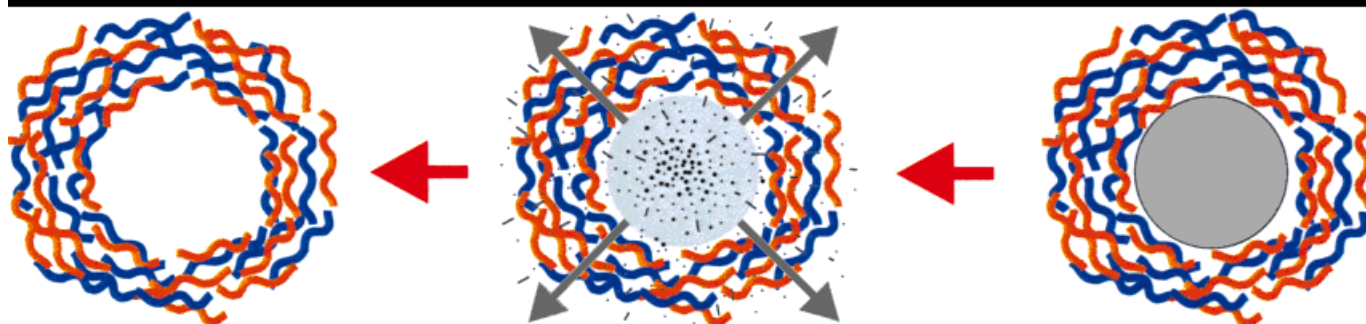


**P**olyelectrolyte shells with controlled thickness and composition are fabricated by stepwise adsorption of oppositely charged polyelectrolytes onto melamin resin templates which are subsequently solubilized.



**T**he confocal micrograph of a shell that is 8  $\mu\text{m}$  in diameter and made up of nine layers demonstrates both the integrity and deformability of the shell walls. See the following pages.



# Novel Hollow Polymer Shells by Colloid-Templated Assembly of Polyelectrolytes\*\*

Edwin Donath,\* Gleb B. Sukhorukov, Frank Caruso, Sean A. Davis, and Helmuth Möhwald

The fabrication of micro- and nano-sized capsules (or shells) which enable the encapsulation of various materials are of both scientific and technological interest.<sup>[1]</sup> Particles embedded in a solid shell (core-shell particles) have been extensively used as microcapsules for the controlled release and targeting of drugs as well as for the protection of sensitive agents such as enzymes and proteins.<sup>[1, 2]</sup> Such particles can be prepared by interfacial polymerization or by phase separation from a polymer-solvent mixture.<sup>[3]</sup> There are, however, a number of common problems associated with their fabrication including polydispersity, uneven shell coverage, and core solidification. Lipid liposomes are another well-known example of systems which have been used to encapsulate a variety of inorganic and organic materials.<sup>[4]</sup> Although liposomes are employed as delivery systems for various species in the pharmaceutical and cosmetic industries, their limited stability and low permeability for polar molecules presents serious limitations for general use.

A method for preparing multilayer ultrathin organic films by the consecutive deposition of oppositely charged polyelectrolytes from dilute aqueous solution onto charged solid substrates was recently introduced by Decher et al.<sup>[5]</sup> This technique utilizes the electrostatic attraction and complex formation between polyanions and polycations to form supramolecular multilayer assemblies of polyelectrolytes. The majority of studies have thus far focused on film formation on macroscopically flat substrates (e.g. silicon, glass, gold wafers). Techniques such as X-ray reflectivity, UV/Vis and IR spectroscopy, ellipsometry, neutron scattering, and

quartz crystal microbalance gravimetry have been employed to follow polyelectrolyte multilayer film growth as well as their structures and properties.<sup>[5, 6]</sup> As an extension of this technique, a variety of materials (e.g. biological macromolecules, surfactants, phospholipids, nanoparticles, inorganic crystals, and multivalent dyes) have been successfully incorporated into polyelectrolyte films by replacing one of the polyelectrolytes with another species of the same charge to fabricate composite polyelectrolyte multilayer films.<sup>[7]</sup>

Recently, we demonstrated that the step-wise adsorption of polyelectrolytes can also be performed onto charged colloidal polystyrene latex particles in solution to produce multilayer films.<sup>[8]</sup> Whilst the complex formation of polyelectrolytes in bulk solution has been intensively studied,<sup>[9]</sup> the template-based polyelectrolyte step-wise adsorption technique has not been applied to produce hollow polyelectrolyte shells of given size and topology. Such shells represent an interesting class of stable structures in the nano- to micrometer size range.

