Giant Surfactants Based on Molecular Nanoparticles: Precise Synthesis and Solution Self-assembly

Xinfei Yu,[1]* Yiwen Li,[1]* Xue-Hui Dong,[1] Kan Yue,[1] Zhiwei Lin,[1] Xueyan Feng,[1] Mingjun Huang,[1] Wen-Bin Zhang,[1,2] Stephen Z. D. Cheng[1]

[1]Department of Polymer Science, College of Polymer Science and Polymer Engineering, The University of Akron, Akron, Ohio 44325-3909
[2]Department of Polymer Science and Engineering, Key Laboratory of Polymer Chemistry and Physics of Ministry of Education, College of Chemistry and Molecular Engineering, Center for Soft Matter Science and Engineering, Peking University, Beijing 100871, People's Republic of China
Correspondence to: S. Z. D. Cheng (E-mail: scheng@uakron.edu) or W.-B. Zhang (E-mail: wenbin@pku.edu.cn)

Received 24 May 2014; revised 23 July 2014; accepted 24 July 2014; published online 25 August 2014
DOI: 10.1002/polb.23571

ABSTRACT: Giant surfactants are polymer-tethered molecular nanoparticles (MNPs) and can be considered as a subclass of giant molecules. The MNPs serve as functionalized heads with persistent shape and volume, which may vary in size, symmetry, and surface chemistry. The covalent conjugation of MNPs and polymer tails affords giant surfactants with diverse composition and architecture. Synthetic strategies such as "grafting-from" and "grafting-onto" have been successfully applied to the precise synthesis of giant surfactants, which is further facilitated by the emergence of "click" chemistry reactions. In many aspects, giant surfactants capture the essential features of small-molecule surfactants, yet they have much larger sizes. They bridge the gap between small-molecule surfactants and traditional amphiphilic macromolecules. Their self-assembly behaviors in solution are summarized in this Review. Micelle formation is affected not only by their primary chemical structures, but also by the experimental conditions. This new class of materials is expected to deliver general implications on the design of novel functional materials based on MNP building blocks in the bottom-up fabrication of well-defined nanostructures. © 2014 Wiley Periodicals, Inc. J. Polym. Sci., Part B: Polym. Phys. **2014**, *52*, 1309–1325

KEYWORDS: amphiphilic polymer; fullerene; giant surfactant; micelles; polyhedral oligomeric silsesquioxanes (POSS); polyoxometalates (POM); proteins

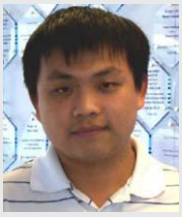
INTRODUCTION Amphiphiles contain chemically distinct parts (e.g., hydrophilic and hydrophobic parts) connected via primary chemical bonds. Traditional amphiphiles were recognized as small-molecule surfactants and lipids in the early days, and later expanded to include amphiphilic block copolymers.[1–8] Small-molecule surfactants and lipids usually consist of a hydrophilic ionic head and hydrophobic tail(s). Typical examples are sodium stearate (soaps), alkylbenzenesulfonates, fatty alcohol ethoxylates, and alkylphenol ethoxylates, which are all produced in industrial scales for everyday uses.[9] Based on their topological differences, these surfactants can be identified as the simplest small-molecule surfactants with single-head/single-tail, or lipids with single-head/two-tails,[1] or more complex gemini surfactants,[10,11] bolaform surfactants,[12] and multiheaded/multitailed surfactants.[13,14] On the other hand, amphiphilic linear block copolymers consisting of chemically distinct blocks such as hydrophilic and hydrophobic blocks have drawn great attentions during the past three decades due to their promising applications.[15,16] A combination of both features of small-molecule surfactants and block copolymers is expected to expand the scope of amphiphiles and bring in unique properties.

Recently, a new class of amphiphiles called giant surfactants has been developed based on molecular nanoparticles (MNPs).[17,18] The MNPs possess unique features such as persistent shape and volume, precisely defined chemical structures and surface functionalities. Typical MNPs include but are not limited to [60]fullerenes (C_{60}),[19] polyhedral oligomeric silsesquioxanes (POSS),[20] polyoxometalates (POM),[21] and folded globular proteins.[22] When these functionalized MNPs are covalently connected with polymer tail(s), giant surfactants are constructed. Giant surfactants with various topologies can also be readily designed and synthesized. Figure 1 illustrates the structural difference among small-molecule surfactant, diblock copolymer, and the simplest giant surfactant

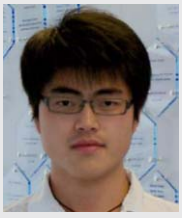
*Xinfei Yu and Yiwen Li contributed equally to this work

Xinfei Yu received his B.S. degree in Polymer Chemistry at Fudan University in 2005 and a Ph.D. degree in Polymer Science at the University of Akron in 2012. He is currently a postdoctoral research associate in the Materials Science and Engineering Division at the National Institute of Standards and Technology under the supervision of Dr. Wen-li Wu and Dr. Dean M. DeLongchamp.

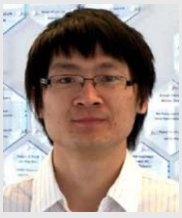
Yiwen Li received his B.S. degree in Chemistry at University of Science and Technology of China in 2008. After his graduation, he joined Department of Polymer Science at the University of Akron and received his Ph.D. degree in August 2013. In the fall of 2013, he moved to the Department of Chemistry and Biochemistry at the University of California, San Diego, as a postdoctoral fellow in Prof. Nathan Gianneschi's group.



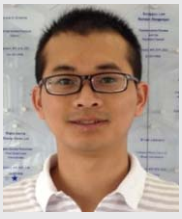
Xue-Hui Dong graduated with a B.S. degree in Polymer Chemistry from University of Science and Technology of China in 2008. He joined Department of Polymer Science at the University of Akron as a graduate student and received his Ph.D. degree in December 2013. He has joined Prof. Bradley Olsen's research group at MIT as a postdoctoral fellow in early 2014.



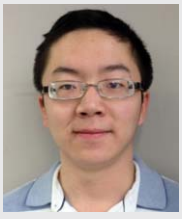
Kan Yue received his B.S. degree in Chemistry at Peking University in 2008. He then jointed Department of Polymer Science at The University of Akron in 2009 and received his Ph.D. degree in Polymer Science in December 2013. He continued at the University of Akron for his postdoctoral research for 5 months, before joining Prof. Ali Khademhosseini's research group at Harvard Medical School as a postdoctoral fellow in June 2014.



Zhiwei Lin received his B.S. degree in Polymer Science and Engineering and M.S. degree in Material Science and Engineering at Beijing University of Chemical Technology in 2008 and 2011. He joined Department of Polymer Science at The University of Akron as a Ph.D. student in August 2011. His research topics focus on precise synthesis and self-assembly of fullerene-based molecular Janus particles and giant surfactants.

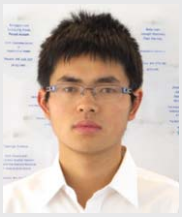


Xueyan Feng received his B.S. degree in Department of Chemistry at University of Science and Technology of China in 2011. He joined Department of Polymer Science at The University of Akron as a Ph.D. student in August 2011. His research topic focuses on precise synthesis and self-assembly of functionalized polyhedral oligomeric silsesquioxanes-based giant molecules.

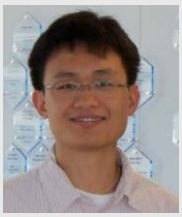


with single head and single tail.[17] Small-molecule surfactants are composed of a compact polar head and a hydrophobic alkyl tail typically containing 12–16 carbon atoms [Fig. 1(a)], while amphiphilic linear diblock copolymers have polymeric, covalently linked hydrophilic and hydrophobic blocks [Fig. 1(c)]. In contrast, the giant surfactants with single head and

Mingjun Huang earned his B.S. degree in the College of Chemistry and Molecular Engineering from Peking University in 2010. He is currently a Ph.D. candidate in the department of Polymer Science at the University of Akron. His research currently focuses on self-assembly behavior of novel tetrahedral giant polyhedra based on polyhedral oligomeric silsesquioxanes molecular nanoparticles.



Wen-Bin Zhang received his B.S. in Organic Chemistry from Peking University and his Ph.D. in Polymer Science from the University of Akron. He continued at the University of Akron for his postdoctoral research for 1 year, before he moved to Caltech for a second postdoctoral training with Prof. David Tirrell. Dr. Zhang is currently an Assistant Professor at the Department of Polymer Science and Engineering, College of Chemistry and Molecular Engineering, and Center for Soft Matter Science and Engineering of Peking University. His current research interests include the development of materials that integrates synthetic and biological systems for energy and health-related applications.



Stephen Z. D. Cheng received his Ph.D. degree at Rensselaer Polytechnic Institute at Troy, New York, in 1985. His research interests are in chemistry, physics and engineering of polymers and advanced functional materials. He holds the Frank C. Sullivan Distinguished Research Professor, the R. C. Musson and Trustees Professor and served as the Dean of the College of Polymer Science and Polymer Engineering at the University of Akron during 2007–2014. He is the recipient of Presidential Young Investigator Award (1991), John H. Dillon Medal (APS, 1995), Polymer Physics Prize (APS, 2013), and other awards and recognitions. He has been elected as a member of the National Academic of Engineering of US (2008).

single tail possess a hydrophilic head with definite shape and size and a linear, hydrophobic polymeric tail with a size ratio that resembles the typical structure of a small-molecule surfactant [Fig. 1(b)].

Surfactants and block copolymers are commonly capable of forming various thermodynamically stable micellar structures in dilute solutions including spheres, cylinders, and vesicles. The self-assemblies of small-molecule surfactants and block copolymers have been well studied and extensively reviewed in the literatures.[23–25] We thus only provide a brief summary about small-molecule surfactant and block copolymer micelles to serve as the basis of our understandings in the self-assembly behaviors of giant surfactants. Generally speaking, there are two categories of parameters that determine the final micellar structures. One is the structural parameter such as chemical structures of immiscible parts, the size and molecular architecture of each individual component and the overall molecule.[26–28] The other is the physical characteristics of experimental environments such as the properties of solvents (common solvents and usually, selective solvents), the common solvent/selective solvent ratio, the surfactants/block copolymer concentrations and sometimes, the blend compositions, pH value, additives (*e.g.*, salts, ions), and temperature.[29–33]

In small-molecule surfactants, a dimensionless packing parameter, $P = V/AL$, has been proposed by Israelachivili et al. to explain the self-assembled structures, where V and L are the volume and length of the hydrophobic tail, and A is the equilibrium interfacial area of the ionic (hydrophilic) head at the critical micelle concentration.[1] This packing parameter is not merely a geometrical argument. The interfacial area term A is critically associated with the ionic interactions among the heads, which are affected by the degree of ionization in solution. The formation of various micelle structures is thus characterized by the value of P. If $P < 1/3$, spherical micelles are formed; if $1/3 < P < 1/2$, cylindrical micelles are favored; if $1/2 < P < 1$, bilayers with a spontaneous curvature (vesicles) are produced; if P approaches 1, planar bilayers are expected; while if $P > 1$, reversed micelle structures are constructed. A similar argument also holds in the self-assembly of block copolymers.

