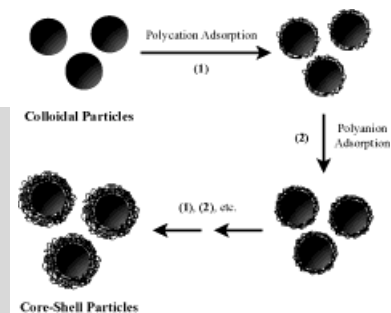


# Nanoengineering of Particle Surfaces\*\*

By Frank Caruso\*

*The creation of core-shell particles is attracting a great deal of interest because of the diverse applicability of these colloidal particles; e.g., as building blocks for photonic crystals, in multi-enzyme biocatalysis, and in drug delivery. This review presents the state-of-the-art in strategies for engineering particle surfaces, such as the layer-by-layer deposition process (see Figure), which allows fine control over shell thickness and composition.*



## 1. Introduction

In recent years, considerable effort has been devoted to the design and controlled fabrication of nanostructured materials with functional properties. The interest in nanoscale materials stems from the fact that their properties (optical, electrical, mechanical, chemical, etc.) are a function of their size, composition, and structural order. Therefore, effective strategies to build tailored nanomaterials reliably and predictably are required in order to meet the ever-increasing demands (e.g., structural and compositional complexity) placed on materials synthesis and performance by nanotechnology. Colloidal particles represent attractive building blocks from which to create ordered and complex materials. They are also of widespread interest in chemical engineering, pharmaceutical and biological applications. Over the last decade there have been immense efforts to fabricate core-shell colloidal materials with tailored structural, optical, and surface properties.<sup>[1–6]</sup> Investigations have largely been spurred by the applicability of such colloids in modern materials science, and by their technological importance: Composite colloids are utilized in the areas of coatings, electronics, catalysis, separations, and diagnostics.<sup>[1–6]</sup> The creation of core-shell colloidal particles is also of interest from a fundamental and academic viewpoint, especially in the areas of colloid and interface science. They can be utilized as model systems to investigate factors governing colloidal interactions and stabilization<sup>[7–9]</sup> and to gain valuable information on the properties of concentrated dispersions.<sup>[10]</sup>

The term used to describe the synthesis of core-shell particles with defined morphologies and properties can be referred

to as particle engineering.<sup>[2]</sup> This typically involves tailoring the surface properties of particles, often accomplished by coating or encapsulating them within a shell of a preferred material. Particle coating is carried out for a myriad of reasons.<sup>[1–6]</sup> For example, the shell can alter the charge, functionality, and reactivity of the surface, and can enhance the stability and dispersibility of the colloidal core. Magnetic, optical, or catalytic functions may be readily imparted to the dispersed colloidal matter depending on the properties of the coating. Encasing colloids in a shell of different composition may also protect the core from extraneous chemical and physical changes.<sup>[11–13]</sup>

Core-shell particles often exhibit improved physical and chemical properties over their single-component counterparts, and hence are potentially useful in a broader range of applications. Therefore, methods to “engineer” such materials with controlled precision have long been sought.<sup>[1–3]</sup> Although a variety of procedures have been employed for their manufacture, difficulties associated with their production have limited the application of the final colloidal materials.<sup>[2,14]</sup> Furthermore, despite the fact that the advantages of uniformly coated and stable colloidal particles have been recognized for years,<sup>[1–3,15]</sup> the controlled coating of colloids with organized layers has for many years remained a technical challenge. A major requirement pertaining to the procedures used to coat particles is that they do not cause aggregation, thus rendering the particles unusable for many purposes. Optimization of the surface characteristics of particles through coating processes is also of primary importance for the successful application of composite particles. Recent methods offer new alternatives for the controlled synthesis of novel, stable and functional core-shell type materials.

This article provides an overview of the various methods used to synthesize core-shell particles in the nanometer to the micrometer size range, detailing early and very recent developments in the area. Current and future possible applications of these materials are also discussed. Facile and flexible synthetic routes are the key to the production of uniform nanocomposite colloids; therefore, emphasis is placed on widely

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used strategies and their utilization in the construction of nanostructured colloidal entities. Primary emphasis is given only to the most common forms of synthesized particles; namely, composite colloidal systems that comprise solid cores (i.e., latex, inorganic, or metal) coated with polymers, inorganics, or biomacromolecules. The special case of liquid colloidal cores (e.g., emulsions) is not covered here. Details on the methods used to produce liquid cores surrounded by organic or inorganic materials can be found elsewhere.<sup>[16–21]</sup> It should also be noted that colloid modification with alkanethiol monolayers will not be described here; readers interested in obtaining further information are referred to a recent review.<sup>[22]</sup> The purpose of this review is not to provide an exhaustive summary of the literature but rather to present a cohesive discussion of the main strategies and most significant developments in the area of particle engineering. Since the current article encompasses the surface modification of solid polymer, metal, and inorganic colloidal particles, it is worthy to note literature relevant to the production of the core particles. The synthesis of latex particles and the various types that can be produced have been extensively documented.<sup>[23]</sup> A detailed review on the preparation of monodisperse (metal) particles has been given.<sup>[12]</sup> Methods for the synthesis of various inorganic cores can be found in the relevant publications associated with their coatings (as referenced). Finally, although there is much interest in the arrangement of nanostructured colloidal entities into complex functional structures, here only the design and surface modification is discussed and illustrated.

## 2. Polymer Coatings

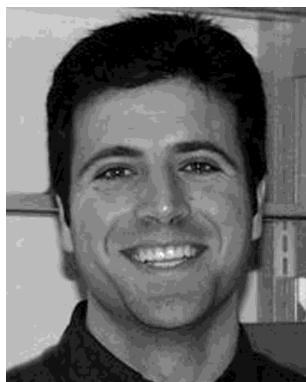
Polymer-coated particles offer interesting prospects in a broad spectrum of applications, ranging from catalysis to additives and pigments, where they are exploited in the manufacture of cosmetics, inks, and paints.<sup>[5]</sup> The synthetic routes that have been developed in order to produce polymer-coated particles fall into two main classes: polymerization at the particle surface or adsorption onto the particles. Hofman-Caris has comprehensively reviewed the processes used to obtain particles that consist of an inorganic core and a polymer shell through polymerization and chemical coupling procedures

prior to 1994.<sup>[5]</sup> The following will deal with more recent strategies used to coat particles with polymers, stressing polymerization approaches and the self-assembly of polymers from solution.

### 2.1. Surface Modification via Polymerization Processes

A number of polymerization-based methods have been employed to produce particles that consist of solid cores coated with a shell of polymeric materials.<sup>[5]</sup> These include monomer adsorption onto particles followed by subsequent polymerization,<sup>[24–30]</sup> heterocoagulation–polymerization,<sup>[31]</sup> and emulsion polymerization.<sup>[5,32–34]</sup> In the first approach— one of the most frequently employed to achieve polymer coatings on solid particles—the polymerization reaction can be either catalyzed by an initiator to promote the process or by the colloidal particles themselves. Matijevic et al. reported the coating of aluminum hydrous oxide-modified silica particles with poly(divinylbenzene) (PDVB) layers by pre-treatment of the inorganic cores with coupling agents such as 4-vinylpyridine or 1-vinyl-2-pyrrolidone, followed by subsequent admixing of divinylbenzene and a radical initiator.<sup>[24]</sup> Polymer layers of poly(vinylbenzyl chloride) (PVBC), copolymers of PDVB–PVBC, and double shells of PDVB and PVBC were also synthesized around inorganic particles using a similar approach.<sup>[25]</sup> The surface characteristics of the silica cores were substantially altered, as evidenced by electrophoresis measurements. Polymer coating of the particles allowed cores incorporating dyes (pigments) to be retained as the polymer shell is permeable to small inorganic ions but not to the dye molecules.<sup>[24]</sup>

The use of electrochemical or soluble initiators can be eliminated by utilizing catalytically active cores to effect polymerization of monomers adsorbed on the surface of particles. This approach was employed to obtain poly(pyrrole) coatings on a range of inorganic cores by using the active sites on the metal oxide surfaces to initiate the polymerization of pyrrole.<sup>[26,27]</sup> Hematite ( $\alpha$ -Fe<sub>2</sub>O<sub>3</sub>), silica-modified hematite, and cerium(IV) oxide (CeO<sub>2</sub>) were coated with poly(pyrrole) by exposing the inorganic cores to the polymerization medium of pyrrole in an ethanol/water mixture and heating to 100 °C.



