ACCOUNTS
of chemical research

Soft Vesicles in the Synthesis of Hard Materials

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RECEIVED ON MAY 8, 2011

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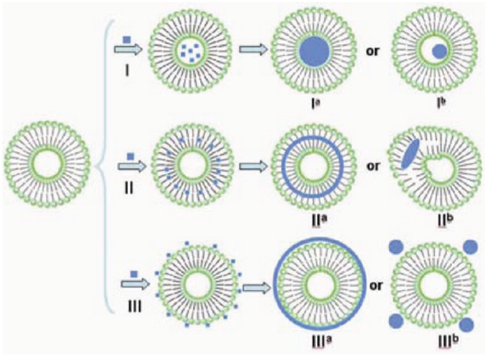

Vesicles of surfactants in aqueous solution have received considerable attention because of their use as simple model systems for biological membranes and their applications in various fields including colloids, pharmaceuticals, and materials. Because of their architecture, vesicles could prove useful as “soft” templates for the synthesis of “hard materials”. The vesicle phase, however, has been challenging and difficult to work with in the construction of hard materials.

In the solution-phase synthesis of various inorganic or macromolecular materials, templating methods provide a powerful strategy to control the size, morphology, and composition of the resulting micro- and nanostructures. In comparison with hard templates, soft templates are generally constructed using amphiphilic molecules, especially surfactants and amphiphilic polymers. These types of compounds offer advantages including the wide variety of available templates, simple fabrication processes under mild conditions, and easy removal of the templates with less damage to the final structures. Researchers have used many ordered molecular aggregates such as vesicles, micelles, liquid crystals, emulsion droplets, and lipid nanotubes as templates or structure-directing agents to control the synthesis or assembly hard micro- and nanomaterials composed from inorganic compounds or polymers. In addition to their range of sizes and morphologies, vesicles present unique structures that can simultaneously supply different microenvironments for the growth and assembly of hard materials: the inner chamber of vesicles, the outer surface of the vesicles, and the space between bilayers. Two main approaches for applying vesicles in the field of hard materials have been explored: (i) *in situ* synthesis of micro- or nanomaterials within a specific microenvironment by vesicle templating and (ii) the assembly or incorporation of guest materials during the formation of vesicles.

This Account provides an in-depth look at the research concerning the association of soft vesicles with hard materials by our laboratory and others. We summarize three main principles of soft vesicle usage in the synthesis of hard materials and detailed procedures for vesicle templating and the characterization of the synthetic mechanisms. By use of these guiding principles, a variety of inorganic materials have been prepared, such as quantum dots, noble metal nanoparticles, mesoporous structures, and hollow capsules. Polymerization within the vesicle bilayers enhances vesicle stability, and this strategy has been developed to synthesize hollow polymer materials. Since 2004, our group has pursued a completely different strategy in the synthesis of micro- and nanomaterials using vesicles as reactive templates. In this method, the vesicles act not only as templates but also as reactive precursors. Because of the location of metal ions on the bilayer membranes, such reactions are restricted to the interface of the vesicle membrane and solution. Finally, using the perspective of soft matter chemistry, we stress some basic criteria for vesicle templating.

Introduction

Vesicles, usually spherical, are enclosed and hollow lamellar aggregates with a curved bilayer membrane comprised of amphiphilic molecules.[1] Not only can they be stably dispersed in and filled with water[1] or organic solvents,[2] vesicles can also be obtained as nearly perfect hollow capsules on solid surfaces.[3] Depending on the fabrication method, vesicles generally exhibit three morphologies: oligovesicular, multilamellar, and unilamellar;[4] the dimensions of vesicles generally vary from 10 nm to 50 μm. On the basis of the unique architectures available, current functional applications of vesicles have focused on

Published on the Web 01/18/2012 www.pubs.acs.org/accounts
10.1021/ar200124g

biological membrane models, drug delivery systems, microreactors, or soft templates for synthesizing hard materials.[5,6]

Two main approaches for applying vesicles in the field of hard materials have been explored: (i) *in situ* synthesis of micro- or nanomaterials within a specific microenvironment by vesicle templating and (ii) the assembly or incorporation of guest materials during the formation of vesicles. In this Account, we summarize recent progress on the relationship between soft vesicles and hard materials from the unique perspective of vesicle characteristics, and focus on material synthesis by vesicle templating. Vesicles provide multiple microenvironments, which can restrict the guest species and direct their growth and packing. The synthesis of hard materials via soft vesicles has been explored using three main strategies:[6,7] (i) reaction compartmentalization within the hydrophilic vesicle chamber (Figure 1, I), (ii) membrane-restricted reaction within the bilayers (Figure 1, II), and (iii) surface-reactive templating and synthesis at the vesicle outer surface (Figure 1, III). A comprehensive picture of the templating functions of soft vesicles is therefrom highlighted, including detailed procedures of vesicle templating, the confirmation of synthetic mechanisms, and the properties of the expected materials, which we expect to further promote using soft matter in hard materials applications.