Here we describe a method for constructing hollow polyelectrolyte shells by colloid-templated consecutive polyelectrolyte adsorption followed by decomposition of the templating core (Figure 1). Micron-size polyelectrolyte shells

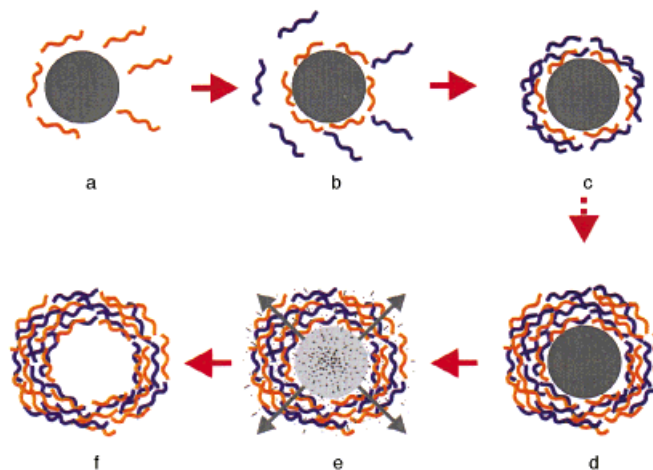


Figure 1. Schematic illustration of the polyelectrolyte deposition process and of subsequent core decomposition. The initial steps (a–d) involve step-wise film formation by repeated exposure of the colloids to polyelectrolytes of alternating charge. The excess polyelectrolyte is removed by cycles of centrifugation and washing before the next layer is deposited. After the desired number of polyelectrolyte layers are deposited, the coated particles are exposed to 100 mm HCl (e). The core immediately decomposes, as evidenced by the fact that the initially turbid solution becomes essentially transparent within a few seconds. Three additional washings with 100 mm HCl ensure removal of the dissolved MF oligomers. Finally, a suspension of free polyelectrolyte hollow shells is obtained (f).

of poly(sodium styrenesulfonate) (PSS) and poly(allylamine hydrochloride) (PAH), with thicknesses ranging from a few to tens of nanometers, have been produced. The stability, selectivity, and permeability of these polyelectrolyte shells make them rather distinct from hollow core-shell particles or liposomes currently available.

The first stage of shell fabrication involves step-wise deposition of polyelectrolytes from dilute aqueous solutions onto monodisperse weakly cross-linked melamine formaldehyde (MF) colloidal particles.<sup>[10]</sup> These particles decompose in

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aqueous media at pH values below 1.6. The polyelectrolyte multilayer film is formed by the alternate adsorption of oppositely charged polyions, beginning with adsorption of the negatively charged polyanion (PSS) onto the positively charged MF particles. After each adsorption step the non-adsorbed polyelectrolyte in solution is removed by repeated centrifugation and washing. In this way, the desired number of polyelectrolyte layers can be deposited, allowing control of the multilayer film thickness.<sup>[8]</sup>

As illustrated in Figure 1, subjecting the polyelectrolyte-coated MF particles to low pH results in decomposition of the core. Time-of-flight mass spectrometry experiments reveal that MF oligomers consisting mostly of 5–10 monomers of tetramethylol-melamine are produced.<sup>[11]</sup> The MF oligomers, which have a characteristic cross-sectional extension of about 1 nm,<sup>[12]</sup> are expelled from the core and permeate through the polyelectrolyte layers forming the shells. This observation is consistent with the finding that polyelectrolyte-coated MF particles are readily permeable to molecules of a few nanometers in size.<sup>[13]</sup> The MF oligomers are finally separated from the hollow shells by centrifugation.

The polyelectrolyte shells fabricated were characterized with scanning electron microscopy (SEM), transmission electron microscopy (TEM), and atomic force microscopy (AFM). A SEM image of nine-layer [(PSS/PAH)<sub>4</sub>/PSS] polyelectrolyte shells is shown in Figure 2. The numerous folds and creases observed are attributed to drying of the shells. The shells are also flattened and some spreading is noticed; the diameters (both short- and long-axis) of the shells