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The poly(pyrrole)-coated  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> and CeO<sub>2</sub> particles were found to be electrically conductive.<sup>[26]</sup> In a subsequent study, it was shown that CeO<sub>2</sub> and copper(II) oxide (CuO) react with the adsorbed pyrrole molecules through a reductive-dissolution process that involves oxidation of the monomers and release of the metal ions, whilst  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> and silica (SiO<sub>2</sub>) were found to be inactive in the polymerization.<sup>[27]</sup> Uniform poly(pyrrole) coatings surrounding the core can be obtained using this approach, as displayed in Figure 1 for poly(pyrrole)-coated SiO<sub>2</sub> particles.<sup>[27]</sup> It was further shown that the

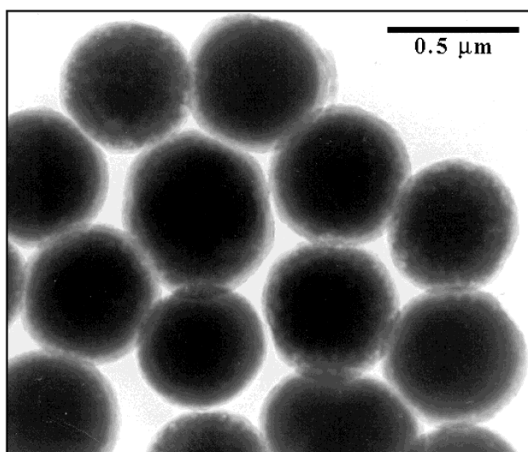
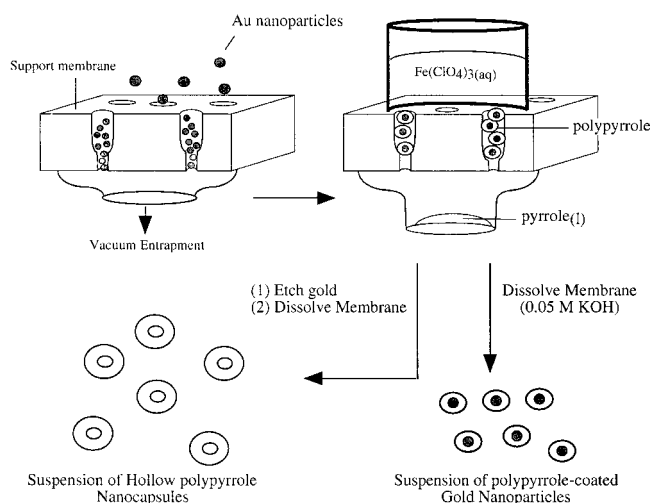


Fig. 1. TEM of SiO<sub>2</sub> particles coated with poly(pyrrole). The polymer coatings, seen as a shell around the SiO<sub>2</sub> cores, were prepared by exposing the inorganic particles to pyrrole in an ethanol/water mixture and heating at 100 °C for 67 h in air. (Reproduced from [27]. Copyright 1995 Materials Research Society.)

thickness of the polymer coating can be controlled by varying the contact time of the cores with the polymerization solution and that the polymer layer thickness is dependent on the type of core used and the presence of additional polymer (e.g., polyvinyl alcohol).<sup>[27]</sup> In some cases, however, it may be difficult to finely tune the polymer layer thickness. The fact that the core affects the thickness and composition of the shell (this is determined by the specific oxidative process by the core materials) may also limit the formation of polymer layers of a well-defined thickness on colloidal cores of choice. Nevertheless, this method represents an attractive means to deposit polymer layers on particles, allowing a broad range of core-shell type materials with different properties to be prepared.

An elegant strategy recently introduced by Feldheim and co-workers for the formation of polymer-coated colloids involves trapping and aligning the particles in the pores of membranes by vacuum filtration, followed by polymerization of a conducting polymer inside the pores (Scheme 1).<sup>[28–30]</sup> This approach begins with gold nanoparticles being filtered into a porous Al<sub>2</sub>O<sub>3</sub> support membrane with a pore size of 200 nm. Initiator (Fe(ClO<sub>4</sub>)<sub>3</sub>) was then poured into the top of the membrane and several drops of the monomer (pyrrole or *N*-methylpyrrole) were placed underneath the membrane. Upon diffusion of the monomer vapor into the membrane it contacted the initiator to form polymer, with deposition preferentially occurring on the surface of the gold particles. This



Scheme 1. Schematic diagram of the membrane-based method for synthesizing gold-core/polymer-shell nanoparticles. The particles are first trapped and aligned in the membrane pores by vacuum filtration and subsequently coated with poly(pyrrole), which occurs via polymerization of the monomer vapor when it diffuses into the membrane and interacts with the initiator (Fe(ClO<sub>4</sub>)<sub>3</sub>). The membrane is then dissolved, leaving behind nanoparticle composites. The gold can also be etched first and the membrane then dissolved, resulting in hollow poly(pyrrole) nanocapsules. (Reproduced from [30]. Copyright 1999 American Chemical Society.)

resulted in the formation of hybrid polymer-encapsulated gold nanoparticles that were conveniently isolated by dissolution of the membrane material in basic solution. It was shown that poly(pyrrole) and composite poly(*N*-methylpyrrole)/poly(pyrrole) multilayers of a predetermined thickness can be formed on gold nanoparticles of 30 nm diameter (Fig. 2). Controlling the thickness and the composition of the polymer coatings are attractive features of this strategy. The thickness is dependent on the polymerization time and can be varied from 5 to 100 nm. Long polymerization times resulted in the formation of aggregated particles, or pseudo-one-dimensional strings of nanoparticles.<sup>[28,29]</sup> Multilayer composites were also produced by simply replacing the first monomer with a second and allowing polymerization to proceed. Using this technique, fine control over the shell thickness and coating may be difficult depending on the particle packing in the membrane. In addition, the particle type appears to be limited to those that fit in the membrane supports used. However, this method shows promise for the coating of various template particles with a range of polymers and is to be extended to biomacromolecules.<sup>[30]</sup>

A different approach to the formation of core-shell particles that comprise a solid core encased in a polymer layer is that of heterocoagulation of small particles with larger ones followed by heating.<sup>[31]</sup> For example, cationic particles of poly(butyl methacrylate) (PBMA) (167 nm in diameter) were heterocoagulated onto negatively charged polystyrene microspheres (600 nm in diameter). The PBMA particles had a non-ionic polymer layer grafted onto their surface and this stabilized the resulting cluster. Subsequent heating of the sample to approximately 45 °C above the glass-transition temperature of PBMA caused it to spread while the nonionic