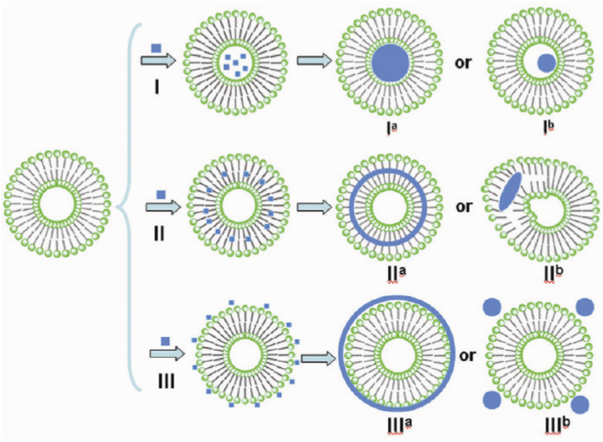

FIGURE 1. Schematic routes of the three principal uses of soft vesicles in the synthesis of hard materials: I, reaction compartmentalization; II, membrane-restricted microreactor; III, surface-reactive templating and synthesis.

Synthesis of Hard Nanocrystals in the Vesicle Chamber

In the first strategy, vesicles offer the inner chamber for reaction compartmentalization (Figure 1, I). In aqueous solution, the bilayer membrane serves as a barrier to isolate two discontinuous aqueous phases, i.e., the interior aqueous cavity and the "bulk" solution outside the vesicles. Hence, one potential application of vesicles depends on the presence of a hydrophilic cavity, which can carry and disperse various hydrophilic cargos by encapsulation.[8] For materials fabrication, pioneering work in the synthesis of nanoparticles (NPs) in the vesicle chamber was carried out by Tricot and Fendler in the mid-1980s.[9] Rh-coated ca. 40 Å diameter CdS NPs were synthesized *in situ* and stabilized in single-component dihexadecylphosphate vesicles; the vesicles doped with NPs were further utilized for transmembrane photoelectron transfer and hydrogen generation. Subsequently, this approach has been successfully applied in solution synthesis of core–shell metal sulfide nanocrystals.[10]

In this fabrication process, ion exchange technology is frequently used in order to ensure the formation of particles only within the vesicle chamber. For instance, in the synthesis of nanometer-sized CdS particles in unilamellar lipid vesicles by Korgel and Monbouquette,[10] the Cd^{2+} ions external to the vesicles were removed by passing the dispersion through a cation exchange column (Figure 2, left), leaving only the encapsulated Cd^{2+}. After desalting, an ion selective electrode confirmed that no Cd^{2+} permeated out of the unilamellar vesicular bilayer, presumably due to its semipermeable character. With the addition of $(NH_4)_2S$, the

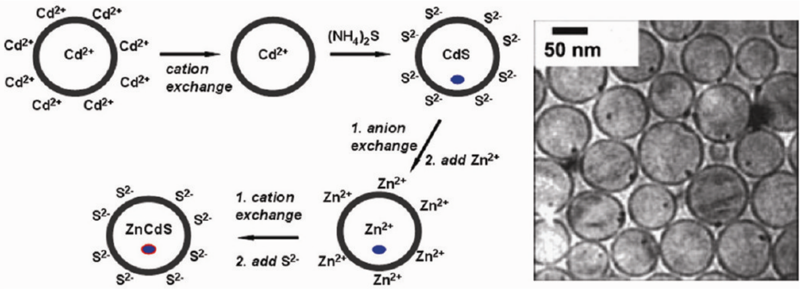

FIGURE 2. A schematic of the synthetic steps for CdS and ZnCdS NP formation in vesicle chambers (left). A cryo-TEM image of ~60 Å CdS particles encapsulated within ~70 nm phosphatidylcholine (PC) vesicles. Only a single particle forms per vesicle (right). Modified with permission from ref 10. Copyright 2000 American Chemical Society.

precipitation reaction of oppositely charged ions was constrained in the vesicle chamber and CdS particles with ∼60 Å diameter were formed. Interestingly, cryo-TEM observation confirmed the product was in the vesicle chamber and indicated that only a single CdS particle forms per vesicle (Figure 2, right). Further, adding Zn^{2+} into the dispersion with trapped CdS NPs resulted in the formation of mixed ZnCdS nanocrystals with limited size in the vesicle chamber by repeated utilization of ion exchange. These colloidal semiconductor nanocrystals, also called quantum dots (QDs), have been used as unique luminescent materials for many purposes due to their size-dependent emission properties, such as light-emitting diodes, high-efficiency lasers, and biomedical labeling. The vesicles serve as nanoreactors that control the crystal growth and stabilize the QDs in aqueous solution.

As described, to achieve the goal of controlling the material's synthesis in the vesicle chamber, at least three aspects have to be considered: (i) the unloaded or unreactive ions external to the vesicles should be removed, leaving only the reactive ions entrapped within the chamber; (ii) the bilayers act as a semipermeable membrane to allow the selective passage of ions; and (iii) the vesicles are stable enough to retain their morphology and contain the reactive ions in their pool. Generally, unilamellar vesicles are favored for synthesizing homogeneous materials due to their nearly monodisperse size. Cryo-TEM has proven to be a powerful technique in studying the original morphology of the vesicles and confirming the reaction site.

