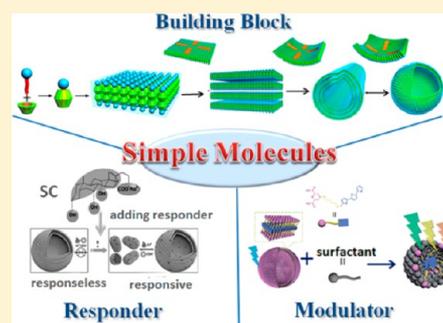


## Advanced Molecular Self-Assemblies Facilitated by Simple Molecules

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**ABSTRACT:** Advanced materials are often based on smart molecular self-assemblies that either respond to external stimuli or have hierarchical structures. Approaches to this goal usually stem from complicated molecular design and difficult organic synthesis. In this invited feature article, we demonstrate that desired molecular self-assemblies can be made conveniently by introducing simple functional molecules into amphiphilic systems. We show that upon introducing specific small molecules which serve as responders, modulators, or even building blocks, smart supramolecular architectures can be achieved which avoid complicated organic synthesis. We expect that this could be a general and economical way to produce advanced materials in the near future.



## 1. INTRODUCTION

Molecular self-assembly,<sup>1–3</sup> the spontaneous association of molecules into structurally well-defined entities, is ubiquitous throughout basic science, technology, and nature.<sup>4</sup> It provides a general route to achieving order from disorder at various length scales.<sup>5–7</sup> Extensive effort has been exerted for surfactants,<sup>8</sup> polymers,<sup>9</sup> colloidal particles,<sup>4</sup> and even large biological molecules,<sup>10</sup> where these building blocks organize into larger-scale ordered structures.<sup>11</sup> Molecular self-assembly not only leads to a better understanding of biological systems but also enriches rational building units for complex and functional materials.

There are thousands of natural and artificial molecules known to mankind, but their functions are far beyond being fully recognized. For instance, many previously discovered drugs are found to be efficient in treating new diseases, and a simple combination of some ordinary molecules may produce amazing materials or structures. It is expected that the employment of the existing simple molecules may be an economical approach that leads to advanced materials.

This critical review aims to elucidate the versatility and fantastic functions of simple molecules in self-assembling systems developed in our laboratory. The contents are arranged in the following way: (1) general principles of using simple molecules; (2) a brief description of the advanced systems built up with specific simple molecules where they serve as the responder, modulator, or building block; and (3) perspectives on the impact of simple molecules on the future of material science.

## 2. GENERAL PRINCIPLES OF USING SIMPLE MOLECULES

Simple molecules refer to those with low molecular weight which are obtained easily either from nature or by laboratory synthesis. Usually, small molecules themselves are not able to self-assemble although they bear functional groups. However, they are able to interact with most amphiphiles by noncovalent interactions, such

as electrostatic interactions, hydrophobic interaction, hydrogen bonding, coordination, or  $\pi$ - $\pi$  stacking. In this way, the functional groups can be introduced to the self-assembled structures of amphiphiles. Of course, these simple molecules may contribute to the self-assembling structures as well in the form of formation via coassembly. Upon employment of different combinations of simple molecules and amphiphiles, one may expect bulk materials based on various self-assembled structures. Since the functional groups provided by simple molecules may change their conformation or structure upon exerting a stimulus, such as photo, chemical, pH, shearing, or temperature, the self-assembled structures change accordingly, as will be expressed as the responsiveness to the corresponding stimulus of the bulk materials.

Clearly, one need only choose a simple molecule which contains groups that respond to the desired stimulus in order to fabricate a smart material that responds to a certain stimulus. Then combine this responsive simple molecule with an amphiphile so that they may interact through noncovalent interactions. This avoids tedious synthesis chemistry and leads to convenient supramolecular self-assemblies. It is well known that supramolecular chemistry is one of the major approaches toward advanced materials. The characteristic feature of advanced materials lies mainly in their smart responsiveness to external stimuli and their hierarchical structures. From this point of view, the role of simple molecules in molecular self-assemblies can be briefly categorized as (1) stimuli responders, which endow the stimuli inert systems with responsiveness to various external stimuli, such as photo, chemicals, temperature, pH, and salt; (2) structural modulators, which assist in the formation of different structures other than the original molecular self-assemblies formed by the amphiphilic component; and (3) structure

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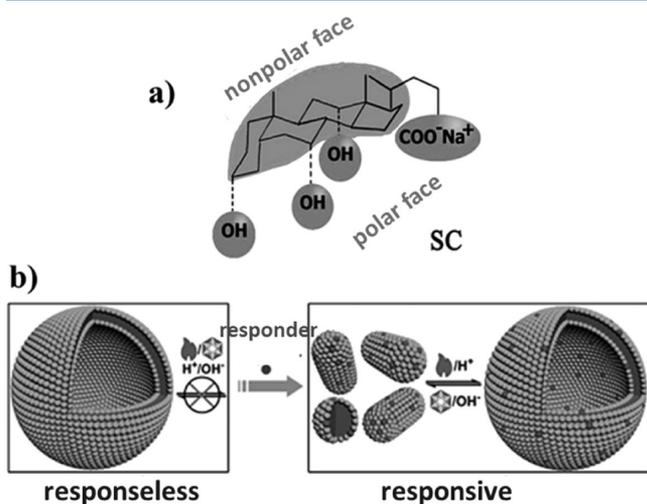
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makers, namely, acting as key building blocks which have never been realized to form novel self-assemblies. In the following text, we briefly introduce approaches taken in our laboratory to fabricate advanced molecular self-assemblies on the basis of simple molecules.

### 3. SIMPLE MOLECULE AS A FUNCTIONAL RESPONDER

Smart materials which are able to respond to external fields or stimuli have attracted intense attention in nanoscience and nanotechnology. In past decades, great effort has been input to create various novel molecules to achieve this goal.<sup>2,12–17</sup> This not only involves complicated organic synthesis but also confronts the problem of bulk fabrication. Therefore, simple protocols that avoid organic synthesis are highly desired to fabricate responsive materials that have applicable potential. It is realized that it is not necessary that all of the structure-forming molecules be responsive to stimuli; in most cases, the responsiveness produced by a small fraction of molecules may already produce a strong-enough effect for the whole system. As examples for demonstration, we will introduce some responsive self-assemblies completed in our laboratory upon introducing a simple molecule into a nonresponsive self-assembled system.

**3.1. Sodium Cholate (SC) as a Temperature and pH Dual Responder.** Sodium cholate (SC) is a member of the bile salts, which are different from conventional “head-and-tail” surfactants and are well known as facial amphiphiles composed of a polar face and a nonpolar face.<sup>18</sup> In addition, SC has three temperature-responsive hydroxyl groups, a pH-responsive carboxylate group, and a hydrophobic steroid skeleton<sup>18</sup> (Figure 1a). When a small amount of SC was added to a stimuli-inert



**Figure 1.** (a) Molecular structure of SC. Its facially amphiphilic structure is highlighted. Its hydroxyl groups and carboxylate group are sensitive to temperature and pH, respectively. (b) Adding a responder (SC) endows responseless catanionic surfactant vesicles with temperature- and pH-responsive abilities. Copyright 2008, Royal Society of Chemistry.