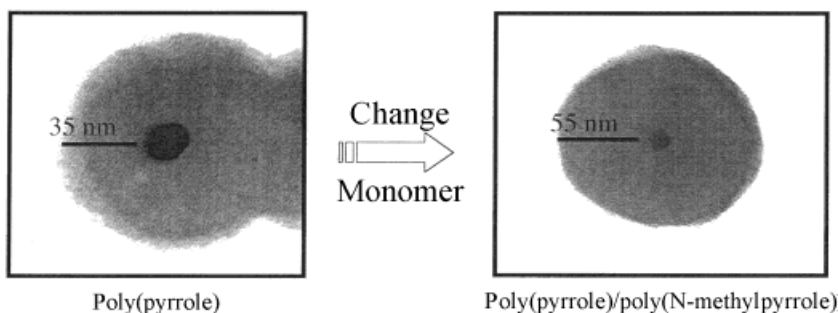


Fig. 2. TEMs of core-shell gold-polymer nanoparticles prepared by the membrane-based strategy (Scheme 1). Gold-poly(pyrrole) nanoparticle composites, and poly(pyrrole)/poly(*N*-methylpyrrole)-coated gold nanoparticles, prepared by sequentially depositing poly(pyrrole) and poly(*N*-methylpyrrole). An increase in polymer shell thickness is apparent with the subsequent deposition of poly(*N*-methylpyrrole). In both micrographs the gold nanoparticle is seen in the center as a dark core. (Reproduced from [30]. Copyright 1999 American Chemical Society.)

polymer migrated to the outer surface and acted as a steric stabilizing layer. The resulting particles comprised a polystyrene core coated with a relatively uniform shell of PBMA (Fig. 3). While this is an interesting method, difficulties exist in obtaining the desired coating of smaller particles that will in turn form a continuous film on the larger colloids. Colloidal stability may also be compromised when irregular coatings are obtained.

An alternative and widely used strategy for the creation of core-shell particles is that of emulsion polymerization.<sup>[5]</sup> This approach has been used to encapsulate submicrometer- and micrometer-sized organic and inorganic particles with polymer layers.<sup>[32,33]</sup> A major limitation of this method has been that it often leads to aggregated particles embedded in a polymer matrix. However, a recent study by Quaroni and Chumanov has demonstrated the encapsulation of individual silver nanoparticles by a polymer shell comprising polystyrene and methacrylate via emulsion polymerization.<sup>[34]</sup> Polymerization of styrene and/or methacrylic acid in emulsions of oleic acid

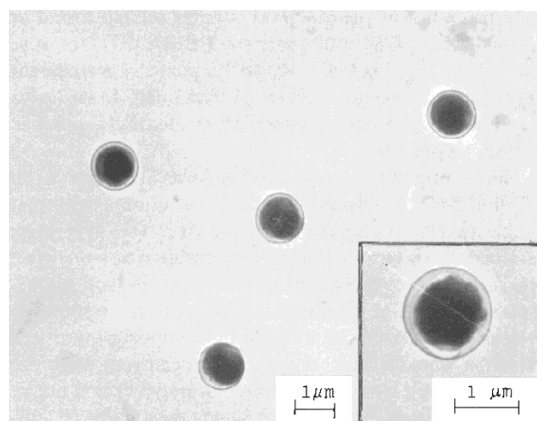


Fig. 3. TEMs of polystyrene core particles coated with a shell of PBMA. The particles were produced by heterocoagulation of larger polystyrene particles and PBMA nanoparticles, followed by heating to about 45 °C above the PBMA glass-transition temperature, which caused it to spread on the polystyrene particle surface. The dark inner region is polystyrene and the light outer region is PBMA. (Reproduced from [31]. Copyright 1997 Springer-Verlag.)

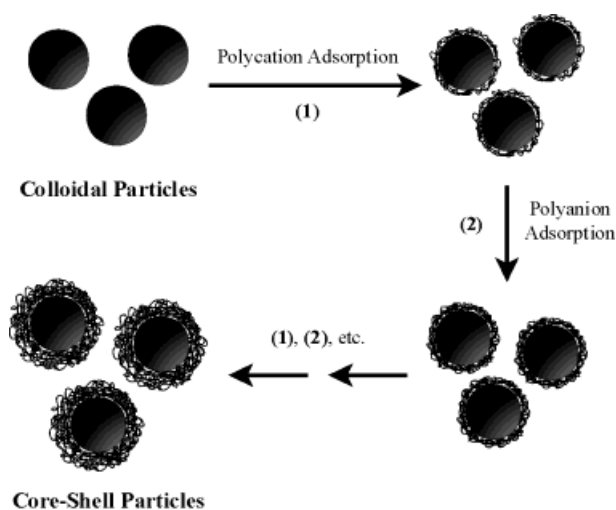
afforded a uniform polymer layer around the metal core, the thickness of which could be easily controlled in the range 2–10 nm by altering the concentration of monomers. This coating process appears to be best applicable to the formation of thin coatings as they follow the shape of the metal core, while thicker ones (>10 nm) take on a globular geometry and form irregular coatings. It was also found that, unlike the uncoated particles, the polymer-encapsulated cores could be routinely centrifuged and redispersed, they exhibited a strong resistance toward etching, and could be functionalized via protein attachment. This investigation is a prime example of the marked influence

that a thin coating can have on the properties of a colloidal particle, thus making the previously single-component particles useful for other studies and even applications.

## 2.2. Self-Assembled Polymer Layers

The evolution of self-assembly techniques for film construction has led to a wealth of research on the construction and applications of nanostructured thin film materials.<sup>[35,36]</sup> In contrast, considerably less attention has been paid to the controlled modification of colloidal particle surfaces via classical self-assembly strategies. This is particularly the case for the assembly of organized layered materials as a thin shell on the colloids, despite the fact that for centuries colloidal particles have been coated and stabilized by the direct adsorption of polymers from solution onto their surface.<sup>[37]</sup> Generally, the polymers used are charged (i.e., polyelectrolytes) and their stabilizing influence arises from both electrostatic and steric (polymeric) effects. Conversely, under certain conditions such polymers can also induce flocculation of colloidal materials and this has been widely exploited in many industrial processes.<sup>[38]</sup> Such colloidal destabilization has in the past hampered efforts to uniformly coat particles with polymer layers, particularly with respect to the formation of composite polymer coatings on colloids.

However, recent advances in particle coating strategies have made it possible to coat colloids with uniform single- and multilayers of polyelectrolytes. Latex particles have been coated with a variety of polyelectrolytes by electrostatic self-assembly.<sup>[39–43]</sup> In this approach (Scheme 2), termed the layer-by-layer (LbL) colloid templating strategy,<sup>[43]</sup> a polymer solution in excess concentration of that required for saturation adsorption was added to a colloidal dispersion. The polymer selected had an opposite charge to that on the latex particles, hence predominantly adsorbing through electrostatic interactions. The coated particles were subsequently centrifuged and washed. Evidence that the polymer adsorbed was



Scheme 2. Schematic illustration of the LbL process for forming polyelectrolyte multilayers on particles. The scheme is shown for negatively charged particles. The process entails the sequential deposition of oppositely charged polyelectrolytes onto colloidal particles, exploiting primarily electrostatic interactions for polymer multilayer build-up. Following deposition of each polymer layer, excess polyelectrolyte is removed by centrifugation or filtration, with intermediate water washings. The key to the formation of the polyelectrolyte multilayers is that not all of the cationic (or anionic) groups of the deposited polyelectrolyte interact with the particle surface (or the underlying polymer layer beneath). Hence, non-utilized charged groups, which cause charge overcompensation, facilitate the electrostatic binding of the subsequently adsorbed layer. Finally, a polyelectrolyte multilayer film of tailored thickness is obtained on the colloidal template via this strategy.

obtained by electrophoresis, which showed a reversal in surface charge for the polymer-coated particles.