Synthesis of Hard Inorganic Particles within the Vesicle Bilayers

The second strategy utilizes the core of the vesicle bilayer membrane as a spatially restricted microreactor, having similar effects on material synthesis as a vesicle chamber (see Figure 1, II). However, in aqueous systems, the interior of the bilayers favors localization of hydrophobic species. To accomplish synthesis within vesicle bilayers, it should first be emphasized that the reactive components permeate the hydrophobic core of the bilayer after the formation of vesicles and form expected materials within the limitation of the bilayer environment. Typically, hydrophobic monomers are solubilized in the hydrophobic part of the bilayers, and polymerization reactions of the organic monomers can be restricted to the bilayer interior. In this process, a homogeneous distribution of monomers favors the formation of polymer chain networks that can retain the shape of the template to form hollow polymer capsules (Figure 1, II^a).[11] In contrast, an asymmetric distribution of monomer can promote a phase separation between the polymer chains and bilayer, resulting in a "parachute-like" structure (Figure 1, II^b).[7] Therefore a number of polymer products with complex forms can be obtained using vesicles. Of course, decorated NPs preformed with a protective surfactant, can also be incorporated into vesicle membranes due to hydrophobic interactions during the formation of vesicles, but this is generally regarded as a separate, though important, assembly behavior.[12−14] The technology is largely dependent on size restrictions (i.e., particle size and spacing of bilayers), the penetrability of the modified NP, and the stability of the bilayer membrane.

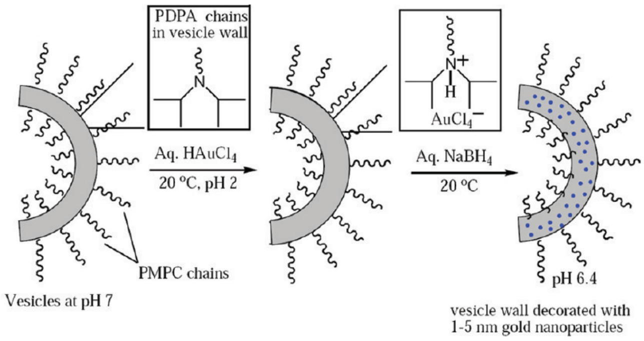

FIGURE 3. Schematic illustration of the formation of PMPC-*b*-PDPA diblock copolymer vesicles in aqueous phase and subsequent Au NP synthesis within the bilayers. Modified with permission from ref 16. Copyright 2005 American Chemical Society.

Synthesis within bilayers offers an especially effective strategy to prepare hydrophobic NPs in an aqueous environment. In another approach to hard materials, an oil-in-water microemulsion procedure helps stabilize the hydrophobic NPs in an aqueous phase.[15] The advantage of this method is that the entrapped NPs can be stabilized without the need of other surfactants. NPs with excellent dispersity have been produced, and the uniform particle sizes can enhance their efficiency in applications in adsorption, catalysis, and sensors. Gold NPs have been prepared in bilayers after controlling the entrance of the precursor $HAuCl_4$. Du et al.[16] prepared pH-sensitive vesicles by directly dissolving a copolymer, poly[2-(methacryloyloxy)ethylphosphorylcholine]-*block*-poly[2-(diisopropylamino)ethyl methacrylate] (PMPC-*b*-PDPA) in purely aqueous solution. The hydrophilic PMPC chains face toward the water, while the hydrophobic PDPA chains reside in the interior of the bilayer. With the addition of aqueous $HAuCl_4$ solution, the nitrogen atoms of the PDPA groups were partially protonated, leading to the incorporation of $AuCl_4^-$ in the bilayer as a counterion. Finally, a large amount of Au NPs with the size of 4.4 ± 1.6 nm were synthesized within the copolymer vesicle walls after *in situ* reduction of tetrachloroaurate by $NaBH_4$ (Figure 3). The incorporation *in situ* of Au NPs into vesicles also creates a versatile hybrid for drug delivery, image tracking, or catalysis.

Using the bilayer as a template has also been successfully applied to the synthesis of silica materials. In order to avoid template disruption during the fabrication process, polymer materials are typically used to construct vesicles. Compared with conventional liposomes or surfactant vesicles, the bilayers of polymersomes have superior stability and toughness due to their higher molecular weight.[17,18] The membrane thickness can be also controlled by the molecular weight of the hydrophobic block of the polymer. In addition, it is believed that the presence of quaternary ammonium groups, acting as a catalyst, is favorable for silica growth.[19] Thus, cationic polymers or surfactants with quaternary ammonium groups are common templating materials in synthesizing silica solids or hollow microspheres. For instance, the amphiphilic, biocompatible zwitterionic diblock copolymer poly(ε-caprolactone)-*block*-poly[2-(methacryloloxy)ethyl phosphorylcholine] (PCL-*b*- PMPC) was directly combined with hot water to form vesicles.[20] The PCL chains are somewhat hydrophobic and form the core of the vesicle bilayer (Figure 4). After addition of tetramethylorthosilicate (TMOS), the water-immiscible silica precursor is initially solubilized within the vesicle walls by the hydrophobic interactions. Under mild catalytic action by the quaternary ammonium groups of PMPC,[20−23] the entrapped TMOS is fully hydrolyzed to form silica after a long duration sol−gel reaction. The silicification is confined within the hydrophobic PCL wall, leading to the final formation of membrane silicified vesicles. We note that, for silicification within the membrane, the TMOS silica precursor should be encapsulated in the membrane prior to hydrolysis. Hence, it is important that the vesicular solution with a neutral pH is controlled to slow down the hydrolysis.

