can adapt to environmental changes, such as biomimetic surfaces and self-cleaning surfaces[2—6]. Generally, the various properties of interfaces facilitate the formation of molecular assemblies with controlled structures and architectures over a broad range of complexity. It should be noted that whereas many device functions work well in solution, there are issues when the same systems are transferred onto solid surfaces and other interfaces.

The use of supramolecular chemistry for fabrication and functionalization of interfacial supramolecular structures is desirable for many potential applications. The most commonly used methods for fabricating supramolecular interfaces are Langmuir-Blodgett (LB) films[7], Layer-by-layer (LbL) assembly[8] and self-assembled monolayers (SAM)[9]. Particularly, the formation of SAMs through chemisorptions of surface-active molecules at the liquid-solid interface is a powerful method for modifying the physical and/or chemical properties of surfaces.

The transfer of azobenzene and cyclodextrin (CD) complexes from solution to surfaces for fabrication of stimuli-responsive surfaces with novel interfacial functions is discussed in this article. Stimuli-responsive supramolecular assemblies formed on the basis of the host-guest interaction of azobenzene and CD have been well established in solution[10—16]. For example, stimuli-responsive vesicles formed from an azobenzene derivative and CD can undergo reversible assembly and disassembly by the photocontrolled inclusion and exclusion reaction of an azobenzene-containing surfactant with α-CD[17]. We have been attempting to employ the supramolecular chemistry between azobenzene and CD to fabricate functional surfaces with different properties, including tunable surface wettability, reversible protein adsorption and resistance, and photo-switchable bioelectrocatalysis (Fig. 1)[18—22].

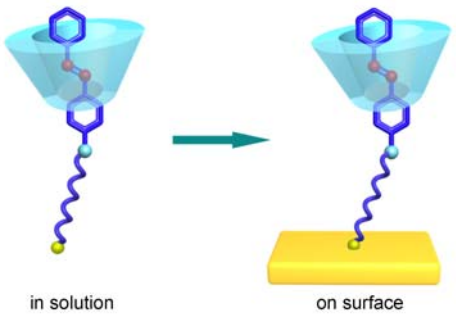

Fig. 1 Stimuli-responsive supramolecular assembly of azobenzene and CD from solution to surface

2 Photocontrolled interfacial molecular shuttle for tunable surface wettability

Artificial molecular shuttles formed on the basis of host-guest interactions of azobenzene and α-CD are mostly studied in solution[23]. These systems are termed artificial molecular shuttles, because a ring can slide back and forth like a shuttle between two stations in response to external stimuli[24,25]. We have demonstrated the fabrication of an interfacial photocontrolled molecu-

lar shuttle based on SAMs of the α-CD/azobenzene inclusion complex on rough gold surfaces, which can reversibly switch the surface wettability[19]. As shown in Fig. 2, an azobenzene-containing building block with a mercapto end-group (CF_3AzoSH) is pre-assembled with α-CD (α-CD/CF_3AzoSH) in water as a result of the host-guest interaction between azobenzene and α-CD. Meanwhile, the fluorocarbons of the fluorinated azobenzene may act as a blocking group for α-CD[26—29]. This α-CD/CF_3AzoSH inclusion complex is able to form a mixed SAM with *n*-butylthiol (*n*-C_4H_9SH) on a gold substrate. The purpose of the mixed SAM is to ensure that there is enough free space for the photoisomerization of CF_3AzoSH between the *cis* and the *trans* form, which is necessary for the photocontrolled up-down motion of α-CD in the CF_3AzoSH SAMs on the gold substrate upon UV/Vis irradiation.

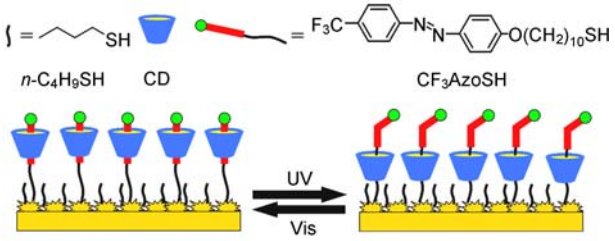

Fig. 2 Photocontrolled reversible molecular shuttles on a rough surface[19]. Reproduced with permission. Copyright 2008 The Royal Society of Chemistry

