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Microcapsules of PEGylated Gold Nanoparticles Prepared by Fluid–Fluid Interfacial Assembly

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ABSTRACT

Amphiphilic, PEGylated gold nanoparticles, of ∼2 nm average core diameter, were synthesized by reduction of hydrogen tetrachloroaurate in the presence of the ligand (1-mercaptoundec-11-yl)tetra(ethylene glycol). These PEGylated gold nanoparticles were found to assemble cleanly at the oil–water interface. This self-assembly process gave a microencapsulated oil phase, water as the continuous phase, and a monolayer of gold nanoparticles at the oil–water interface. The capsules could be cross-linked from the organic phase by reaction of the chain-end hydroxyl groups of the PEG ligands with suitable electrophiles such as terephthaloyl chloride.

The development of reliable syntheses of well-defined nanoparticles has opened many new opportunities in the areas of nanoscience and nanocomposites.[1−4] Being able to control the assembly of such well-defined nanoparticles is critically important for effectively harnessing the unique properties of the nanoparticles, which arise from their nanometer-scale dimensions.[5−8] Tailoring the ligand periphery of nanoparticles is proving useful for their dispersion and assembly in polymers and fluids, for example, within homopolymers to give dispersed nanocomposites,[9−12] within block copolymers and block copolymer templates to give hybrid assemblies with predictable spatial location of the nanoparticles,[13−16] and at the interface of immiscible fluids.[17−28]

It is well-established that microparticles strongly segregate to the interface of immiscible fluids, driven by a reduction of interfacial energy.[29−31] The driving force responsible for the analogous fluid−fluid interfacial segregation of nanoparticles is much weaker, due to the small size of the particles, and the role of thermal energy (Brownian motion) in disrupting weakly held assemblies (on the order of a few k_BT). Nonetheless, several cases of nanoparticle assemblies at fluid−fluid interfaces have been observed and characterized.[17−28] When the nanoparticles used in these interfacial assemblies are decorated with functional ligands, the assemblies can be stabilized and transformed into robust materials by performing chemistry on the functional groups contained within the ligand structure. This chemistry has provided a route to robust nanoparticle-based materials such as capsules and ultrathin sheets.[19,32] In general, the combination of intrinsic nanoparticle properties, such as fluorescence, conductivity, and magnetic properties, combined with control over their spatial location by assembly at the fluid−fluid interface, carries potential in numerous applications in which multifunctional nanostructured materials, including encapsulants and delivery systems, are needed.[33−36]

Cadmium selenide and gold represent two examples of nanoparticles that can be prepared with finely controlled average diameters and excellent reproducibility.[2,4] Both cadmium selenide and gold nanoparticles are stabilized by alkane-based hydrophobic ligands that render the particles soluble in organic solvents. While tri-*n*-octylphosphine oxide (TOPO)-covered CdSe quantum dots were found to segregate to the oil−water interface, *n*-dodecanethiol-covered gold nanoparticles exhibit no such interfacial segregation, but rather prefer the oil phase. The literature contains only a few examples in which gold nanoparticles segregate to the oil−water or air−water interface.[18,22−28] Most of these methods utilize citrate-stabilized gold nanoparticles (5−50 nm in diameter) that must be modified subsequently to enable the assembly,[18,22−26] while one example describes bromopropionate-functionalized gold nanoparticles that give very large (millimeter diameter) oil-in-water droplets when mixed with silver nanoparticles.[27] Another example uses carboxylic acid terminated ligands on the gold nanoparticles, again to produce millimeter diameter droplets of oil (hexane) in water, where the droplets are seen to coalesce quickly.[37] Previously, we showed that gold nanoparticles covered with a mixture of hydrophobic and hydrophilic ligands, prepared by ligand