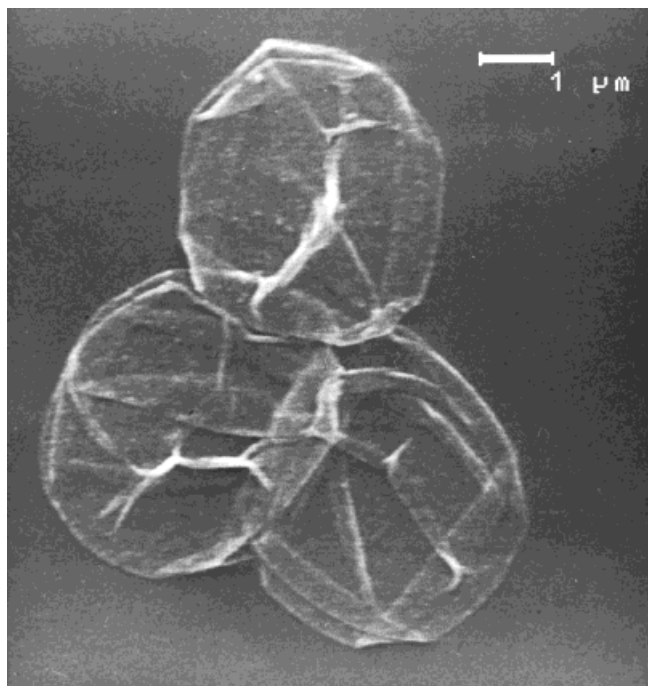


Figure 2. SEM image of nine-layer [(PSS/PAH)<sub>4</sub>/PSS] polyelectrolyte shells after solubilization of the MF core. The outer layer is PSS. The strong electrostatic attraction of the shells to the positively charged PEI-coated glass surface leads to some spreading of the polyelectrolyte shell. The drying process induces a number of folds and creases. Drying, together with the topological constraints of the closed surface, results in a completely folded upper hemisphere.

lie within the value  $4.0 \pm 0.5 \mu\text{m}$ , which is larger than that of the MF particle ( $3.3 \mu\text{m}$ ). This increase in diameter is ascribed to a combination of drying and the forces exerted on the shells upon their electrostatic immobilization onto the PEI-coated glass substrates [PEI = poly(ethyleneimine)]. The shells also exhibit a somewhat rough surface texture. This may be characteristic of the polyelectrolyte film, although some residual MF is present in the shells. Within the limit of resolution of the SEM technique, no holes or traces of rupture are identified in the shells.

The TEM images of hollow nine-layer [(PSS/PAH)<sub>4</sub>/PSS] polyelectrolyte shells are displayed in Figure 3. The homogeneous curvature of the shells proves that, provided the interior

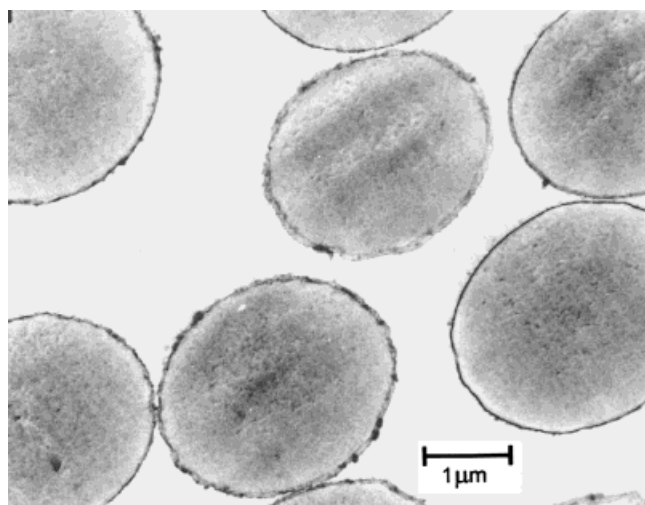


Figure 3. TEM image of nine-layer [(PSS/PAH)<sub>4</sub>/PSS] polyelectrolyte shells. The template MF particles used have a diameter of  $2 \mu\text{m}$ . The stained polyelectrolyte layer surrounding the less stained shell interior can be clearly identified. The polyelectrolyte layer thickness is of the order of 20 nm. Some surface roughness of the outer layer is observed. Apart from some longitudinal deformation, an artefact of thin sectioning the shell, the shells are close to spherical.

aqueous solution has not been removed, the fabricated shells preserve both the diameter and the spherical shape of the template particles. This is further evidence that the creases and folds seen in the SEM pictures are due to bending and tension forces exerted on the polyelectrolyte shell upon drying. Additional support for this comes from the real-time monitoring of decomposition of the MF core of a three-layer [PSS/PAH/PSS] or seven-layer [(PSS/PAH)<sub>3</sub>/PSS] polyelectrolyte-coated MF particle in solution with high-resolution video microscopy, which confirms that the shells retain their integrity upon dissolution of the core.<sup>[14]</sup> From the TEM image it can also be deduced that the thickness of the polyelectrolyte film is of the order of 20 nm for the nine-layer polyelectrolyte film. This value is consistent with the layer thickness obtained for polyelectrolyte-coated polystyrene latex particles from single-particle light-scattering data.<sup>[8]</sup> This suggests that the nature of the colloid in these cases, does not significantly affect the thickness of the polyelectrolyte layers. In agreement with the SEM data, the outer surface of the polyelectrolyte

film is also seen to be rough, and there is no evidence of a distinct layered structure to the film. In addition, the TEM image does not provide any evidence of existing holes larger than a few nanometers in the polyelectrolyte shells.