A novel and intriguing result arose from the subsequent addition of a second solution of oppositely charged polyelectrolyte to the polymer-coated particles; adsorption of a second layer on the particle surface occurred through electrostatic self-assembly in the same way that multilayered polymer films have been assembled on planar substrates.<sup>[44,45]</sup> Again, a reversal in surface charge was observed. Repetition of this process resulted in the formation of multiple bilayers on the particle surface in a controlled fashion. This was verified by single particle light scattering (SPLS) experiments.<sup>[46,47]</sup> The average thickness of adsorbed polyelectrolyte layers on polystyrene cores of 640 nm diameter was approximately 1.5 nm per layer (see Table 1).<sup>[41]</sup> These data demonstrate the remarkable nanoscale control that can be exerted over the shell thickness; the calculated average layer thickness increases with the number of polyelectrolyte layers deposited. Both SPLS and transmission electron microscopy (TEM) provided evidence that no significant aggregation of the coated polystyrene particles occurred. Figure 4 shows a TEM image of 640 nm diameter polystyrene particles coated with 21 layers of poly(allylamine hydrochloride) and poly(styrenesulfonate). The average diameter of the coated particles is approximately 710 nm.

The main advantages of the LbL technique are apparent: First, the thickness of the polymer coatings can be fine tuned by altering the number of layers deposited and the solution conditions from which the polymers are adsorbed.<sup>[45]</sup> Second,

Table 1. Thickness of polyelectrolyte multilayer films assembled onto polystyrene latexes [a].

Number of layers	Film thickness [nm] [b]	
	PAH/PSS	PDADMAC/PSS
1	1.2	1.4
3	3.4	3.3
5	5.6	6.6
7	8.4	8.5
9	11.5	11.7
11	15.0	–
15	24.8	–
21	33.9	–

[a] PAH = poly(allylamine hydrochloride), PSS = poly(styrenesulfonate), PDADMAC = poly(diallyldimethylammonium chloride). [b] Values were derived from SPLS data by using the Rayleigh–Debye–Gans theory and a refractive index of 1.47 for the polymer layers. (Reproduced from [41]. Copyright 1999 American Chemical Society.)

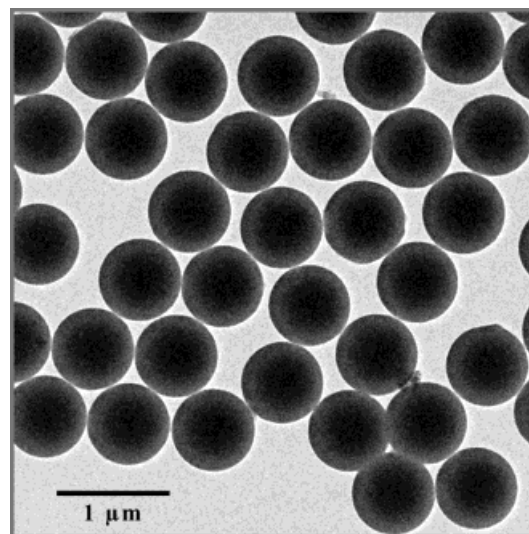


Fig. 4. TEM of polystyrene core particles (negatively charged) coated with 21 alternating layers of poly(allylamine hydrochloride) (PAH) and poly(styrenesulfonate) (PSS). The particles were prepared by the consecutive adsorption of PAH and PSS, as depicted in Scheme 2. The coating cannot be clearly seen as the contrast of the polymer is similar to that of the polystyrene core in the electron beam. However, a noticeable increase in particle diameter occurred; the average diameter of the coated particles is approximately 710 nm, compared with 640 nm for the polystyrene core particles. The total thickness of the 21 PAH/PSS shell is about 34 nm (Table 1), corresponding to an average layer thickness of about 1.5 nm for each polymer layer, as determined by single particle light scattering [41].

multicomposite polymer films can be assembled through choice of a large variety of polymers.<sup>[39–43]</sup> Third, colloids of different sizes, shapes and composition can be employed as templates since polyelectrolytes self-assemble onto numerous surfaces.<sup>[43]</sup> For example, latex particles of 70 nm diameter (Fig. 5a)<sup>[42]</sup> as well as biocolloids larger than 10 μm (Fig. 5b)<sup>[48]</sup> have been successfully coated using this approach. Perhaps the biggest limitation of the LbL strategy is the time-consuming sequential polyelectrolyte deposition cycles and purification steps. Filtration-based purification methods have shown to simplify and speed up the process, thus making it suitable for large-scale up.<sup>[49]</sup> Overall, the self-assembly of

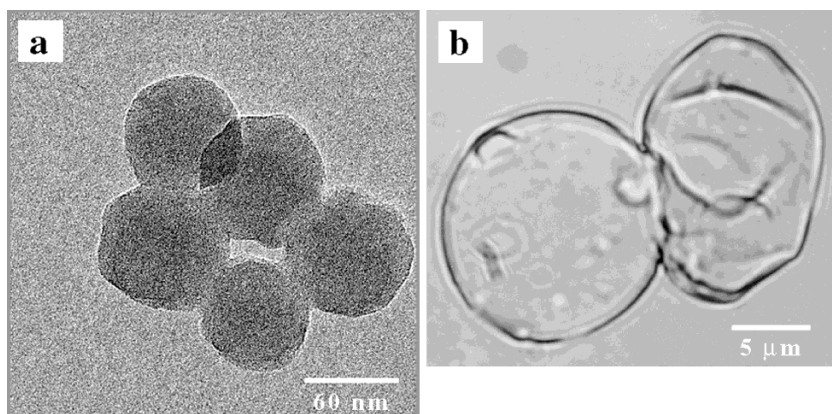


Fig. 5. Micrographs of colloidal particles coated using the LbL strategy, showing the range of particle sizes and different colloidal materials that can be used. a) TEM of 70 nm diameter cationic polystyrene particles coated with 15 layers of PSS and an Fe<sup>II</sup>-metallosupramolecular polyelectrolyte. The uneven surface seen is evidence for successful coating of the particles (uncoated particles exhibit smooth surfaces). (Reproduced from [42]. Copyright 1999 American Chemical Society.) b) Optical micrograph of solubilized enzyme (catalase) in polymer multilayer capsules. The polymer multilayers (comprising eight layers of PSS and PAH) were deposited on catalase crystal colloidal templates and the enzyme was subsequently dissolved by changing the solution pH. The enzyme was retained within the semi-permeable polymer multilayer capsules. (Reproduced from [48]. Copyright 2000 American Chemical Society.)

polyelectrolytes onto particles via the LbL technique allows the production of composite colloidal materials with tailored compositions and well-defined morphologies.

### 3. Inorganic and Composite Coatings

Various procedures have been employed in the fabrication of inorganic and hybrid coatings on particles, allowing a broad range of materials with different properties to be prepared. The specific methods of solid-core inorganic/hybrid-shell particle preparation can be classified into two general categories:

- i) precipitation and surface reactions and
- ii) the controlled deposition of preformed inorganic colloids.

