Self-Assembled, Sub-Micrometer Diameter Semipermeable Capsules

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Self-assembly is an elegant and simple approach to the design of new materials relevant to problems in catalysis, sensor design, biological chemistry, and materials science.[1] The many applications of two-dimensional arrays such as those derived from thiol-self-assembly on gold and other metals illustrate the potential of macroscopic organized molecular assemblies.[2] However, while self-assembly has proven to be a very versatile and useful method for modifying the reactivity and chemistry of two-dimensional macroscopically planar surfaces, less attention has been paid to the use of self-assembly to modify the surfaces of one and zero dimensional fibers and particles. This oversight is now being addressed. The work highlighted here illustrates the potential of self-assembly both as a method for modifying surfaces of particles and as a method in the fabrication of micrometer- and submicrometer-sized hollow spheres. This work by Möhwald et al. and Wooley et al. spans a range of materials and length scales and promises to provide chemists with new sorts of materials that should be useful in applications in areas as diverse as biological chemistry, synthesis, and catalysis.[3–7]

Micrometer- and submicrometer-sized containers are not new; nature uses them in various ways in intracellular apparatus. Chemists too use structures such as liposomes in applications such as drug delivery and in other chemistry. Still smaller materials such as micelles are easily prepared, but they have only modest stability as discrete nanoscopic objects. More stable dendritic structures comparable in size to micelles can also be prepared.[8] Moreover, since dendrimers are covalently assembled in a step-by-step approach from smaller molecules they can be engineered to have considerable chemical diversity. However, dendrimer synthesis is a tedious, costly process. Recent work by Möhwald et al. and Wooley et al.[3–7] shows how synthetically less complex self-assembly approaches can be used to prepare particles or spherical hollow shells. This work shows that self-assembly can be a powerful, but simple, synthetic method for the fabrication and surface modification of nanometer- to micrometer-sized hollow spheres and particles.

The approaches of Möhwald et al. to the synthesis of surface modified sub-micrometer particles and spheres relies on surface modification chemistry developed for two-dimensional surfaces by Decher.[9] This chemistry uses a series of layer-by-layer deposition steps as shown in Figure 1. This polyelectrolyte self-assembly has proven to be broadly applicable as a method for the modification of two-dimensional surfaces and has been used successfully in many ways on a wide variety of substrates.

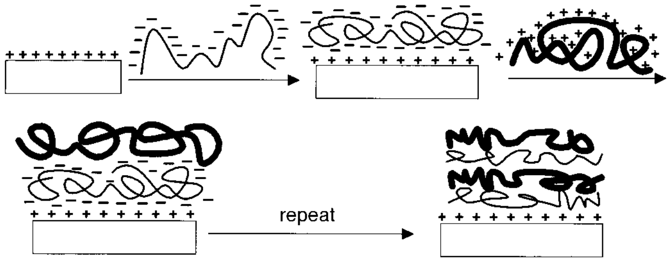

Figure 1. Layer-by-layer ionic self-assembly on a planar surface.

Möhwald et al. have shown that micrometer- and sub-micrometer-sized particles can be modified by ionic self-assembly in the same way Decher modifies planar surfaces by electrostatic self-assembly. For example, the approach by Möhwald et al. begins with a colloidal organic polymer support.[10] Micrometer-sized melamine–formaldehyde colloidal particles 2 or 3.3 µm in diameter were used as substrates. These polymer particles were suspended in a dilute aqueous solution containing 0.5 M NaCl and 1 mg mL^{-1} of sodium polystyrene sulfonate (NaPSS). After repeated centrifugation and washing, a second, cationic polyelectrolyte, poly(allylamine hydrochloride) (PAH), was added. Repetition of this process leads to multiple bilayers on the melamine–formaldehyde support. In this chemistry the anionic polyelectrolyte sodium polystyrene sulfonate initially self-assembles onto the cationic melamine–formaldehyde particle. Since all the sulfonated groups are not consumed by electrostatic interactions with the particle surface there are sulfonate groups in random, polydisperse sections of the polymer that are available for further ion exchange with the cationic polyelectrolyte. Thus, polyvalent ionic interactions with the support entropically favor deposition of the polymer onto the sub-micrometer particular support, and the first deposition of an anionic polyelectrolyte sets the stage for subsequent deposition of a second, positively charged polyelectrolyte. This sequential deposition of polyelectrolytes eventually produces a multilayer mat of polyelectrolyte polymers on the underlying particle.