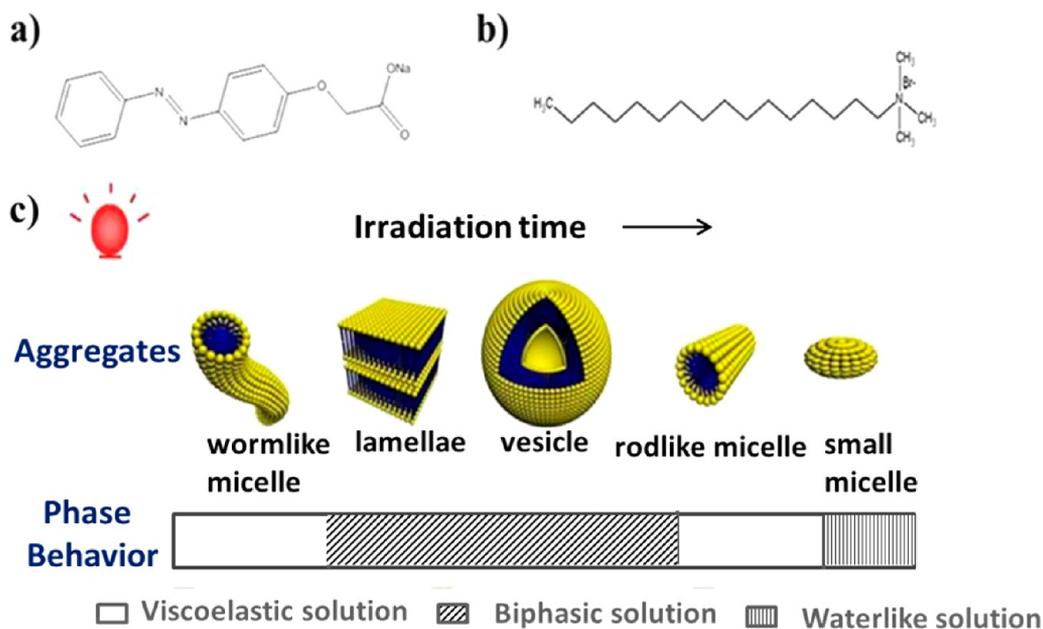
vesicular system formed with dodecyltriethylammonium bromide (DEAB)/ sodium dodecyl sulfonate (SDS),<sup>19</sup> the DEAB/SDS vesicles exhibited temperature and pH dual responsiveness. The system underwent a micelle-to-vesicle transition (MVT) upon heating or acidifying, and the reverse process occurred when cooling or alkalifying (Figure 1b). It is well known that catanionic surfactants have a superior ability to form vesicles, but these vesicles are inert to external stimuli, which makes them less applicable on many occasions. However, upon introducing the

responsive SC into the DEAB/SDS system we are able to make the system both pH- and temperature-sensitive. Since temperature and pH responsiveness are relevant to many biological processes and smart materials, our strategy makes it possible to gain scientific insight or to construct responsive materials using simple catanionic surfactants.

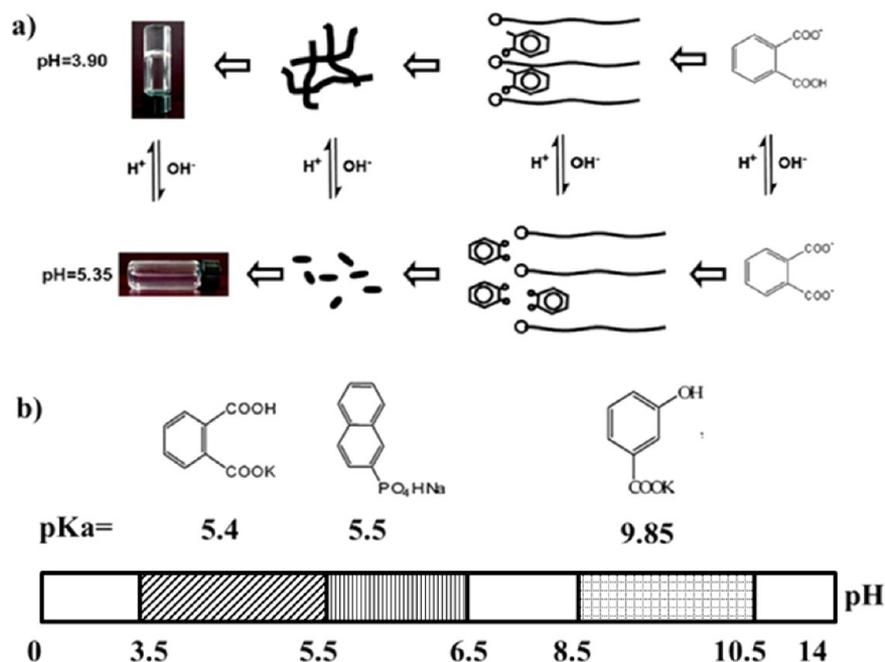
**3.2. Sodium (4-Phenylazo-phenoxy)-acetate (AzoNa) as a Photoresponder.** Azobenzene compounds are very often used to build photosensitive molecular self-assemblies.<sup>20–23</sup> The often-employed strategy is to synthesize complicated amphiphiles which contain azobenzene groups.<sup>24,25</sup> Upon exerting UV irradiation, the azobenzene groups undergo trans–cis isomerization, which triggers the phase and structure differences in the self-assemblies.<sup>26</sup> For instance, this has been utilized to switch on or switch off supramolecular processes such as host–guest chemistry,<sup>27</sup> the reversible self-assembly of amphiphiles,<sup>20</sup> the fabrication of molecular machines,<sup>21</sup> changing the wettability of modified surfaces,<sup>28</sup> and control over drug release.<sup>22</sup>

Considering that the synthesis of photoresponsive self-assembled molecules is usually quite complicated and often not available in many laboratories, the employment of simple molecules which possess photoresponsive groups together with an amphiphile seems very promising. The two form mixed self-assemblies where the photoresponsive molecules act as the responder. Then upon light irradiation the photoresponder changes its properties, which leads to a change in the original self-assemblies. For instance, when a small sodium acetate azobenzene molecule (AzoNa) was introduced into the aqueous solution of cetyltrimethylammonium bromide (CTAB), dramatic phase and microstructures were triggered.<sup>29</sup> The light-triggered trans–cis transition of AzoNa caused a significant change in its dipole moment. This led to a weaker interaction between the CTAB molecules and *cis*-AzoNa so that the mode of molecular packing in the CTAB/AzoNa mixed system was changed accordingly. Depending on the UV irradiation time, four phase states resulting from multiscale nanostructures were obtained in the mixed system, namely, the viscoelastic phase of a long, flexible wormlike micelle, a biphasic solution of global vesicles and planar lamellae, a viscous fluid of rodlike micelles, and a waterlike system of small micelles (Figure 2). It is anticipated that the concept of photomodulated multistate and multiscale self-assembling systems may be extended to related research areas such as molecular devices, logic gates, and sensors.

**3.3. Hydrophobic Salt as pH Responder.** Hydrophobic salt has been widely used to tune the self-assembled structure of amphiphiles. These are a class of salts that bear an aromatic group (hydrophobic) and an ionic group (hydrophilic).<sup>30</sup> They cannot self-assemble in water but may facilitate the self-assembly of other amphiphiles.<sup>31–33</sup> For instance, Hoffmann et al. reported that nanofibers can be formed upon addition of a hydrophobic salt to the surfactant solution of tetradecyldimethyl amine oxide (C14DMAO).<sup>34,35</sup> Raghavan et al. found that the rheological behavior of fluids formed with amphiphiles can be considerably changed upon introduction of various hydrophobic salts into the system.<sup>36</sup> Lin et al. in our group found that by careful selection of a hydrophobic salt, a system can be endowed with pH responsiveness using commercially available compounds.<sup>37</sup> According to this route, pH-sensitive viscoelastic fluids can be easily obtained by introducing a pH-responsive hydrophobic salt such as potassium phthalic acid (PPA) into a solution of CTAB. This fluid can be switched between a gellike state and a waterlike state within a narrow pH range (Figure 3a). Rheology and DLS results revealed that the pH-sensitive flow behavior was



**Figure 2.** (a) Molecular structure of AzoNa. (b) Molecular structure of CTAB. (c) Structural evolution and phase behavior in the solution of 30 mM CTAB and 50 mM AzoNa varying with UV irradiation time.