Giant surfactants arrest the essential structural features of their small-molecule counterparts but possess much larger sizes. They are thus recognized as size-amplified versions of small-molecule surfactants and serve to bridge the gap between small molecules and amphiphilic block copolymers.[34] It has been found that giant surfactants are able to self-assemble into highly diverse, thermodynamically

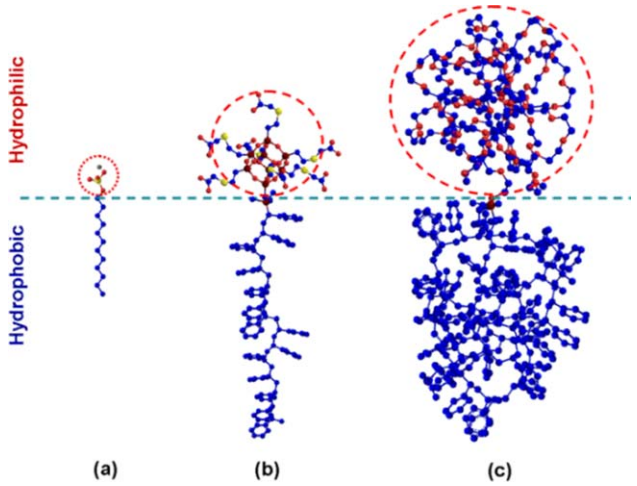


FIGURE 1 Structural comparison between (a) a typical small-molecule surfactant (such as sodium dodecyl sulfate); (b) a giant surfactant, (such as seven carboxylic acid groups functionalized POSS with a polystyrene tail); and (c) a typical amphiphilic block copolymer (such as polystyrene-*block*-poly(ethylene oxide)). Reproduced from ref. 17 with permission from American Chemical Society.

stable and metastable micelles in solution. In this Review, we will summarize recent progress on giant surfactants with regard to their precise synthesis and self-assembly in solution. A comparison among giant surfactants, small-molecule surfactants, and amphiphilic block copolymers reveals that giant surfactants, as a unique class of new materials, open up numerous possibilities in using MNP building blocks, or so-called nanoatoms,[34] in the bottom-up fabrication of well-defined nanostructures with technological relevance.

DESIGN AND SYNTHESIS OF GIANT SURFACTANTS

Molecular Nanoparticles

MNPs are a group of building blocks with well-defined molecular structures and rigid three-dimensional (3D) conformations at nanometer scale. MNPs can be formed either by covalently bonded, or folded/assembled cage structures. Figure 2 shows several typical examples, including [60]fullerene (C_{60}),[18] POSS,[20] POM,[21] and folded globular protein.[22]

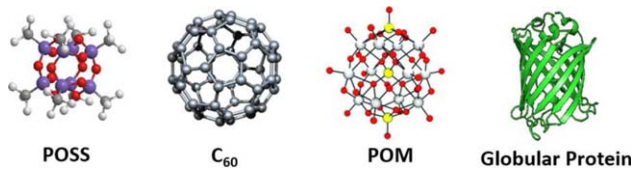


FIGURE 2 Molecular nanoparticles: polyhedral oligomeric silsesquioxane (POSS), [60]fullerene (C_{60}), polyoxometalate (POM), and globular protein.

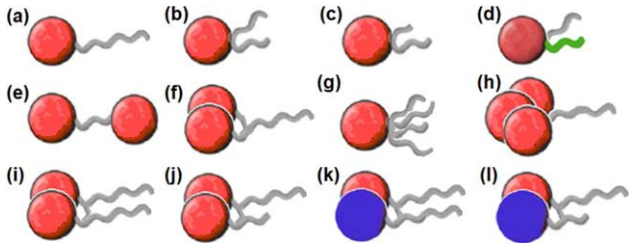


FIGURE 3 The cartoons of giant surfactants including giant surfactants (a), giant lipids with symmetric (b), and asymmetric tails (c and d), giant bola-form surfactants (e), multitailed and multiheaded giant surfactants (f–h), and symmetric/asymmetric giant gemini surfactants (i–l).

Though MNPs also can be constructed by multiple components as in the case of "tennis ball" reported by Rebek et al.,[35–37] or DNA origami,[37] we will focus on the single-molecule MNPs in this Review. MNPs provide a library of essential building blocks to construct various "giant molecules,"[34] such as molecular Janus particles,[38–42] giant polyhedra,[34] and giant surfactants.[17,18]

Fullerene

Fullerenes are a class of carbon allotropes, consisting solely of carbon atoms arranged in five- and six-member rings.[43] Among them, C_{60} is the smallest stable fullerene and is also the most abundant one. It has a spherical shape with truncated icosahedral (I_h) symmetry. The well-defined structure and high symmetry make fullerenes an excellent structural motif for constructing giant surfactants. Physical properties of fullerene could be tuned via surface modification by addition reactions such as [4+2] Diels–Alder reaction, [3+2] cycloaddition of diazomethane, and the Bingel–Hirsch reaction which have been thoroughly studied and documented.[44–48] Among these reactions, the Bingel-Hirsch reaction is particularly suitable for preparing multiadducts of fullerenes and thus, tuning of their surface properties.[49,50] Fullerene amphiphiles and Janus fullerenes have been successfully synthesized and shape-persistent micelles have also been observed in solutions.[42,51]

Polyhedral Oligomeric Silsesquioxanes

Silsesquioxanes are organic–inorganic hybrid molecules with an empirical formula of $RSiO_{1.5}$, where R represents hydrogen, alkyl, aryl, or other functional substituents.[20] Specifically, POSS is a family of silsesquioxane compounds with cage structures, among which the cubic T_8 cage is the most common one with a diameter of ~1 nm (depending on the periphery R groups). POSS is usually prepared from condensation reactions of silane/silanol precursors. Depending on the side chains, POSS molecules show varying solubility and miscibility with other materials.[52] Mono-functionalized POSS are routinely utilized to construct giant surfactants. They can be prepared via the following approaches: (1) substitution or addition reactions of one reactive corner group on the POSS cage; (2) "co-hydrolysis of tri-functional organo- or

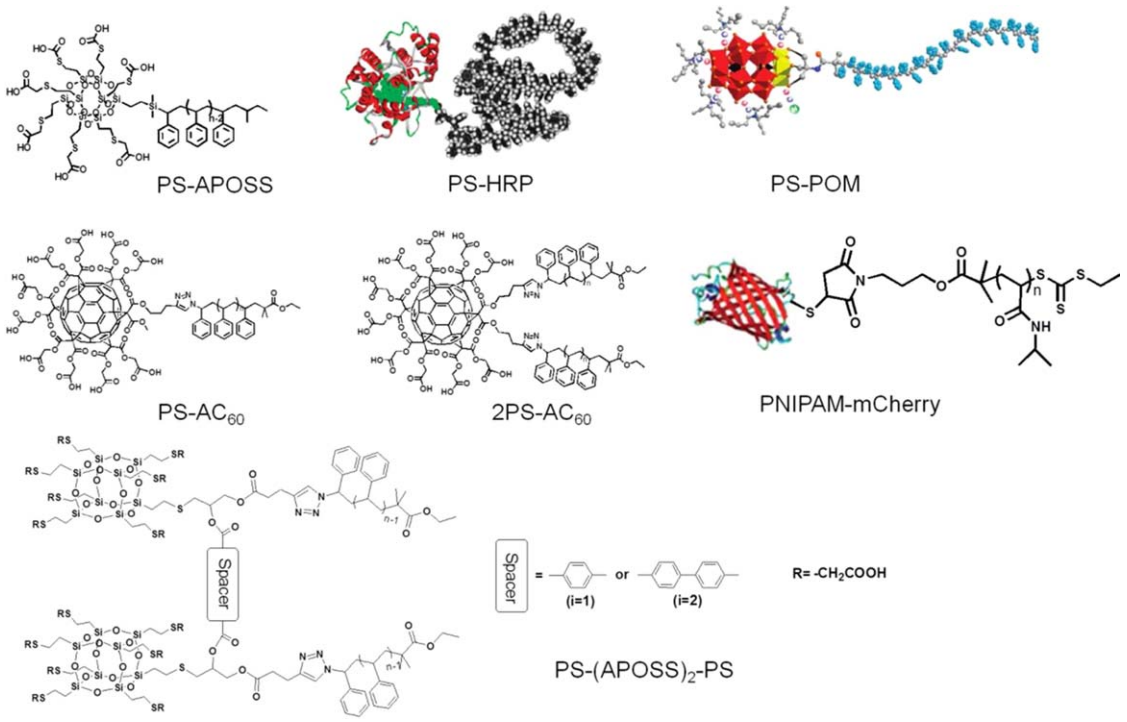


FIGURE 4 Giant surfactants based on various hydrophilic MNPs including POSS, POM, C_{60}, and folded protein.[17,22,63–66]

hydro-silanes"; and (3) corner-capping reactions.[20] Most monofunctional POSS compounds obtained by the third strategy have one functional group for further organic reaction or polymerization and inert groups such as isobutyl, phenyl, isooctyl, cyclopentyl, and so forth, at other corners. Octavinyl POSS is an ideal structural motif due to the versatility of vinyl functional groups by methods such as hydrosilylation, olefin metathesis, and thiol-ene "click" chemistry.[17,53] Feher et al. developed mono-substituted POSS based on octavinyl POSS, which has provided an anisotropic modification of POSS cage.[54] The multi-vinyl functionalized POSS cage (VPOSS) has thus become a versatile POSS derivative. Recently, we have also developed an efficient strategy to prepare mono-substituted POSS using the thiol-ene "click" chemistry.[55]

Polyoxometalate

POMs are a large family of inorganic polyatomic ions with large, closed 3D frameworks formed by transition metals (mostly Mo, W, V, Nb, and Ta) in their high oxidation states and oxo ligands, which are widely utilized as catalysts, photoelectronic/magnetic materials, and so forth,[56,57] POMs exhibit a remarkable diversity in size, structure and symmetry, and their surface properties can be tuned by sophisticated chemistry.[57] POMs are usually highly negatively charged and are soluble as macroanions in solutions. Mono- and multifunctionalized POMs have been demonstrated via covalent linkage with organic species.[58] Conjugation between hydrophilic POM particle with hydrophobic polymers leads to giant surfactants that can generate various intriguing micellar structures in solution.

Folded Protein Domains

Folded proteins have well-defined 3D structures and surface chemistries, and they could also be utilized as the functional head in giant surfactants. Such protein-based giant surfactants have exhibited significantly improved stability and biocompatibility in the field of biotechnology and medicine.[59] The conventional approach to prepare protein-based giant surfactant is to synthesize polymers with protein-reactive chain ends, such as activated esters, which facilitate the coupling reaction between the polymer and the protein, or with an active initiating group for further growing a polymer tail on the protein surface.[60] Functional groups at specific locations could be changed through site-directed mutagenesis at the genetic level or through the enzyme-assisted incorporation of noncanonical amino acids.[61] Some folded proteins, like green fluorescent protein, have well-defined shape and superior stability.[62] The folding of proteins could also be controlled by the solvent, concentration of salts, pH, or the temperature, which endow them multiple responsive behaviors.

