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Communications

Fabrication of Au@CaCO₃ Nanoparticles by in Situ Mineralization in Hydrogel Microspheres

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Enormous effort has been continually devoted to the preparation of colloidal gold nanoparticles (NPs) with various sizes and shapes since Michael Faraday's pioneering work on colors of Au NP suspensions in 1857.¹ As a result of the particle-geometry confinement of conduction electrons, Au NPs exhibit size and shape tunable colors, so-called plasmon resonances, which are usually exceedingly sensitive to the separation distance between the particles and their surrounding media.² This sensitive plasmon resonance and their biocompatibility make Au NPs good candidates for use in biolabeling.³ However, the colloidal stability of hydrophilic Au NPs, either directly created in aqueous media or transferred from organic media, is rather poor, as they strongly tend to aggregate upon environmental variation, thus limiting their applicability in the complicated biological milieu.

To enhance the stability of aqueous Au NPs and their dispersibility in water, particularly to protect them from extraneous chemical and physical changes, the creation of hydrophilic dielectric shells on Au NPs is necessary.

Recently, various polymeric coatings have been constructed on Au NPs based on layer-by-layer self-assembly of polymers⁴ or surface initiated polymerization.⁵ Liz-Marzán et al.^{6a} have developed a deliberate way to grow silica shells on Au NPs using controlled deposition. Their approach is difficult to extend to other metal oxide coatings as the precursors used are rather sensitive to surrounding moisture.

From the materials science point of view, biomimetic mineralization paves a simple and efficient way to produce various inorganic materials.⁷ To date, there exist a fairly limited number of reports on extending this methodology to create mineral shells on Au NPs as a result of the poor colloidal stability of the Au NPs. It is obvious that the addition of metallic cations such as Ca²⁺ into Au NP suspensions should cause aggregation of the particles in the mineralization process. Tremel and co-workers have recently used *p*-sulfanylphenol-stabilized Au NPs as preformed nuclei to control the mineralization of CaCO₃ to obtain micrometer-sized spherules.^{8a} Kim's group has demonstrated the forma-

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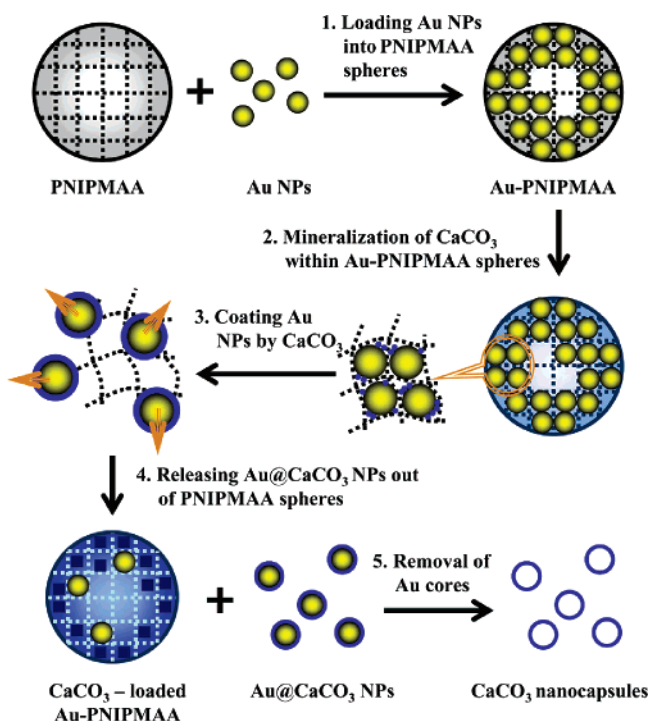


Figure 1. Schematic illustration of in situ mineralization of CaCO_3 in Au-PNIPMAA spheres and formation of Au@ CaCO_3 NPs and the corresponding CaCO_3 nanocapsules.

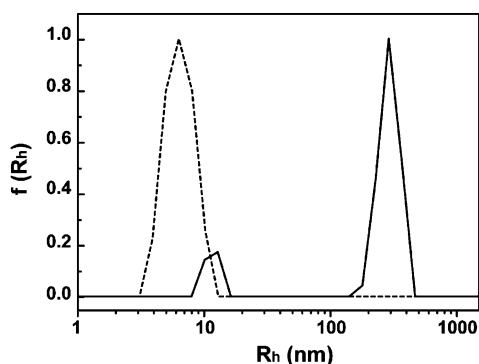


Figure 2. Hydrodynamic radius distribution profiles of 16 nm citrate-stabilized Au NPs (dotted) and of CaCO_3 -loaded Au-PNIPMAA spheres and Au@ CaCO_3 NPs, obtained from in situ mineralization of CaCO_3 within Au-PNIPMAA spheres (solid).