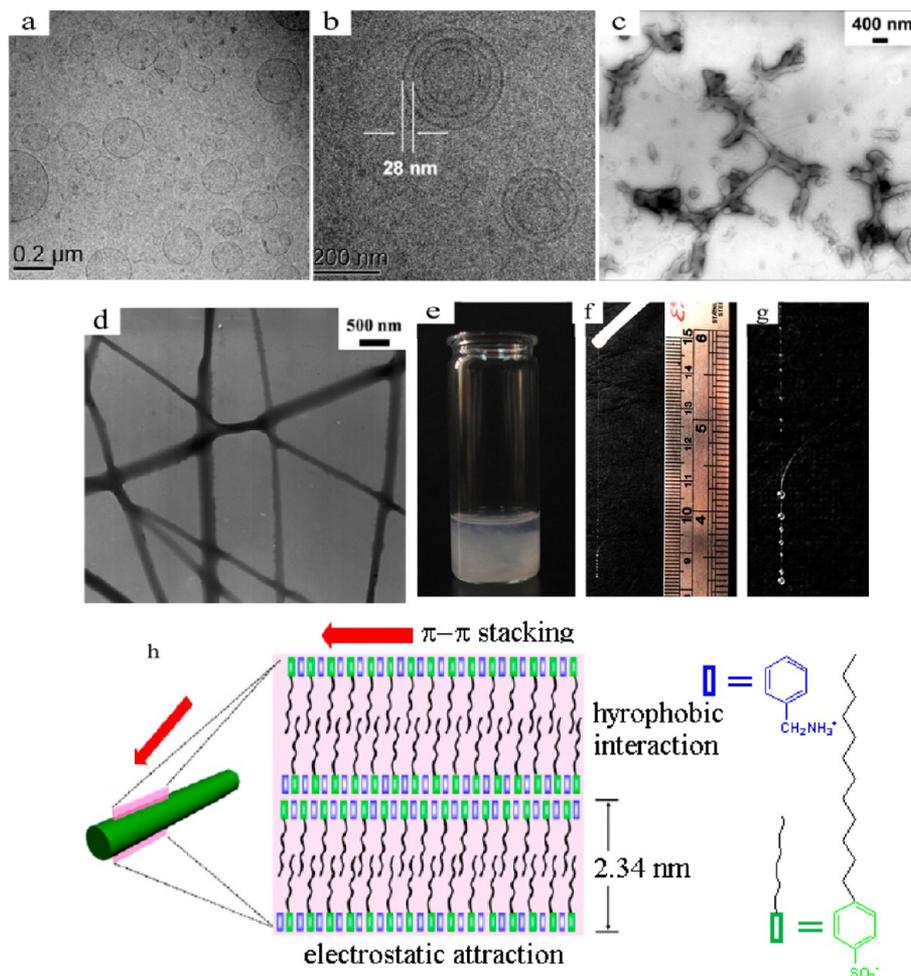


**Figure 3.** (a) Illustration of the self-assembled structures from wormlike micelles to short cylindrical micelles with pH variation. (b) Schematic of the responsive pH window for the 60 mM CTAB system upon addition of 40 mM different hydrophobic salts: pH 3.5–5.5, potassium phthalic acid (oblique line region); pH 5.5–6.5, 2-naphthyl phosphate monosodium (vertical bar region); pH 8.5–10.5, 3-hydroxybenzoic acid (gridding region).

attributed to the microstructural transition between wormlike micelles and short cylindrical micelles. Replacing PPA with other hydrophobic salts such as 2-naphthyl phosphate monosodium and 3-hydroxybenzoic acid may also lead to pH-responsive viscoelastic fluids (Figure 3b). Because the viscoelasticity of the fluids changes sharply around the  $pK_a$  of the hydrophobic salt, this allows us to design smart fluids over a wide spectrum of pH simply by the employment of hydrophobic salts with the desired  $pK_a$ .

#### 4. SIMPLE MOLECULE AS A STRUCTURAL MODULATOR

Recently, tuning the morphologies or the properties of molecular self-assemblies has attracted increasing attention since structural transitions are important processes in biological and materials science.<sup>38–40</sup> The transition of molecular self-assemblies in the presence of other small molecules is of particular importance in understanding the evolution of disease and the performance of materials. In the following text, we summarize some representative work in our laboratory concerning tuning the self-assembled structures with simple molecules.



**Figure 4.** (a–d) Microscopic structure of the unilamellar vesicles (a, cryo-TEM), multilamellar vesicles (b, cryo-TEM), aggregates of vesicles (c, TEM), and fibers (d, TEM) formed in the mixed system of SDBS/BzCl. (a, b) From mixed systems aged for 24 h; (c, d) systems aged for 1 and 6 months, respectively. (e–g) Macroscopic appearance of SDBS/BzCl solution that is kept for 6 months (e); ultralong fibers lifted up from the SDBS/BzCl solution (f, a ruler is also placed on the right to indicate the length of surfactant fiber); and water droplets spreading on ultralong fibers (g). The fibers were prepared in a 10 mM/10 mM SDBS/BzCl solution. (h) Schematic illustration of the molecular packing mode for the fibers formed in the SDBS/BzCl mixed system. Copyright 2012, Elsevier.

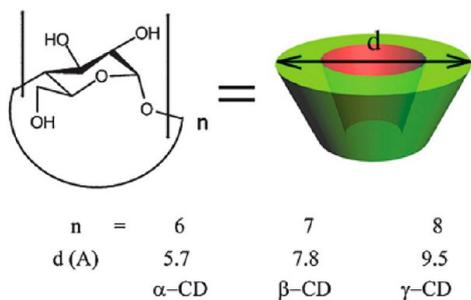
#### 4.1. Inducing Self-Assembly with a Hydrophobic Salt.

Surfactants may form spherical micelles in solution. This is usually not interesting in view of molecular self-assemblies. However, in the presence of small hydrophobic salts, the self-assembling ability of surfactants can be drastically enhanced. Lin et al. in our group reported that anionic surfactant sodium dodecylbenzenesulfonate (SDBS) may be induced to form vesicles by adding hydrotropic salt benzylamine hydrochloride (BzCl).<sup>41</sup> These vesicles can further aggregate to form ultralong fibers. BzCl was found to facilitate the close packing of surfactants, thus inducing the structural transformation from SDBS micelles to unilamellar vesicles (Figure 4a) and multilamellar vesicles (Figure 4b). The multilamellar vesicles could transform into macroscale fibers (Figure 4c,d) after standing still for months, which was long enough to be visualized with the naked eye (Figure 4f). In particular, these fibers were hydrophobic (water droplets may reserbed on the surface of the fiber, Figure 4g) and robust enough to be conveniently separated from the solution. The combined effect of noncovalent interactions such as the hydrophobic effect, electrostatic attractions, and  $\pi$ – $\pi$  interactions was supposed to be responsible for the robustness of the fibers, in which  $\pi$ – $\pi$  interactions

provide the directional driving force for fiber growth. In this recipe, ultralong nanofibers were produced with only two economical molecules upon simple combination, which indicates that advanced materials can indeed be made from existing simple molecules. Obviously, this will greatly simplify the procedure of fabrication and may produce a significant impact on the development of materials science.

#### 4.2. Tuning the Stoichiometry with Cyclodextrins (CDs).

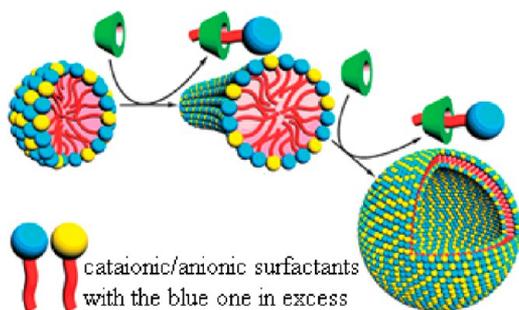
In recent decays, CDs are widely applied in fabricating smart molecular devices owing to their uniquely truncated doughnut-shaped structures.<sup>42</sup> These are oligosaccharides of six, seven, or eight D-glucopyranose ( $C_6H_{10}O_5$ ) units (named  $\alpha$ -,  $\beta$ -, and  $\gamma$ -CD, respectively) linked by  $\alpha$ -1,4 glycoside bonds. The hydrophobic  $CH_2$  groups are located in the cavity which forms a hydrophobic environment, whereas the hydrophilic OH groups in the exterior make the outer surface hydrophilic.<sup>38,43–45</sup> (Figure 5). When such a structure encounters an amphiphile in solution, the hydrophobic portion of the amphiphile will insert into the cavity of CD to make the amphiphile hydrophilic.<sup>46</sup> This was used to disassemble the aggregated structures which were driven by hydrophobic interaction, such as the release of DNA and RNA from the package of polymers.<sup>47</sup> As charged macromolecules,



**Figure 5.** Structure of cyclodextrins (CDs) and approximate values of the largest diameter of their nanocage. Copyright 2011, Royal Society of Chemistry.