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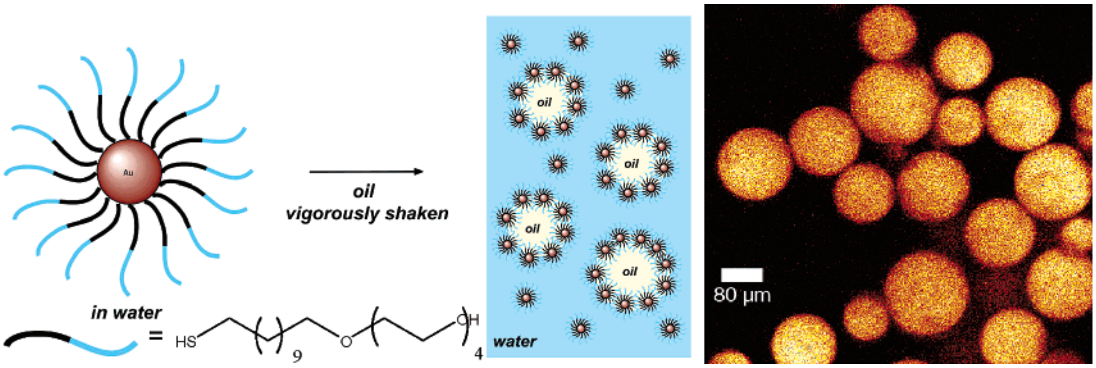

Figure 1. Left: schematic depiction of PEGylated gold nanoparticles assembling at the oil−water interface; right: confocal fluorescence microscopy image of oil-in-water droplets, containing coumarin 153 in TCB, stabilized by gold nanoparticles at the oil−water interface. The fluorescence in the TCB phase confirms the hydrophobic interior of the capsules.

exchange chemistry, gave microcapsules of oil in water.[38] In that case, a narrow ratio of hydrophobic (*n*-dodecanethiol) to hydrophilic (11-mercapto-1-undecanol) ligands on the gold nanoparticle surface was needed to provide the desired interfacial assembly. While this method provides chain-end hydroxyl groups for subsequent reactivity, it is limited to a narrow range of ligand ratios and works only for select organic solvents. A more generally effective method for interfacial assembly of gold nanoparticles in fluids is thus needed to integrate the properties of gold nanoparticles into self-assembled materials in fluids.

Here we demonstrate the interfacial segregation of gold nanoparticles containing an amphiphilic ligand periphery consisting of PEGylated alkane thiols in which the thiols bind to the nanoparticle surface, the alkane provides a spacer group, and the PEG is exposed to the surrounding aqueous medium. The methods described overcome the solubility and stability limitations that have been problematic in other gold nanoparticle interfacial assemblies and lead to cleanly assembled, micron-sized oil droplets in an aqueous medium in which the oil droplets are covered with the gold nanoparticles. These assemblies are obtained with considerable simplicity and are amenable to capsule sizing and nanoparticle cross-linking methods that are highly desirable in encapsulation strategies. The gold nanoparticle assemblies described here encapsulate hydrophobic liquids and solutes in the oil phase and are relevant for potential applications that utilize the properties of the gold nanoparticles, including their conductive and optical properties as well as their biocompatibility.

The PEGylated gold nanoparticles used in these studies were synthesized in the presence of (1-mercaptoundec-11-yl)tetra(ethylene glycol) (ligand **1**) according to the procedures of Brust and co-workers.[39] These gold nanoparticles are dispersible in water and methanol and at low concentrations in chloroform. Fluid−fluid interfacial assemblies were formed by first dispersing the nanoparticles in water, followed by addition of the organic solvent as the minor phase, to give a ~1:10 ratio of organic solvent-to-water. This mixture was shaken vigorously by hand to give spherical droplets ranging in diameter from 60 to over 200 μm. As seen in Figure 1, the droplets formed by this process are visible by confocal laser scanning microscopy when coumarin 153 (a hydrophobic dye) is present in the organic phase. Gold nanoparticles covered with PEG-OH ligand **1** proved exceptionally effective in this oil−water interfacial stabilization process with any of a variety of organic solvents, including, for example, hexanes, ethyl acetate, perfluorodecalin, 1,2,4-trichlorobenzene (TCB), and toluene. Chloroform was the only solvent tested that proved incompatible with this interfacial segregation due to an appreciable dispersion of the PEGylated gold nanoparticles in chloroform. PEGylated gold nanoparticles with different chain ends were also found to segregate to the oil−water interface. For example, (1-mercaptoundec-11-yl)tetra(ethylene glycol) trimethylammonium methanesulfonate,[40] ligand **2**, was used to functionalize gold nanoparticles by ligand-exchange chemistry on the PEG-OH (**1**-covered) particles. These ammonium-functionalized gold nanoparticles were found to segregate to the oil−water interface, also giving oil droplets in water, with numerous organic solvents (including chloroform, unlike the PEG-OH case). While the positively charged particles were found to assemble at the oil−water interface, the assemblies were not stable for long time periods (hours as compared to weeks for the PEG-OH case). These assemblies are being investigated further for the effects of charge in the ligand periphery on the stability of interfacial assembly.