#### 3.1. Precipitation and Surface Reactions

Previous investigations have demonstrated that polymeric and inorganic particles dispersed in aqueous solutions can be coated with layers of various inorganic materials either by precipitation of the coating materials onto the cores or by direct surface reactions utilizing specific functional groups on the cores to induce coating.<sup>[4,11,50–76]</sup> The inorganic coatings prepared using these approaches include silica,<sup>[4,11,50–64,67–72,74]</sup> yttrium basic carbonate,<sup>[54]</sup> titania,<sup>[65,66,73]</sup>

titanium nitride,<sup>[75]</sup> and zirconia.<sup>[76]</sup> Early work focused on the coating of titania microparticles with silica layers; however, significant particle clumping and coalescence took place during silica deposition.<sup>[50]</sup> Using the precipitation method, in which the coating material is precipitated directly onto the core, Ohmori and Matijevic optimized coating conditions and coated spindle-shaped hematite ( $\alpha$ -Fe<sub>2</sub>O<sub>3</sub>) particles with silica layers by hydrolysis of the alkoxide tetraethoxysilane (TEOS) in 2-propanol.<sup>[11,53]</sup> (This method is known as the Stöber process, which is based on the hydroxide-catalyzed hydrolysis of an alkoxy-silane and condensation of the resulting silanol groups<sup>[77]</sup>). Uniform silica coatings on individual  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> particles were obtained when the kinetics of the TEOS hydrolysis was properly controlled (Fig. 6a). Dispersions of uniform submicrometer spherical particles consisting of silica cores and yttria coatings, as well as yttria cores with silica coatings

(Fig. 6b), were also prepared by a similar method.<sup>[54]</sup> The SiO<sub>2</sub>-coated particles behaved like pure silica, and the coating protected the yttrium core material against dissolution. As illustrated in Figure 6, the size of the particles and the thickness of the shells could be varied. The TEM in Figure 6a shows 0.5  $\mu$ m  $\alpha$ -Fe<sub>2</sub>O<sub>3</sub> particles coated with an approximately 50 nm thick shell,<sup>[53]</sup> while Figure 6b shows yttrium basic carbonate cores (86 nm) covered with a 10 to 20 nm thick silica coating.<sup>[54]</sup> More recently, submicrometer-sized silica spheres have also been coated with titania (submonolayer to 7 nm thick) by hydrolysis of titanium alkoxide precursors.<sup>[65]</sup> It was found that the ratio of the titanium alkoxide to water and the dilution of the reactant mixture in ethanol controlled the nature of the coating. By

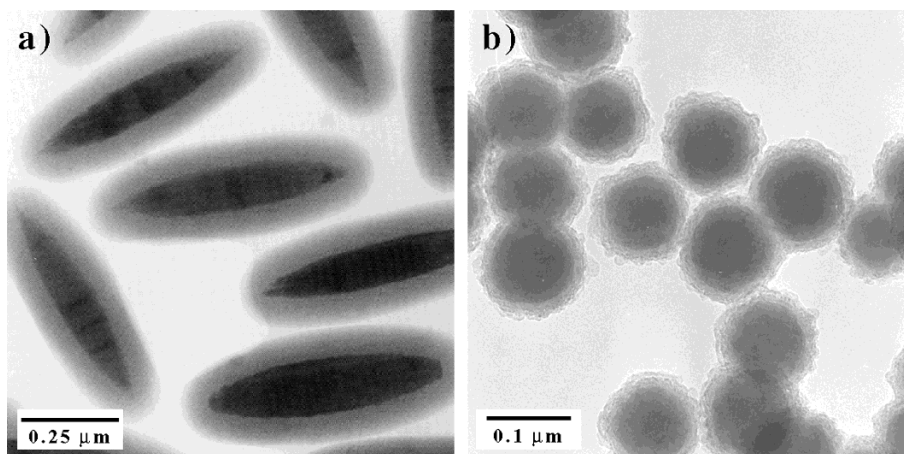
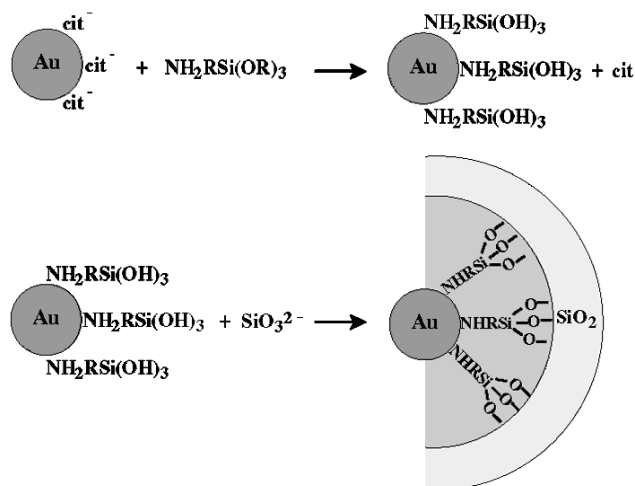


Fig. 6. TEMs of uniformly coated inorganic particles. a) TEM image of hematite ( $\alpha$ -Fe<sub>2</sub>O<sub>3</sub>) particles coated with silica, prepared by hydrolysis of TEOS in 2-propanol and aging at 40 °C for 15 h. (Reproduced from [11]. Copyright 1993 Academic Press.) b) TEM image of yttrium basic carbonate particles (diameter ca. 80 nm) coated with silica, prepared by dispersing the inorganic cores in an ethanol/water/ammonia solution, slowly adding TEOS, and aging at 80 °C. Thin silica shells (10–20 nm) were obtained. (Smoother and thinner silica coatings (5–10 nm) were obtained when the coating reaction was carried out at room temperature [54].) (Reproduced from [54]. Copyright 1994 Materials Research Society.)

repeating this process several times, the thickness of titania layers on silica microspheres could be increased to 46 nm.<sup>[66]</sup> In a novel two-step silica-coating process comprising a sol-gel step followed by a dense liquid coating exposure, maghemite surfaces were coated with silica, affording a magnetic nanocomposite.<sup>[67]</sup>

In the aforementioned inorganic coating methods, the size and quantity of the core particles as well as the relative ratios of the reactants (e.g., alkoxide, organic solvent, and water) considerably influence the quality and thickness of the coating. Hence, systematic experiments are usually required in order to establish optimum conditions for particle coating. For example, when very thick coatings are required, the inorganic materials are also precipitated in solution in the form of nanoparticles, which then heterocoagulate with the core, resulting in irregular coatings and/or particle aggregation. Compatibility between the particle surface and the precursor inorganic solutions is also required to achieve regular coatings without aggregation of the particles. Furthermore, these procedures have generally been applied to coat particles >100 nm in diameter that have a significant chemical or electrostatic affinity for the inorganic material. It has been indicated that they are not directly applicable to coating vitreophobic materials such as gold or silver nanoparticles.<sup>[4,69]</sup> An early study<sup>[68]</sup> aimed at overcoming the vitreophobic character of gold involved the heterocoagulation of gold nanoparticles onto silica colloids dispersed in water, followed by growth of the composite particles in ethanol by the Stöber method. This resulted in the incorporation of the gold particles inside only about 3% of the silica spheres, i.e., a mixture of labeled and unlabeled silica particles were obtained.<sup>[68]</sup> For gold or silver dispersions, surface chemical derivatization is often undertaken prior to the formation of inorganic layers. In a series of studies,<sup>[4,56–58]</sup> Liz-Marzan, Mulvaney, and co-workers modified the surface of citrate-stabilized gold nanoparticles with the silane coupling agent (3-aminopropyl)trimethoxysilane, thereby rendering the gold surface vitreophilic via its complexation with the amine groups of the silane (Scheme 3). A sodium silicate solution (pH 10–11) was then added to the surface-modified gold sol with continuous stirring. Upon standing, the active silica polymerized onto the gold particle surface, yield-

ing a silica shell of thickness 2–4 nm after 24 h.<sup>[4]</sup> In this method, care was required with both the pH and silicate concentration. A pH of 8–10 was suitable for coating: it reduced the solubility of the silicate species in solution and optimized the precipitation rate to homogeneously coat the particles, whilst avoiding the formation of new silica nuclei. A large excess of silica resulted in a thicker layer in a shorter time. Using the Stöber method, thick silica layers from TEOS were then grown on the thin silica-coated gold colloids in ethanol/water mixtures.<sup>[4]</sup> Figure 7 displays silica-coated gold nanoparticles with different shell thicknesses produced via this procedure.<sup>[4]</sup> The silica shell thickness was varied from about 10 to 80 nm. An important aspect of the growth process is that the TEOS concentration must be kept low to prevent the formation of new silica nuclei, which would then preferentially grow instead of coating the gold particles. Eliminating the first silica coating in water (Scheme 3) caused problems with aggregation of the nanoparticles before TEOS hydrolysis could be effected. The coating process was also extended to silver<sup>[58,69,70]</sup> and cadmium sulfide<sup>[61]</sup> particles. A similar approach has been



Scheme 3. Schematic diagram of the surface reactions occurring in the process of forming a thin silica shell on citrate-stabilized gold particles. The first step involves reaction with (3-aminopropyl)trimethoxysilane, thereby making the gold surface vitreophilic. Secondly, sodium silicate solution (pH 10–11) is added and the silica polymerizes onto the gold particle surface.