tion of submicrometer- to micrometer-sized Au@ CaCO_3 particles by conducting mineralization on 4-mercaptobenzoic acid-stabilized Au NPs.^{8b} In all of these reports, the capping of Au NPs with thiol ligands bearing functional terminal groups, such as hydroxyl and carboxylic groups, is necessary to create the nucleation sites of CaCO_3 mineralization. This was implemented by ligand exchange, which is usually associated with a deterioration of the colloidal stability of Au NPs, leading to aggregation of the particles. To enhance the colloidal stability of Au NPs in the presence of Ca^{2+} , herein we employed hydrogels to stabilize the Au NPs on the basis of our recent success.⁹ As shown in Figure 1, the preformed Au NPs were embedded into hydrogel spheres prior to CaCO_3 mineralization. Afterward, we

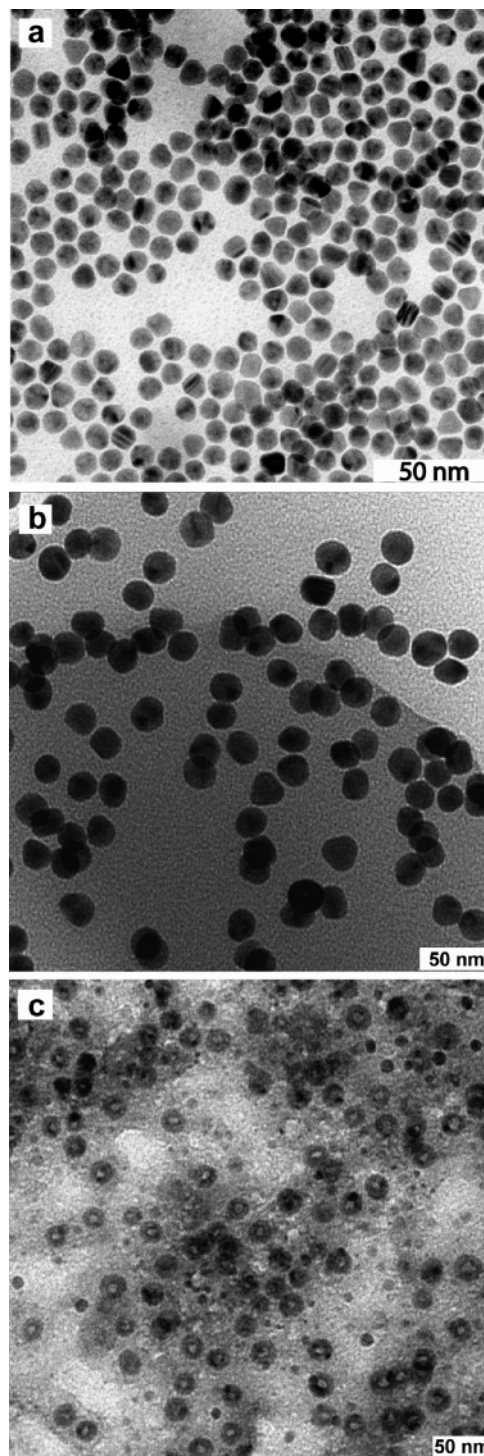


Figure 3. TEM pictures of 12 nm Au NPs (a), Au@ CaCO_3 NPs from in situ mineralization of CaCO_3 within Au-PNIPMAA spheres (b), and CaCO_3 nanocapsules obtained by etching out Au cores of Au@ CaCO_3 NPs (c).

conducted in situ mineralization within the hydrogel spheres loaded with Au NPs, creating CaCO_3 shells on the NPs.

Recently, our group and others have succeeded in incorporating various aqueous NPs, such as CdTe quantum dots and Au NPs, into hydrogel spheres, relying on the physical entrapment of the gel network.^{9,10} Especially in the case of

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Au NPs, their loading in hydrogel spheres is mainly due to the dimensional similarity between the Au NPs and the pores within the hydrogel spheres.^{9a} The gel networks sufficiently protect the loaded Au NPs from aggregation in the presence of salts and different solvents.^{9a} Encouraged by this success, in the current work, 1 μm hydrogel spheres of poly(*N*-isopropylacrylamide-*co*-methacrylic acid) (PNIPMAA) were employed to embed 12 nm citrate-stabilized Au NPs (Supporting Information). The resulting composite gel spheres are marked as Au–PNIPMAA. As depicted in Figure 1, after incubating the Au–PNIPMAA spheres in aqueous CaCl_2 solution, followed by slow diffusion of CO_2 , the mineralization of CaCO_3 occurred in the aqueous solution within the gel spheres. After 5 h of calcification, followed by filtration of the precipitates, the resulting dispersions were analyzed by dynamic light scattering (DLS). Figure 2 indicates that there exist two types of particles in the dispersions; one is about 720 nm in size and the other is about 22 nm. This coexistence of large and small particles is also clearly confirmed by scanning electronic microscopy (SEM; Supporting Information, Figure S1). As suggested in our previous study,^{9c} the large particles are expected to result from mineralization of CaCO_3 within Au–PNIPMAA spheres, say, CaCO_3 -loaded Au–PNIPMAA composite spheres.

