

A Simple Route to Multimodal Composite Nanoparticles

Kim Y. van Berkel,[†] Ashley M. Piekarski,[†]
Paul H. Kierstead,[†] Eric D. Pressly,[†] Paresh C. Ray,[‡] and
Craig J. Hawker^{*†}

Materials Research Laboratory and Departments of
Materials, Chemistry and Biochemistry, University of
California, Santa Barbara, California 93106, and
Department of Chemistry, Jackson State University, Jackson,
Mississippi 39217

Received December 24, 2008

Revised Manuscript Received February 2, 2009

Inorganic nanostructures of various shapes and sizes, and consisting of various metal, metal oxide, and semiconductor materials, are finding increasing application in a diverse range of fields, from optical physics to cancer therapy. For example, the use of gold and silver nanoparticles,¹ nanoshells,² and nanowires³ as substrates for surface-enhanced Raman spectroscopy (SERS) in sensing and diagnostics⁴ is presently the subject of intense research interest. Similarly, the preparation of magnetic nanoparticles has enabled the development of new agents for magnetic resonance imaging (MRI)⁵ and protein separation.⁶

As new uses are found for inorganic nanoparticles, an enticing prospect is the ability to combine different functions within a single nanomaterial, giving rise to so-called “multimodal” materials.⁷ A variety of strategies for fabricating such nanostructures has appeared in the literature. These include combining nanoparticles with functional small molecules (e.g., fluorophores or metal complexes⁸); the creation of nanoparticle alloys, containing domains of different inorganic materials;^{9,10} and more elaborate processes to create multilayered composite nanoparticles, e.g., consisting of multiple metallic domains bound together by a silica or organic polymer matrix.^{11,12} In general, these existing procedures often require multiple reaction and/or purification steps, and moreover the resulting materials are generally restricted to specific combinations of inorganic nanoparticle types. Considerable opportunity therefore exists to develop a convenient and general method for preparing multimodal nanoparticles that overcomes many of these limitations.

Herein, we describe a new synthetic method, based on miniemulsion polymerization, for the preparation of composite polymer–inorganic nanoparticles, which readily enables incorporation of two different populations of inorganic nanoparticles within the same composite particle interior. While the incorporation of inorganic nanoparticles into miniemulsion polymerizations to give composite particles has previously been demonstrated,¹³ not only do these reports typically present rather poorly defined composite nanoparticles, but to the best of our knowledge, there are no reports of composite miniemulsion polymerization demonstrating coencapsulation of different inorganic nanoparticles in a single polymerization step.

The present synthetic strategy is illustrated schematically in Figure 1. We exemplify this approach by the coencapsulation of MnFe₂O₄ and Au nanoparticles, which yields as its product composite particles exhibiting both magnetic and surface

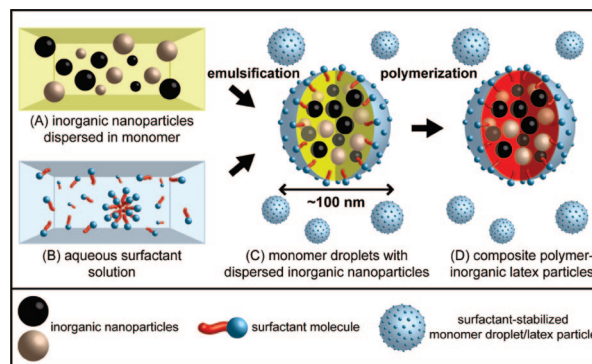


Figure 1. Schematic illustration of composite polymer–inorganic particle formation by miniemulsion polymerization: (A) polystyrene-grafted inorganic nanoparticles are dispersed in monomer (divinylbenzene) and emulsified with aqueous surfactant solution (B) to form small, uniform monomer droplets (C); free radical polymerization yields cross-linked poly(divinylbenzene) latex particles with inorganic nanoparticles embedded in the interior (D).

plasmon resonance characteristics. First, MnFe₂O₄ and Au nanoparticles grafted with short polystyrene ligands are dispersed in the monomer, divinylbenzene. This monomer/nanoparticle solution is then emulsified with an aqueous solution of surfactant (cetyltrimethylammonium bromide, CTAB), via ultrasonication, to generate an emulsion of submicrometer monomer droplets containing the inorganic nanoparticles. The free radical polymerization of these droplets (using 2,2′-azobis(2-amidinopropane) dihydrochloride, or “V-50”, as initiator) yields cross-linked poly(divinylbenzene) latex particles with inorganic nanoparticles embedded in the interior.