Möhwald et al. have also shown[4, 5] that functionalized polystyrene latex particles are also suitable substrates for ionic self-assembly chemistry. In this work a cationic polyelectrolyte, an anionic polyelectrolyte, and finally a cationic electrolyte were first sequentially adsorbed onto negatively charged, 640-nm diameter polystyrene latex particles. This initial set of deposition experiments produced a uniformly positively charged outer surface that could then be used in sequential adsorption of negatively charged 25-nm SiO_2 particles and cationic poly(diallyldimethylammonium chloride) (PDADAC) polyelectrolyte. Layers with thicknesses ranging from tens to hundreds of nanometers were prepared with this procedure. The alternating surface charge postulated in these syntheses was verified by electrophoretic mobility

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measurements of particles at intermediate stages in the synthesis.

The coated particles obtained from the work of Möhwald et al. can then be transformed into hollow spheres (Figure 2). In reference [3] exposure of the coated particles to an acidic solution ($pH < 1.6$) dissolves the acid-sensitive melamine–formaldehyde colloidal core. Transmission electron microscopy (TEM) and scanning electron microscopy (SEM) images of nine-layer $[(PSS/PAH)_4PSS]$ hollow shells that were obtained show that the resulting hollow capsules are approximately 4 µm in diameter. The TEM studies indicate that the nine-layer polyelectrolyte film is about 20 nm thick. Mass spectroscopic studies of the dissolved melamine–formaldehyde products show that oligomers consisting of 5–10 monomers of tetramethylol–melamine are produced. Molecular dynamics simulations indicated that these oligomers are about 1 nm in diameter. This observation indicates that the shells formed by this chemistry are permeable.

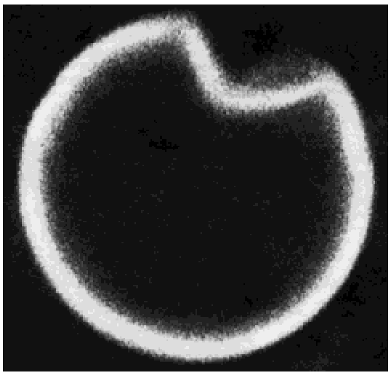

Figure 2. A confocal micrograph of an 8-µm hollow sphere illustrating the stability and deformability of a $[(PSS/PAH)_4PSS]$ hollow shell.[3]

They have also described several procedures for forming hollow spheres from SiO_2/poly(diallyldimethylammonium chloride) nanocomposite-coated particles. With polystyrene latex cores, calcining thermally destroys the core (Figure 3). This thermal process generates product spheres that are mostly whole but also produces some ruptured spheres. Milder procedures for core removal generate more whole spheres. For example, dissolution of the core by a good solvent (THF) leads to more unruptured hollow spheres. When a chemically reactive core such as the melamine–formaldehyde colloid is used in place of polystyrene, acid treatment such as that described in reference [3] can be used to chemically dissolve the core to form hollow spheres.

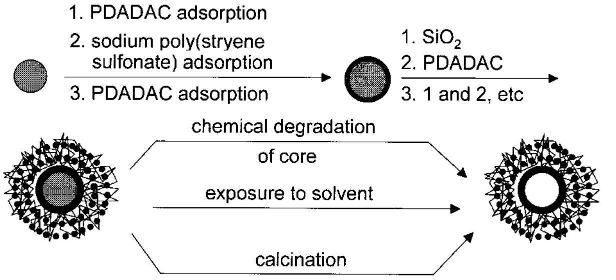

Figure 3. Procedures for preparing hollow spheres with a hybrid SiO_2/PDADAC shell (solvent extraction of core or chemical degradation of the core).

Still smaller particles may be prepared as reported recently by Wooley's group.[6, 7] This work uses a conceptually different synthetic approach that relies on the synthesis of block copolymers and the assembly of these block copolymers into polymeric micelles. Such micellarization is precedented and produces materials whose dimensions are smaller than those of colloids prepared by emulsion polymerization. By varying the conditions of micellarization polymeric micelles with diameters in the 10–100 nm range can be prepared from polymers such as polyisoprene or polystyrene for the core and polymers such as poly(acrylic acid) and poly(*tert*-butyl acrylate) for the shells. Such polymer micelles can be designed to have significant stability, interesting morphologies, and can be chemically manipulated by cross-linking.[11–13] The innovative feature of the work by Wooley et al. is the subsequent cross-linking of these block copolymer micelles to form shell- or core-cross-linked particles whose reactive interiors can be chemically degraded to give hollow spheres with nanometer-sized cavities.[7]