Synthesis of Hollow Materials on the Outer Surface of Vesicles

In the third route, the outer surface of the vesicles is considered a specific reaction site for materials synthesis, which can lead to a direct, transcriptive templating process (Figure 1, III^a). In the transcriptive process, the precursors initially adsorb and react at the vesicle surface. Next, the products nucleate, grow, and gradually cover the vesicle. Complete coating of the vesicle can create a cast of the vesicle morphology, leaving the vesicle as a filler of the materials. After removal of the vesicle material, hollow micro- or nanocapsule structures with well-organized morphologies have been successfully constructed. This technology has been suitably developed and applied in fabrication of inorganic hollow materials.[24] A key factor in this approach is to use charged vesicle bilayers so that the precursors can initially adsorb at the interface between the vesicle and the solution via electrostatic interactions. Furthermore, by controlling the vesicle composition or precursors, different product structures can also be obtained at the vesicle surface, such as anchoring NPs (Figure 1, III^b).

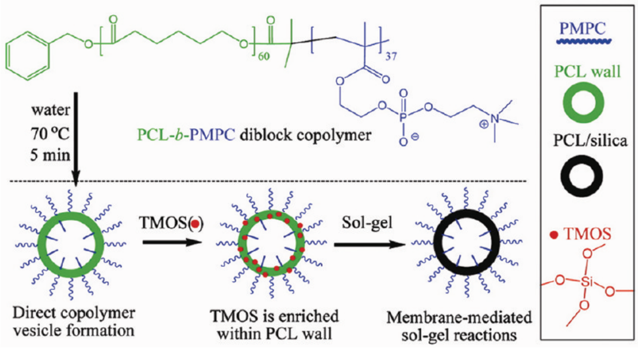

FIGURE 4. Schematic illustration of the formation of PCL-*b*-PMPC diblock copolymer vesicles and subsequent silica synthesis within the bilayers without any external catalyst. Reproduced with permission from ref 20. Copyright 2009 American Chemical Society.

As one of the most popular inorganic matrices, hollow silica particles synthesized by the vesicle-transcriptive templating method have been widely studied.[19,21−23,25,26] Furthermore, silicified vesicle complexes with relatively high mechanical strength and hydrothermal stability can be prepared, which have many potential applications in encapsulation, drug delivery, nanocatalysts, and high-capacity adsorptions. Hubert et al.[19] prepared unilamellar siliceous vesicles in basic conditions ($pH = 8$) by taking a single component, dioctadecyldimethylammonium bromide (DODAB), for the vesicle composition and using TMOS as the silica precursor. The measurements of ζ-potential for the vesicle ($+73 \pm 3$ mV) and the product (-37 ± 2 mV) solutions indicate that the vesicles were completely covered with silica. The positively charged outer surface of vesicles interacts with the negatively charged silica species, leading to the formation of the coating. The silica shell thickness was determined to be approximately 9 nm by cryo-TEM (Figure 5a) and dynamic light scattering (DLS). Subsequently, Kaler et al.[21] prepared hollow silica particles ranging in size from about 60 to 120 nm using cationic and anionic (catanionic) surfactant vesicles (in the cationic-rich region) with excess salt as templates and TMOS as silica precursor in acidic conditions (pH = 3). Their research suggests that the ratio of surfactant and silica precursor plays a key role in the silicification, and a higher TMOS concentration resulted in the formation of solid silica particles in addition to the silica hollow spheres. Methanol generated in the silicification reaction can destroy the stability of the vesicle bilayer and can even lead to the transformation of vesicles into flat lamellar aggregates. Another key factor, the temperature effect, was studied in the silica synthesis using unilamellar didodecyldimethylammonium bromide (DDAB) vesicles.[22] Typically, when the reaction temperature was 20 °C, the majority of the silica particles were mesostructured solid spheres, while at 8 °C multilamellar hollow silica spheres were obtained as the major products (Figure 5b). Zemb et al. prepared catanionic vesicles with a faceted, hollow polyhedral morphology by mixing cetyltrimethylammonium hydroxide (CTAOH) and myristic acid ($C_{13}H_{27}COOH$), used these vesicles as a template to synthesize hollow silica icosahedra (Figure 5c), and systematically investigated various parameters that influenced the synthesis.[23] They found that the rate of silica deposition is faster in acidic rather than in basic conditions. The surface charge of siliceous vesicles depended on the solution pH. Further it was confirmed that a higher silica precursor concentration led to the destruction of the vesicles.

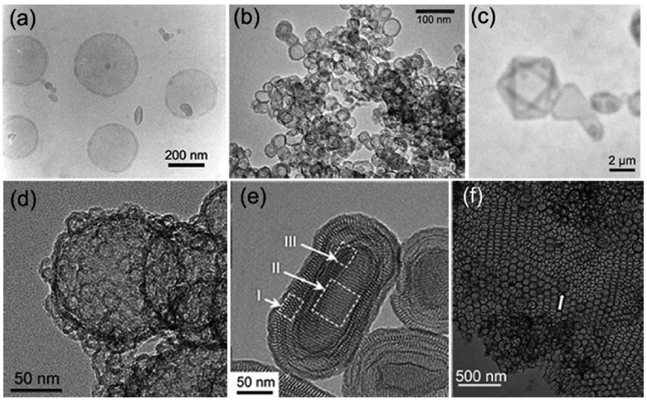

FIGURE 5. Morphologies of hollow silica materials. A typical cryo-TEM image of a silica-coated unilamellar vesicle (a). TEM images of (b) multilamellar, (c) icosahedra-like, (d) raspberry-like, and (e) cocoon-like hollow silica structures. TEM image of siliceous foams (f). Modified with permission from refs 19,22,23,25,26, and 27, respectively. Copyright 2000 and 2007 Wiley-VCH, Copyright 2003 Royal Society of Chemistry, Copyright 2007 American Chemical Society, Copyright 2007 Wiley-VCH, and Copyright 2006 American Chemical Society.