Capsules stabilized by gold nanoparticles covered with thiol **1** are stable for at least several weeks without coalescence. Any excess of gold nanoparticles in the major (aqueous) phase can be removed following the initial assembly by exchanging the aqueous solution with pure water. These nanoparticle assemblies can then be dried on different substrates for further characterization. Figure 2a shows a transmission electron microscopy (TEM) image of a nanoparticle-stabilized droplet dried on a carbon-coated copper grid. The low magnification TEM image shows the edge of one droplet following drying. No nanoparticles are observed outside of the droplet structure, confirming the adherence of the nanoparticles to the interface during the drying process. At higher magnification, individual gold nanoparticles are seen. It should be noted that the spatial arrangement of the nanoparticles seen in the TEM image does not necessarily reflect the assembly at the oil−water interface; future studies using grazing incidence small-angle

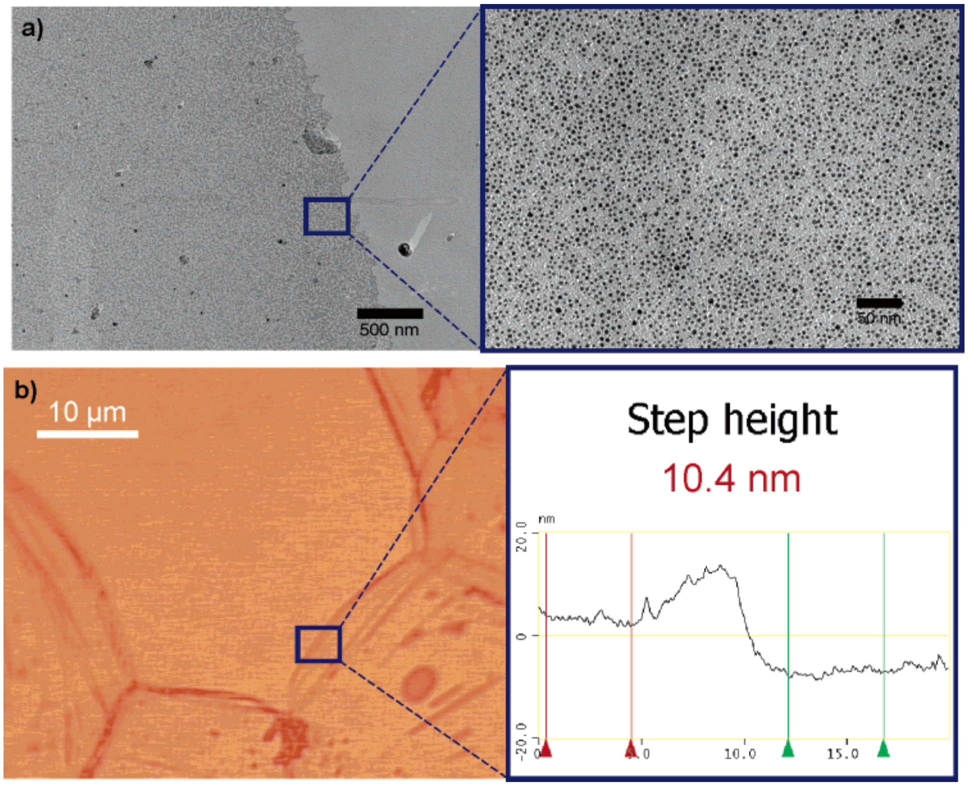

Figure 2. (a) TEM image of a dried droplet of PEG-OH-covered gold nanoparticles, formed initially at the water−TCB interface then dried on a carbon-coated copper grid. Individual nanoparticles are observed in the body of the droplet. (b) SFM image of a dried droplet on a silicon wafer. The observed step height of ∼10 nm corresponds to two nanoparticles plus the surface-bound ligands, confirming the monolayer nature of the interfacial assembly.