DNAs or RNA can form mixed micelles with oppositely charged surfactants; upon addition of  $\beta$ -CD, they are able to be released from the mixed micelles due to the formation of  $\beta$ -CD–surfactant inclusion complexes, which breaks the micelles.

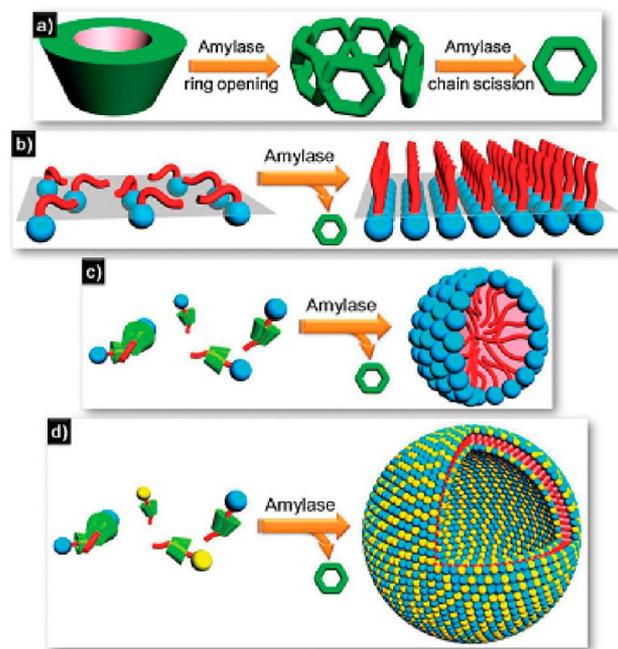
Different from the disassembly of aggregates with CD, we found that CDs can also be used to tune the morphology of the self-assemblies. This smart design was created by Jiang in our group.<sup>48,49</sup>  $\beta$ -CD was added to the mixed cationic/anionic surfactant systems. It exhibited selective binding toward the major component (molar fraction >0.5) in the cationic/anionic surfactant mixture, which changed the effective mixing ratio between the cationic and anionic surfactant. This shifted the system toward a ratio in which the charge was balanced. This composition variation enhanced the electrostatic attractions between the oppositely charged surfactant headgroups and led to self-assemblies with smaller curvature. As a result, the spherical micelles elongated gradually and finally transformed into vesicles. From this point of view,  $\beta$ -CD is a “stoichiometry booster” for the whole class of cationic/anionic surfactant systems (Figure 6).



**Figure 6.** Scheme of the aggregate growth induced by  $\beta$ -CD in nonstoichiometrical cationic/anionic surfactant systems. Upon selective binding of the excess component, the composition in the aggregates gradually approaches 1:1, which is accompanied by aggregate growth. Reprinted with permission from the American Chemical Society, copyright 2009.

A similar strategy is embodied in the work of other groups. For instance, Signorell et al.<sup>50</sup> and Degrip et al.<sup>51</sup> utilized the selective extraction of detergents by CD from the mixed micelles of detergent/lipid/protein to prepare the 2D crystallization of protein. Before CD addition, the detergent/lipid/protein mixture formed mixed micelles due to the presence of a considerable amount of the micelle-forming detergent. After CD addition, the detergent was selectively extracted by CDs, whereas the vesicle-forming lipid and the protein were left to form protein-containing vesicles (a micelle-to-vesicle transition).

**4.3. Tuning the Aggregating States with Enzyme.** Enzyme is known to decompose certain chemical bonds.<sup>52–56</sup> For instance,  $\alpha$ -amylase can cleave  $\alpha$ -1,4 linkages between glucose units of starch molecules including CDs, which will degrade CDs in two steps (ring opening and chain scission) giving glucose in the end (Figure 7a).<sup>54</sup> This was smartly used to

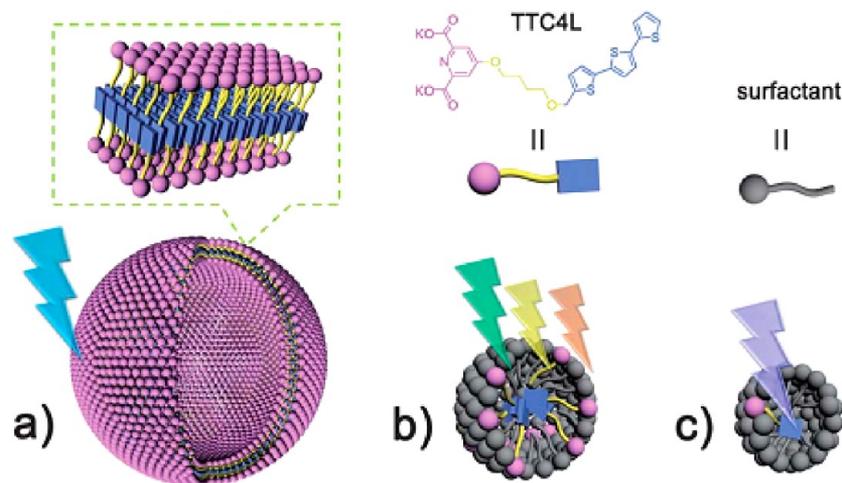


**Figure 7.** Schematic illustrations of the degradation of  $\beta$ -CD by  $\alpha$ -amylase (a), enzyme-triggered monolayer formation (b), enzyme-triggered micellization (c), and enzyme-triggered vesicle formation (d). Copyright 2012, Royal Society of Chemistry.

tune the self-assembly transition in the host–guest system by Jiang et al.<sup>57</sup> The addition of  $\alpha$ -amylase to surfactant/CD mixtures resulted in releasing the included surfactant molecules. For dilute surfactant/CD solutions, this led to the occurrence of adsorbed film on the surface and resulted in a dramatic decrease in the surface tension (Figure 7b). For surfactant/CD solutions close to its CMC, the addition of  $\alpha$ -amylase switched on the formation of micelles (Figure 7c). Similarly, for systems far beyond the CMC, the addition of  $\alpha$ -amylase triggered the formation of vesicles (Figure 7d). It is worth mentioning that the abnormal increase in  $\alpha$ -amylase is intimately associated with acute pancreatitis, thus the  $\alpha$ -amylase-triggered self-assembly might be of potential use in their early detection and clinical treatment.

#### 4.4. Tuning the Molecular Distance with Surfactant.

The coassembly of surfactant with other amphiphiles has been widely applied in molecular self-assemblies, especially in inducing the self-assembly of insoluble molecules. This actually changes the distance between the strongly interacting molecules. Therefore, we expect that surfactant can be specially used to tune the distance between interacting molecules. To this end, we employed a cationic surfactant, dodecyltriethylammonium bromide (DEAB), to tune the distance between amphiphiles containing thiophene groups TTC4L to obtain multicolor emissions (Figure 8).<sup>58</sup> The rationale is that the emission of oligo thiophene is intermolecular-distance-dependent. Oligo-thiophene amphiphile TTC4L self-assemble into vesicles in solution which exhibits blue emission. Upon tuning the



**Figure 8.** Illustration of the arrangement of TTC4L molecules under various conditions. (a) Self-assembly formed by TTC4L. (b, c) Coassemblies between TTC4L and surfactants with increasing surfactant concentration. The lightning bolts represent different emitted colors by the various assemblies. Copyright 2012, Royal Society of Chemistry.