Preliminary experiments were carried out to demonstrate that the present synthetic approach produces well-defined composite latex particles based on just a single type of inorganic nanoparticle. Particular note should be made of the importance of the surface stabilizing group in successful composite latex particle formation. Attempts to use inorganic nanoparticles (either Au or MnFe₂O₄) stabilized by small organic ligands—such as dodecyl or oleyl groups^{10,12,14}—resulted in substantial nanoparticle aggregation upon redispersion in divinylbenzene monomer and also significantly limited the level of nanoparticle incorporation into composite latex particles (see Figure 2a). An effective solution to this problem was to graft the inorganic nanoparticles with short polystyrene ligands ($M_n \sim 3000$ – 6000 g/mol; see Supporting Information for details), enabling the inorganic material to be conveniently isolated in the form of a dry film and readily redispersed in divinylbenzene monomer for composite miniemulsion polymerization. Inspection by transmission electron microscopy (TEM), exemplified in Figure 2b, verified that these polymer-grafted Au nanoparticles resulted in well-defined composite latex particles, consisting of multiple inorganic domains fully encapsulated by a spherical poly(divinylbenzene) matrix. In both cases, the wt % of Au nanoparticle in the starting polymerization mixture was 12%; however, significant agglomeration and flocculation of the Au nanoparticles were observed for oleylamine, resulting in a significantly lower wt % in the actual polymeric composite. This is also in agreement with the poorly defined nanostructures formed with traditional, low molecular weight surfactants when compared to the polymer grafted systems.

In order to generate multimodal composite particles, the same procedure was employed for a mixture of MnFe₂O₄ and Au

^{*} Corresponding author. E-mail: hawker@mrl.ucsb.edu.

[†] University of California, Santa Barbara.

[‡] Jackson State University.

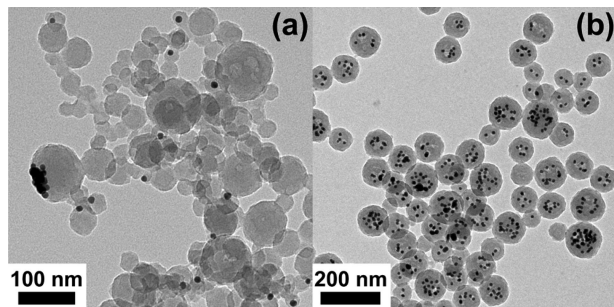


Figure 2. TEM images of composite poly(divinylbenzene)-Au latex particles, based on Au nanoparticles with either (a) oleylamine or (b) polystyrene thiol ligands as surface stabilizing groups. In both cases the wt % of Au was 12%.

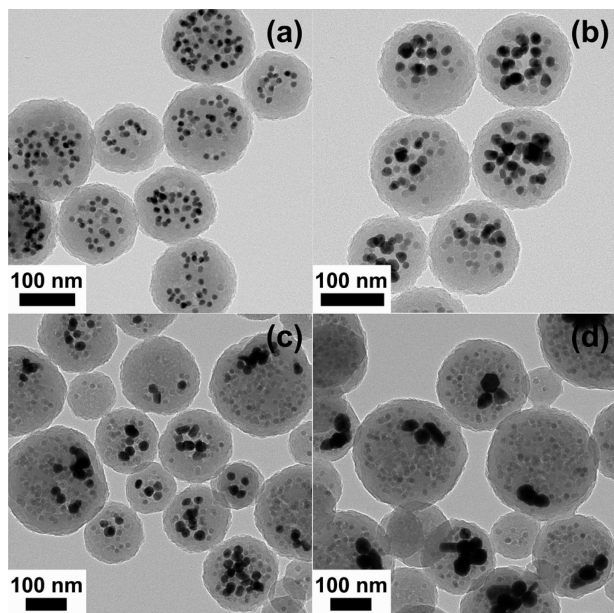


Figure 3. TEM images of multimodal composite poly(divinylbenzene)-inorganic latex particles prepared by coencapsulation of MnFe_2O_4 nanoparticles (11 nm average diameter) and Au nanoparticles of average diameter 13 (a), 18 (b), 24 (c), or 46 nm (d). In each case the wt % loading of the MnFe_2O_4 was 10 wt % and the Au 19 wt %.

nanoparticles. A series of coencapsulation experiments were carried out using MnFe_2O_4 particles with 11 nm average diameter and four different populations of Au nanoparticles, with average diameters ranging from 13 to 46 nm. TEM analysis, as shown in Figure 3, clearly revealed the formation of spherical composite latex particles encapsulating both MnFe_2O_4 (smaller nanoparticles with lower TEM contrast) and Au nanoparticles of various average sizes (larger nanoparticles with higher TEM contrast).