X-ray scattering (GISAXS) will probe this aspect of these gold nanoparticle assemblies.

The gold nanoparticle-covered capsules were dried onto a silicon wafer for characterization by scanning force microscopy (SFM), as shown in Figure 2b. The edges of multiple droplets are seen in the image, scanned along the surface of the wafer. Step height analysis reveals that the height from the substrate to the middle of the droplet is approximately 10 nm, which corresponds approximately to the diameter of two nanoparticles and their ligands (the outer edge of the droplet measures higher than 10 nm as a consequence of the drying process). This suggests that the gold nanoparticles had assembled as a monolayer at the oil−water interface. Such clean assemblies are of interest for subsequent nanoparticle exchange at the interface and for understanding the properties of ultrathin sheets composed primarily of nanoparticles.

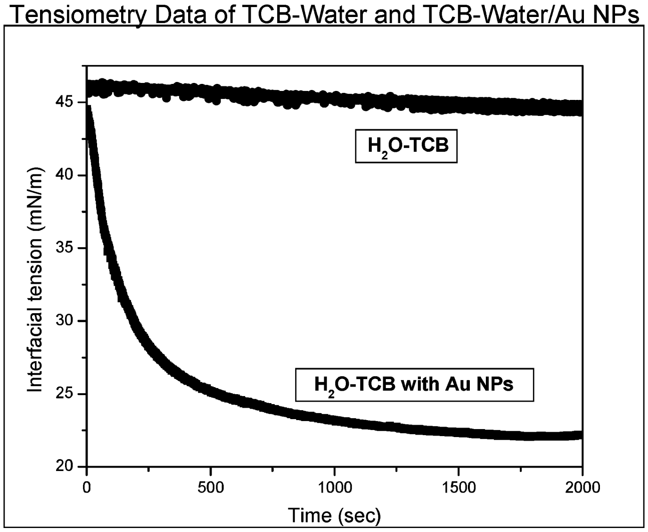

Figure 3. Pendant drop tensiometry measurement on PEG-OH-covered gold nanoparticles at the TCB−water interface. The upper curve represents the interfacial tension between TCB and water, while the downward sloping curve reflects the observed reduction in interfacial tension upon assembly of the nanoparticles at the TCB−water interface.

The effect of the PEGylated gold nanoparticles on measured interfacial tension was evaluated using pendant drop tensiometry, with TCB as the minor (drop) phase and water as the major phase. A drop of TCB was introduced into an aqueous dispersion of nanoparticles, and based on the droplet shape, the interfacial tension between the two fluids is obtained. Figure 3 shows the measured reduction in interfacial tension between TCB and water as a result of introduction of gold nanoparticles covered with PEG-OH ligand **1**. The TCB−water interfacial tension, approximately 45 mN/m initially, fell rapidly upon introduction of the gold nanoparticles, eventually reaching a steady value of ∼22 mN/m. This result is consistent with the theoretical and experimental studies, for example, by Pieranski[29] and Binks and co-workers,[30,31] in which particle assemblies at the interface of immiscible fluids is described as driven by particle mediation of interfacial interactions.