The motion of the molecular shuttles at the interface is influenced by the structure of the SAMs, which is indicated by the different surface wettability changes. As shown in Fig. 3a, after the chemisorption of the pure inclusion complex of α-CD/CF_3AzoSH on a rough gold surface, the surface is superhydrophilic because of the hydrophilic outside of α-CD and the amplification of contact angles by the rough surface (Fig. 3a)[2]. Upon UV light irradiation, the surface is still superhydrophilic because the densely packed α-CD/CF_3AzoSH-containing SAMs prohibit the photoisomerization of CF_3AzoSH which results in downwards motion of α-CD in CF_3AzoSH SAMs. By introducing the enormous spacer *n*-C_4H_9SH into the α-CD/CF_3AzoSH-containing SAMs, the surface becomes superhydrophobic from the mixed SAM containing very few of the α-CD/CF_3AzoSH complexes (Fig. 3b). Under UV light irradiation, the photoisomerization of CF_3AzoSH and the subsequent up-down motion of α-CD in CF_3AzoSH SAMs is allowed, however, the surface wettability change is slight. Optimization of the mixed SAMs yielded successfully with a ~5∶1 ratio of *n*-C_4H_9SH to α-CD/CF_3AzoSH. With this optimized SAM, the surface wettability can be switched between 70 ± 2° and 120 ± 2° reversibly upon UV/Vis light irradiation, indicating the photo-induced up-down movement of α-CD in CF_3AzoSH-SAMs on the gold substrate from the formation of the interfacial molecular shuttles (Fig. 3c). It is anticipated that such a line of research may provide a way to visualize microscopic molecular motions by observing the change of a macroscopic property and also applications in molecular motors and energy converters.

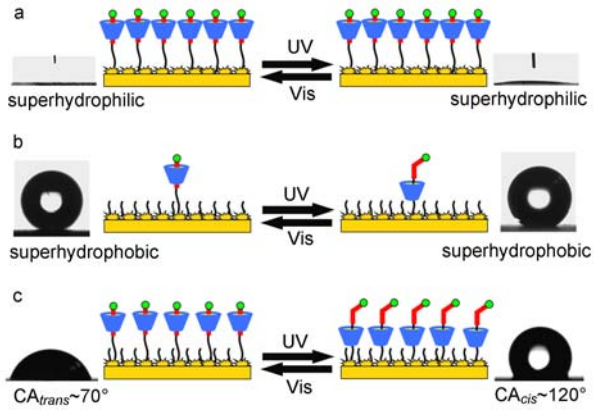

Fig. 3 Surface wettability changes from different mixed SAMs containing photocontrolled interfacial molecular shuttles upon UV/Vis irradiation[19]. Reproduced with permission. Copyright 2008 The Royal Society of Chemistry

3 Dual-controlled reactivated biointerface for reversible protein immobilization

The attachment of CD onto polymers can lead to the fabrication of polymeric surfaces capable of molecular recognition. By optimizing the chain length of alkylthiol spacers and the ratio of spacer to azobenzene-containing alkylthiol, cyclodextrins or polymer-grafted cyclodextrins (polymer-*g*-CD) can be reversibly assembled and disassembled from the azobenzene-containing SAMs due to the photocontrolled inclusion and exclusion reaction between azobenzene and CD (Fig. 4). Because of the good biocompatibility of cyclodextrin

and many polymers, this light-driven surface reactivation can be developed in diverse interfacial biological and medical applications for controllable biomacromolecule adsorption and desorption.

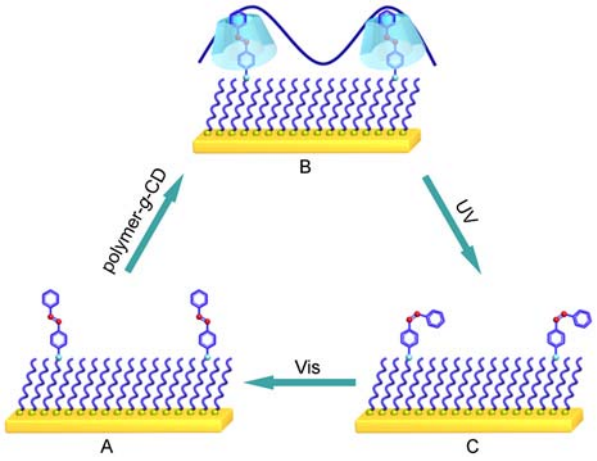

Fig. 4 Reversible assembly and disassembly of polymer-grafted cyclodextrins from the azobenzene-containing SAMs

Effective immobilization of proteins on surfaces without inducing conformation change and denaturation is crucial for applications in the areas of protein electrochemistry, bioassays, bioseparation, and bioengineering[30]. Recently, numerous attempts have been focused on carboxylic-acid-terminated SAM-modified gold electrodes to irreversibly adsorb cytochrome c (Cyt c), a heme-containing metalloprotein that can be entrapped into the mitochondrial membrane and act as an electron carrier in the respiratory chain[31]. However, in spite of advances in the fields of biosciences and biotechnology, it remains a challenge to design flexible, functionalized biocompatible interfaces that can reversibly immobilize bioactive proteins or carry out other biomimetic biomembrane functions[32].