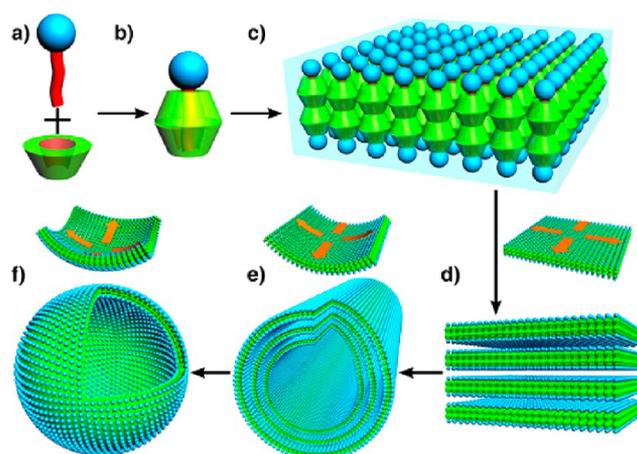
intermolecular distance between the terthiophene groups by changing the self-assembly of TTC4L to its coassembly with various surfactants, Zhao et al. obtained emissions from violet to orange which cover most of the visible-light region. It is worth noting that this approach avoids changing and modifying the structure of the TTC4L and achieves multicolor emission on a one-molecule platform. We expect that it is a general approach applicable to many surfactants and fluorescent molecules with similar properties.

## 5. SIMPLE MOLECULE AS A BUILDING BLOCK

According to experiences in the past, advanced self-assemblies are usually constructed with complicated molecules.<sup>4,6</sup> Recently, it was found that advanced building blocks can also be made with simple molecules. In this section, we will introduce some typical illustrations completed in our laboratory to serve as a modest spur to future contributions in this field.

**5.1. Surfactant @ 2CD as a Building Block.** It has long been considered that the addition of cyclodextrins (CDs) disfavors the self-assembly of surfactants in dilute solutions since the hydrophobic effect is destroyed upon the formation of the hydrophilic CD/surfactant inclusion complex. But in a series of works by Jiang et al., it was found when the tail of a surfactant is completely buried in the cavity of CD, the supramolecular complex may act as a novel hydrophilic building block to form nonamphiphilic self-assemblies. For instance, as the molar ratio of SDS and  $\beta$ -CD was 1:2 in aqueous media, channel-type dimers of  $\beta$ -CD can be formed with the tail of SDS going through the cavities. This led to an SDS@2 $\beta$ -CD supramolecular complex (Figure 9a,b). At high enough concentrations, the supramolecular tile of SDS@2 $\beta$ -CD is able to self-assemble into well-defined lamellae (Figure 9d), tubes (Figure 9e), and vesicles (Figure 9f), depending simply on concentration.<sup>59–61</sup>

As shown in Figure 9, all three classes of aggregates share a consistent SDS@2 $\beta$ -CD building block, which forms the channel-type crystalline bilayer membrane (Figure 9c); the membrane will laterally expand into infinite 2D lamellar structures at high concentrations (Figure 9d), extend in one direction, and scroll up in the perpendicular direction to form 1D multilayer microtubes (Figure 9e) or close up along two in-plane axes to generate dispersed vesicles (Figure 9f).

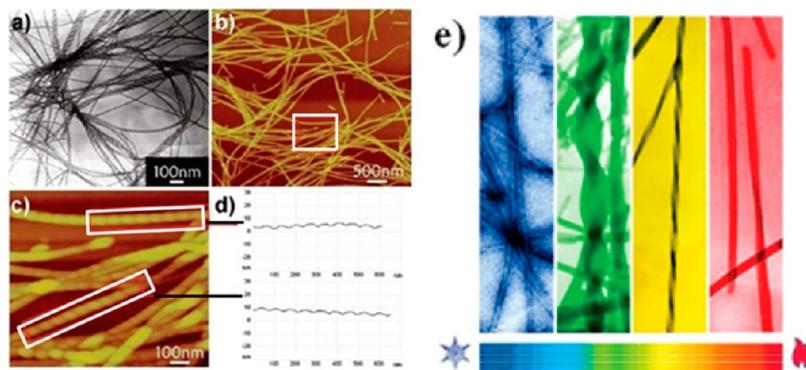


**Figure 9.** Schematic self-assembly behavior of SDS@2 $\beta$ -CD. (a) SDS and  $\beta$ -CD monomers. (b) SDS@2 $\beta$ -CD complex. (c) SDS@2 $\beta$ -CD bilayer membrane with a channel-type crystalline structure. (d–f) The aggregates transform upon dilution from lamellae via microtubes to vesicles. Copyright 2011, Royal Society of Chemistry.

These self-assembled structures are driven by hydrogen bonding. For this reason, they are sensitive to temperature. At temperature above 42 °C, the hydrogen bonding in this system is greatly retarded so that the tubes tend to transform into vesicle and the vesicles tend to break.<sup>62</sup>

Electrostatic interactions were found to determine the critical self-aggregation concentration of the system. The presence of ionic repulsion requires a higher concentration to form self-assembled structures, whereas in nonionic surfactant systems this aggregation concentration is greatly lowered. For instance, in an ionic surfactant SDS system, the critical aggregation concentration at 25 °C is 5%, whereas that in the nonionic surfactant Tween 20 system is only 0.02 mM.<sup>63</sup>

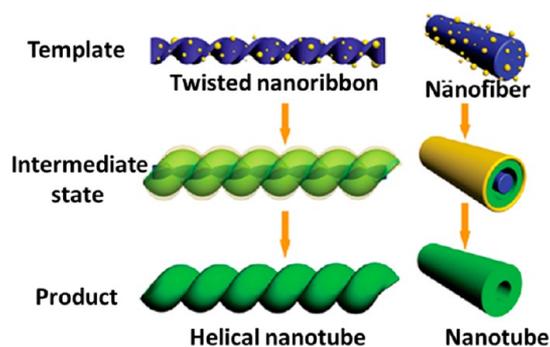
**5.2. Sodium Cholate as a Building Block.** Sodium cholate (SC) is well known for its superior self-assembly properties. As mentioned in previous text, this molecule has an ionic carbonate group.<sup>64–66</sup> Because many metal ions may coordinate with the carbonate group, we expect multivalent metal ions to connect at least two such groups to form 1D or 3D structures. This is indeed the case. Well-defined right-handed helical nanoribbons in



**Figure 10.** Morphology of calcium cholate supramolecular nanohelices. (a) Typical unstained TEM image of right-handed nanohelices; (b) tapping-mode AFM height image revealing the helical undulation feature; (c) high magnification of the boxed area in (b); (d) corresponding cross-sectional analysis of nanohelices showing uniform pitches; and (e) representative scheme of the temperature-dependent nanostructural evolution of the hydrogel.

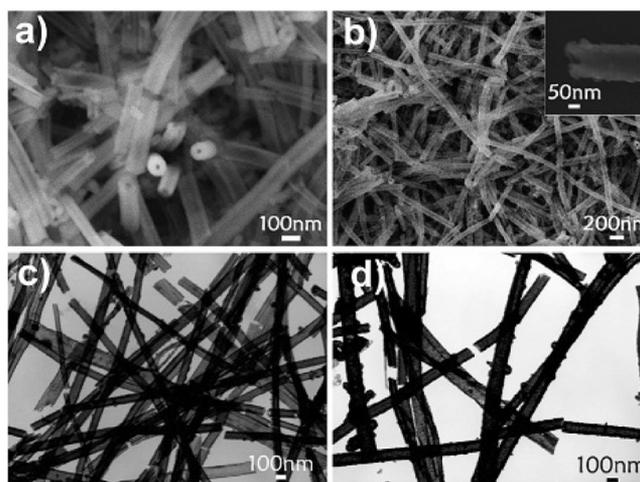
calcium cholate systems were obtained (Figure 10).<sup>67,68</sup> The entanglement of 1D nanostructures was demonstrated to give rise to a fascinating “superhydrogel”, which can realize water gelation at extremely low concentration.<sup>69</sup> Normally, self-assembled hydrogels may undergo a gel–sol phase transition as the temperature increases, accompanied by a decrease in mechanical strength. But the lanthanum cholate supramolecular hydrogel, however, exhibited increased mechanical intensity with increasing temperature.<sup>69</sup> This was attributed to continuous growth in the size of the self-assembled nanostructures in this system. Because hydrogen bonding plays an important role in the self-assembly of the SC metal system, increasing temperature caused larger self-assembling domains. Namely, the initial nanotubes gradually transformed into helical ropes, then twisted nanoribbons, and finally into plain nanoribbons as the temperature increased (Figure 10e).