Currently, the various vesicular silica materials that have been fabricated by vesicle-transcriptive templating methods include unilamellar and multilamellar mesoporous structures, and icosahedra-like, raspberry-like (Figure 5d),[25] or cocoon-like (Figure 5e)[26] hollow silica structures. Yu's group further produced macroporous (~110 nm in diameter) ordered siliceous foams through a supra-assembly approach.[27] Cooperative silica-coated triblock copolymer (P123) vesicles were preformed at 35 °C in pH = 5 buffer solutions in the absence of organic solvent, fused, and packed to form honeycomb-patterned structures (Figure 5f). The above structures are dependent on the reaction conditions, including the

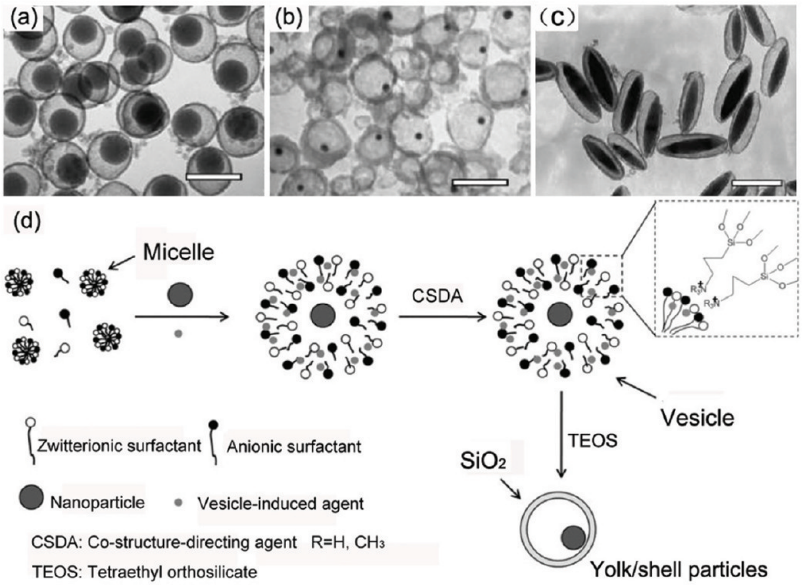

FIGURE 6. TEM images of yolk/SiO_2 shell structures encapsulating different kinds of NP cores: (a) 90 nm SiO_2 NPs, (b) 10 nm Au NPs, and (c) spindle-like Fe_2O_3 particles. Scale bars: (a, c) 200 nm; (b) 100 nm. (d) A schematic procedure for producing yolk/SiO_2 shell particles using vesicle templates. Modified with permission from refs 28 and 29. Copyright 2009 American Chemical Society and copyright 2010 Wiley-VCH.

vesicle-constructing systems, the silica precursor composition, pH, temperature, aging time, and ionic strength. Recently, a novel "yolk/SiO_2 shell" structure has been described using mixed surfactant vesicles as the template.[28,29] In this unique structure, SiO_2, noble metal (Au), or magnetic (Fe_2O_3) NPs can be encapsulated as mobile cores in hollow silica capsules (Figure 6a–c). Initially, preformed NPs were encapsulated into a 1:1 mol ratio aqueous mixture of lauryl sulfonate betaine (LSB) and sodium dodecyl benzenesulfonate (SDBS). A co-structure-directing agent, 3-amino-propyltriethoxysilane (APS), was used to induce the vesicle formation, and then was anchored on the vesicle surface by electrostatic interactions. After addition of TEOS, the silica shell with a shell thickness of ~10 nm was produced by hydrolysis of the APS and TEOS. A detailed procedure is shown in Figure 6d. We note that only one NP is encapsulated per silica capsule. This technology may promote the applications of hollow silica materials as delivery systems, catalysts, sensors, storage materials, photonic materials, or microreactors.