We have demonstrated the fabrication of a light or pH dual-responsive reactivated biocompatible interface using the reversible host-guest interaction between photo-responsive azobenzene-containing self-assembled monolayers (Azo SAM) and the pH-responsive poly(acrylic acid) polymer grafted with β-cyclodextrin moieties (PAA-*g*-CD). These assemblies are used for reversible immobilization of redox proteins triggered by dual external stimuli (Fig. 5)[20]. First, the Azo SAM (Fig. 5A) can be formed through chemisorption of the thiol groups onto gold-coated surfaces. These SAMs can reversibly assemble with PAA-*g*-CD through the host-guest interaction of azobenzene and CD to allow photoactivated switching between a bare Azo SAM and PAA-*g*-CD-protected interface (PAA-*g*-CD/Azo SAM, Fig. 5B). Second, the PAA-*g*-CD protected interface can be switched between its electronegative (Fig. 5B) and electroneutral states (Fig. 5C) by pH variation. Third, the photoactivated reversibly-protected interfaces can be used for light-activated adsorption (Fig. 5 from B to D) and release (Fig. 5 from D to A) of Cyt c along with the reversible attachment and detachment of PAA-*g*-CD. Last, pH-responsive switchable biointerfaces can be employed for pH-responsive reversible immobilization (Fig. 5 from B to D) and release (Fig. 5 from D to C) of Cyt c. The integration of pH-sensitivity and photoactivated switching to form dual-responsive reactivated biointerfaces for reversible adsorption and release of electroactive Cyt c meets the modern requirements of bioscience and biotechnology, and is anticipated to provide an excellent platform for potentially wide-ranging applications in biomimetics, biomembranes, stimuli-responsive biomedical technologies, and optobioelectronic devices.

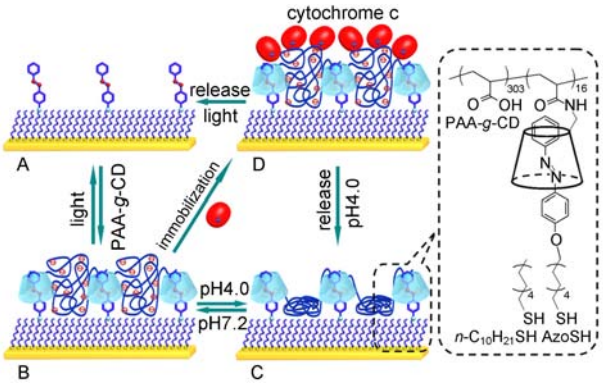

Fig. 5 Dual-controlled reactivated biointerface and reversible protein immobilization[20]. Reproduced with permission. Copyright 2009 John Wiley and Sons

4 Nearly complete and reversible interfacial resistance of cytochrome c

The effective resistance of proteins on surfaces is very desirable for potential applications, including biomedical implants, in vitro diagnostics, biosensors, coatings for ship hulls, carriers for targeted drug delivery, and more[33]. Among various protein-resistant ma-

terials, poly(ethylene glycol) (PEG)-based materials have been extensively employed for decades to prevent nonspecific protein adsorption and cell adhesion. Recently, numerous attempts have been focused on using PEG-coated surfaces to resist protein adsorption irreversibly[34]. However, it still remains a challenge to design reactivated flexible biointerfaces that can reversibly prevent protein adsorption in response to external stimuli[35].