Molecular Design of Giant Surfactants

Giant surfactants are size-amplified versions of small-molecule surfactants with MNPs as the head(s) and polymers as the tail(s). Since MNPs are compact and rigid, giant surfactants retain the essential structural features of small-

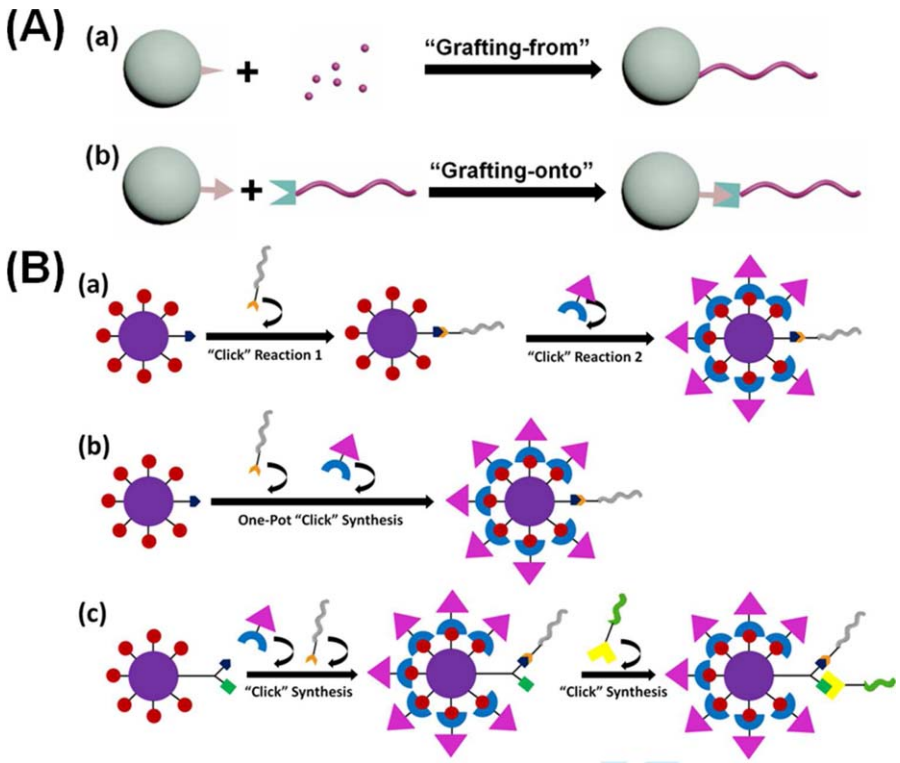


FIGURE 5 (A) Illustration of general synthetic strategies including "grafting-from" and "grafting-onto." (B) Illustration of the specific synthetic methods using combined "click" methodologies toward complex macromolecular structures: (a) sequential click approach,[84,85] (b) one-pot orthogonal assembly,[86] and (c) fractal iterative synthesis.[86]

molecule surfactants. In a simple analogy to small-molecule surfactants, giant surfactants can be designed as shown in the cartoons of Figure 3, which include, but are not limited to, giant lipids, giant bola-form surfactants, multiheaded/multitailed giant surfactants, and symmetric/asymmetric giant gemini surfactants. Apparently, giant surfactants are much more versatile than small-molecule surfactants since they provide a broad platform for structural engineering. For example, the heads can be made with heterogeneous functionalities (a patchy head); the tails can be in cyclic,[67]

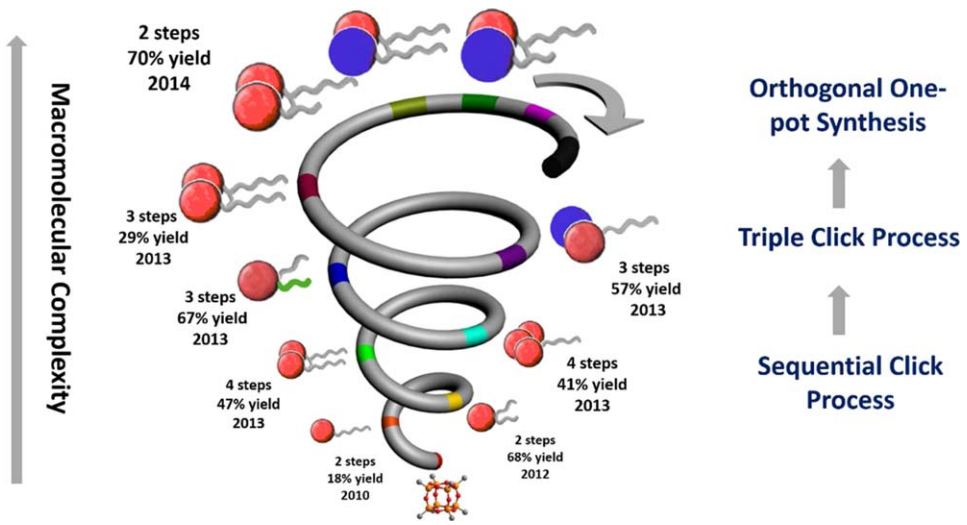


FIGURE 6 An overview of the giant surfactants developed by our group over the past several years. Reproduced from ref. 68 with permission from The Royal Society of Chemistry.

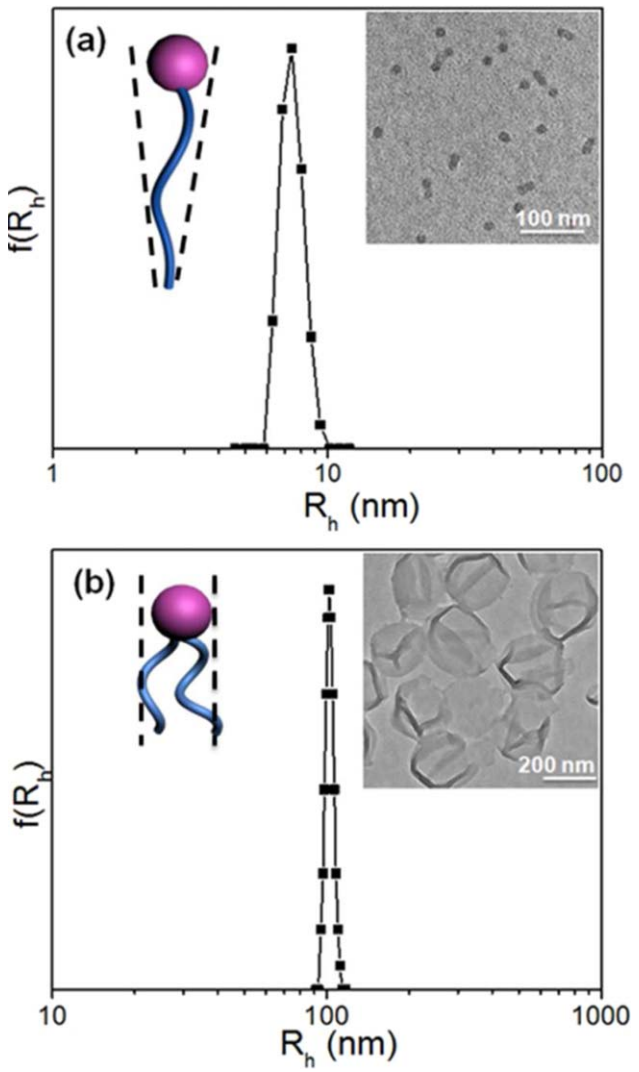


FIGURE 7 Self-assembled morphologies of PS_{44}-AC_{60} (a) and $2PS_{23}$-AC_{60} (b) in solution with a mixture of 1,4-dioxane and DMF (w/w = 1/1) as the common solvent and water as the selective solvent. Adapted from ref. 63 with permission from American Chemical Society.

branched topologies, or of heterogeneous composition, such as block copolymers. These features render a high structural complexity in giant surfactants and thus, more self-assembly behaviors and tunable functional properties of the materials.[67–69]

Figure 4 shows recent examples of giant surfactants based on various functionalized MNPs including carboxylic-functionalized POSS,[17,65] carboxylic-functionalized C_{60},[63] POM,[21,64,70–74] and proteins.[75–83] Molecular topology could also be precisely controlled for these giant surfactants. As an example, PS-AC_{60} (PS: polystyrene; AC_{60}: C_{60} with 10 carboxylic acid groups where "A" denotes carboxylic acid groups) has one tail, while 2PS-AC_{60} has two tails with the same hydrophilic polar head.[63] Our group has also successfully synthesized giant gemini surfactants, in which two giant surfactants are connected via a rigid spacer.[31]

Precise Synthesis of Giant Surfactants

Precise control of the functionalities on the periphery of MNP heads, and of the chemical composition and macromolecular architecture of the polymer tails, is essential in constructing giant surfactants. The primary chemical structure plays the key role in determining its solution self-assembly behaviors and physical properties. Generally speaking, chemical modification of pristine MNPs brings various functionalities onto the MNP surface, providing remarkable opportunities for tuning the properties of the resulting giant surfactants. It is thus a prerequisite to achieve site-selective mono-/multifunctionalization or regio-selective multifunctionalization of MNPs in order to further conjugate them with polymer tails via either "grafting-from" or "grafting-onto" methodologies [Fig. 5(A)].[55]

"Grafting-From" Approach

The grafting-from methodology involves the polymerization of hydrophobic monomers starting from the MNP macroinitiators with exact numbers of initiation sites [Fig. 5A(a)].

This grafting-from strategy circumvents the incompatibility and steric hindrance between preformed polymer tails and MNP-based macroinitiators which may be problematic in the grafting-onto strategy (see Grafting-onto" Approach section).[87] In addition, tedious purification procedures involved in the removal of unreacted MNP precursors, free polymers, and higher adducts that might exist in the crude products of the grafting-onto approach is no longer necessary.[87] In general, the success of the grafting-from approach highly relies on the compatibility of MNP-based macroinitiators with the polymerization mechanisms. Among the most important and widely established methods employed for grafting-from techniques are atom transfer radical polymerization (ATRP),[88] reversible addition-fragmentation chain transfer (RAFT) polymerization,[89] and ring opening polymerization (ROP).[90]

A large number of reports on the grafting-from methodology in the literatures involve the synthesis of giant surfactants by the ATRP technique. By establishing a dynamic equilibrium between low concentration active propagating species and high concentration dormant chains, polymers can be grown from different MNP macroinitiators in a controlled fashion with respect to both molecular weight and polydispersity.[91] For example, polymerization from globular protein-based macroinitiators by attaching an ATRP initiation group onto protein surface [i.e., bovine serum albumin (BSA)[77]] offers a promising path toward various bio-related giant surfactants.[78,92] In this way, different polymeric tails including poly(*N*-isopropylacrylamide) (PNIPAM),[93] polystyrene,[77] poly(mPEG-metharylate),[94] and many others can be directly introduced. In addition, the ATRP technique has also been fully explored in the POM,[64] C_{60},[95] and POSS[86] systems.

RAFT polymerization is another important controlled radical polymerization method. It is associated with several

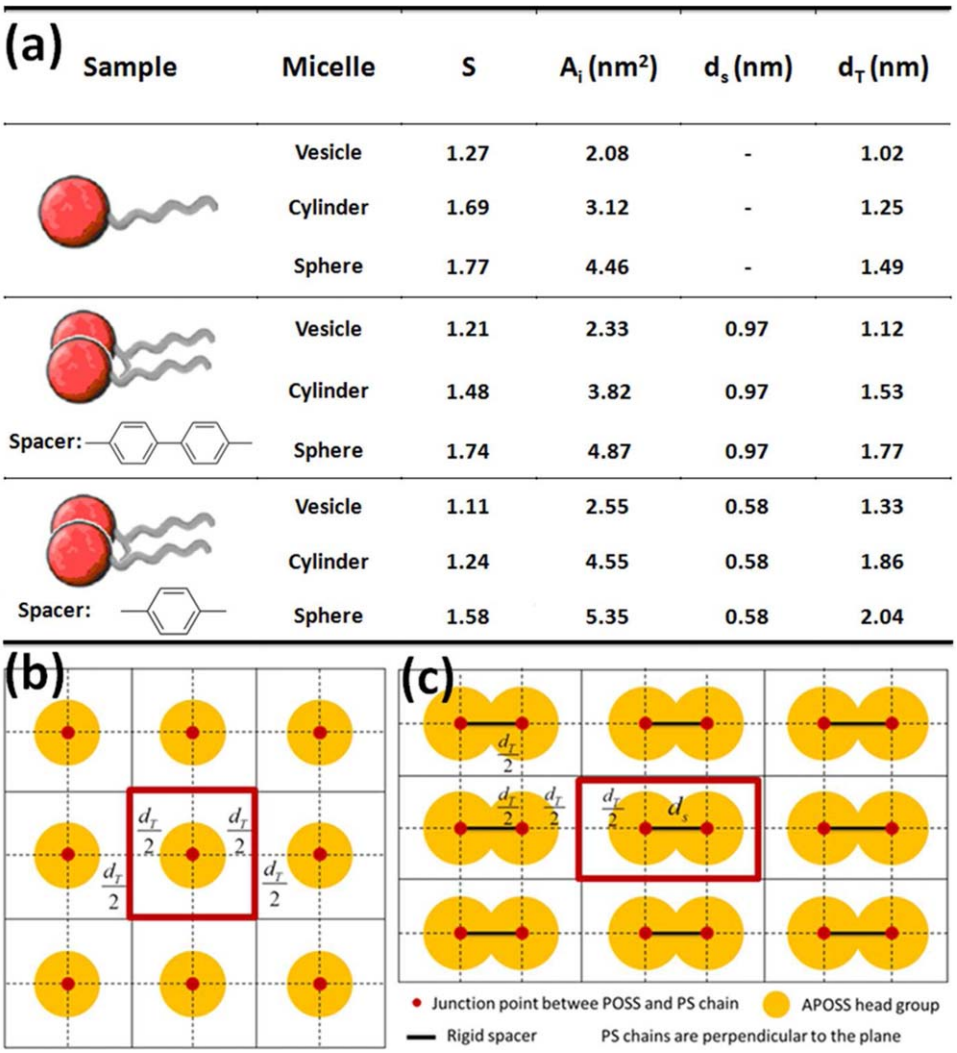


FIGURE 8 Morphologies and physical parameters of giant surfactant and corresponded giant gemini surfactants with different spacers; (a) Proposed models of giant surfactants, (b) and giant gemini surfactants, (c) packing on the micelle surface. (S: stretchiness of polymer tail; A_i: surface area per two chains; d_s: spacer length; d_T: intermolecular distances). Adapted from ref. 65 with permission from The Royal Society of Chemistry.

