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Polymersomes and Multicompartment Polymersomes Formed by the Interfacial Self-Assembly of Gold Nanoparticles and Amphiphilic Polymers

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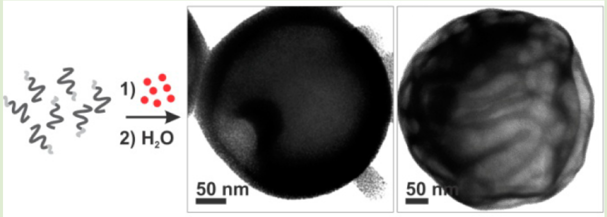
S *Supporting Information*

ABSTRACT: Here, we report the formation of polymer vesicles (polymersomes) uniformly decorated with gold nanoparticles (AuNPs) through the interfacial self-assembly of 11-mercapto-1-undecanol (MUL)-stabilized AuNPs and two prototypical amphiphilic polymers (i.e., polystyrene-*block*-poly(acrylic acid) (PS-*b*-PAA), poly(ethylene oxide)-*block*-polylactide (PEO-*b*-PLA)). The addition of MUL-capped nanoparticles during the self-assembly process was found to stabilize colloidal polymer assemblies that otherwise tend to form macroscopic aggregates in water. Multicompartment polymersomes with complex internal membrane structures were formed at high nanoparticle volume percent, demonstrating that the interfacial assembly of nanoparticles can be used to create interesting new types of polymer assemblies while providing additional functionalities. This strategy offers a simple method for the formation of nanoparticle-loaded polymersomes that is applicable to various types of amphiphilic polymers.

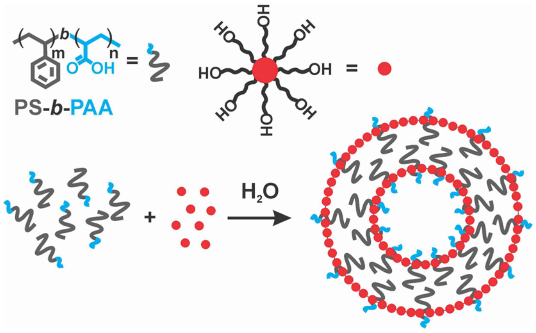


Biological and synthetic vesicles have impacted many areas of science and technology ranging from biophysics to medicine.[1−6] In particular, vesicles made of amphiphilic polymers, so-called polymersomes, are of great interest owing to their stability and chemical diversity.[2,3,7−9] Membrane properties of polymersomes including permeability and fluidity can be controlled by changing the molecular weight and chemical structure of polymers.[7,10,11] Functional molecules such as drugs, near-IR dyes, and MRI contrast agents have been successfully loaded into the polymersome membrane or in the water pool inside the polymersome for drug delivery and bioimaging applications.[8,9,12,13]

As an alternative to the conventional molecular probes, there has been increasing interest in combining the useful membrane properties of polymersomes and unique size-dependent physical properties of inorganic nanoparticles.[14−27] Several different strategies have been developed for the formation of nanoparticle-loaded polymersomes.[18] For example, polymer-grafted nanoparticles have been assembled into polymersomes with nanoparticles located at the center of the polymersome wall[25] or at the interface between the polymersome wall and corona,[15] depending on the polymer composition on nanoparticles. Similarly, we[14] and others[20,28] have shown that ligand-stabilized hydrophobic nanoparticles can be loaded into the membrane of polymersomes.

Here, we report that the simultaneous self-assembly of amphiphilic polymers and quasi-hydrophobic gold nanoparticles (AuNPs) capped with 11-mercapto-1-undecanol (MUL) can lead to the formation of polymersomes decorated with AuNPs at two interfaces between the hydrophobic polymersome wall and the hydrophilic corona (Scheme 1).

Scheme 1. Binary Self-Assembly of Gold Nanoparticles and PS_{149}-*b*-PAA_{49} into Polymersomes



Furthermore, we have fabricated multicompartment polymersomes with highly structured internal morphology based on this approach, demonstrating that the interfacial self-assembly of nanoparticles can induce interesting morphology changes of polymer bilayers while providing additional functionalities.