By introducing protein-resistant PEG into the main chain of pH-responsive PAA-*g*-CD, we have successfully fabricated a pH-responsive reactivated biointerface through the inclusion complex between an azobenzene-containing SAM (Azo SAM) and a pH-responsive PEG-PAA block copolymer grafted with cyclodextrin (PEG-PAA-*g*-CD). First, the pH-responsive block copolymer PEG-PAA-*g*-CD can be assembled on Azo SAM by the host-guest interaction between azobenzene and CD (Fig. 6). The interface of PEG-PAA-*g*-CD and Azo SAM can be reversibly switched between an electronegative state to immobilize Cyt c (Fig. 7A) and an electroneutral state to resist Cyt c adsorption (Fig. 7B). The pH-responsive interface can be switched between an extended state and a relaxed state for complete resistance of Cyt c adsorption in cooperation with protein-resistant PEG, compared to only ~80% release of immobilized Cyt c under pH variation reported

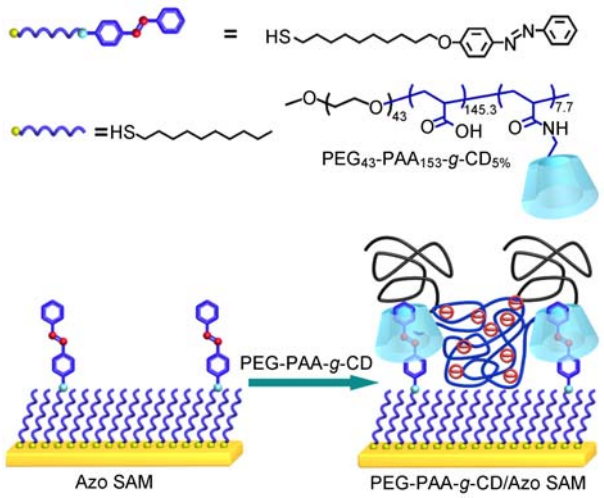

Fig. 6 pH-responsive reactivated biointerface by the inclusion reaction of PEG-PAA-*g*-CD on Azo SAM modified surface. Reproduced with permission.[21] Copyright 2010 American Chemical Society

in our previous work[21]. This type of interfacial supramolecular chemistry can be further extended to fabricate different functional biointerfaces by combining PEG and other stimuli-responsive materials.

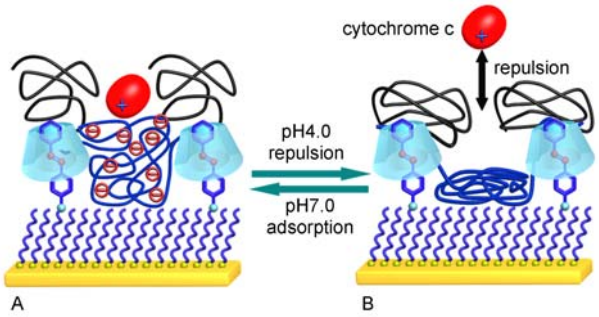

Fig. 7 Nearly complete and reversible interfacial resistance of Cyt c on pH-responsive reactivated biointerface[21]. Reproduced with permission. Copyright 2010 American Chemical Society.

5 Host-guest chemistry at interfaces for photoswitchable bioelectrocatalysis

The construction of signal-triggered bioelectrocatalysis attracts substantial research efforts because of the potential applications in many fields, such as stimuli-responsive biosensors, optoelectronic systems, energy conversion, and information storage and processing[36]. Recently, stimuli-responsive monolayer coated electrodes integrated with redox enzymes for controlled bioelectrocatalysis have been well established[37]. Compared to monolayer surfaces, smart polymer surfaces can provide more flexibility and enable the inclusion of functional groups.

One can employ the following four steps to fabricate a photoswitchable bioelectrocatalyzed oxidation of glucose by GO_x using a ferrocene-labeled polymer, which can be reversibly immobilized on surfaces by irradiation with light[22]. First, PAA-*g*-CD can be assembled onto an Azo SAM modified gold surface through the host-guest interaction of azobenzene and CD (Fig. 8 from A to B). Although some CDs in PAA-*g*-CD were immobilized onto the surface, there were still many free CDs left to incorporate the electron mediator ferrocene-methanol (Fc) on the basis of host-guest interactions between Fc and CD (Fig. 8 from B to C). As a result, ferrocene-labeled polymer coated

surfaces (PAA-*g*-CD-Fc/Azo SAM) were formed. The ferrocene-coated surfaces could be deactivated by the release of PAA-*g*-CD-Fc from Azo SAM through the photocontrolled exclusion between *cis*-azobenzene and CD upon UV light irradiation (Fig. 8 from C to D). Finally, *cis*-Azo SAM was isomerized by visible light irradiation to *trans*-Azo SAM (Fig. 8 from D to A), restarting the cycle of reversible immobilization of PAA-*g*-CD-Fc.