Atomic force microscopy in the tapping mode (TM) was employed to investigate the topography of the fabricated polyelectrolyte shells in more detail. All AFM images in Figure 4 indicate that the three-dimensional polyelectrolyte shells are continuous films which, in accordance with the SEM observations (Figure 2), exhibit creases and folds resulting from evaporation of the aqueous content. Figure 4A shows an AFM image of polyelectrolyte shells consisting of three

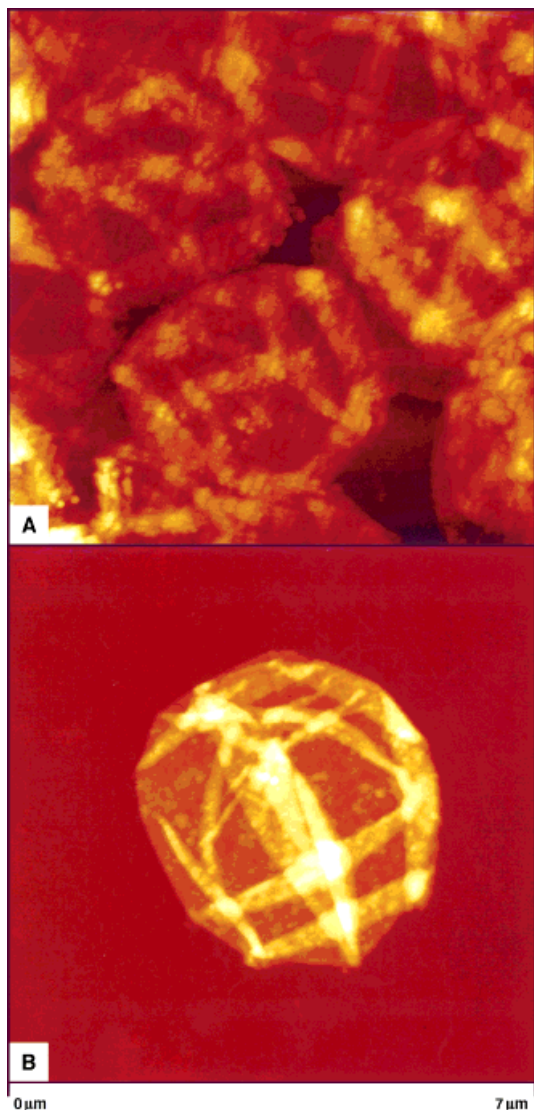


Figure 4. AFM images (tapping mode) of three-layer [PSS/PAH/PSS; A] and nine-layer [(PSS/PAH)<sub>4</sub>/PSS; B] polyelectrolyte shells prepared on MF particle templates of 3.3  $\mu\text{m}$  in diameter. The maximum height of the shell in image A is of the order of 50 nm, and 100 nm for the shell in image B.

layers [PSS/PAH/PSS]. This image is an example of the exceptionally strong electrostatic forces involved in the formation of these ultrathin polyelectrolyte layers. The diameter of the shell in Figure 4A is approximately 3  $\mu\text{m}$ . In this image it appears that some of the shells are overlaying

others beneath them. The average thickness of the shells (obtained from height measurements), is about 50 nm, suggesting that even when dried the shells are not completely flattened. Although some remaining MF material is seen in the shells, some lower regions (darker spots in the images) have a minimum height comparable to about two superimposed shell walls (ca. 10 nm). Figure 4B presents an AFM image of a shell consisting of nine polyelectrolyte layers [(PSS/PAH)<sub>4</sub>/PSS]. An increase in both the diameter (ca. 4  $\mu\text{m}$ ) and in the height (maximum value ca. 120 nm) of the shell, compared to that of the three-layer shell, is observed. Some residual MF is also clearly seen in the shell.