The majority of composite latex particles contained both inorganic nanoparticle types, with only small subpopulations (less than 5%) of monomodal composite latex particles (containing only MnFe_2O_4 or Au nanoparticles). Only in the case of coencapsulation using the largest Au nanoparticles (Figure 3d) did the subpopulations of monomodal (MnFe_2O_4 -containing) (~10–20%) appear. UV-vis spectroscopy of the multimodal composite particles confirmed the incorporation of Au nanoparticles—with their signature absorption maximum at ~520 nm (see Figure 4b)—while the magnetism conferred by the incorporated MnFe_2O_4 was evident from the ability to harvest the composite particles using a simple bar magnet (Figure 4a). A UV-vis spectrum obtained for the residual solution after magnetic

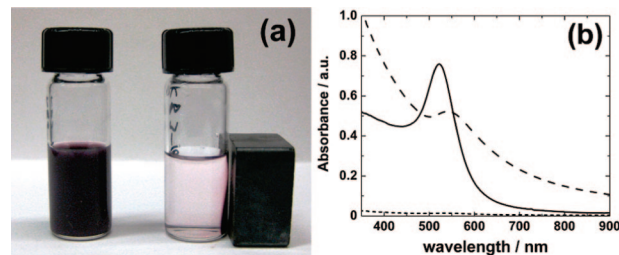


Figure 4. (a) Magnetic isolation of multimodal particles. (b) UV-vis spectra of Au nanoparticles prior to encapsulation (—), multimodal composite latex particles (---), and residual solution after magnetic removal of multimodal particles (---).

removal of composite latex particles revealed no significant absorbance maximum at 520 nm—as is expected for a sample in which the vast majority of latex particles incorporate both types of nanoparticles, mixing of discrete nanocomposites containing just MnFe_2O_4 or Au did not lead to the same results. Importantly, comparison of the UV-vis spectrum for the composite latex particles with that of the starting Au nanoparticles showed only a small shift in the absorption maximum (to 540 nm). This clearly indicates the Au nanoparticles did not undergo any significant aggregation during redispersion and encapsulation, and they retained their surface plasmon resonance properties.

Importantly, inspection by TEM confirmed that all inorganic material was located inside composite latex particles, with no observation of free (unencapsulated) manganese ferrite or gold nanoparticles. Furthermore, it was apparent that the inorganic nanoparticles were not exposed at the composite particle surface, but rather they were protected by a thin layer of cross-linked polymer (e.g., see Figure 3b). This protective polymer layer has subsequently been shown to be impermeable to small molecule etchants.¹⁵ In all four cases, the number-average particle diameter measured for each composite latex (determined from TEM particle sizing) was relatively consistent: 130 ± 20 nm for the latex using 13 nm Au nanoparticles; 140 ± 25 nm for 18 nm Au nanoparticles; 175 ± 25 nm for 24 nm Au nanoparticles; 220 ± 25 nm for 46 nm Au nanoparticles. Interestingly, the dispersion of the inorganic nanoparticles within the polymeric matrix was size dependent. For the small, 11 nm MnFe_2O_4 nanoparticles, random dispersion throughout the matrix was observed. In direct contrast, at comparable dimensions (13 and 18 nm) the Au nanoparticles were observed to be randomly distributed; however, on increasing to 24 nm and finally 46 nm, aggregation of the Au was observed, and the particle segregation that we observe at higher particle size ratios (i.e., with larger Au particles) is consistent with theoretical predictions.¹⁶

The composite nanoparticles obtained from miniemulsion polymerization were stabilized by charged surface groups (from the initiator, V-50, and surfactant, CTAB) and remained well-dispersed in aqueous solution. However, these nanoparticles were found to be unstable upon redispersion in organic solvent, as shown in Figure 5 (left sample). A convenient strategy for improving the stability of these composite nanoparticles was therefore developed and involved the attachment of poly(ethylene glycol) (PEG) chains to the nanoparticle surface using thiol-ene chemistry and takes advantage of the orthogonal nature of thiol-ene chemistry and the presence of residual double bonds in the polymeric matrix. The thiol-ene approach has recently emerged as a highly useful methodology for synthesis and modification of polymers and other macromolecular structures.¹⁷ In the present work, it was possible to