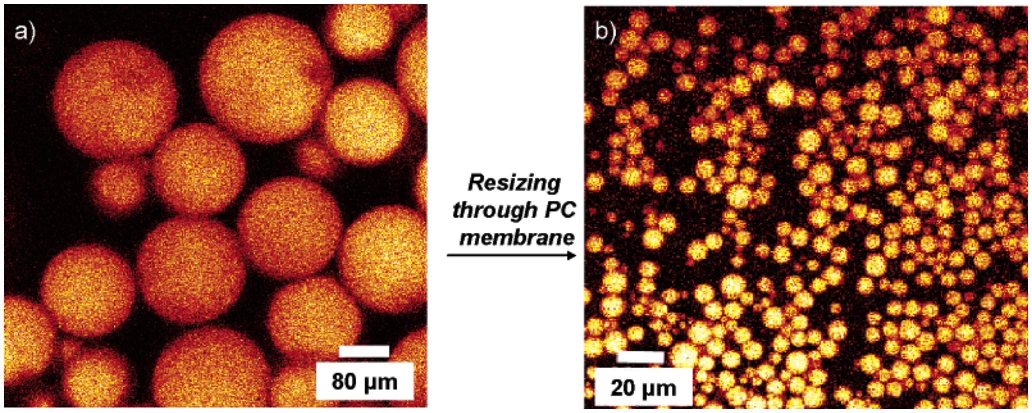

Figure 4. (a) Confocal fluorescence image of vigorously shaken (by hand) assemblies of gold nanoparticles at the TCB−water interface, with coumarin 153 dye in the TCB phase. (b) Confocal image of droplets following extrusion through the polycarbonate track-etch membranes (1 μm pore size membrane, 50 passes).

The gold nanoparticle-coated droplets formed by vigorous shaking possess a broad size distribution, as seen in Figure 1, with most droplets in the 60−200 μm diameter size range. Quantum dot-stabilized droplets, of similar size and size distribution to these gold nanoparticle droplets, can be resized very simply by extrusion through polycarbonate track-etch membranes of known and well-defined pore size.[41] In analogy to sizing methods for vesicles,[42,43] extrusion of the droplets through the small pores imparts forces that exceed the lysis tension of the droplets. However, the interfacial activity of the nanoparticles leads to a reformation of the droplets during extrusion, producing droplets much smaller than those of the original samples and with a more narrow size distribution. As seen in Figure 4, passing gold nanoparticle-coated TCB droplets 50 times through a track-etch polycarbonate membrane containing 1 μm diameter pores reduces their size from the initial 60−200 μm diameter range to <10 μm in diameter. The fluorescent dye in the TCB phase following the extrusion process enables visualization of these smaller nanoparticle-coated droplets by confocal fluorescence microscopy.

To increase the stability of the gold nanoparticle-coated capsules by creating robust capsule walls, small molecules were introduced into the minor (organic) phase for reaction with the chain-end hydroxyl groups of the PEGylated ligands (for **1**-covered nanoparticle assemblies); this process cross-links the assemblies by polymerization at the interface. Ideally, such cross-linking additives would be soluble and reactive from within the minor, encapsulated phase so as to minimize interdroplet cross-linking. In this study, the most suitable system found was a toluene solution of terephthaloyl chloride as the minor phase, which was added to the continuous major phase of **1**-covered gold nanoparticles in water. This is expected to give interfacial polymerization through the ligands that form the capsule wall, cross-linking the assemblies, and providing an aromatic polyester shell about the nanoparticle periphery. To confirm the expected interfacial polymerization, the assemblies formed with terephthaloyl chloride present in the organic phase were observed by optical microscopy initially, then imaged again following addition of methanol to remove the oil−water interface. Washing with methanol caused the spherical structures to collapse into nonspherical but intact capsular structures. When the cross-linking procedure is not performed, the nanoparticles simply disperse in the methanol, and no micron-sized capsules or other objects are observed microscopically. Future studies on these cross-linked capsules of gold nanoparticles will center on their ability to withstand break-up against applied mechanical force as well as their release properties with respect to encapsulated reagents.

In summary, gold nanoparticles with PEGylated ligands, containing either hydroxyl or ammonium chain ends, were found to assemble cleanly at the oil−water interface, with water as the major phase and a variety of organic liquids (with or without dissolved solutes) as the encapsulated minor phase. These nanoparticle assemblies were characterized by a number of microscopic techniques that suggest the monolayer nature of the interfacial nanoparticle assembly and that demonstrate the amenability of the capsules to sizing techniques by extrusion and cross-linking by chemical reactions on the ligand periphery.

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Supporting Information Available: A description of the ligand and gold nanoparticle synthesis is reported, as well as the conditions used for droplet extrusion and characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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