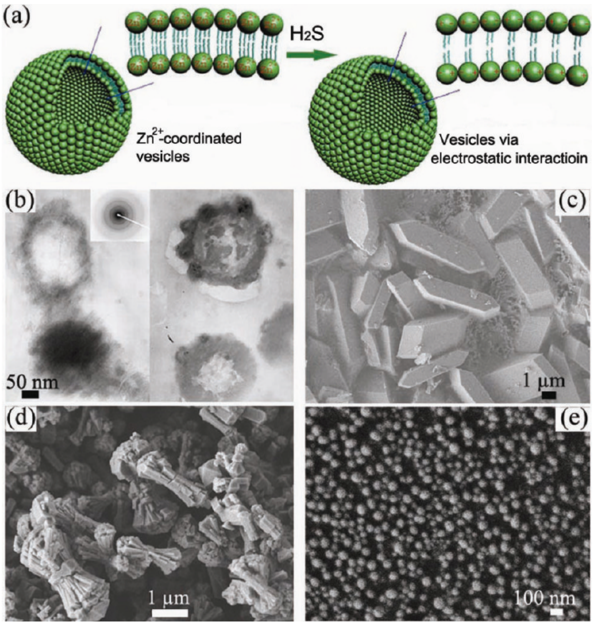

FIGURE 7. Scheme illustrating the transition from vesicles composed of Zn^{2+}–ligand complexes to vesicles held together by ionic interactions. ZnS NPs were prepared in this transition process (a). TEM image of ring-like ZnS particles with encapsulated central ZnS precipitates (b). SEM images of CaC_2O_4 crystals produced from Ca^{2+}–ligand coordinated vesicles: elongated hexagonal and dumbbell-like structures (c, d). SEM image of Zn NPs synthesized by electrochemical deposition from a vesicular solution (e). Modified with permission from refs 5,30,31, and 33, respectively. Copyright 2009 Elsevier Inc. and Copyright 2005, 2008, and 2009 American Chemical Society.

Vesicles as Reactive Templates To Induce Crystal Growth

Reactive templates here refer to vesicles that act not only as templates but also as reactive precursors. In our research,[4,30–32] these reactive templates are generally composed of long-chain alkyldimethylamine oxide and multivalent metal anionic surfactant complexes formed via coordination interactions between metal ions and the N–O group. Although these vesicles are involved in the reaction, they are not consumed but preserved, because catanionic vesicles can be produced again after introducing acidic gas as a reagent to precipitate the metal ions from the vesicles.

We dissolved zinc 2,2-dihydroperfluorooctanoate [$Zn(OOCCH_2C_6F_{13})_2$] and single-chain zwitterionic tetradecyldimethylaminoxide ($C_{14}DMAO$) in water to prepare Zn^{2+} coordinated vesicles.[30] In these vesicles, the Zn^{2+} ions, as the central ions forming the membrane, are tightly associated with the head groups of two surfactant molecules. Therefore, the vesicles are positively charged, but the surface charge is not shielded because there is no free salt in the vesicular solution. After addition of H_2S, Zn^{2+} ions are precipitated from the vesicle surface to form ZnS NPs. After this reaction, a catanionic $C_{14}DMAOH^+{-}^-OOCCH_2C_6F_{13}$ vesicle phase is produced via electrostatic interactions, because the zwitterionic $C_{14}DMAO$ is protonated by H^+ released from H_2S. The detailed transition process is illustrated in Figure 7a. The resulting ZnS exhibits ring-like structures with rings encapsulating ZnS precipitates corresponding to polycrystalline zinc-blende (Figure 7b). The final catanionic vesicular solution is still salt-free after removal of ZnS precipitates. We have also designed a series of metal–ligand coordination systems for vesicles by mixing $C_{14}DMAO$ with different multivalent metal anionic surfactants including calcium tetradecylamidomethyl sulfate,[31] calcium or barium oleate,[5] and aluminum laurate.[32] Directed by the Ca^{2+}-ligand vesicles as reactive templates, CaC_2O_4 crystals with different morphologies are produced via the hydrolysis of dimethyl oxalate ($CH_3OOCCOOCH_3 + H_2O \rightarrow 2\ CH_3OH + H_2C_2O_4$ and $Ca^{2+} + H_2C_2O_4 \rightarrow CaC_2O_4\downarrow + 2H^+$). The resulting materials include elongated hexagonal crystals (Figure 7c)[31] and dumbbell-like morphologies (Figure 7d).[5]

During the synthesis, the reaction does not occur in the bulk solution but is restricted to the interface of the vesicles due to the presence of the metal ions on the bilayer membranes. Once the control of the material morphology and size is successful, using metal–ligand complexes as reactive templates should open up avenues to prepare a number of inorganic materials. Another advantage to this method is that the reformation of vesicles means the template is not destroyed. Recently, we have successfully prepared zinc nanospheres (Figure 7e) on an ITO (indium tin oxide) electrode surface from $C_{14}DMAO/Zn(OOC(CH_2)_{10}CH_3)_2$ vesicular solution by electrochemical deposition.[33] This provides another new templating and surface modification route from metal–ligand coordinated soft vesicles.

Polymerization within Vesicle Bilayers

Polymerization within a vesicle bilayer provides an additional route to enhance vesicle stability and preserve vesicles from deformation during changes to their environment; polymers entrapped within bilayers may also control the permeability of the membrane. This method has been developed to fabricate hollow polymer capsules, based on the bilayer capturing hydrophobic monomers (along with cross-linkers and hydrophobic initiators) in its interior while the monomer-loaded vesicle retains its previous morphology. The polymer scaffold is then formed as a part of the vesicle membrane by cross-linking the monomers. Hollow polymer capsules can be prepared after removal of the vesicle templates.[24]

Different strategies have been applied to promote polymerization reactions in vesicle membranes, including thermal initiation, pH response, and UV irradiation. Kaler et al.[34] prepared polymerized vesicles based on catanionic equilibrium complexes that were fortified through the cross-linking of divinylbenzene (DVB) and styrene monomers after being induced by an initiator at 60 °C. After polymerization, cryo-TEM observations suggested that the vesicle templates were largely intact in the hybrid product. After removal of the templates, the obtained particles are robust and successfully transcribe the template shape. Kepczynski et al.[35] also studied polymerization within catanionic vesicle membrane and prepared inorganic/organic hybrid vesicles. Using methanol washing to remove the surfactants, they obtained silicone ($[R_2SiO]_n$) nanocapsules filled with water (Figure 8a). The polymerization reaction was induced by pH adjustment rather than thermal initiation. In the case of an anionic-rich vesicular solution, silicone capsules were synthesized by acid-catalyzed polycondensation of 1,3,5,7-tetramethylcyclotetrasiloxane, whereas a base-catalyzed ring-opening polymerization was performed in a cationic-rich solution. Though the reaction mechanisms in the above catanionic vesicles are different, the polymerization process is restricted to within the vesicle membrane, and a homogeneous distribution of monomer units leads to the formation of hollow polymer capsules.