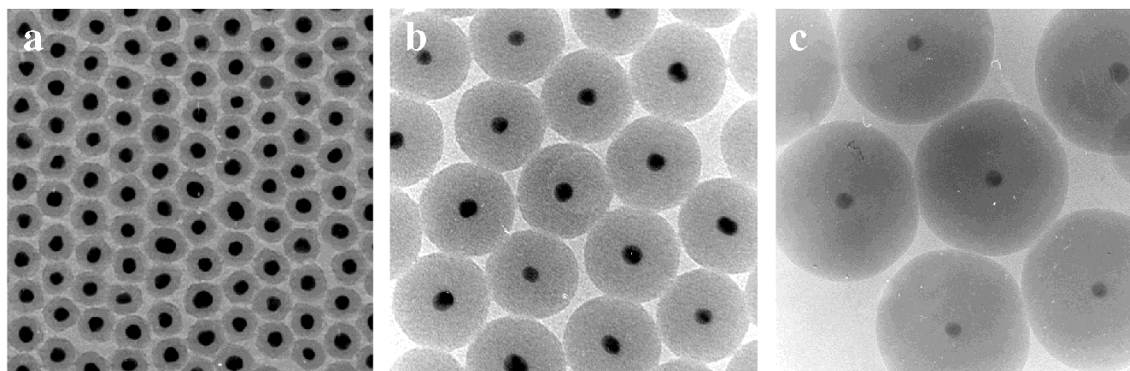


Fig. 7. TEMs of silica-coated gold nanoparticles, prepared according to Scheme 3 and subsequently further growing the silica shell via the hydrolysis of TEOS (Stöber method) in an ethanol/water mixture. The silica shell thickness on the 15 nm gold nanoparticles was varied from approximately a) 10 through b) 60 to c) 80 nm during growth of the silica shell.

employed by Philipse et al. to produce silica-coated magnetite particles,<sup>[63]</sup> and Bruggen adapted the work to produce colloidal boehmite core–thin silica shell rods with adjustable aspect ratios.<sup>[71]</sup> Hall and co-workers used a modified version of the above process to synthesize gold–organosilica core–shell particles using a base-catalyzed cocondensation of TEOS and organoethoxysilane precursors in the presence of surface-modified gold particles.<sup>[72]</sup> Organo-functionalities were covalently linked both within and on the surface of the regular 7 nm thick organosilica shell structure. Liz-Marzan et al. have also demonstrated that a thin shell of titanium dioxide can be produced on silver nanoparticles by the simultaneous reduction of silver and condensation of titanium butoxide.<sup>[73]</sup> A very recent study has shown that under certain conditions, silica shells can be formed on silver nanoparticles without pretreatment of the particle surface using the Stöber method.<sup>[74]</sup>

The inorganic and inorganic–organic shell coatings not only stabilize the particles against coalescence, but also allow tuning of their optical properties.<sup>[4]</sup> In addition, they provide silica surfaces that can subsequently be functionalized using silane coupling reactions, or already surface-functionalized silica ready for further reaction. The inorganic-coated particles can catalyze redox reactions on their surface,<sup>[70]</sup> be used to probe direct chemical reactions within them,<sup>[58]</sup> or be assembled into multilayered thin films.<sup>[78]</sup>

Surface chemical reactions have also been exploited to modify particle surfaces with metal nanoparticles. Akashi and co-workers have produced platinum nanoparticles on polystyrene microspheres with surface-grafted poly(*N*-isopropylacrylamide) via the reduction of hexachloroplatinate(IV) hydrate by ethanol.<sup>[79,80]</sup> The immobilized Pt colloids acted as active and stable heterogeneous catalysts for the hydrogenation of allyl alcohol in water, and they could be recycled several times whilst retaining their activity. The immobilized platinum colloids displayed higher activity than the polymer-stabilized colloidal platinum sol, and the activity of the immobilized catalyst could be enhanced by increasing the temperature.<sup>[80]</sup> Using a similar method, Dokoutchaev et al. formed metal particles of 2–4 nm diameter on polystyrene microspheres by depositing a precursor metal (palladium) oxide or hydroxide onto the spheres, followed by reduction to give fine metal particles on the surface.<sup>[64]</sup> The synthesis of polymer-coated microspheres with silver colloids on their surface using free radical chemistry has also been reported.<sup>[81]</sup> The metal salt and organic monomers are mixed together in solution. Dispersion polymerization of styrene and the reduction of silver ions to free atoms in solution then occurs simultaneously, leading to the in-situ formation of silver colloids on the surface of polystyrene microspheres. This method can potentially be applied to synthesize other monometallic or bimetallic colloids on polymer microspheres. However, low coverage and irregular metal nanoparticle coatings on the larger particles are often achieved by these methods.<sup>[64,79–81]</sup>

Sonochemistry is an alternative technique that can be employed for the production of coated particles. In sonochemical processes, the chemical effects of ultrasound arise from the

formation, growth and implosive collapse of bubbles in liquid (known as acoustic cavitation).<sup>[82]</sup> This phenomena has been exploited to prepare a variety of metal, oxide and composite nanoparticles,<sup>[64,82–84]</sup> and has recently been extended to produce core–shell type materials.<sup>[64,85–87]</sup> These composite particles are formed via the generation of nanoparticles in the presence of larger colloids. Semiconductor nanoparticles (ZnS) on submicrometer sized silica particles were prepared by the ultrasound irradiation of a slurry of silica, zinc acetate and thioacetamide in water at near room temperature.<sup>[85]</sup> The ZnS nanoparticles (of 1–5 nm in diameter) covered the colloidal silica surface either as thin layers or nanoclusters, depending on the reactant concentrations. Ultrasound-induced cavitation has also been used to coat nanosized nickel on alumina microspheres<sup>[86]</sup> and cobalt clusters on silica spheres,<sup>[87]</sup> imparting a magnetic function to the particles. Sonication of PdCl<sub>4</sub><sup>2-</sup> in aqueous solution leads to large Pd colloids that precipitate immediately, whereas conducting the sonication reaction in the presence of amine-functionalized polystyrene microspheres results in deposition of 8 nm Pd colloids on the particles.<sup>[64]</sup> The sonochemical approach is an attractive means for coating particles. It appears to be best suited for the modification of particle surfaces with nanoparticles, but not necessarily for forming regular coatings of these materials. The interest in such particles decorated with smaller active nanoparticles arises from their potential use as substrates for surface-enhanced Raman scattering, heterogeneous catalysts, and because of their relevance in electronic and optical sensor applications.