To further analyze the small particles obtained, the CaCO_3 -loaded Au–PNIPMAA spheres were removed by centrifugation at 2000g. The resulting supernatants were visualized by transmission electron microscopy (TEM). Figure 3b reveals that these small particles consist of Au cores, whose sizes are similar to those of the initial Au NPs (Figure 3a). This indicates that these small particles are derived from the Au NPs. Their increased dimension should arise from the formation of the CaCO_3 coating on the Au NPs, as the carboxylic acid groups of citrates capped on the Au NPs used in our work may provide nucleation sites for mineralization of CaCO_3 .⁸ As shown in Figure 1, CaCO_3 was, therefore, generated not only inside the pores of the hydrogel networks but also on the Au NPs. As the mineralization of CaCO_3 proceeded, the accumulation of CaCO_3 on Au NPs led to formation of CaCO_3 shells on the Au NPs, thus creating Au@ CaCO_3 NPs. Note that Au NPs can be embedded within hydrogel spheres only when their sizes are comparable to the pore sizes of the hydrogel networks; otherwise, the NPs will be excluded outside the gel spheres.^{9a} The resulting Au@ CaCO_3 NPs were obviously bigger than the initial Au NPs, so the pores of the PNIPMAA gel network should not be able to confine these composite NPs, thus releasing them into the surrounding media (Figure 1). By means of centrifugation, we can easily separate the Au@ CaCO_3 composite NPs from CaCO_3 -loaded hydrogel spheres. By combining the DLS and TEM data, the CaCO_3 shell should be around 5 nm thick.

Note that a number of Au NPs and their aggregates, coated with CaCO_3 , remained inside or on the gel spheres (Supporting Information, Figure S1), as indicated by the light

red color of the sediments of the gel spheres after centrifugation. This incomplete release of Au@ CaCO_3 NPs and the low loading amount of Au NPs in the hydrogel spheres decreased the efficiency of our approach. Our current efforts are devoted to increasing the production of Au@ CaCO_3 NPs.

As a result of their low electron contrast the CaCO_3 shells on the Au NPs are hard to observe in TEM imaging. To demonstrate the CaCO_3 coating on the Au NPs, we incubated the resulting composite NPs in aqueous solutions of a mixture of KI and I_2 for 10 min to etch out the Au cores.¹¹ After removal of the composite hydrogel spheres by three cycles of centrifugation at 2000g and washing with water, one may observe hollow spheres of 18–22 nm in size in TEM images (Figure 3c), clearly demonstrating the core–shell feature of Au@ CaCO_3 NPs. The resulting CaCO_3 shell is about 3–5 nm thick. The X-ray diffraction patterns of the resulting CaCO_3 nanocapsules testified to the formation of the calcite crystalline phase (Supporting Information, Figure S2). Note that, in our work, prolonging the mineralization period has little influence on the dimension of Au@ CaCO_3 NPs and CaCO_3 nanocapsules. Mann and co-workers have recently fabricated calcium phosphate/polymer composite hollow spheres of 50–70 nm in size using block polymer micelles or polymer nanocages as templates for mineralization.¹² To the best of our knowledge, the current study represents a first report on the generation of sub-50 nm hollow spheres of CaCO_3 via the templating of Au NPs.

In summary, we have demonstrated a simple way to construct Au@ CaCO_3 NPs via in situ mineralization within hydrogel spheres loaded with Au NPs. The hydrogel spheres were used both as stabilizers and as reservoirs of the NPs. The resulting Au@ CaCO_3 NPs exhibit good colloidal stability and dispersibility in aqueous media, which are hard to fabricate otherwise. The removal of Au cores resulted in CaCO_3 nanocapsules. Following a similar procedure, we also succeeded in creating calcium phosphate shells on Au NPs. Thus, our methodology should open up a hydrogel-assisted bio-inspired methodology to encapsulate NPs with various biominerals and in turn to create biomineral nanocapsules. Additionally, our previous study suggests that Au–PNIPMAA spheres can be transferred into various solvents such as ethanol and toluene without deteriorating the Au NP properties; thus, our method can be expected to be extendable to nonaqueous mineralization. Further work will also focus on the exploitation of the resulting biomineral coated Au NPs and the corresponding nanocapsules in applications such as bioimaging and drug delivery.

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Supporting Information Available: Experimental details of loading Au NPs into PNIPMAA spheres, in situ mineralization within Au–PNIPMAA spheres, and etching out Au NPs; a SEM image of CaCO_3 -loaded Au–PNIPMAA composite spheres and Au@ CaCO_3 ; and X-ray diffraction of the resulting CaCO_3 nanocapsules (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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