Wooley et al. describe their shell-cross-linked polymeric micelles as knedels.[14] The cross-linked shell of these knedels is semi-permeable similar to the shells of the hollow micrometer-sized spheres Möhwald et al. have prepared. By using controlled anionic polymerization, Wooley and co-workers have prepared a variety of diblock copolymers. These diblock copolymers are then assembled into polymeric micelles by using the general concepts associated with the formation of polymer micelles that have been developed over a number of years by others. By design, Wooley et al. have chosen block copolymer systems where either the exterior or interior diblock contains polymerizable groups or cross-linkable groups. For example, when knedels with a poly(acrylic acid) and a polyisoprene core are prepared the shell can be chemically cross-linked by treatment with an activating agent and a diamine (Figure 4). Ongoing work has shown that suitable cores can be chemically removed to yield smaller hollow spheres than are available by the methods Möhwald et al. have developed.[7] In this latest work, Wooley's group used polymeric micelles derived from poly(isoprene-*b*-acrylic

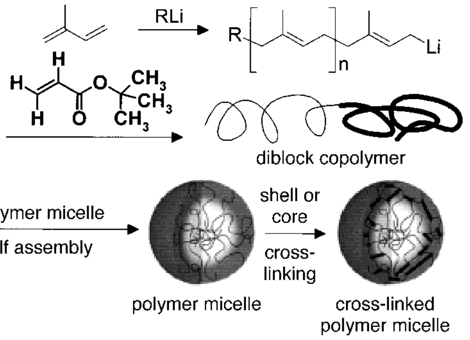

Figure 4. Shell cross-linked knedel nanospheres prepared from an amphiphilic diblock copolymer by 1) assembly of the amphiphilic diblock copolymer into multi-molecular micelles and 2) intramicellar cross-linking of the shell domain through reactions along the hydrophilic segment of the diblock copolymer.

acid) that were cross-linked with α,ω-diamino(polyethylene glycol).[15] Ozonolysis was then used to chemically degrade the polyisoprene core into small molecules that diffuse into solution and leave a hollow-sphere product. The hollow spheres were characterized by dynamic light scattering and were visualized by TEM and atomic force microscopy (AFM). Control experiments showed that noncross-linked polymeric micelles disintegrated on ozonolysis, which shows that a cross-linked shell was required. The diameter of the hollow-sphere products is controllable and dependent both on the degree of polymerization of the diblock copolymers originally used to form the micelle and on the nature of the cross-linking diamine used to prepare the Knedel.

Applications of these materials have been proposed but not yet realized. However, the authors have each described some general ideas. Drug delivery seems to be an especially likely application and may be especially interesting since shells can be designed or fabricated that will be biocompatible and permeable. However, other applications could also be envisioned. These materials are not likely to be permeable to macromolecular reagents or catalysts so reagents, substrates, and catalysts can be prepared that will be localized inside or outside of these hollow shells. It should thus be be possible to incorporate enzymatic catalysts or other catalysts into these hollow shells and to mix these shell-immobilized enzymes with other shells containing other catalysts or reagents. Since the immobilized reagents in such systems are precluded from diffusing into contact with one another such systems could capitalize on some of the early ideas espoused by others working with solid-phase organic synthesis where so-called "wolf and lamb" systems were designed in which mixtures of incompatible species were rendered compatible by diffusional restraints.[16]

Hollow shells could also be useful in other areas such as combinatorial synthesis, catalysis, sensor chemistry, and in materials chemistry. For example, if a library of precatalysts were enclosed in these hollow shells and if these catalysts were then used to produce a colored product that was constrained to remain in the nanoscopic reactor, hollow spheres could serve to differentiate good, efficient catalysts form their less efficient cousins. The small size of these materials and the potential chemical versatility of the shells makes them candidates as synthesis supports because of shell permeability and high surface area. The permeability of these shells and the potential to load shells with recognition elements that cannot readily diffuse out of the shell also make them potentially useful in sensor chemistry. The shells or particles themselves can also presumably be immobilized on various surfaces, which leads to new sorts of chemically responsive functional grafts. Regardless of what specific applications are developed, the synthetic versatility and simplicity inherent in the syntheses of sub-micrometer diameter semipermeable capsules by Möhwald et al. and Wooley et al. make intriguing new materials available for further use in basic and applied chemistry.

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