### 3.2. Controlled Assembly of Preformed Nanoparticles

Electrostatic interactions between nanoparticles and larger particles via solution self-assembly have been widely exploited to prepare core–shell materials.<sup>[64,88–102]</sup> Homola et al. reported the coating of  $\gamma$ -Fe<sub>2</sub>O<sub>3</sub> particles with preformed smaller silica particles by combining the particle mixtures under conditions where the two types of particles are oppositely charged.<sup>[88–90]</sup> This resulted in better dispersion and less aggregation of the magnetic particles. Similarly, nanosized silica was deposited on a range of larger inorganic particles, thus forming a protective layer.<sup>[91,92]</sup>

Nanocomposite multilayers can be assembled on particle surfaces by using the LbL method based on colloidal templates, as described in Section 2.2. Several research groups have employed the above procedure to fabricate particles consisting of a solid core covered with either a single layer of nanoparticles or a composite multilayer shell.<sup>[64,93–101]</sup> Keller et al. prepared alternating composite multilayers of exfoliated zirconium phosphate sheets and charged redox polymers on (3-aminopropyl)-triethoxysilane-modified silica particles.<sup>[93]</sup> Chen and Somasundaran deposited nano-sized alumina particles in alternation with poly(acrylic acid), which acts as the bridging polymer, on submicrometer-sized alumina core particles.<sup>[94]</sup> Evidence for the formation of the composite particles

in the latter work was provided by adsorption and electrophoresis data. Dokoutchaev et al. recently reported the alternating assembly of metal nano-sized particles and oppositely charged polyelectrolyte onto polystyrene microspheres.<sup>[64]</sup> In that work,<sup>[64]</sup> low gold nanoparticle coverage and non-uniform coatings were obtained, although the nanoparticle loading was increased by repeated depositions of nanoparticle and polyelectrolyte in the LbL manner. Using the same strategy, Caruso et al. demonstrated the step-wise formation of regular nanoparticle layers on colloidal particles.<sup>[95–99]</sup> Silica<sup>[95,96]</sup> and iron oxide<sup>[97,98]</sup> nanoparticle multilayer coatings on submicrometer-sized particles were prepared with nanometer-scale control over the thickness. Growth of the individual layers and morphology of the resulting coated particles were followed by electrophoresis, light scattering and electron microscopy. For the silica coatings, it was found that approximately one monolayer of nanoparticles were adsorbed with each deposition step.<sup>[95,96]</sup> The TEM images in Figure 8 illustrate the regularity of the coatings and the nanoscale control over shell layer thickness and the composite particle diameter through simple variation of the number of deposition cycles. The colloidal-core/silica-shell particles prepared in this way exist as single, unaggregated particles in solution.<sup>[95,96]</sup> Regular coatings were observed when the silica nanoparticles were deposited from salt solutions; deposition from pure water immediately produced aggregated particles. The salt screens charge on the silica nanoparticles and allows them to pack closely together on the surface.<sup>[95,96,103]</sup> This highlights the importance of controlling the solution conditions to effect uniform nanoparticle coatings on larger colloids when using the LbL technique. Submicrometer-sized composite particles with multilayer arrays of Fe<sub>3</sub>O<sub>4</sub>,<sup>[97,98]</sup> TiO<sub>2</sub>,<sup>[99]</sup> and clay<sup>[99]</sup> nanoparticles, lumi-

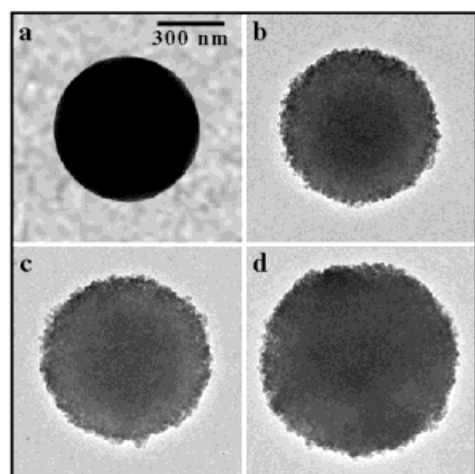


Fig. 8. TEMs of silica nanoparticle–polymer multilayer shell growth on 640 nm polystyrene particles prepared by the LbL method. a) Bare polystyrene particle. b)–d) Polyelectrolyte-modified polystyrene particles coated with one, two and four SiO<sub>2</sub> nanoparticle–poly(diallyldimethylammonium chloride) bilayers, respectively. The increased surface roughness is due to deposition of the 25 nm SiO<sub>2</sub> nanoparticles. A systematic increase in the diameter of the coated particles with increasing layer number is observed. The scale bar corresponds to all four TEM images shown. (Reproduced from [95]. Copyright 1998 American Chemical Society.)

nescent semiconductors,<sup>[100,101]</sup> as well as nanoparticle composites have also been produced via this approach.

Using a combination of self-assembly of preformed nanoparticles onto larger spheres and colloid reduction chemistry, Halas et al. reported a general strategy for the formation of solid-core/metal-nanoshell particles.<sup>[102]</sup> Small (1–2 nm diameter) gold nanoparticles were covalently bound via amine group linkages on 120 nm diameter 3-aminopropyltriethoxysilane-modified silica particles. This resulted in a surface coverage of gold nanoparticles of approximately 30%. The gold-coated silica particles were subsequently used as nucleation sites for the reduction of a mixture of chloroauric acid and potassium carbonate by sodium borohydride, thus increasing the coverage of gold on the surface.<sup>[102]</sup> The seed colloids increase in size as the reduction reaction proceeds until they finally coalesce to form a continuous metallic shell (Fig. 9).<sup>[102]</sup> Optical studies showed that the optical resonances of the particles could be varied over hundreds of nanometers in wavelength by variation of the relative sizes of the core and shell.<sup>[102,104–106]</sup> Surface enhanced Raman scattering was also observed when *p*-mercaptoaniline was present in solution with the gold-coated particles, with the largest enhancements observed when the gold coating formed an almost complete metal shell.<sup>[104]</sup> This procedure opens new avenues to the production of materials with tailored optical properties. The same group also studied the deposition of preformed gold nanoparticles onto 100 nm silica particles functionalized with various compounds.<sup>[107]</sup> The type of functional group present on the silica nanoparticles was found to have a

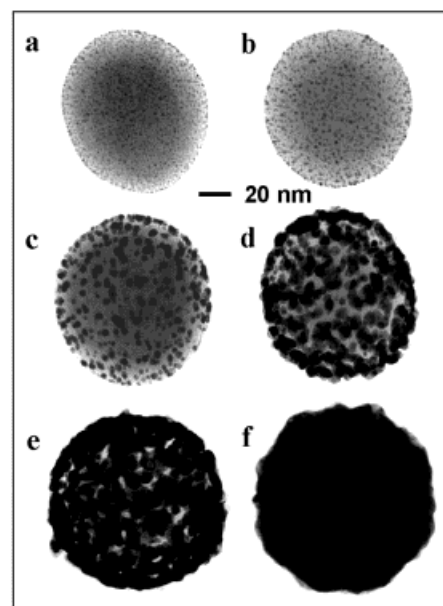


Fig. 9. TEMs of metal shell growth on 120 nm diameter silica particles. a) Gold-coated silica nanoparticle, prepared by adsorption of 1–2 nm diameter gold colloids onto (3-aminopropyl)trimethoxysilane-modified silica particles. b)–f) Progression of growth and coalescence of the gold nanoparticles on the surface of the silica, effected via the reduction of a mixture of chloroauric acid and potassium carbonate by sodium borohydride using the gold-coated silica particles as nucleation sites for the reduction. A continuous metallic shell is finally obtained (f). (Reproduced from [102]. Copyright 1998 Elsevier Science.)

profound influence on the coverage of gold nanoparticles and clusters on the silica particles: amino and thiol functional groups bound the gold nanoparticles, whilst only minimal attachment to methyl and diphenylphosphine moieties was observed. Mostly non-uniform nanoparticle coatings were obtained in this work, although increasing the content of ethanol in the aqueous solution from which the nanoparticles were deposited enhanced the degree of cluster formation and the quantity adsorbed.<sup>[107]</sup> The low degree of surface coverage is a common finding for the direct adsorption of metal nanoparticles onto larger particles. However, as described above, the nanoparticles on the surface may be used as nucleation sites for the growth of a thin metallic shell.