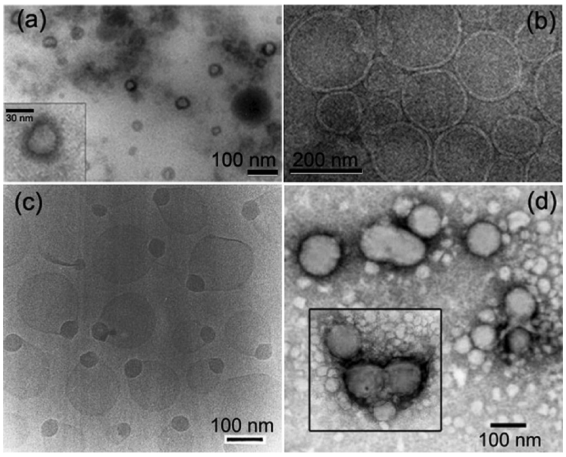

FIGURE 8. TEM image of silicone nanocapsules (a). Cryo-TEM images of mixed liposome/polymer capsules (b) and polystyrene/DODAB hybrid vesicles of parachute-like structures (c). TEM observation of polymer nanocapsules from cross-linking of DVB and TBS (d). Modified with permission from refs 35,36,37, and 38, respectively. Copyright 2004 Wiley-VCH and Copyright 2006, 1997, and 2010 American Chemical Society.

Initiating polymerization in vesicles by UV irradiation is popular due to its high reaction rate. Unlike pH adjustment or thermal initiation procedures, UV irradiation uses shorter reaction times and causes little change in the vesicular environment, which can further reduce the deformation of vesicle templates. The process is very simple, and common procedures are described in Figure 9a. By control of monomer addition, ratio of surfactant to monomer, initiation mode, etc., polymer materials with different morphologies may be synthesized, including hollow capsules[11] and solid spheres entrapped in so-called "parachute structures".[7] In a study by Meier et al.,[11] giant, hollow polymer spheres of several micrometers in diameter were prepared through UV-initiated polymerization of dual functional monomers in DODAC vesicles. These authors also developed nanometer-sized bioreactors by incorporating a water-soluble enzyme into the chamber and a channel protein into the membrane of fortified lipid vesicles.[39] These vesicles were stabilized by polymerization of *n*-butyl methacrylate (BMA) and ethylene glycol dimethacrylate (EGDMA) under UV irradiation. Cryo-TEM showed that no phase separation occurred in the polymerized vesicles (Figure 8b).[36] Due to the size selectivity of the entrapped channel protein, the functionalized vesicle bilayers can control the penetration of the reactive ions and protect the enzyme against the outer environment.

In contrast, Jung et al.[7,37,40] reported a novel polystyrene/DODAB hybrid vesicle with a parachute-like architecture. This structure results from a typical phase separation between polymer and amphiphilic bilayers after polymerization

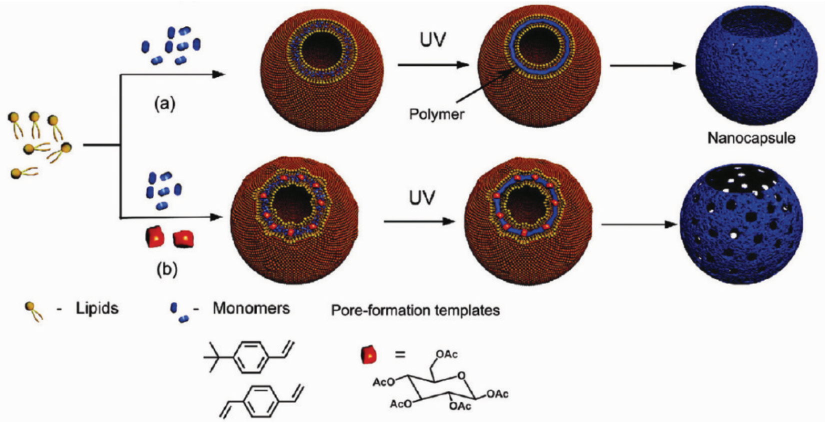

FIGURE 9. Synthesis of hollow polymer nanocapsules by polymerization within bilayers under UV irradiation (cutaway view). In pathway a, stable vesicles with loaded monomers (and initiator) are formed, and then polymer/vesicle hybrids are prepared under UV irradiation. After removal of the vesicle templates, hollow nanocapsules are obtained. If monomers and pore-formation templates are encapsulated together in the bilayer, as in pathway b, nanoporous polymer nanocapsules can be fabricated. Modified with permission from ref 38. Copyright 2010 American Chemical Society.