reversible addition–fragmentation steps based on the degenerative chain transfer process.[96] Compared with ATRP, it offers many unique advantages to prepare giant surfactants, especially for protein–polymer bioconjugates.[78] In 2007, Davis' group reported the *in situ* synthesis of BSA-based "smart" giant surfactants using RAFT polymerization in a single step.[97] In addition, Sumerlin and coworkers developed a general approach toward well-defined protein-polymer biohybrids with RAFT agent immobilization via the "R-group" strategy.[79]

ROP is commonly regarded as the most efficient technique to generate giant surfactants with biocompatible and biodegradable polymer tails, such as polylactide,[98] poly(ε-caprolactone) (PCL),[86,99,100] and many other possible polyesters, with much higher molecular weights than those from the ATRP and RAFT methods. For instance, Xia et al. successfully prepared a giant surfactant with POM tethered with two PCL tails using ROP of ε-caprolactone monomer initiated by two hydroxyl groups on the two sides of a POM cluster.[99] In addition, the compatibility between VPOSS and ROP has been demonstrated by our group,[86,98,100] which provides numerous opportunities for the facile and modular postpolymerization functionalization of VPOSS–polymer conjugates toward various giant surfactants.

"Grafting-Onto" Approach

Although the grafting-from technique is widely established in the design and synthesis of giant surfactants, its scope is largely limited by the choice of monomers, the compatibility between MNPs and the polymerization methods, which may be further complicated by inefficient initiation.[101] The grafting-onto strategy is an alternative technique to construct

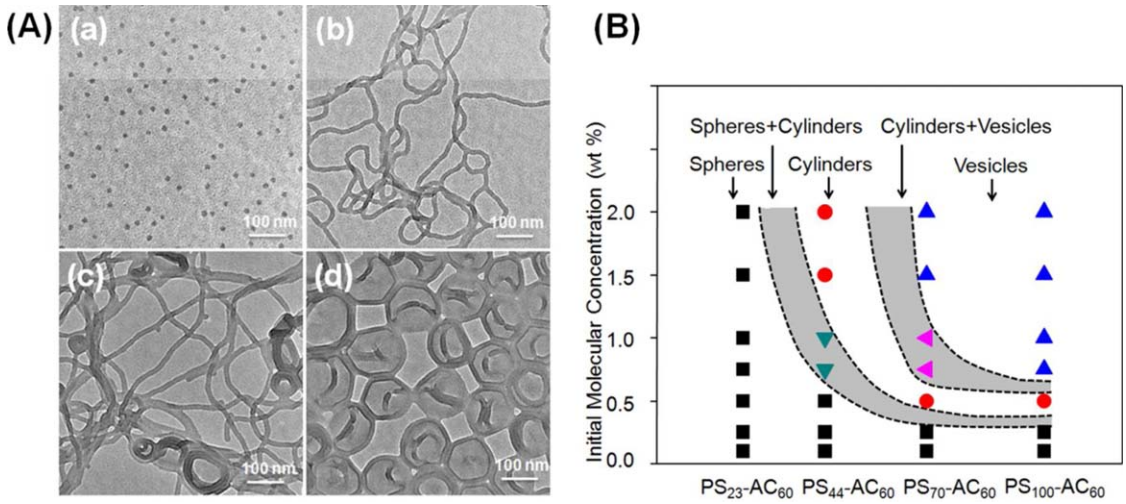


FIGURE 9 (A) TEM images of self-assembly morphologies of PS_{70}-AC_{60} with different initial concentrations in the 1,4-dioxane/DMF/water system. Initial polymer concentration: (a) 0.1 wt %; (b) 0.5 wt %; (c) 1.0 wt %; (d) 2.0 wt %. (B) Morphological phase diagram of PSn-AC60 self-assemblies in the 1,4-dioxane/DMF/water system depending on the PS tail length and polymer concentration. Adapted from ref. 63 with permission from American Chemical Society.

diverse giant surfactants with well-controlled molecular weight, chemical composition, molecular weight distribution, and macromolecular architectures [Fig. 5A(b)].[84,86]

Many conjugation chemistries have been widely employed for the synthesis of giant surfactants via grafting-onto strategy. For example, hydrosilylation reaction was employed to incorporate silylhydride-functionalized PS onto VPOSS by our group.[17] The resulting mono-tethered VPOSS–PS precursor can be obtained by fractional precipitations[17] or flash column chromatography purification.[100] In addition, various conjugation methods have been applied for the grafting-onto synthesis of giant surfactants based on C_{60}-polymer hybrids including the "radical addition" approach,[102,103] the "anion addition" approach,[104,105] and the "azido" approach (the reaction between an azide and C_{60} affords azafulleroid).[106,107] However, the limited selectivity and reactivity of those methods usually require drastic reaction conditions and lead to the unavoidable multiple additions and potential polymer backbone degradation, which could make purification a daunting task. Moreover, the grafting-onto strategy also involves both covalent bioconjugation approach and noncovalent complexation approach to prepare protein-based giant surfactants.[78] Nevertheless, those methodologies usually suffer from several experimental restrictions. For example, the conjugate sites are sometimes limited to specific domain of the proteins with steric crowded surfaces.[108] Therefore, it is highly desirable to develop a facile, modular and efficient approach toward various MNP-based giant surfactants with precisely defined macromolecular structures.

Copper-catalyzed azide–alkyne cycloaddition (CuAAC), the most popular "click" reaction, is a solid conjugation method for the synthesis of giant surfactants. Due to its orthogonal reactivity to most other reactions, CuAAC can be widely applied in the coupling reactions between the MNP heads and the polymer tails. For example, Cornelissen's group employed CuAAC reaction to straightforwardly construct a biohybrid giant amphiphiles composed of a PS tail and a peptide or protein head.[109] In addition, a giant surfactant of POM tethered with two PCL tails was also successfully achieved by Wang's group via CuAAC coupling reaction between a bis-azido organosilyl derivative of Wells-Dawson-type POM (one POM with two azido groups) with a propargyl-terminated PCL chains.[73] These promising results indicate that CuAAC can be potentially extended to the preparation of many other giant surfactants with different MNPs and polymers. Moreover, the azido-functionalized polymers can also be efficiently coupled with alkyne-modified fullerenes (including [5:1]-hexakisadducts of C_{60})[63,110] using CuAAC. The compatibility of VPOSS cage with CuAAC allows us to develop a general postpolymerization functionalization approach to generate a library of giant amphiphiles with diverse surface functionalities.[84]

Thiol-ene click chemistry (TECC), including thiol-ene free-radical reaction and thiol–Michael addition reaction, refers to the addition reaction of thiol group across double bonds, resulting in stable thiol ether bonds.[111–113] It is another type of "click" reaction that has been widely applied in giant surfactant synthesis as a grafting-onto approach. For instance, Nolte and co-workers firstly reported the synthesis of protein-based giant surfactant through direct conjugation of a maleimide appended hydrophobic tail to a thiol-functionalized enzyme via thiol–Michael addition reaction.[78]

SPAAC between cyclooctynes and azides has emerged as a bio-orthogonal, metal-free, and highly efficient "click" chemistry.[114] Interestingly, the distinctly different chemical reactivity between strained cyclooctyne and terminal alkyne in the absence of Cu(I) enables the sequential use of triple "click"

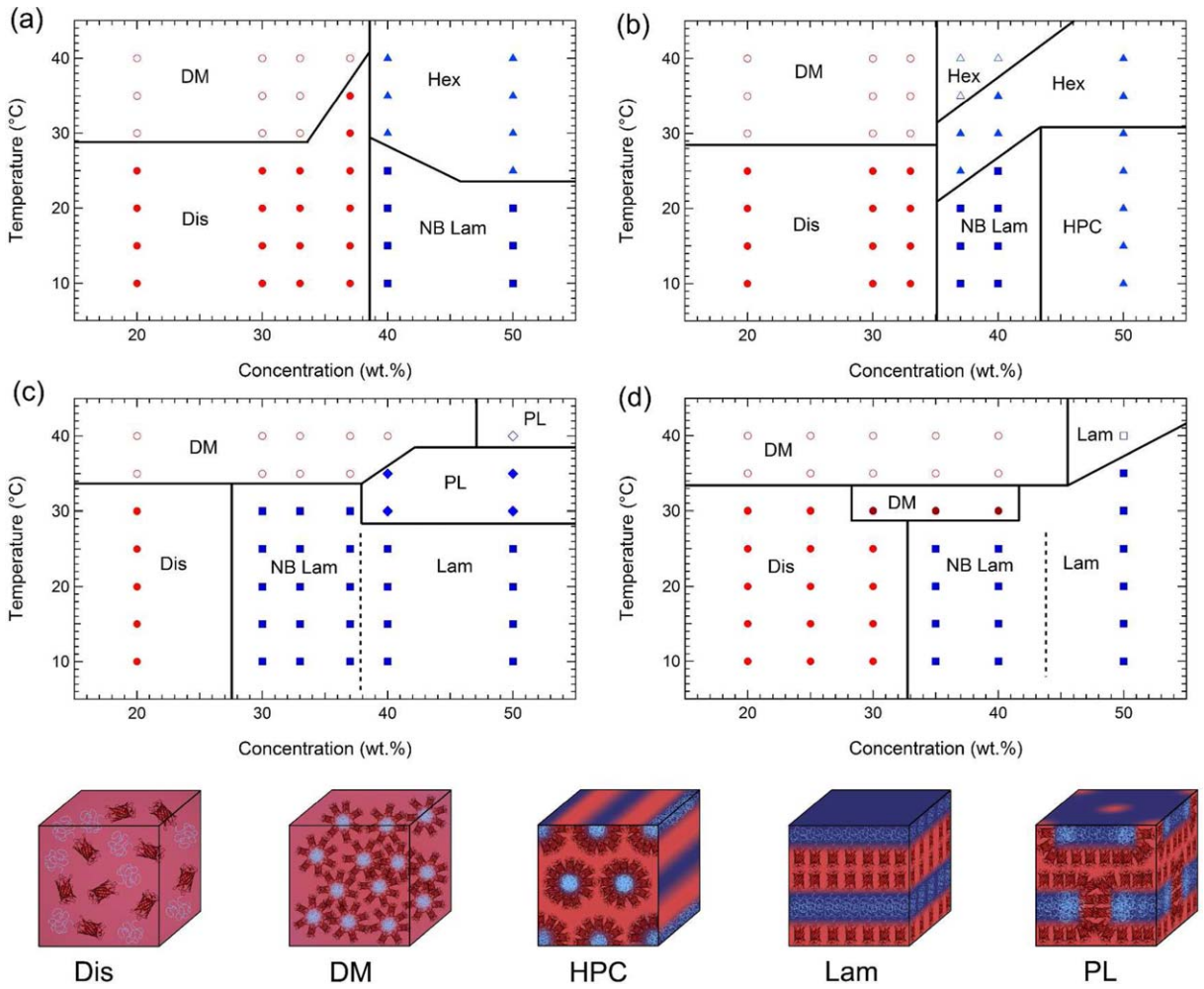


FIGURE 10 Phase diagrams of mChP8 (a), mChP17 (b), mChP30 (c), and mChP57 (d) as a function of temperature and concentration. The various phases are denoted as disordered (Dis), disordered micelle (DM), nonbirefringent lamellar (NB Lam), lamellar (Lam), nonbirefringent hexagonal (Hex), hexagonally packed cylinders (HPC), and perforated lamellar (PL). Open symbols represent regions where macrophase separation between a conjugate-rich ordered phase and a water-rich phase is observed. Reproduced from ref. 83 with permission from The Royal Society of Chemistry.

chemistries (SPAAC, CuAAC, and TECC) to develop new multi-headed/multi-tailed giant surfactants with complex macromolecular architectures.[85] Many important molecular parameters of each block in giant surfactants, including chemical composition, molecular weight, and polydispersity, could be rigorously controlled and systematically varied. Notably, SPAAC-based sequential "click" methodology might have general implications for the synthesis of various giant surfactants based on other MNPs, such as protein, POM, and C_{60}.