Moreover, the metal cholate supramolecular systems were appealing soft templates for designing inorganic helical materials. For instance, we obtain SiO<sub>2</sub> tubes by hydrolysis tetraethyl orthosilicate (TEOS) in the hydrogel system.<sup>70</sup> Meanwhile, the metal ions also serve as the inorganic precursor (Figure 11).



**Figure 11.** Schematic diagram of the self-templating protocol. Copyright 2011, American Chemical Society.

Since the nanohelices or nanoribbons were formed in the coordinating self-assembly of metal ions and SC, 1D inorganic materials ZnS, CuS, NiS, CdS, CoS, ZnSe, and ZnTe nanotubes (Figure 12) were obtained simply by introducing Na<sub>2</sub>S, thioacetamide, and sodium hydrogen selenide into the hydrogel.<sup>70</sup> This strategy is therefore believed to provide a simple and convenient route to creating 1D inorganic nanomaterials with controllable shape, size, and helicity.



**Figure 12.** Zinc chalcogenide nanotubes prepared by the self-templating strategy. SEM images (a, b) and TEM images (c, d) for ZnSe nanotubes (a, c) and ZnTe nanotubes (b, d). Copyright 2011, American Chemical Society.

## 6. CONCLUSIONS AND PERSPECTIVES

The invention and fabrication of advanced materials are permanent goals of mankind. People on the one hand like improved functions, and on the other hand, they hope to have economic bulk fabrication. In the latter regard, strategies based on simple molecules have become very promising in the development of materials science. The examples given in this review are only some primary explorations of our group. We expect that this may shed some light on constructing advanced or smart materials based on supramolecular self-assembly.

The main advantage of using existing simple molecules as functional groups is convenience. However, this may also bring up another question: are the materials based on these strategies as robust as those made with synthetic compounds? This is a bottleneck that limits the future of materials based on simple molecules. Therefore, studying the synergism effect of non-covalent interaction between the existing simple molecules and given amphiphilic molecules will be very important. This requires the construction of new model systems to demonstrate the correlation between the synergism effect and the strength of materials. Obviously, combinations based on other simple molecules with specific functions and structures are highly desired. We look forward to seeing much more comprehensive

work in this regard. We also envision that the interplay between molecular and colloidal self-assembly may provide a fruitful pathway toward novel functional materials. This may be a simple and promising strategy for fabricating stimuli-responsive organized structures based on commercial compounds, which is expected to connect fundamental research to practical applications.

## AUTHOR INFORMATION

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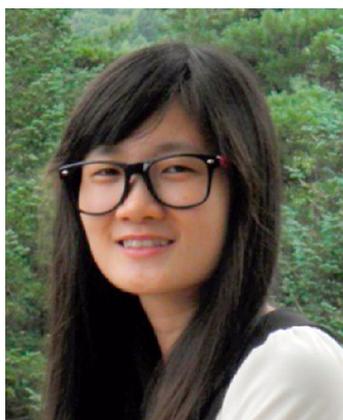
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### Notes

The authors declare no competing financial interest.

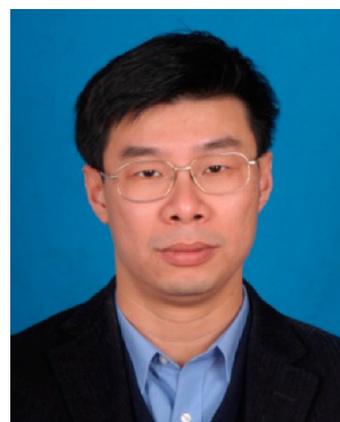
### Biographies



Zheng Wu is currently a Ph.D. candidate at Peking University. She obtained her bachelor's degree at China Agricultural University in 2012 and is expecting the Ph.D. degree at Peking University in 2017. Her study focuses on metallo-supramolecular assemblies and the electrostatic self-assembly of polyelectrolytes. She will also try to explore other interesting aspects in the field of self-assembly in the future.



Yun Yan earned her bachelor's degree at Northeast Normal University (1997) and the Ph.D. degree at Peking University (2003), China. After two postdoctoral studies at Bayreuth University (Germany, with professor Hoffmann) and Wageningen University (The Netherlands, with professor Martien A. Cohen Stuart) in colloid science, she joined Peking University as an associate professor in 2008. She was selected for the New Century Training Program for the Talents by the State Education Commission of China in 2009 and was named an Outstanding Young Professor of Colloid Science of China in 2013. Her current interest is solution-based molecular self-assembly and the application of molecular self-assembly in various advanced materials.



Jianbin Huang obtained his bachelor's (1987), master's (1990), and Ph.D. (1993) degrees at Peking University, China. After a postdoctoral study at the same university, he was nominated as an associate professor in 1995 and as a full professor in 2001 and was named an "Outstanding Young Scientist of China" in 2004. His main research interests include the soft self-assembly of amphiphiles and 1D nanomaterials that are synthesized using soft templates. He is currently the senior editor of *Soft Matter* and also on the editorial board of *Langmuir*.

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## REFERENCES

- (1) van de Manakker, F.; van der Pot, M.; Vermonden, T.; van Nostrum, C. F.; Hennink, W. E. Self-assembling Hydrogels Based on Beta-cyclodextrin/cholesterol Inclusion Complexes. *Macromolecules* **2008**, *41*, 1766–1773.
- (2) Wang, Y.; Ma, N.; Wang, Z.; Zhang, X. Photocontrolled Reversible Supramolecular Assemblies of an Azobenzene-containing Surfactant with Alpha-cyclodextrin. *Angew. Chem., Int. Ed.* **2007**, *46*, 2823–2826.
- (3) Alarcon, C. D. H.; Pennadam, S.; Alexander, C. Stimuli Responsive Polymers for Biomedical Applications. *Chem. Soc. Rev.* **2005**, *34*, 276–285.
- (4) Whitesides, G. M.; Grzybowski, B. Self-assembly at All Scales. *Science* **2002**, *295*, 2418–2421.
- (5) Ku, T.-H.; Chien, M.-P.; Thompson, M. P.; Sinkovits, R. S.; Olson, N. H.; Baker, T. S.; Gianneschi, N. C. Controlling and Switching the Morphology of Micellar Nanoparticles with Enzymes. *J. Am. Chem. Soc.* **2011**, *133*, 8392–8395.
- (6) Lehn, J. M. Toward Complex Matter: Supramolecular Chemistry and Self-organization. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 4763–4768.
- (7) Nayak, S.; Lyon, L. A. Soft Nanotechnology with Soft Nanoparticles. *Angew. Chem., Int. Ed.* **2005**, *44*, 7686–7708.
- (8) Svenson, S. Controlling Surfactant Self-assembly. *Curr. Opin. Colloid Interface Sci.* **2004**, *9*, 201–212.
- (9) Wu, L.; Lal, J.; Simon, K. A.; Burton, E. A.; Luk, Y.-Y. Nonamphiphilic Assembly in Water: Polymorphic Nature, Thread Structure, and Thermodynamic Incompatibility. *J. Am. Chem. Soc.* **2009**, *131*, 7430–7443.
- (10) Guo, J.; Zhuang, J. M.; Wang, F.; Raghupathi, K. R.; Thayumanavan, S. Protein And Enzyme Gated Supramolecular Disassembly. *J. Am. Chem. Soc.* **2014**, *136*, 2220–2223.
- (11) Guo, D. S.; Wang, K.; Wang, Y. X.; Liu, Y. Cholinesterase-Responsive Supramolecular Vesicle. *J. Am. Chem. Soc.* **2012**, *134*, 10244–10250.
- (12) Ahn, S.-K.; Kasi, R. M.; Kim, S.-C.; Sharma, N.; Zhou, Y. Stimuli-responsive Polymer Gels. *Soft Matter* **2008**, *4*, 1151–1157.