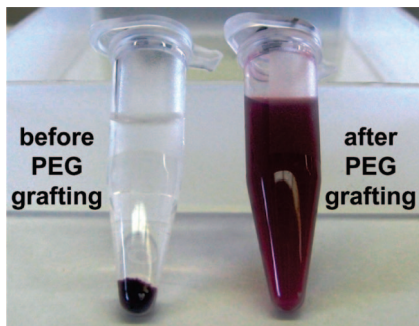
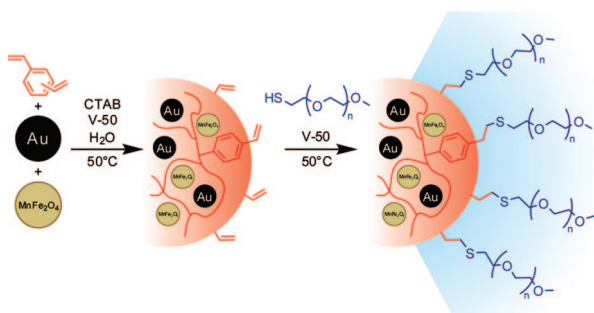


Figure 5. Photographs of composite latex particles redispersed in tetrahydrofuran (left sample) and after attachment of poly(ethylene glycol) (PEG) surface groups by thiol–ene chemistry and redispersion in THF (right sample).

Scheme 1. Preparation of Multimodal Latex Particles by Composite Miniemulsion Polymerization, Followed by Attachment of Poly(ethylene glycol) (PEG) Chains to the Surface of Composite Particles Using Thiol–Ene Chemistry



exploit residual vinyl (“ene”) groups present in the poly(divinylbenzene) matrix of as-prepared composite nanoparticles (Scheme 1).¹⁸ Addition of thiol-terminated PEG chains ($M_n = 2000$ g/mol), and V-50 as a free radical source, resulted in successful attachment of PEG to the nanoparticle surface as evidence by NMR, IR, and physical property differences.

These PEG-grafted composite nanoparticles were found to be completely stable upon redispersion in a variety of solvents, such as *N,N*-dimethylformamide, chloroform, water, and tetrahydrofuran (see Figure 5, right sample). Moreover, TEM analysis showed that the composite latex particle structure remains intact after redispersion in organic solvents due to the highly cross-linked nature of the poly(divinylbenzene) matrix.¹⁵

In summary, the present synthetic method represents a convenient and highly modular method for the preparation of multimodal composite nanoparticles, consisting of a spherical, cross-linked poly(divinylbenzene) matrix embedded with two different types of inorganic core materials. Importantly, these particles exhibit a combination of properties characteristic of the incorporated inorganic material—in this case, magnetism due to $MnFe_2O_4$ nanoparticles and UV–vis absorption due to the surface plasmon resonance of Au nanoparticles. To our knowledge, this is the first report of miniemulsion polymerization used to generate dual-core inorganic composite nanoparticles. It is envisaged that this synthetic approach will provide a general method for the preparation of multimodal polymer–inorganic

nanoparticles, using a variety of inorganic nanoparticle combinations.

Acknowledgment. Financial support from the National Science Foundation through the PREM program (DMR-0611539), the UCSB Materials Research Laboratory (NSF Grant DMR05-20415), an NSF Graduate Fellowship (A.M.P.), and the New Zealand Foundation for Research Science and Technology Postdoctoral Fellowship program (K.V.B.) is gratefully acknowledged.

Supporting Information Available: Experimental details for polymer and nanoparticle synthesis. This material is available free of charge via the Internet at <http://pubs.acs.org>.