The oxime ligation describes the efficient condensation reaction between an aminoxy group and an aldehyde or ketone to form an oxime linkage and has attracted considerable attentions as another type of highly reactive, bio-orthogonal "click" reaction under physiological conditions.[115] This reaction is chemoselective and compatible with most functional groups in biomolecules, and the rate of this reaction can be enhanced by protic or nucleophilic catalysts. Maynard et al. utilized this reaction to conjugate *N*-levulinyl lysine-modified BSA with aminooxy-terminated synthetic polymers within 30 min to obtain "smart" protein-based giant surfactant.[93] In addition, due to its orthogonal nature to CuAAC/SPAAC/TECC, oxime ligation can be incorporated into the "click" chemistry toolbox to achieve the one-pot synthesis of giant surfactants based on POSS and other MNPs.[86]

In recent years, our group has designed and synthesized various types of POSS-based giant surfactants in analogy to their small-molecule counterparts, such as giant surfactants,[84] giant lipids,[116] giant gemini surfactants,[65] giant bola-form surfactants,[117] and multi-headed/multi-tailed giant surfactants.[85,117] This series of molecular design also denotes an evolution toward complex macromolecular structures (Fig. 6) yet with increasingly facile synthesis. Combination of

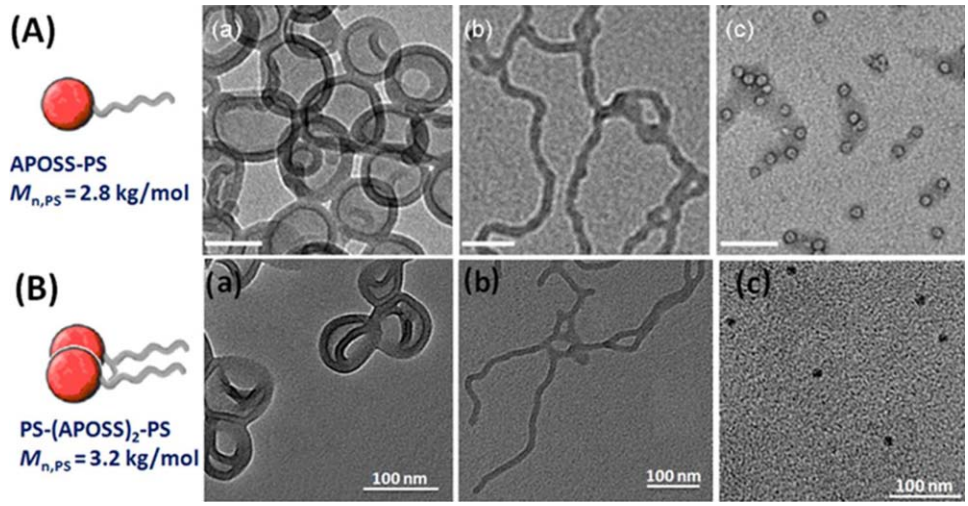


FIGURE 11 TEM images of self-assembly morphologies of different giant surfactants. (A) APOSS-PS micelles in solution with an initial concentration of 0.8% and a final water content > 50% using 1,4-dioxane (a), DMF (b), and DMF/NaOH (c) (scale bar is 80 nm). Adapted from ref. 17 with permission from American Chemical Society. (B) PS-(APOSS)$_2$-PS micelles in solution with an initial concentration of 2.8% and a final water content >70% using 1,4-dioxane (a), DMF (b), and DMF/NaOH (c) (scale bar is 100 nm). Adapted from ref. 65 with permission from The Royal Society of Chemistry.

different "click" reactions in a sequential manner [Fig. 5B(a)], a one-pot process [Fig. 5B(b)], and a fractal iterative strategy [Fig. 5B(c)] offers numerous opportunities in generating complex macromolecular structures for giant surfactants. Using such methodologies, several important molecular parameters of giant surfactants, including overall molecular weight, surface functionalities of the nanoparticle, polydispersity, weight fraction of heads/tails, asymmetry of head/tail could be independently controlled and systematically varied. Above all, echoing the structural evolution and increasing sophistication of giant surfactant via combined "click" methodology, a library of POSS-based giant surfactants can be constructed for systematic investigation of their self-assembly behavior and hierarchical micelle structure formation in solution (Fig. 6).

Self-Assembly of Giant Surfactants

Self-assembly of giant surfactants has been studied by Glotzer et al. using computer simulations.[118–121] Multiple self-assembly morphologies are observed including spherical micelles, cylinders, and lamellae.[118] Specifically, transition from cylindrical structure to perforated lamellae and further to lamellar structure was observed as increasing the concentration from 30 to 50%.[122] Most computer simulations are conducted under concentrated solution with a surfactant volume fraction of 20 to 60%. Recently, we have systematically studied the self-assembly of giant surfactants in dilute solution with polystyrene-(carboxylic acid-functionalized POSS) conjugate (PS-APOSS) as our starting point.[17] Multiple morphologies including spheres, cylinders, and vesicles were observed when tuning the degree of ionization of carboxylic acids on the POSS cage. Moreover, the PS tails in the micelle cores were found to be highly stretched in comparison with those in traditional amphiphilic block copolymers. This feature well resembles the self-assembly behaviors of small-molecule surfactants.[17,65] Here, we are going to focus only on reviewing the general self-assembly behaviors of these new materials and illustrating the effects of molecular structure, solvent properties, and molecular concentrations in the following sections.

Effects of Molecular Architecture

Physical properties of giant surfactants are intimately dependent on their primary chemical structures. To emphasize this, we have investigated the different self-assembly behaviors of topological isomers of giant surfactants that possess identical compositions but distinct polymer topologies in solution. Consider as an example the simplest case mentioned in the previous section: PS_{44}-AC_{60} versus $2PS_{23}$-AC_{60}. Both of them possess identical volume fraction of the PS tail (subscript denotes the degree of polymerization). The PS tail of PS_{44}-AC_{60} is about twice longer than that of $2PS_{23}$-AC_{60}.[59] Certainly, the hydrophilic polar head can also be other functionalized MNPs such as APOSS, DPOSS, POM, and so forth. This class of materials is an interesting and promising extension of simple giant surfactants and can be used to qualitatively and systematically study the effects of topology on the self-assembly behaviors. In this class of materials, other than the traditional order parameter (the volume fraction), additional parameters are required to describe the phase separation and structure formation. The parameters must be associated with the geometrical shapes, macromolecular architectures, and topological variation. For example, one important structural parameter called asymmetry of tail (A_{tail}), which originates from small-molecule amphiphiles system,[123] can be employed to quantitatively describe the spontaneous curvature formation between hydrophilic head region and hydrophobic tail region of giant surfactants. The value of A_{tail} $(0 \leq A_{tail} \leq 100\%)$ can be

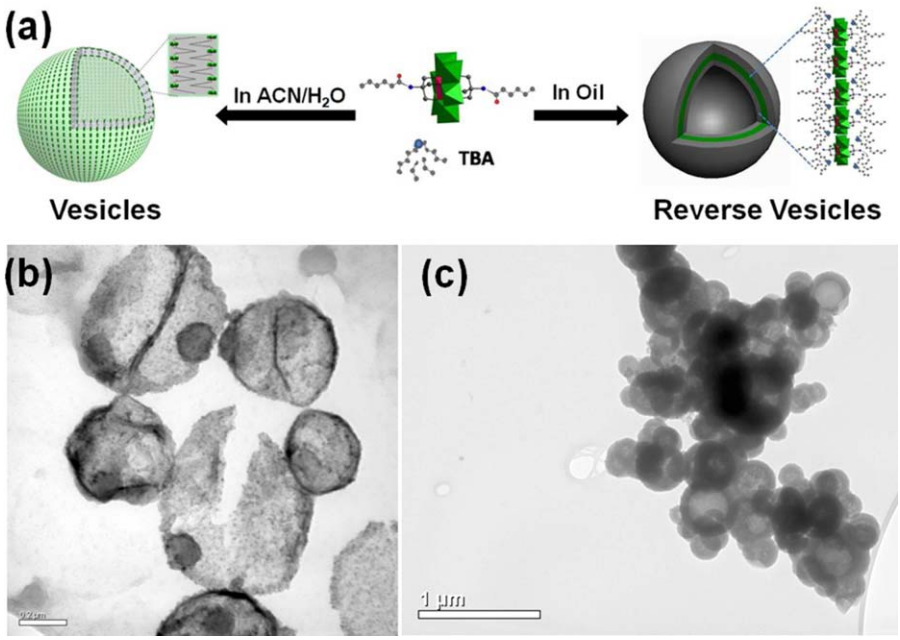


FIGURE 12 (a) Formation of vesicles and reverse vesicle structures in polar and nonpolar solvent, respectively. (b) TEM image of vesicular structure formed by Mn-Anderson-C_{16} in MeCN/water solution. (c) TEM image of reverse-vesicular structure by Mn-Anderson-C_{16} in MeCN/toluene solution. Adapted from ref. 70 with permission from American Chemical Society, and ref. 125 with permission from Wiley-VCH.

calculated based on molecular weight of tail 1 (M_{tail1}) and tail 2 (M_{tail2}) as in eq 1 if both tails possess the same chemical structure/composition:

$$A_{tail}=\left|\frac{M_{tail_1}-M_{tail_2}}{M_{tail_1}+M_{tail_2}}\right|\times 100\% \quad (1)$$

We currently limit this library into three kinds of topological isomeric giant surfactants: (1) giant surfactant ($A_{tail} = 100\%$) [Fig. 3(a)]; (2) asymmetric giant lipid ($0 < A_{tail} < 100\%$) [Fig. 3(c)]; and (3) symmetric giant lipid ($A_{tail} = 0$) [Fig. 3(b)].[86] Similar argument can be applied in giant gemini surfactants: (1) double-headed giant surfactant ($A_{tail} = 100\%$) [Fig. 3(f)]; (2) asymmetric giant gemini surfactant ($0 < A_{tail} < 100\%$) [Fig. 3(j)]; and (3) symmetric giant gemini surfactant ($A_{tail} = 0$) [Fig. 3(i)].[68]

The exceptional sensitivity of giant surfactants' self-assembly to topological variation has also been observed in solution (Fig. 7).[63] A PS_{44}-AC_{60} with a single PS tail formed spherical micelle, while $2PS_{23}$-AC_{60} with two PS chains formed bilayer vesicles under the identical conditions. The topological effects of the AC_{60}-based giant surfactants on their self-assembly behaviors can be revealed by shape aspect ratio (P), which describes the ratio between cross-sectional areas of the head and tail region of giant surfactants.