- (13) Morimoto, N.; Ogino, N.; Narita, T.; Kitamura, S.; Akiyoshi, K. Enzyme-responsive Molecular Assembly System with Amylose-primer Surfactants. *J. Am. Chem. Soc.* **2007**, *129*, 458–459.
- (14) Mart, R. J.; Osborne, R. D.; Stevens, M. M.; Ulijn, R. V. Peptide-based Stimuli-Responsive Biomaterials. *Soft Matter* **2006**, *2*, 822–835.
- (15) Medina, J. C.; Gay, L.; Chen, Z. H.; Echegoyen, L.; Gokel, G. W. Redox-switched Molecular Aggregates - The 1st Example of Vesicle Formation From Hydrophobic Ferrocene Derivatives. *J. Am. Chem. Soc.* **1991**, *113*, 365–366.
- (16) Reeves, P. J.; Hwa, J.; Khorana, H. G. Structure and Function in Rhodopsin: Kinetic Studies of Retinal Binding to Purified Opsin Mutants in Defined Phospholipid-detergent Mixtures Serve as Probes of the Retinal Binding Pocket. *Proc. Natl. Acad. Sci. U.S.A.* **1999**, *96*, 1927–1931.
- (17) Winnik, F. M.; Whitten, D. G.; Urban, M. W. Stimuli-responsive Materials: Polymers, Colloids, and Multicomponent Systems. *Langmuir* **2007**, *23*, 1–2.
- (18) Tung, S. H.; Huang, Y. E.; Raghavan, S. R. A New Reverse Wormlike Micellar System: Mixtures of Bile Salt and Lecithin in Organic Liquids. *J. Am. Chem. Soc.* **2006**, *128*, 5751–5756.
- (19) Jiang, L.; Wang, K.; Ke, F.; Liang, D.; Huang, J. Endowing Catanionic Surfactant Vesicles With Dual Responsive Abilities via a Noncovalent Strategy: Introduction of a Responder, Sodium Cholate. *Soft Matter* **2009**, *5*, 599.
- (20) Sakai, H.; Matsumura, A.; Yokoyama, S.; Saji, T.; Abe, M. Photochemical Switching of Vesicle Formation Using an Azobenzene-modified Surfactant. *J. Phys. Chem. B* **1999**, *103*, 10737–10740.
- (21) Song, X. D.; Perlstein, J.; Whitten, D. G. Supramolecular Aggregates of Azobenzene Phospholipids and Related Compounds in Bilayer Assemblies and Other Microheterogeneous Media: Structure, Properties, and Photoreactivity. *J. Am. Chem. Soc.* **1997**, *119*, 9144–9159.
- (22) Dugave, C.; Demange, L. cis-trans Isomerization of Organic Molecules and Biomolecules: Implications and Applications. *Chem. Rev.* **2003**, *103*, 2475–2532.
- (23) Ferri, V.; Elbing, M.; Pace, G.; Dickey, M. D.; Zharnikov, M.; Samori, P.; Mayor, M.; Rampi, M. A. Light-powered Electrical Switch Based on Cargo-lifting Azobenzene Monolayers. *Angew. Chem., Int. Ed.* **2008**, *47*, 3407–3409.
- (24) Hayashita, T.; Kurosawa, T.; Miyata, T.; Tanaka, K.; Igawa, M. Effect of Structural Variation Within Cationic Azo-surfactant Upon Photoresponsive Function in Aqueous-solution. *Colloid Polym. Sci.* **1994**, *272*, 1611–1619.
- (25) Ikeda, T.; Tsutsumi, O. Optical Switching and Image Storage by Means of Azobenzene Liquid-crystal Films. *Science* **1995**, *268*, 1873–1875.
- (26) Kumar, G. S.; Neckers, D. C. Photochemistry of Azobenzene-containing Polymers. *Chem. Rev.* **1989**, *89*, 1915–1925.
- (27) Shimizu, T.; Masuda, M.; Minamikawa, H. Supramolecular Nanotube Architectures Based on Amphiphilic Molecules. *Chem. Rev.* **2005**, *105*, 1401–1443.
- (28) Eastoe, J.; Zou, A.; Espidel, Y.; Glatter, O.; Grillo, I. Photo-labile Lamellar Phases. *Soft Matter* **2008**, *4*, 1215–1218.
- (29) Lin, Y.; Cheng, X.; Qiao, Y.; Yu, C.; Li, Z.; Yan, Y.; Huang, J. Creation of Photo-modulated Multi-state and Multi-scale Molecular Assemblies via Binary-state Molecular Switch. *Soft Matter* **2010**, *6*, 902–908.
- (30) Eastoe, J.; Hatzopoulos, M. H.; Dowding, P. J. Action of Hydrotropes and Alkyl-hydrotropes. *Soft Matter* **2011**, *7*, 5917–5925.
- (31) Hodgdon, T. K.; Kaler, E. W. Hydrotropic Solutions. *Curr. Opin. Colloid Interface Sci.* **2007**, *12*, 121–128.
- (32) Abdel-Rahem, R. The Influence of Hydrophobic Counterions on Micellar Growth of Ionic Surfactants. *Adv. Colloid Interface Sci.* **2008**, *141*, 24–36.
- (33) Israelachvili, J. N.; Mitchell, D. J.; Ninham, B. W. Theory of Self-assembly of Hydrocarbon Amphiphiles into Micelles and Bilayers. *J. Chem. Soc., Faraday Trans. 2* **1976**, *72*, 1525–1568.
- (34) Hoffmann, H.; Ulbricht, W. Vesicle Phases of Surfactants and Their Behaviour in Shear Flow. *Tenside Surfact. Deterg.* **1998**, *35*, 421–438.
- (35) Schonfelder, E.; Hoffmann, H. From Vesicle to Micelles. *Ber. Bunsen-Ges. Phys. Chem. Chem. Phys.* **1994**, *98*, 842–852.
- (36) English, R. J.; Raghavan, S. R.; Jenkins, R. D.; Khan, S. A. Associative Polymers Bearing n-alkyl Hydrophobes: Rheological Evidence for Microgel-like Behavior. *J. Rheol.* **1999**, *43*, 1175–1194.
- (37) Lin, Y.; Han, X.; Huang, J.; Fu, H.; Yu, C. A Facile Route to Design pH-responsive Viscoelastic Wormlike Micelles: Smart Use of Hydrotropes. *J. Colloid Interface Sci.* **2009**, *330*, 449–455.
- (38) Dorrego, A. B.; Garcia-Rio, L.; Herves, P.; Leis, J. R.; Mejuto, J. C.; Perez-Juste, J. Micellization Versus Cyclodextrin-surfactant Complexation. *Angew. Chem., Int. Ed.* **2000**, *39*, 2945–2948.
- (39) Mao, M.; Huang, J. B.; Zhu, B. Y.; Ye, J. P. The Transition from Vesicles to Micelles Induced by Octane in Aqueous Surfactant Two-phase Systems. *J. Phys. Chem. B* **2002**, *106*, 219–225.
- (40) Renoncourt, A.; Vlachy, N.; Bauduin, P.; Drechsler, M.; Touraud, D.; Verbavatz, J. M.; Dubois, M.; Kunz, W.; Ninham, B. W. Specific Alkali Cation Effects in the Transition From Micelles to Vesicles Through Salt Addition. *Langmuir* **2007**, *23*, 2376–2381.
- (41) Lin, Y.; Qiao, Y.; Cheng, X.; Yan, Y.; Li, Z.; Huang, J. Hydrotropic Salt Promotes Anionic Surfactant Self-assembly into Vesicles and Ultralong Fibers. *J. Colloid Interface Sci.* **2012**, *369*, 238–244.
- (42) Akiyoshi, K.; Sasaki, Y.; Kuroda, K.; Sunamoto, J. Controlled Association of Hydrophobized Polysaccharide by Cyclodextrin. *Chem. Lett.* **1998**, 93–94.
- (43) Akiyoshi, K.; Ueminami, A.; Kurumada, S.; Nomura, Y. Self-association of Cholesteryl-bearing Poly(L-lysine) in Water and Control of Its Secondary Structure by Host-guest Interaction with Cyclodextrin. *Macromolecules* **2000**, *33*, 6752–6756.
- (44) De Lisi, R.; Lazzara, G.; Milioto, S.; Muratore, N. Characterization of the Cyclodextrin-surfactant Interactions by Volume and Enthalpy. *J. Phys. Chem. B* **2003**, *107*, 13150–13157.
- (45) Saenger, W. R.; Jacob, J.; Gessler, K.; Steiner, T.; Hoffmann, D.; Sanbe, H.; Koizumi, K.; Smith, S. M.; Takaha, T. Structures of the Common Cyclodextrins and Their Larger Analogues - Beyond the doughnut. *Chem. Rev.* **1998**, *98*, 1787–1802.
- (46) van de Manacker, F.; Kroon-Batenburg, L. M. J.; Vermonden, T.; van Nostrum, C. F.; Hennink, W. E. Supramolecular Hydrogels Formed by Beta-cyclodextrin Self-association and Host-guest Inclusion Complexes. *Soft Matter* **2010**, *6*, 187–194.
- (47) Carlstedt, J.; Gonzalez-Perez, A.; Alatorre-Meda, M.; Dias, R. S.; Lindman, B. Release of DNA From Surfactant Complexes Induced by 2-hydroxypropyl-beta-cyclodextrin. *Int. J. Biol. Macromol.* **2010**, *46*, 153–158.
- (48) Jiang, L. X.; Yan, Y.; Huang, J. B.; Yu, C. F.; Jin, C. W.; Deng, M. L.; Wang, Y. L. Selectivity and Stoichiometry Boosting of beta-Cyclodextrin in Cationic/Anionic Surfactant Systems: When Host-Guest Equilibrium Meets Biased Aggregation Equilibrium. *J. Phys. Chem. B* **2010**, *114*, 2165–2174.
- (49) Jiang, L. X.; Deng, M. L.; Wang, Y. L.; Liang, D. H.; Yan, Y.; Huang, J. B. Special Effect of beta-Cyclodextrin on the Aggregation Behavior of Mixed Cationic/Anionic Surfactant Systems. *J. Phys. Chem. B* **2009**, *113*, 7498–7504.
- (50) Signorell, G. A.; Kaufmann, T. C.; Kukulski, W.; Engel, A.; Remigy, H. W. Controlled 2D Crystallization of Membrane Proteins Using Methyl-beta-cyclodextrin. *J. Struct. Biol.* **2007**, *157*, 321–328.
- (51) DeGrip, W. J.; VanOostrum, J.; Bovee-Geurts, P. H. M. Selective Detergent-extraction From Mixed Detergent/lipid/protein Micelles, Using Cyclodextrin Inclusion Compounds: a Novel Generic Approach for the Preparation of Proteoliposomes. *Biochem. J.* **1998**, *330*, 667–674.
- (52) Amir, R. J.; Zhong, S.; Pochan, D. J.; Hawker, C. J. Enzymatically Triggered Self-Assembly of Block Copolymers. *J. Am. Chem. Soc.* **2009**, *131*, 13949–13951.
- (53) Azagarsamy, M. A.; Sokkalingam, P.; Thayumanavan, S. Enzyme-Triggered Disassembly of Dendrimer-Based Amphiphilic Nanocontainers. *J. Am. Chem. Soc.* **2009**, *131*, 14184–14185.