Furusawa et al. used electrostatic and polymerization processes to achieve the encapsulation of magnetic nanoparticle-coated polystyrene particles within a polystyrene shell.<sup>[108]</sup> In the process, magnetic nanoparticles were heterocoagulated with larger polystyrene microspheres, followed by seed polymerization to form a polystyrene layer around the composite particles. The advantage of this method is that the composite particles can be controlled by the diameter of the core latexes that are initially used. This study also shows the successful combination of multiple methods to form nanocomposite particles.

The above studies demonstrate the versatility of procedures based on colloidal templates, allowing an unprecedented means to the fabrication of a novel type of “heterocomposite” (multicomposite), nanostructured core-shell particles. Apart from the previously mentioned applications of such novel colloidal materials, they are attractive candidates for use in combinatorial chemistry. For example, multi-dye loaded silica particles attached to the surface of polystyrene microspheres can be used to identify compounds synthesized on the larger particle by means of fluorescence microscopy.<sup>[109]</sup>

#### 4. Biomacromolecule Layers

There has been an abundance of research concerning the immobilization of proteins onto solid supports, mainly because of the importance of proteins in biotechnology.<sup>[110–117]</sup> The potential applications of colloidal particles with attached biological molecules (e.g., enzymes, antibodies, and antigens) have long been recognized.<sup>[115,115]</sup> Particles that have biomolecules coupled to their surface can specifically react with antigens, target cells or viruses and can be used for *in vitro* or *in vivo* applications.<sup>[115,117]</sup> Application areas of these immunoparticles are diverse, ranging from immunoassays, bioseparations and hybridization assays through to biochemical or enzymatic reactions, affinity chromatography, clinical analysis and diagnostics, localization and markers in electron or standard light microscopy.<sup>[115,115–117]</sup> For example, Peula et al. used polymer colloids as carriers of adsorbed proteins in latex agglutination immunoassay techniques to enhance antibody-antigen interactions.<sup>[118–120]</sup> Gold colloids attached to proteins are routinely applied as immunocytochemical markers.<sup>[117]</sup> Biofunctionalized magnetically responsive colloidal particles are of

particular interest as these can be directed and isolated by exploiting their magnetic properties.<sup>[121,122]</sup> More recently, there has been interest in bio-modified nanoparticles for constructing nanoparticle-based assemblies through specific biomolecular interactions.<sup>[123–126]</sup> Studies by Mirkin et al.<sup>[123]</sup> and Alivisatos et al.<sup>[124]</sup> showed that complementary deoxyribonucleic acid (DNA) could be used to self-assemble DNA-modified gold nanoparticles into dimers and trimers<sup>[124]</sup> or higher-order aggregates.<sup>[123]</sup> Similarly, gold nanoparticles with chemisorbed antibodies<sup>[125]</sup> or a disulfide biotin-analogue<sup>[126]</sup> were cross-linked through the introduction of bivalent antigens and streptavidin, respectively, to form aggregated structures of the nanoparticles.

Biological molecules have long been immobilized onto solid surfaces by a variety of techniques, including passive adsorption, covalent bonding, sol-gel entrapment, specific recognition, and electrostatic self-assembly methods.<sup>[115,127–130]</sup> Many of these procedures have been utilized for the coupling of biomolecules to particles such as polystyrene, polyacrylamide, and azalactone.<sup>[115]</sup> The passive (non-covalent) adsorption method is one of the most frequently employed procedures for the immobilization of biomolecules onto particles.<sup>[115,127–130]</sup> Using this approach, particles can be coated with proteins or antibodies. However, passively adsorbed proteins can be readily lost from the surface and are prone to denaturation, thereby losing activity. Furthermore, small substances do not adhere very well to, for example, hydrophobic polystyrene surfaces through passive adsorption. Covalent coupling between suitable groups on the protein and the solid support is an alternative and widely used approach to tether biological molecules to particles.<sup>[115,127–130]</sup> The vast number of surface modification and coupling chemistries exploited to covalently bind the molecules has been well documented.<sup>[115]</sup> By covalently attaching proteins to particle surfaces, problems of instability, reversibility or inactivation can be overcome.

In contrast to planar substrates,<sup>[110]</sup> the vast majority of studies concerning the coupling of proteins to particle surfaces have focused on the formation of a single biological layer. Recently however, the aforementioned LbL approach has been shown to be a suitable means to assemble protein multilayer architectures on colloidal particles.<sup>[131–133]</sup> Multilayer films of bovine serum albumin (BSA),<sup>[131]</sup> immunoglobulin G (IgG),<sup>[131]</sup>  $\beta$ -glucosidase ( $\beta$ -GLS),<sup>[132]</sup> glucose oxidase (GOD),<sup>[133,134]</sup> and horseradish peroxidase (POD)<sup>[134]</sup> have been assembled on polystyrene microspheres by the alternate deposition of the protein and oppositely charged polymer. The protein multilayer shell could be varied from several nanometers in thickness to hundreds of nanometers.<sup>[131]</sup> Biomacromolecule multilayers are of interest in, for example, applications where the signal, as a result of biological interaction, needs to be amplified for the successful detection of various species, or where a higher efficiency of product from enzyme-substrate reactions is required.<sup>[135–137]</sup> This strategy permits the preparation of functional films on colloids with a high density of biomolecules. These and related biomultilayer colloids are expected to find new applications in biological applications.

## 5. Conclusions and Outlook

Research efforts over the last decade have led to a host of new strategies being developed for the modification of particle surfaces. Earlier methods have primarily focused on achieving single-component coatings on particles through surface chemical modification and conventional polymerization and precipitation reactions. More recent approaches, particularly those based on solution self-assembly, have been shown to be highly effective in producing multicomposite, nanostructured coatings. These methods permit remarkable control over the coating uniformity and thickness, and thus the assembled components and experimental conditions can be readily manipulated to prevent aggregation of the coated colloids. Although the method of choice highly depends on the coating required and the end use of the composite particles, the synthetic approaches outlined provide a high level of flexibility, thus allowing the design, structure and properties of the resultant particles to be varied tremendously. In addition, combinations of these methods are likely to allow new functional and composite layers to be manufactured on the surfaces of particles. Accordingly, nanoengineered core-shell particles are expected to find new and exciting applications in the chemistry, bioscience and materials science fields. Core-shell particles have already been assembled into colloidal crystals for photonic applications,<sup>[101]</sup> used as heterogeneous catalysts<sup>[79,80]</sup> and multi-enzyme biocatalysts,<sup>[132–134]</sup> and in surface enhanced Raman scattering applications.<sup>[104]</sup> An interesting extension of the composite particles is the production of hollow capsules by removal of the core particle,<sup>[29,30,42,43,48,49,98,99,138–140]</sup> these hollow materials may find applications in drug delivery, or as reactor or specific recognition systems.

Many of the approaches for constructing composite-colloidal entities are still in their infancy and much remains to be accomplished with respect to engineering the surfaces of particles. It is envisioned that future research will, to a large extent, continue to be focused on optimizing existing approaches, as well as developing new procedures, in order to create functional, multicomposite particles, with the individual components organized into ordered and complex architectures. This is likely to pave the way for the fabrication of nanostructured particles with designed interface structure-property relationships, similar to that observed for planar substrates over the last decade, and hence narrowing the gap that currently exists between thin film fabrication on planar surfaces and colloidal particles. Therefore, it is foreseen that the realm of technological applications of colloids will rapidly expand. This is certain to inspire multidisciplinary research on the particle edge well into the new millennium.

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