Besides topological variation, effects of other structural parameters on solution behaviors of giant surfactants have also been discussed. For example, our recent study has shown that the spacer length could greatly affect the self-assembly behaviors of symmetric gemini-type giant surfactants containing two identical APOSS heads and two identical PS tails in solution.[65] First, it was observed that the PS tails are usually less stretched in the micelle cores of these giant gemini surfactants comparing to those of the corresponding single-tail giant surfactant [Fig. 8(a)]. Second, the conformation of PS tails in the micelles is influenced by the spacer length where the one with longer spacer exhibits more stretched PS tail conformations [Fig. 8(a)]. Both findings may be explained by the macromolecular architectural constraint imposed by the rigid spacer and anisotropic local charge density distribution of gemini surfactants [Fig. 8(b,c)].[65] Based on the proposed model in Figure 8(b,c), the rigid short spacer of giant gemini surfactants could push the two APOSS heads closer to each other, leading to an increased local charge density for attracting more counter-ions around the POSS head than that in the single-chained giant surfactant. The intermolecular distances (d_T) should be increased to reduce the actual electrostatic repulsive energy, resulting in more inter-molecular space for the chain to relax and thus a less stretched chain conformation.[58] Similarly, giant gemini surfactant possessing shorter spacer is able to increase the local charge density and d_T even more effectively, which may allow the polymer tails in the micellar core become less stretched.[65]

Effects of Initial Concentration

We have recently constructed the phase diagram of a set of representative PS-AC_{60} giant surfactants based on both the initial molecular concentration and the PS tail length.[63] Figure 9(A) is a set of TEM bright-field images of self-assembled micelles of PS_{70}-AC_{60} at various initial molecular concentrations in

solution. Self-assembly structures change from spherical micelles to worm-like cylinders and further to vesicles when the initial molecular concentration increased from 0.1 to 2.0 (wt) % in 1,4-dioxane/DMF/water, where 1,4-dioxane/DMF is a mixed common solvent and water is a selective solvent for AC_{60}. On the other hand, the change of self-assembled structure can also be found by increasing the PS tail length while keeping the initial molecular concentration constant. A sophisticated phase diagram was plotted based on the PS tail length and initial polymer concentrations as shown in Figure 9(B), which reflects a balance between two parameters during the micelle formation: an aggregation number of micelles and the degree of ionization.[63]

Olsen et al. systematically studied the phase behaviors of globular protein–polymer giant surfactant, mCherry-*b*-PNIPAM (mChP), in concentrated aqueous solution as a function of the giant surfactant concentration, the solution temperature, and the PNIPAM coil fraction. Both order–order transition and order–disorder transition were observed.[82,83] Figure 10 shows the phase diagrams for mChP with different coil fractions. By increasing the concentration, the system undergoes a transition from a disordered phase to a lamellar phase and then, to a hexagonally packed cylinder phase with temperature below the lower critical solution temperature of PNIPAM in solution. Changing the polymer fraction generates a large impact on the phase behaviors (Fig. 10).

Effects of the Solvent

The nature of common solvent plays an important role in the micelle formation of giant surfactants in solution. Similar to many traditional macromolecular amphiphiles such as diblock copolymers, the packing behaviors of hydrophilic MNP heads and hydrophobic polymeric tails of giant surfactants can be strongly affected by the solvent in which they are initially dissolved. The strength of the steric interactions between the functionalized MNP heads on micelle surface depends mainly on the charge density (usually, the degree of ionization) of the MNPs, which are usually dominated by the nature of common solvents used (i.e., solubility parameter and the dielectric constant). Considering the conformational rigidity and shape persistence of MNPs, their repulsion force usually affects the thermodynamic distance between two heads of neighboring giant surfactants, which could further influence the formation of different micelle structures. On the other hand, the nature of common solvent may also have effects on the micelle structural transitions by tuning the chain mobility and conformation of hydrophobic polymer tails of giant surfactants. Both parameters of the solvents are able to tune the final thermodynamically stable, yet different micelle structures of giant surfactants in solution. For example, our group systematically investigated the effects of common solvents on the phase behaviors of a giant surfactant model system of PS-APOSS,[17] and its corresponding giant gemini surfactants, PS-$(APOSS)_2$-PS.[31,65] Figure 11 shows a

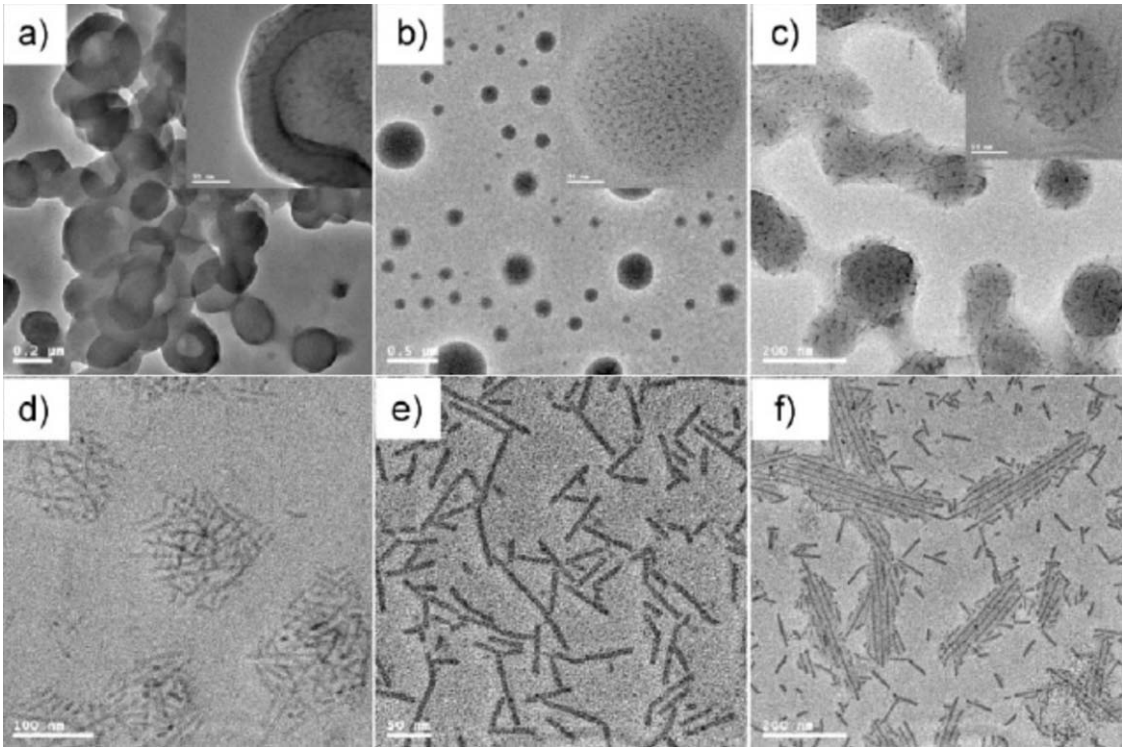


FIGURE 13 Morphology evolution of POM-PS in solution: (a) partially deteriorated hybrid vesicles; (b) initial stage of the tubular aggregates in spherical aggregates; (c) fine and tubular aggregates embedded inside the deteriorated spherical aggregates; (d) tubular aggregates released from the spherical aggregates; (e) randomly oriented tubular aggregates; and (f) domains where the tubular aggregates arrange parallel to each other. Reproduced from ref. 131 with permission from Wiley-VCH.

set of TEM images of PS-APOSS [Fig. 11A(a–c)]) and PS-$(APOSS)_2$-PS micelles [Fig. 11B(a–c)] formed in different common solvents. The micelle structure changes from vesicles with 1,4-dioxane as the common solvent, to cylinders with DMF as the common solvent, and to spheres with DMF/NaOH as the common solvent. The structural transformations were attributed to the increasing degree of ionization of the carboxylic acid groups, which was estimated by the ratio between the peak intensity of ν(COO–) to the intensity sum of ν(COO–) and ν(COOH) in FTIR spectrum. When increasing the degree of ionization, the charge density on the APOSS cage increased, resulting in stronger repulsion among the APOSS cages. For the PS-APOSS micelles, the occupied surface area per chain, A, was increased from 1.04 to 1.56 nm^2, and further to 2.23 nm^2 to minimize the electrostatic free energy of the APOSS heads. Similar effects have also been observed on the giant gemini surfactants as shown in Figure 11B(a–c).[65] Therefore, the tuning of the common solvent can be employed as an effective tool for controlling the micelle structures of giant surfactants.

POM-based giant surfactants usually contain bulky organic cationic counterions, such as tetrabutylammonium (TBA), which are strongly associated with the charged POM heads via electrostatic interactions in nonpolar solvents. The interactions between TBAs and POM heads can be controlled by tuning the polarity of solvents. Generally speaking, with increasing solvent polarity, the electrostatic interaction between POM heads and counter-ions will be increasingly screened. The reduce in the strength of electrostatic interaction can be directly confirmed by the different diffusion coefficients between the TBA and the anionic hybrids based on 2D NMR studies and leads to different self-assembled morphology.[21,124] For example, Mn-Anderson-C_{16} giant surfactants yielded vesicles in a polar solvent, while reversed vesicles were formed in a nonpolar solvent (Fig. 12).[70,125]

Kinetically Trapped, Metastable Structures of Giant Surfactants

In addition to those classical micelle structures, many unconventional morphologies have also been observed. In most cases, these unusual micelle structures are not thermodynamic stable. Rather, they are trapped in metastable states most likely due to kinetic reasons. Generally speaking, these metastable micelle structures are in a local free energy minimum, but not in thermodynamic equilibrium states. The height of transition barrier that leads to this metastable state determines whether this metastable state can be relatively easy or difficult to experimentally observe following its phase transition pathway. Moreover, the life time of this metastable state is also determined by the height of the transition barrier that prevents it from transferring to other more stable phases.[126] This is particularly interesting when the molecular weights of amphiphilic copolymers are large and entanglements are non-negligible during the micelle formation process. Also, these metastable structures are also sensitively dependent on the preparation processes[127] due to the large volume and slow mobility of amphiphilic copolymers and other phase transition processes such as vitrification and crystallization.

In amphiphilic block copolymers, kinetically trapped, metastable micelle morphologies are often observed when solvent-phobic block is glassy or semicrystalline in nature, or the micelle formations are so fast that the polymers do not have enough time to relax into their equilibrium states. Jain et al. observed cylindrical undulations and octopus-like aggregates with cylindrical micelles emanating from a single bilayer core,[128] while Pochan et al. observed the transition from regular cylindrical micelles to undulating cylinders during aging.[129,130]

Giant surfactants may also form metastable micelle structures due to the interactions generated by multiple hydrogen bonds between polar heads and the tail that may form glassy state at a low temperature even in solution. Wang et al. studied the evolution of self-assembled morphologies of POM-PS during the annealing process.[131] Figure 13 shows a set of TEM bright-field images of self-assembly aggregates after different thermal annealing time. Spherical aggregates gradually change to tubular structure after annealing as shown in Figure 13(a–e). Figure 13(f) is the micelle structure after 21 days of annealing, in which the tubular aggregates arrange themselves parallel to each other. It clearly indicates that the metastable micelles are slowly transferred to a more stable or a final micelle structure in equilibrium.

CONCLUSIONS AND OUTLOOK

The synthetic strategies and self-assembly behaviors in solution of giant surfactants based on functional MNPs are reviewed. Functional MNPs include derivatives of POSS, C_{60}, POM, and globular protein, which possess persistent shape and volume, and can be designed as the hydrophilic/ionic heads of the giant surfactants in which polymer chains serve as the hydrophobic tails. Two synthetic strategies (grafting-from and grafting-onto) have been developed for their precise syntheses. Self-assembly behaviors of these giant surfactants have been extensively investigated and found to be dependent on both the intrinsic molecular structures (such as molecular weight and molecular architecture) and the external experimental conditions (such as solvent used and initial molecular concentration, etc.). This class of giant surfactants captures the essential features of their small-molecule counterparts, yet has much larger sizes. They can be recognized as size-amplified versions of small-molecule surfactants and bridge the gap between small-molecule surfactants and traditional block copolymers. Our current efforts are to elucidate universal principles underlying the self-assemblies in order to apply the knowledge from these model systems to guide the design of new nanomaterials for different technologically relevant applications. Several challenges remain unresolved in this area: (1) theoretical studies, especially in dilute solutions as well as in the bulk, are necessary for a deeper and more thorough understanding of their self-assembly thermodynamics and the influence of various factors in their formation kinetics; (2) phase transitions between equilibrium states (spheres, cylinders, and vesicles) and their transition

mechanism are of great interest for investigation; (3) hierarchical self-assembled structure based on these giant surfactants need to be widely explored. The outlook for giant surfactants points to an emerging broad and bright field with many scientific challenges to be addressed. Giant surfactants are also anticipated to find many technological interests in biotechnology, optoelectronic and others.