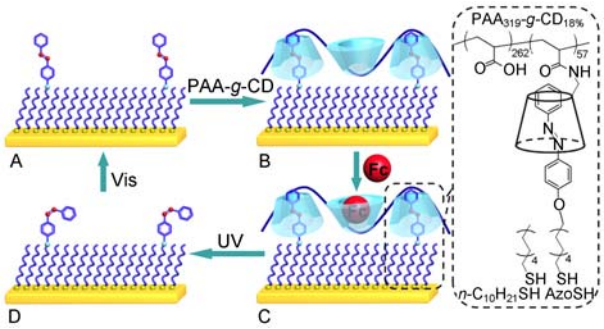

Fig. 8 Photocontrolled reversible immobilization of ferrocene-labeled PAA-*g*-CD. Reproduced with permission.[22] Copyright 2011 The Royal Society of Chemistry

The ferrocene-labeled polymer-coated surfaces can be used as mediators to provide an oxidative electron path from glucose oxidase (GO_x) for bioelectrocatalyzed oxidation of glucose to gluconic acid (Fig. 9A). Meanwhile, after light-driven release of PAA-*g*-CD-Fc, glucose cannot be oxidized to gluconic acid because of the lack of the ferrocene mediator in PAA-g-CD-Fc (Fig. 9B). Therefore, the activation and deactivation of the surface's redox activity by the reversible immobilization and release of PAA-*g*-CD-Fc can be employed for the photoswitchable bioelectrocatalyzed oxidation of glucose with GO_x in an "on-off" state. This avenue of research allows for improved applications using functional switchable biosurfaces such as photoswitchable biofuel cells, controlled biosensors, and other stimuli-responsive biomedical technologies.

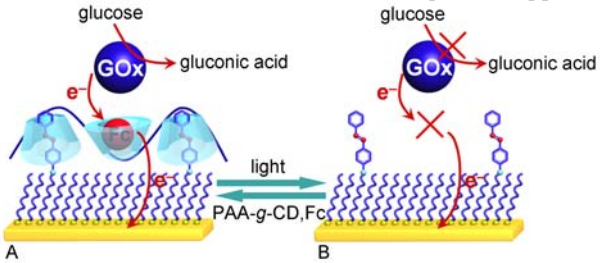

Fig. 9 Photoswitchable interfacial bioelectrocatalysis. Reproduced with permission.[22] Copyright 2011 The Royal Society of Chemistry

6 Conclusions

Based on the host-guest interaction of azobenzene and CD, we have shown that stimuli-responsive surfaces with a variety of tunable or reversible properties can be achieved by transferring supramolecular chemistry from solution to interfaces. Similar methods should hold true for other supramolecular systems. In addition, the marriage of supramolecular chemistry and polymeric systems at the interface can provide a rich structural diversity that can enhance the stability of the system. This line of research extends the horizon of supramolecular chemistry, and provides a new avenue for fabrication of functional surfaces. Further applications for the research covered in this article which are greatly anticipated include photoswitchable biofuel cells, stimuli-responsive biochemical information storage and processing, controlled bioseparation, optobioelectronic devices, and other areas of bioengineering.

Acknowledgement We thank National Basic Research Program (No. 2007CB808000), National Natural Science Foundation of China (No. 50573042), NSFC-DFG TRR61, and Tsinghua University Initiative Scientific Research Program (No. 2009THZ02230).

References

[1] Zhang X, Whitten D G. Langmuir, 2011, 27: 1245—1245
[2] Jiang Y G, Wan P B, Smet M, Wang Z Q, Zhang X. Adv. Mater., 2008, 20: 1972—1977
[3] Jiang Y G, Wang Z Q, Yu X, Shi F, Xu H P, Zhang X, Smet M, Dehaen W. Langmuir, 2005, 21: 1986—1990
[4] Shi F, Niu J, Liu J L, Liu F, Wang Z Q, Feng X Q, Zhang X. Adv. Mater., 2007, 19: 2257—2261
[5] Yu X, Wang Z Q, Jiang Y Q, Shi F, Zhang X. Adv. Mater., 2005, 17: 1289—1293
[6] Zhang X, Shi F, Niu J, Jiang Y Q, Wang Z Q. J. Mater. Chem., 2008, 18: 621—633
[7] Blodgett K B, Langmuir I. Phys. Rev., 1937, 51: 964—982
[8] Decher G. Science, 1997, 277:1232—1237
[9] Nuzzo R G, Fusco F A, Allara D L. J. Am. Chem. Soc., 1987, 109: 2358—2368
[10] Wang Y P, Xu H P, Zhang X. Adv. Mater., 2009, 21: 2849—2864
[11] Liao X J, Chen G S, Liu X X, Chen W X, Chen F E, Jiang M.