(UV irradiation at 25 °C). The polystyrene does not transcribe the morphology of the vesicle templates but grows at one site, leading to only a small polymer sphere linked to the membrane in each vesicle and producing the "parachute" structure (Figure 8c).[37] Temperature appears to have a large influence on the formation of the "parachute" structure;[40] when polymerized at 60 °C, the polymer particles can be separated completely from the vesicle matrix. The increase in temperature lowers the membrane rigidity, resulting in the release of the particles through a more liquid bilayer.

Recently, Pinkhassik et al.[38] have further developed UV-initiated polymerization within bilayers to create nanometer-thin organic materials with nanopores of programmed size. The hydrophobic monomers, DVB and *tert*-butylstyrene (TBS), were incorporated into a liposome membrane, and the polymer scaffold was formed *in situ* after polymerization. At a 3:1 monomer to lipid and 1:1 monomer to cross-linker ratios, the polymer/vesicle hybrids with an average diameter of 100 nm can withstand environmental changes and retain their spherical shape (Figure 8d). When some pore-formation templates (e.g., glucose pentabenzoate) are doped into the monomer mixture (Figure 9b), polymer nanocapsules with nanopores are obtained after the removal of the liposomes and pore-forming templates. Due to the adjustment of the nanopore size or shape, this material has been regarded as a novel delivery device with size selectivity.

Primary Standpoints in Soft Vesicles for Hard Materials

Since its inception, soft vesicle templating has attracted increased interest in the synthesis of polymer or inorganic materials. Due to some misunderstandings about vesicle templating, there are some primary considerations that need to be stressed from the perspective of soft matter chemistry. First, as mentioned above, a stable vesicle phase, but not micelles or a microemulsion, should be prepared as a template prior to the synthetic reactions. Though there are many amphiphilic molecules or mixtures that are able to construct vesicle systems, some cannot perform as templates under certain conditions. By way of example, it is known that CTAB and SDS can be mixed to form catanionic vesicles in water, but a single-component aqueous solution of the anionic surfactant SDS, sodium oleate, or the cationic surfactants CTAB or tetrabutylphosphonium rarely forms flat lamellar aggregates or vesicles. A second critical point is that the vesicle template should retain its original morphology, avoiding destruction in the reaction process, or the vesicle templating strategy fails. Cryo-TEM observation is a powerful tool to directly confirm not only the presence or integrity of the vesicles but also the formation of final products. Finally, the most suitable reaction microenvironment needs to be selected for different reactive ions or molecules. For example, in the case of aqueous solutions, small hydrophobic monomers prefer to be solubilized within vesicle bilayers.

Vesicles have similar advantages as other soft templates, such as normal and reverse micelles (or water-in-oil microemulsion),[6] and liquid crystals, in materials synthesis. The monodisperse size and uniform morphology of the inorganic or polymer materials can be controlled by varying, for example, the amphiphilic molecule types, solvent types, ionic additives, the composition of reagents, and the concentration, to influence the formation of the vesicle templates or the fabrication process of the products. Furthermore, vesicle templating has its own advantages. First, unlike the reverse micelle method, the vesicle method allows the synthesis of particles with excellent dispersity in aqueous solution under mild conditions. Second, with transcriptive templating and polymerization, the vesicle method provides an extremely convenient route to prepare hollow materials. Third, vesicles, especially multilamellar onions, provide different stable microenvironments that can support parallel reactions for the formation of surprisingly complex and multifunctional products.

However, vesicle methods indeed have shortcomings in material synthesis, including the weak reproducibility and stability of the templates. This limits the production of functional materials on a large scale. If new research does not focus on a real technological impact, this field may end without fulfilling its original promise. Hence, the future direction of vesicle methods in the field of materials synthesis is a concern. For example, specific amphiphilic molecules for the formation of novel vesicles are needed for particular chemical reactions or crystal growth processes. To scale up vesicle templating, different models have to be proposed to explain the formation of particles in vesicle microreactors. In addition, taking vesicles as a matrix, smart and multifunctional vesicle hybrids are required to develop effective carriers in biotechnological and catalytic applications. In terms of potential pharmaceutical applications, these hybrids must be biocompatible, load hydrophobic or hydrophilic drugs, respond to pH or temperature, and be easily tracked *in vivo*.

Conclusions and Perspectives

This Account relates recent developments in the use of soft esicles for hard materials fabrication and characterization. The control and understanding of vesicle templating is an important route to study the physical chemistry of hard materials/soft matter organization. Vesicles have provided various means to synthesize different functional materials. However, success in this templating area hinges largely on the stability of the vesicles employed. Therefore, the study of the factors that influence the phase behavior of amphiphilic molecules is another important issue; these factors include solvent selection, composition, temperature, pH, the presence of salts, and pressure. In fact, using amphiphilic molecular aggregates as templates for material synthesis is also a study of the phase behavior of amphiphilic molecules. No matter how materials are prepared using different templating strategies, stable vesicles with expected structures should be preferentially fabricated. As stated succinctly by Kaler et al., "Template synthesis is not only a powerful means for materials synthesis, but it can also contribute to the determination and analysis of self-organized morphologies."[21]

This work was supported by the NSFC (Grant No. 21033005) and the National Basic Research Program of China (973 Program, 2009CB930103).

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FOOTNOTES

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