ACKNOWLEDGMENTS

The authors are indebted to many scientists whose research results are cited here. This work was supported by the National Science Foundation (DMR-1408872) and the Joint-Hope Education Foundation. W.-B. Z. acknowledges the support from the National Thousand Young Talents Program of China.

REFERENCES AND NOTES

1 J. N. Israelachvili, D. J. Mitchell, B. W. Ninham, *J. Chem. Soc. Faraday Trans. 2* **1976**, *72*, 1525–1568.

2 J. N. Israelachvili, D. J. Mitchell, B. W. Ninham, *Biochim. Biophys. Acta* **1977**, *470*, 185–201.

3 R. Nagarajan, E. Ruckenstein, *Langmuir* **1991**, *7*, 2934–2969.

4 L. Leibler, *Macromolecules* **1980**, *13*, 1602–1617.

5 M. Malmsten, B. Lindman, *Macromolecules* **1992**, *25*, 5440–5445.

6 V. Percec, D. A. Wilson, P. Leowanawat, C. J. Wilson, A. D. Hughes, M. S. Kaucher, D. A. Hammer, D. H. Levine, A. J. Kim, F. S. Bates, K. P. Davis, T. P. Lodge, M. L. Klein, R. H. DeVane, E. Aqad, B. M. Rosen, A. O. Argintaru, M. J. Sienkowska, K. Rissanen, S. Nummelin, J. Ropponen, *Science* **2010**, *328*, 1009–1014.

7 S. Jain, F. S. Bates, *Science* **2003**, *300*, 460–464.

8 L. Zhang, A. Eisenberg, *Science* **1995**, *268*, 1728–1731.

9 K. Kosswig, In *Ullmann's Encyclopedia of Industrial Chemistry*, Wiley-VCH, Weinheim, **2000**.

10 Q. Huo, R. Leon, P. M. Petroff, G. D. Stucky, *Science* **1995**, *268*, 1324–1327.

11 F. M. Menger, J. S. Keiper, *Angew. Chem. Int. Ed.* **2000**, *39*, 1906–1920.

12 R. Zana, *Langmuir* **1996**, *12*, 1208–1211.

13 Y.-L. Lin, M.-Z. Wu, Y.-J. Sheng, H.-K. Tsao, *J. Chem. Phys.* **2012**, *136*, 104905.

14 V. K. Aswal, J. Haldar, P. S. Goyal, S. Bhattacharya, *Appl. Phys. A* **2002**, *74*, 352–354.

15 K. Kataoka, A. Harada, Y. Nagasaki, *Adv. Drug Delivery Rev.* **2001**, *47*, 113–131.

16 G. Fuks, R. Mayap Talom, F. Gauffre, *Chem. Soc. Rev.* **2011**, *40*, 2475–2493.

17 X. Yu, S. Zhong, X. Li, Y. Tu, S. Yang, R. Van Horn, C. Y. Ni, D. J. Pochan, R. P. Quirk, C. Wesdemiotis, W.-B. Zhang, S. Z. D. Cheng, *J. Am. Chem. Soc.* **2010**, *132*, 16741–16744.

18 X. Yu, K. Yue, I.-F. Hsieh, Y. Li, X.-H. Dong, C. Liu, Y. Xin, H.-F. Wang, A.-C. Shi, G. R. Newkome, R.-M. Ho, E.-Q. Chen, W.-B. Zhang, S. Z. D. Cheng, *Proc. Natl. Acad. Sci. USA* **2013**, *110*, 10078–10083.

19 F. Giacalone, N. Martín, *Chem. Rev.* **2006**, *106*, 5136–5190.

20 G. Li, L. Wang, H. Ni, C. U. Pittman, *J. Inorg. Organomet. Polym.* **2001**, *11*, 123–154.

21 P. Yin, P. Wu, Z. Xiao, D. Li, E. Bitterlich, J. Zhang, P. Cheng, D. V. Vezenov, T. Liu, Y. Wei, *Angew. Chem. Int. Ed.* **2011**, *50*, 2521–2525.

22 C. S. Thomas, M. J. Glassman, B. D. Olsen, *ACS Nano* **2011**, *5*, 5697–5707.

23 K. Holmberg, B. JÖnsson, B. Kronberg, B. Lindman, In *Surfactants and Polymers in Aqueous Solution*, 2nd ed.; Wiley: England, **2003**.

24 S. Förster, M. Antonietti, *Adv. Mater.* **1998**, *10*, 195–217.

25 Y. Mai, A. Eisenberg, *Chem. Soc. Rev.* **2012**, *41*, 5969–5985.

26 Z. Li, M. A. Hillmyer, T. P. Lodge, *Nano Lett.* **2006**, *6*, 1245–1249.

27 Z. Li, E. Kesselman, Y. Talmon, M. A. Hillmyer, T. P. Lodge, *Science* **2004**, *306*, 98–101.

28 A. H. Gröschel, F. H. Schacher, H. Schmalz, O. V. Borisov, E. B. Zhulina, A. Walther, A. H. E. Müller, *Nat. Commun.* **2012**, *3*, 710.

29 P. Bhargava, J. X. Zheng, R. P. Quirk, S. Z. D. Cheng, *J. Polym. Sci. Part B: Polym. Phys.* **2006**, *44*, 3605–3611.

30 P. Bhargava, Y. Tu, J. X. Zheng, H. Xiong, R. P. Quirk, S. Z. D. Cheng, *J. Am. Chem. Soc.* **2007**, *129*, 1113–1121.

31 L. Wang, X. Yu, S. Yang, J. X. Zheng, R. M. Van Horn, W.-B. Zhang, J. Xu, S. Z. D. Cheng, *Macromolecules* **2012**, *45*, 3634–3638.

32 H. Shen, A. Eisenberg, *J. Phys. Chem. B* **1999**, *103*, 9473–9487.

33 H. Shen, L. Zhang, A. Eisenberg, *J. Am. Chem. Soc.* **1999**, *121*, 2728–2740.

34 W.-B. Zhang, X. Yu, C.-L. Wang, H.-J. Sun, I. F. Hsieh, Y. Li, X.-H. Dong, K. Yue, R. Van Horn, S. Z. D. Cheng, *Macromolecules* **2014**, *47*, 1221–1239.

35 T. Szabo, G. Hilmersson, J. Rebek, *J. Am. Chem. Soc.* **1998**, *120*, 6193–6194.

36 R. P. Goodman, I. A. T. Schaap, C. F. Tardin, C. M. Erben, R. M. Berry, C. F. Schmidt, A. J. Turberfield, *Science* **2005**, *310*, 1661–1665.

37 T. R. Wilks, J. Bath, J. W. de Vries, J. E. Raymond, A. Herrmann, A. J. Turberfield, R. K. O'Reilly, *ACS Nano* **2013**, 8561–8572.

38 Y. Li, W.-B. Zhang, I.-F. Hsieh, G. Zhang, Y. Cao, X. Li, C. Wesdemiotis, B. Lotz, H. Xiong, S. Z. D. Cheng, *J. Am. Chem. Soc.* **2011**, *133*, 10712–10715.

39 H.-J. Sun, Y. Tu, C. L. Wang, R. M. Van Horn, C. C. Tsai, M. J. Graham, B. Sun, B. Lotz, W.-B. Zhang, S. Z. D. Cheng, *J. Mater. Chem.* **2011**, *21*, 14240–14247.

40 W.-B. Zhang, Y. Tu, H.-J. Sun, K. Yue, X. Gong, S. D. Cheng, *Sci. China Chem.* **2012**, *55*, 749–754.

41 H. Liu, C.-H. Hsu, Z. Lin, W. Shan, J. Wang, J. Jiang, M. Huang, B. Lotz, X. Yu, W.-B. Zhang, K. Yue, S. Z. D. Cheng, *J. Am. Chem. Soc.* **2014**, *136*, 10691–10699.

42 Z. Lin, P. Lu, C.-H. Hsu, K. Yue, X.-H. Dong, H. Liu, K. Guo, C. Wesdemiotis, W.-B. Zhang, X. Yu, S. Z. D. Cheng, *Chem. Eur. J.* **2014**, DOI: 10.1002/chem.201402697.

43 K. M. Kadish, R. S. Ruoff, In *Fullerenes: Chemistry, Physics, and Technology*; Wiley-Interscience: New York, **2000**.

44 Y. Rubin, S. Khan, D. I. Freedberg, C. Yeretzian, *J. Am. Chem. Soc.* **1993**, *115*, 344–345.

45 C. Bingel, *Chem. Ber.* **1993**, *126*, 1957–1959.

46 A. Hirsch, I. Lamparth, H. R. Karfunkel, *Angew. Chem. Int. Ed.* **1994**, *33*, 437–438.

47 A. Hirsch, O. Vostrowsky, *Eur. J. Org. Chem.* **2001**, 829–848.

48 A. Hirsch, I. Lamparth, T. Groesser, H. R. Karfunkel, *J. Am. Chem. Soc.* **1994**, *116*, 9385–9386.

49 G. Zhang, Y. Liu, D. Liang, L. Gan, Y. Li, *Angew. Chem. Int. Ed.* **2010**, *49*, 5293–5295.

50 K. Kokubo, K. Matsubayashi, H. Tategaki, H. Takada, T. Oshima, *ACS Nano* **2008**, *2*, 327–333.

51 B. Schade, K. Ludwig, C. Böttcher, U. Hartnagel, A. Hirsch, *Angew. Chem. Int. Ed.* **2007**, *46*, 4393–4396.

52 F. Wang, X. Lu, C. He, *J. Mater. Chem.* **2011**, *21*, 2775–2782.

53 Y.-J. Lee, J.-M. Huang, S.-W. Kuo, F.-C. Chang, *Polymer* **2005**, *46*, 10056–10065.

54 F. J. Feher, K. D. Wyndham, R. K. Baldwin, D. Soulivong, J. W. Ziller, J. D. Lichtenhan, J. D. Lichtenhan, *Chem. Commun.* **1999**, 1289–1290.

55 Y. Li, K. Guo, H. Su, X. Li, X. Feng, Z. Wang, W. Zhang, S. Zhu, C. Wesdemiotis, S. Z. D. Cheng, W.-B. Zhang, *Chem. Sci.* **2014**, *5*, 1046–1053.

56 C. L. Hill, *Chem. Rev.* **1998**, *98*, 1–2.

57 D.-L. Long, E. Burkholder, L. Cronin, *Chem. Soc. Rev.* **2007**, *36*, 105–121.

58 A. Dolbecq, E. Dumas, C. R. Mayer, P. Mialane, *Chem. Rev.* **2010**, *110*, 6009–6048.

59 P. Caliceti, F. M. Veronese, *Adv. Drug Delivery Rev.* **2003**, *55*, 1261–1277.

60 K. L. Heredia, D. Bontempo, T. Ly, J. T. Byers, S. Halstenberg, H. D. Maynard, *J. Am. Chem. Soc.* **2005**, *127*, 16955–16960.

61 P. Carter, *Biochem. J.* **1986**, *237*, 1–7.

62 J.-D. Pedelacq, S. Cabantous, T. Tran, T. C. Terwilliger, G. S. Waldo, *Nat. Biotech.* **2006**, *24*, 79–88.

63 X. Yu, W.-B. Zhang, K. Yue, X. Li, H. Liu, Y. Xin, C.-L. Wang, C. Wesdemiotis, S. Z. D. Cheng, *J. Am. Chem. Soc.* **2012**, *134*, 7780–7787.

64 Y. Han, Y. Xiao, Z. Zhang, B. Liu, P. Zheng, S. He, W. Wang, *Macromolecules* **2009**, *42*, 6543–6548.

65 Z. Wang, Y. Li, X.-H. Dong, X. Yu, K. Guo, H. Su, K. Yue, C. Wesdemiotis, S. Z. D. Cheng, W.-B. Zhang, *Chem. Sci.* **2013**, *4*, 1345–1352.