Angew. Chem. Int. Ed., 2010, 49: 4409—4413
[12] Liu Y, Chen Y. Acc. Chem. Res., 2006, 39: 681—691
[13] Zhang X, Wang C. Chem. Soc. Rev., 2011, 40: 94—101
[14] Wang Y P, Zhang M, Moers C, Chen S L, Xu H P, Wang Z Q, Zhang X, Li Z B. Polymer, 2009, 50: 4821—4828
[15] Wang C, Wang Z Q, Zhang X. Small, 2011, 7: 1379—1383
[16] Klajn R, Stoddart J F, Grzybowski B A. Chem. Soc. Rev., 2010, 39: 2203—2237
[17] Wang Y P, Ma N, Wang Z Q, Zhang X. Angew. Chem. Int. Ed., 2007, 46: 2823—2826
[18] Wan P B. Doctoral Dissertation of Tsinghua University, 2011
[19] Wan P B, Jiang Y G, Wang Y P, Wang Z Q, Zhang X. Chem. Commun., 2008, 5710—5712
[20] Wan P B, Wang Y P, Jiang Y G, Xu H P, Zhang X. Adv. Mater., 2009, 21: 4362—4365
[21] Wan P B, Chen Y Y, Xing Y B, Chi L F, Zhang X. Langmuir, 2010, 26: 12515—12517
[22] Wan P B, Xing Y B, Chen Y Y, Chi L F, Zhang X. Chem. Commun., 2011, 47: 5994—5996
[23] Tian H, Wang Q C. Chem. Soc. Rev., 2006, 35: 361—374
[24] Coronado E, Gavina P, Tatay S. Chem. Soc. Rev., 2009, 38: 1674—1689
[25] Willner I, Pardo-Yissar V. J. Electroanal. Chem., 2001, 497: 172—177
[26] Wenz G, Han B H, Müller A. Chem. Rev., 2006, 106: 782—817
[27] Kawaguchi Y, Harada A. J. Am. Chem. Soc., 2000, 122: 3797—3798
[28] Mahan E J, Dennis J A. Org. Lett., 2006, 8: 5085—5088
[29] Jiao H, Goh S H, Valiyaveettil S. Macromolecules, 2003, 36: 4241—4243
[30] Mendes P M. Chem. Soc. Rev., 2008, 37: 2512—2529
[31] Xu J S, Bowden E F. J. Am. Chem. Soc., 2006, 128: 6813—6822
[32] Zhou J H, Lu X B, Hu J Q, Li J H. Chem. Eur. J., 2007, 13: 2847—2853
[33] Jiang S Y, Cao Z Q. Adv. Mater., 2010, 22: 920—932
[34] Ma H W, Wells M, Beebe T P, Chilkoti A. Adv. Funct. Mater., 2006, 16: 640—648
[35] Mohammed J S, Murphy W L. Adv. Mater., 2009, 21: 2361—2374
[36] Shipway A N, Willner I. Acc. Chem. Res., 2001, 34: 421—432
[37] Niazov T, Shlyahovsky B, Willner I. J. Am. Chem. Soc., 2007, 129: 6374—6375

界面超分子化学与响应性功能表面

万鹏博[1]　Hill Eric H.[2]　张　希[1*]

(1. 有机光电子与分子工程教育部重点实验室 清华大学化学系　北京 100084;
2. 化学和核工程系 生物医学工程中心 新墨西哥大学 阿尔布开克
新墨西哥 87131-1341 美国)

摘　要　超分子化学和界面的结合有效地促进了超分子化学和胶体与界面科学的发展。刺激响应性超分子界面,因在外界刺激作用下能够引起界面物理化学性质的改变并带来新的界面功能,而受到广泛的关注。近年来,溶液中基于偶氮苯-环糊精主客体相互作用的超分子组装体已经得到了广泛的研究。我们将溶液中基于偶氮苯-环糊精主客体作用的可控可逆超分子组装体转移到界面上,构筑了具有刺激响应性的功能化超分子界面,并实现了表面浸润性的可逆调控、生物大分子的可控吸附与脱附、光可控的生物电化学催化等功能。我们期待类似的概念可以拓展到其他超分子体系,构筑具有特定结构的功能界面。

关键词　界面超分子化学　响应性功能界面　主客体化学　蛋白质固定与释放　生物电化学催化
中图分类号: O631.2;O644.1;O647.1　**文献标识码**: A　**文章编号**: 1005-281X(2012)01-0001-07