References and Notes

- (1) (a) Freeman, R. G.; Grabar, K. C.; Allison, K. J.; Bright, R. M.; Davis, J. A.; Guthrie, A. P.; Hommer, M. B.; Jackson, M. A.; Smith, P. C.; Walter, D. G.; Natan, M. J. *Science* **1995**, *267*, 1629–1632. (b) Faulds, K.; Littleford, R. E.; Graham, D.; Dent, G.; Smith, W. E. *Anal. Chem.* **2004**, *76*, 592–598.
- (2) Jackson, J. B.; Halas, N. J. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 17930–17935.
- (3) Qin, L. D.; Zou, S. L.; Xue, C.; Atkinson, A.; Schatz, G. C.; Mirkin, C. A. *Proc. Natl. Acad. Sci. U.S.A.* **2006**, *103*, 13300–13303.
- (4) (a) Cao, Y. C.; Jin, R.; Mirkin, C. A. *Science* **2002**, *297*, 1536–1540. (b) Hirsch, L. R.; Gobin, A. M.; Lowery, A. R.; Tam, F.; Drezek, R. A.; Halas, N. J.; West, J. L. *Ann. Biomed. Eng.* **2006**, *34*, 15–22. (c) Doering, W. E.; Piotti, M. E.; Natan, M. J.; Freeman, R. G. *Adv. Mater.* **2007**, *19*, 3100–3108.
- (5) Yang, J.; Lee, C. H.; Ko, H. J.; Suh, J. S.; Yoon, H. G.; Lee, K.; Huh, Y. M.; Haam, S. *Angew. Chem., Int. Ed.* **2007**, *46*, 8836–8839.
- (6) Lin, P. C.; Chou, P. H.; Chen, S. H.; Liao, H. K.; Wang, K. Y.; Chen, Y. J.; Lin, C. C. *Small* **2006**, *2*, 485–489.
- (7) Tallury, P.; Payton, K.; Santra, S. *Nanomedicine* **2008**, *3*, 579–592.
- (8) (a) Santra, S.; Bagwe, R. P.; Dutta, D.; Stanley, J. T.; Walter, G. A.; Tan, W.; Moudgil, B. M.; Mericle, R. A. *Adv. Mater.* **2005**, *17*, 2165–2169. (b) Sharma, P.; Brown, S. C.; Bengtsson, N.; Zhang, Q.; Walter, G. A.; Grobmyer, S. R.; Santra, S.; Jiang, H.; Scott, E. W.; Moudgil, B. M. *Chem. Mater.* **2008**, 000.
- (9) (a) Lyon, J. L.; Fleming, D. A.; Stone, M. B.; Schiffer, P.; Williams, M. E. *Nano Lett.* **2004**, *4*, 719–723. (b) Lim, D.-K.; Kim, I.-J.; Nam, J.-M. *Chem. Commun.* **2008**, 000.
- (10) Yu, H.; Chen, M.; Rice, P. M.; Wang, S. X.; White, R. L.; Sun, S. *Nano Lett.* **2005**, *5*, 379–382.
- (11) (a) Stoeva, S. I.; Huo, F.; Lee, J. S.; Mirkin, C. A. *J. Am. Chem. Soc.* **2005**, *127*, 15362–15363. (b) Lee, J.; Yang, J.; Ko, H.; Oh, S. J.; Kang, J.; Son, J.-H.; Lee, K.; Lee, S.-W.; Yoon, H.-G.; Suh, J.-S.; Huh, Y.-M.; Haam, S. *Adv. Funct. Mater.* **2008**, *18*, 258–264. (c) Insin, N.; Tracy, J. B.; Lee, H.; Zimmer, J. P.; Westervelt, R. M.; Bawendi, M. G. *ACS Nano* **2008**, *2*, 197–202.
- (12) Kim, B. S.; Taton, T. A. *Langmuir* **2007**, *23*, 2198–2202.
- (13) (a) Erdem, B.; Sudol, E. D.; Dimonie, V. L.; El-Aasser, M. S. *J. Polym. Sci., Part A: Polym. Chem.* **2000**, *38*, 4441–4450. (b) Ramirez, L. P.; Landfester, K. *Macromol. Chem. Phys.* **2003**, *204*, 22–31. (c) Csetneki, I.; Faix, M. K.; Szilagyi, A.; Kovacs, A. L.; Nemeth, Z.; Zrinyi, M. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 4802–4808. (d) Joumaa, N.; Toussay, P.; Lansalot, M.; Elaissari, A. *J. Polym. Sci., Part A: Polym. Chem.* **2008**, *46*, 327–340. (e) Kim, H.; Daniels, E. S.; Li, S.; Mokkaapati, V. K.; Kardos, K. *J. Polym. Sci., Part A: Polym. Chem.* **2007**, *45*, 1038–1054.
- (14) Zheng, N.; Fan, J.; Stucky, G. D. *J. Am. Chem. Soc.* **2006**, *128*, 6550–6551.
- (15) van Berkel, K. Y.; Hawker, C. J. Manuscript in preparation.
- (16) Warren, P. B. *Europhys. Lett.* **1999**, *46*, 295–300.
- (17) (a) Hoyle, C. E.; Lee, T. Y.; Roper, T. *J. Polym. Sci., Part A: Polym. Chem.* **2004**, *42*, 5301–5338. (b) David, R. L. A.; Kornfield, J. A. *Macromolecules* **2008**, *41*, 1151–1161. (c) Killops, K. L.; Campos, L. M.; Hawker, C. J. *J. Am. Chem. Soc.* **2008**, *130*, 5062–5064. (d) Joralemon, M. J.; O'Reilly, R. K.; Hawker, C. J.; Wooley, K. L. *J. Am. Chem. Soc.* **2005**, *127*, 16892–16899.
- (18) Zheng, G.; Stover, H. D. H. *Macromolecules* **2002**, *35*, 6828–6834.

MA802849F