- (54) Park, C.; Kim, H.; Kim, S.; Kim, C. Enzyme Responsive Nanocontainers with Cyclodextrin Gatekeepers and Synergistic Effects in Release of Guests. *J. Am. Chem. Soc.* **2009**, *131*, 16614–16615.
- (55) Ulijn, R. V. Enzyme-responsive Materials: a New Class of Smart Biomaterials. *J. Mater. Chem.* **2006**, *16*, 2217–2225.
- (56) Wang, C.; Chen, Q.; Wang, Z.; Zhang, X. An Enzyme-Responsive Polymeric Superamphiphile. *Angew. Chem., Int. Ed.* **2010**, *49*, 8612–8615.
- (57) Jiang, L.; Yan, Y.; Drechsler, M.; Huang, J. Enzyme-triggered Model Self-assembly in Surfactant–cyclodextrin Systems. *Chem. Commun.* **2012**, *48*, 7347–7349.
- (58) Zhao, L.; Cheng, X.; Ding, Y.; Yan, Y.; Huang, J. A Surfactant-assisted Unimolecular Platform For Multicolor Emissions. *Soft Matter* **2012**, *8*, 10472–10478.
- (59) Jiang, L.; Peng, Y.; Yan, Y.; Deng, M.; Wang, Y.; Huang, J. Annular Ring<sup>r</sup> Microtubes Formed by SDS@2 $\beta$ -CD Complexes in Aqueous Solution. *Soft Matter* **2010**, *6*, 1731–1736.
- (60) Jiang, L.; Peng, Y.; Yan, Y.; Huang, J. Aqueous Self-assembly of SDS@2 $\beta$ -CD Complexes: Lamellae and Vesicles. *Soft Matter* **2011**, *7*, 1726–1731.
- (61) Yan, Y.; Jiang, L.; Huang, J. Unveil the Potential Function of CD in Surfactant Systems. *Phys. Chem. Chem. Phys.* **2011**, *13*, 9074–9082.
- (62) Zhou, C.; Cheng, X.; Yan, Y.; Wang, J.; Huang, J. Reversible Transition between SDS@ 2 $\beta$ -CD Microtubes and Vesicles Triggered by Temperature. *Langmuir* **2014**, *30*, 3381–3386.
- (63) Zhou, C.; Cheng, X.; Zhao, Q.; Yan, Y.; Wang, J.; Huang, J. Self-Assembly of Nonionic Surfactant Tween 20@2 $\beta$ -CD Inclusion Complexes in Dilute Solution. *Langmuir* **2013**, *29*, 13175–13182.
- (64) Jiang, L. X.; Wang, K.; Ke, F. Y.; Liang, D. H.; Huang, J. B. Endowing Catanionic Surfactant Vesicles with Dual Responsive Abilities via a Noncovalent Strategy: Introduction of a Responder, Sodium cholate. *Soft Matter* **2009**, *5*, 599–606.
- (65) Lin, S. C.; Blankschtein, D. Role of the Bile Salt Surfactant Sodium Cholate in Enhancing the Aqueous Dispersion Stability of Single-Walled Carbon Nanotubes: A Molecular Dynamics Simulation Study. *J. Phys. Chem. B* **2010**, *114*, 15616–15625.
- (66) Meyuhas, D.; Bor, A.; Pinchuk, I.; Kaplun, A.; Talmon, Y.; Kozlov, M. M.; Lichtenberg, D. Effect of Ionic Strength on the Self-assembly in Mixtures of Phosphatidylcholine and Sodium Cholate. *J. Colloid Interface Sci.* **1997**, *188*, 351–362.
- (67) Qiao, Y.; Lin, Y. Y.; Wang, Y. J.; Yang, Z. Y.; Liu, J.; Zhou, J.; Yan, Y.; Huang, J. B. Metal-Driven Hierarchical Self-Assembled One-Dimensional Nanohelices. *Nano Lett.* **2009**, *9*, 4500–4504.
- (68) Qiao, Y.; Lin, Y.; Zhang, S.; Huang, J. Lanthanide-Containing Photoluminescent Materials: From Hybrid Hydrogel to Inorganic Nanotubes. *Chem.—Eur. J.* **2011**, *17*, 5180–5187.
- (69) Qiao, Y.; Lin, Y. Y.; Yang, Z. Y.; Chen, H. F.; Zhang, S. F.; Yan, Y.; Huang, J. B. Unique Temperature-Dependent Supramolecular Self-Assembly: From Hierarchical 1D Nanostructures to Super Hydrogel. *J. Phys. Chem. B* **2010**, *114*, 11725–11730.
- (70) Qiao, Y.; Wang, Y.; Yang, Z.; Lin, Y.; Huang, J. Self-Templating of Metal-Driven Supramolecular Self-Assembly: A General Approach toward 1D Inorganic Nanotubes. *Chem. Mater.* **2011**, *23*, 1182–1187.