66 I. C. Reynhout, J. J. L. M. Cornelissen, R. J. M. Nolte, *Acc. Chem. Res.* **2009**, *42*, 681–692.

67 Z. Lin, P. Lu, X. Yu, W.-B. Zhang, M. Huang, K. Wu, K. Guo, C. Wesdemiotis, X. Zhu, Z. Zhang, K. Yue, S. Z. D. Cheng, *Macromolecules* **2014**, *47*, 4160–4168.

68 H. Su, Y. Li, K. Yue, Z. Wang, P. Lu, X. Feng, X.-H. Dong, S. Zhang, S. Z. D. Cheng, W.-B. Zhang, *Polym. Chem.* **2014**, *5*, 3697–3706.

69 K. Wu, M. Huang, K. Yue, C. Liu, Z. Lin, H. Liu, W. Zhang, C.-H. Hsu, A.-C. Shi, W.-B. Zhang, S. Z. D. Cheng, *Macromolecules* **2014**, DOI: 10.1021/ma501017e.

70 J. Zhang, Y.-F. Song, L. Cronin, T. Liu, *J. Am. Chem. Soc.* **2008**, *130*, 14408–14409.

71 P. Yin, D. Li, T. Liu, *Chem. Soc. Rev.* **2012**, *41*, 7368–7383.

72 J. Rieger, T. Antoun, S.-H. Lee, M. Chenal, G. Pembouong, J. Lesage de la Haye, I. Azcarate, B. Hasenknopf, E. Lacôte, *Chem. Eur. J.* **2012**, *18*, 3355–3361.

73 M.-B. Hu, N. Xia, W. Yu, C. Ma, J. Tang, Z.-Y. Hou, P. Zheng, W. Wang, *Polym. Chem.* **2012**, *3*, 617–620.

74 Y. Xiao, Y.-K. Han, N. Xia, M.-B. Hu, P. Zheng, W. Wang, *Chem. Eur. J.* **2012**, *18*, 11325–11333.

75 M. J. Boerakker, J. M. Hannink, P. H. H. Bomans, P. M. Frederik, R. J. M. Nolte, E. M. Meijer, N. A. J. M. Sommerdijk, *Angew. Chem. Int. Ed.* **2002**, *41*, 4239–4241.

76 M. J. Boerakker, N. E. Botterhuis, P. H. H. Bomans, P. M. Frederik, E. M. Meijer, R. J. M. Nolte, N. A. J. M. Sommerdijk, *Chem. Eur. J.* **2006**, *12*, 6071–6080.

77 B. Le Droumaguet, G. Mantovani, D. M. Haddleton, K. Velonia, *J. Mater. Chem.* **2007**, *17*, 1916–1922.

78 K. Velonia, A. E. Rowan, R. J. M. Nolte, *J. Am. Chem. Soc.* **2002**, *124*, 4224–4225.

79 M. Li, P. De, S. R. Gondi, B. S. Sumerlin, *Macromol. Rapid Commun.* **2008**, *29*, 1172–1176.

80 C. Lavigueur, J. G. Garcia, L. Hendriks, R. Hoogenboom, J. J. L. M. Cornelissen, R. J. M. Nolte, *Polym. Chem.* **2011**, *2*, 333–340.

81 C. S. Thomas, L. Xu, B. D. Olsen, *Biomacromolecules* **2013**, *14*, 3064–3072.

82 B. D. Olsen, *Macromol. Chem. Phys.* **2013**, *214*, 1659–1668.

83 C. N. Lam, B. D. Olsen, *Soft Matter* **2013**, *9*, 2393–2402.

84 K. Yue, C. Liu, K. Guo, X. Yu, M. Huang, Y. Li, C. Wesdemiotis, S. Z. D. Cheng, W.-B. Zhang, *Macromolecules* **2012**, *45*, 8126–8134.

85 H. Su, J. Zheng, Z. Wang, F. Lin, X. Feng, X.-H. Dong, M. L. Becker, S. Z. D. Cheng, W.-B. Zhang, Y. Li, *ACS Macro Lett.* **2013**, *2*, 645–650.

86 Y. Li, Z. Wang, J. Zheng, H. Su, F. Lin, K. Guo, X. Feng, C. Wesdemiotis, M. L. Becker, S. Z. D. Cheng, W.-B. Zhang, *ACS Macro Lett.* **2013**, *2*, 1026–1032.

87 R. M. Broyer, G. N. Grover, H. D. Maynard, *Chem. Commun.* **2011**, *47*, 2212–2226.

88 K. Matyjaszewski, *Macromolecules* **2012**, *45*, 4015–4039.

89 D. J. Keddie, G. Moad, E. Rizzardo, S. H. Thang, *Macromolecules* **2012**, *45*, 5321–5342.

90 O. Dechy-Cabaret, B. Martin-Vaca, D. Bourissou, *Chem. Rev.* **2004**, *104*, 6147–6176.

91 K. Matyjaszewski, J. Xia, *Chem. Rev.* **2001**, *101*, 2921–2990.

92 D. J. Siegwart, J. K. Oh, K. Matyjaszewski, *Prog. Polym. Sci.* **2012**, *37*, 18–37.

93 K. L. Heredia, Z. P. Tolstyka, H. D. Maynard, *Macromolecules* **2007**, *40*, 4772–4779.

94 B. S. Lele, H. Murata, K. Matyjaszewski, A. J. Russell, *Biomacromolecules* **2005**, *6*, 3380–3387.

95 P. Zhou, G.-Q. Chen, C.-Z. Li, F.-S. Du, Z.-C. Li, F.-M. Li, *Chem. Commun.* **2000**, 797–798.

96 G. Moad, E. Rizzardo, S. H. Thang, *Aust. J. Chem.* **2005**, *58*, 379–410.

97 C. Boyer, V. Bulmus, J. Liu, T. P. Davis, M. H. Stenzel, C. Barner-Kowollik, *J. Am. Chem. Soc.* **2007**, *129*, 7145–7154.

98 W.-B. Zhang, Y. Li, X. Li, X.-H. Dong, X. Yu, C.-L. Wang, C. Wesdemiotis, R. P. Quirk, S. Z. D. Cheng, *Macromolecules* **2011**, *44*, 2589–2596.

99 N. Xia, W. Yu, Y. Wang, Y. Han, P. Zheng, W. Wang, G. Sakaguchi, K. Matsuda, K. Saijo, M. Takenaka, H. Hasegawa, *Polymer* **2011**, *52*, 1772–1780.

100 J. He, K. Yue, Y. Liu, X. Yu, P. Ni, K. A. Cavicchi, R. P. Quirk, E.-Q. Chen, S. Z. D. Cheng, W.-B. Zhang, *Polym. Chem.* **2012**, *3*, 2112–2120.

101 Y. Li, X.-H. Dong, K. Guo, Z. Wang, Z. Chen, C. Wesdemiotis, R. P. Quirk, W.-B. Zhang, S. Z. D. Cheng, *ACS Macro Lett.* **2012**, *1*, 834–839.

102 P. Zhou, G.-Q. Chen, H. Hong, F.-S. Du, Z.-C. Li, F.-M. Li, *Macromolecules* **2000**, *33*, 1948–1954.

103 C. Weis, C. Friedrich, R. Muelhaupt, H. Frey, *Macromolecules* **1995**, *28*, 403–405.

104 T. Kawauchi, J. Kumaki, E. Yashima, *J. Am. Chem. Soc.* **2005**, *127*, 9950–9951.

105 T. Kawauchi, J. Kumaki, E. Yashima, *J. Am. Chem. Soc.* **2006**, *128*, 10560–10567.

106 X.-D. Huang, S. H. Goh, S. Y. Lee, *Macromol. Chem. Phys.* **2000**, *201*, 2660–2665.

107 O. Stoilova, C. Jérôme, C. Detrembleur, A. Mouithys-Mickalad, N. Manolova, I. Rashkov, R. Jérôme, *Chem. Mater.* **2006**, *18*, 4917–4923.

108 K. Velonia, *Polym. Chem.* **2010**, *1*, 944–952.

109 A. J. Dirks, S. S. Van Berkel, N. S. Hatzakis, J. A. Opsteen, F. L. Van Delft, J. J. L. M. Cornelissen, A. E. Rowan, J. C. M. Van Hest, F. P. J. T. Rutjes, R. J. M. Nolte, *Chem. Commun.* **2005**, 4172–4174.

110 W.-B. Zhang, Y. Tu, R. Ranjan, R. Van Horn, S. Leng, J. Wang, M. J. Polce, C. Wesdemiotis, R. P. Quirk, G. R. Newkome, S. Z. D. Cheng, *Macromolecules* **2008**, *41*, 515–517.

111 A. B. Lowe, *Polym. Chem.* **2010**, *1*, 17–36.

112 C. E. Hoyle, C. N. Bowman, *Angew. Chem. Int. Ed.* **2010**, *49*, 1540–1573.

113 W. Xi, T. F. Scott, C. J. Kloxin, C. N. Bowman, *Adv. Funct. Mater.* **2014**, *24*, 2572–2590.

114 N. J. Agard, J. A. Prescher, C. R. Bertozzi, *J. Am. Chem. Soc.* **2004**, *126*, 15046–15047.

115 Y.-X. Chen, G. Triola, H. Waldmann, *Acc. Chem. Res.* **2011**, *44*, 762–773.

116 K. Yue, J. He, C. Liu, M. Huang, X.-H. Dong, K. Guo, P. Ni, C. Wesdemiotis, R. Quirk, S. D. Cheng, W.-B. Zhang, *Chin. J. Polym. Sci.* **2013**, *31*, 71–82.

117 K. Yue, C. Liu, K. Guo, K. Wu, X.-H. Dong, H. Liu, M. Huang, C. Wesdemiotis, S. Z. D. Cheng, W.-B. Zhang, *Polym. Chem.* **2013**, *4*, 1056–1067.

118 S. C. Glotzer, M. A. Horsch, C. R. Iacovella, Z. Zhang, E. R. Chan, X. Zhang, *Curr. Opin. Colloid Interface Sci.* **2005**, *10*, 287–295.

119 C. R. Iacovella, M. A. Horsch, S. C. Glotzer, *J. Chem. Phys.* **2008**, *129*, 044902.

120 X. Zhang, E. R. Chan, S. C. Glotzer, *J. Chem. Phys.* **2005**, *123*, 184718.

121 E. R. Chan, X. Zhang, C.-Y. Lee, M. Neurock, S. C. Glotzer, *Macromolecules* **2005**, *38*, 6168–6180.

122 C. R. Iacovella, M. A. Horsch, Z. Zhang, S. C. Glotzer, *Langmuir* **2005**, *21*, 9488–9494.

123 R. Oda, I. Huc, S. J. Candau, *Chem. Commun.* **1997**, 2105–2106.

124 C. P. Pradeep, M. F. Misdrahi, F.-Y. Li, J. Zhang, L. Xu, D.-L. Long, T. Liu, L. Cronin, *Angew. Chem. Int. Ed.* **2009**, *48*, 8309–8313.

125 J. Zhang, Y.-F. Song, L. Cronin, T. Liu, *Chem. Eur. J.* **2010**, *16*, 11320–11324.

126 S. Z. D. Cheng, In *Phase Transitions in Polymers: the Role of Metastable States*, 1st ed.; Elsevier: Amsterdam, Boston, **2008**.

127 R. C. Hayward, D. J. Pochan, *Macromolecules* **2010**, *43*, 3577–3584.

128 S. Jain, F. S. Bates, *Macromolecules* **2004**, *37*, 1511–1523.

129 H. Cui, Z. Chen, S. Zhong, K. L. Wooley, D. J. Pochan, *Science* **2007**, *317*, 647–650.

130 D. J. Pochan, Z. Chen, H. Cui, K. Hales, K. Qi, K. L. Wooley, *Science* **2004**, *306*, 94–97.

131 Y. K. Han, Z. J. Zhang, Y. L. Wang, N. Xia, B. Liu, Y. Xiao, L. X. Jin, P. Zheng, W. Wang, *Macromol. Chem. Phys.* **2011**, *212*, 81–87.