It has been shown that the use of soluble cores as templates for the step-wise deposition of polyelectrolytes is a successful pathway to fabricate novel three-dimensional hollow polymer shells. These films combine the advantages of thin organic films of polyelectrolytes with the easy handling and applications of colloids. The most important novel features of the fabricated polyelectrolyte shells are that 1) the composition and thickness of the shells can be controlled, 2) they can be fabricated with controlled physical and chemical properties, and 3) they offer novel structures for micro- and nano-compartmentalization of materials. In addition, unlike liposome structures,<sup>[4]</sup> the fabricated shells are readily permeable by small (ca. 1–2 nm in diameter) polar molecules<sup>[13]</sup> and are extremely stable against chemical and physical influences. It is envisaged that different species can be incorporated into the shell structure giving them unique tailored properties, and making them attractive for a wide range of applications. For example, the incorporation of catalytic materials inside or onto the inner surface of the shells, together with the easy diffusion of reaction products and substrates, is a promising way to both control and increase the efficiency of catalytic processes. The hollow polyelectrolyte shells may also have potential as micro- and nanocarriers for molecules and nanoparticles, as well as biological species for the controlled release and targeting of drugs. They can also serve as cages for chemical reactions in restricted volumes. The control of the chemical composition of the inner surface (or likewise the outer surface) can be used to produce nucleation centers for subsequent crystal growth in constrained environments, which is also a novel way to produce nanocomposites. Preliminary experiments have shown that monodisperse crystals can be successfully grown inside these novel capsules.

#### Experimental Section

PEI ( $M_w = 50\,000$ ), PSS ( $M_w = 70\,000$ ), and PAH ( $M_w = 8\,000 - 11\,000$ ) were obtained from Aldrich. PEI and PAH were used as received, whereas PSS was dialyzed against Milli-Q water (cut-off 14000) and lyophilized before use. The water used in all experiments was prepared in a three-stage Millipore Milli-Q Plus 185 purification system and had a resistivity higher than 18.2 M $\Omega\text{ cm}$ .

Typical adsorption conditions used to form the polyelectrolyte layers on the MF particles were 1 mgmL<sup>-1</sup> of polyelectrolyte in 0.5 M NaCl, and a particle concentration of 0.5% (v/v). The adsorption time was 20 min. The MF particles have a density of 1.5 gcm<sup>-3</sup>. Centrifugation speeds of 2000 min<sup>-1</sup> (Eppendorf rotor) were more than sufficient to settle the polyelectrolyte-coated particles. Three washings in Millipore water were



carried out prior to addition of the next polyelectrolyte to ensure removal of the nonadsorbed polyelectrolyte.

SEM measurements were conducted with a Zeiss DSM 40 instrument operated at an accelerated voltage of 15 kV. After the required number of polyelectrolyte layers were deposited, the MF core was removed by exposure to an aqueous solution of low pH. Samples were prepared by applying a drop of the shell solution to PEI-coated glass. After allowing the shells to settle the slides were extensively rinsed in Millipore water and then dried under a gentle stream of nitrogen.

The TEM specimens were fixed with glutaraldehyde,  $\text{OsO}_4$ , and  $\text{K}_2\text{Cr}_2\text{O}_7$ , and dehydrated in ethanol/acetone. The samples were embedded in Epon 812/Araldite M resin and polymerized in an oven for two days.<sup>[15]</sup> Thin sections (80–100 nm) were cut with a Reichert ultratome, and stained with uranyl acetate and lead citrate. Measurements were performed on a JEOL 100 B electron microscope.

The AFM images were obtained with a Digital Instruments Nanoscope IIIa in the tapping mode. Samples were prepared by applying a drop of the shell solution to PEI-coated glass. After allowing the shells to settle the slides were extensively rinsed in Millipore water and then dried under a gentle stream of nitrogen.

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## Cation-Induced Macroscopic Ordering of Non-Mesomorphic Modules—A New Application for Metallohelicates\*\*

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A major goal in the emerging field of supramolecular chemistry is to relate local molecular architecture to the macroscopic ordering of the system. Such large-scale organization is probably essential for the construction of practical devices from molecular units.<sup>[1–3]</sup> Despite this realization, little genuine progress has been made with regard to the integration of local order into large-scale multidimensional arrays.<sup>[4]</sup> In marked contrast, tremendous advances have been made in the construction of exotic supermolecules by stepwise accretion of simple building blocks.<sup>[5, 6]</sup>

We now present a strategy that exploits a metallohelicate, assembled from non-mesomorphic but lipid-like organic strands, to promote formation of a liquid crystalline state at ambient temperature. The key element of this approach lies with the helix that provides rigidity and polarizability to counterbalance the flexibility and nonpolarizability of the paraffinic chains (amphiphilic character). This subtle balance between organized and chaotic domains controls the fate of the mesomorphic material. This system, the first liquid crystalline metallohelicate, illustrates the tremendous organ-

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