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In typical experiments, AuNPs capped with MUL were synthesized by a modified Brust method[29,30] and used without surface modification. The diameter of gold particles was determined to be 2.3 ± 0.4 nm. In typical self-assembly, an ethanolic solution of AuNPs (150 μL, 3.05 μM) was slowly added to a 1.5 mL tetrahydrofuran (THF) solution of PS$_{149}$-*b*-PAA$_{49}$ (0.01 wt %) at the rate of 10 μL/30 s. Subsequently, 450 μL of water was added dropwise (10 μL/30 s) to the mixture to initiate the assembly of nanoparticles and polymers. After overnight stirring (15 h), 1.5 mL of water was added over 15 min, and the solution was dialyzed against water (17.9 MΩ). The prepared assemblies were characterized by transmission electron microscopy (TEM), scanning transmission electron microscopy (STEM), and energy-dispersive X-ray spectroscopy (EDS).

This procedure led to a homogeneous dispersion of nanoparticle-loaded polymer assemblies in water as shown in the inset of Figure 1a. TEM images of coassemblies formed at a nanoparticle volume percent of 0.6 vol % and 1.2 vol % revealed that nanoparticles and PS-*b*-PAA assembled into well-defined polymersomes uniformly decorated with nanoparticles (Figure 1, Supporting Information). Individual nanoparticles are clearly visible in polymersomes assembled at low nanoparticle volume percents (Figure S3b, Supporting Information). EDS measurements also confirmed that gold particles are indeed associated with polymersomes (Figure 1c). Similarly shaped dimpled polymersomes were formed when the same polymer was assembled in the absence of gold particles under the same conditions (Figure 1d). On the basis of the interfacial energy calculation,[30] MUL-modified gold particles are expected to locate at the interface between PS and PAA as depicted in Scheme 1 to reduce the interfacial energy between the two polymer blocks. MUL-modified nanoparticles can also favorably associate with the PAA layer through hydrogen bonding.

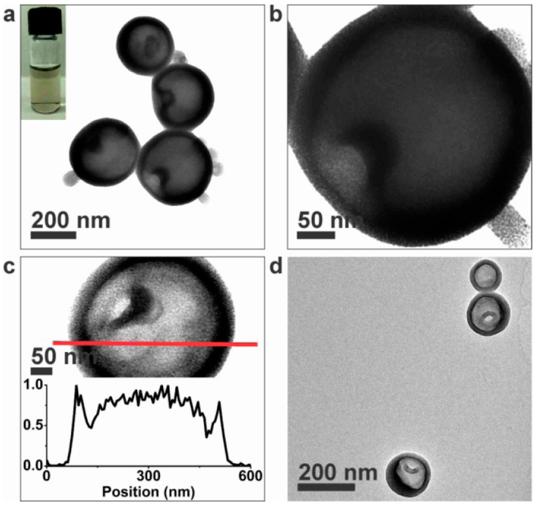

Figure 1. (a, b) TEM images of nanoparticle-decorated polymersomes formed from PS$_{149}$-*b*-PAA$_{49}$ and MUL-stabilized AuNPs at 1.2 vol % of AuNPs. (c) A bright-field STEM image of a nanoparticle-decorated polymersome formed at 1.2 vol % and its EDS Au intensity line profile. (d) A TEM image of polymersomes assembled under the same conditions without AuNPs. The diameters of polymersomes were determined to be 429 ± 129 nm and 239 ± 115 nm for polymersomes with and without nanoparticles, respectively.

The formation of nanoparticle-decorated polymersomes was followed by imaging binary assembly structures at different water contents. As shown in Figure 2, spherical aggregates of nanoparticles and polymers were first formed at low water content (Figure 2b, 48%). A further addition of water led to the formation of large swollen polymersomes decorated with nanoparticles (Figure 2c, 73%). As the water content increases, more particles are expected to be associated with the polymersomes due to the poor water solubility of MUL-stabilized AuNPs (Figure 2d, 100%). The size of polymersomes became smaller with increasing water content as PS packs more tightly to avoid contact with water (Figure 2d, 100%). In this procedure, AuNPs are present both inside and outside of polymersomes. Therefore, nanoparticles can access both inner and outer interfaces of polymersomes as depicted in Figure 2a. This balance is important in stabilizing the polymersome structure. Therefore nanoparticles should be added to the polymer solution before the self-assembly is complete. For example, as an alternative approach, MUL-modified AuNPs were introduced to preformed polymersomes in water to induce the association of nanoparticles with polymersomes, following our recent work.[30] In that study, we have found that the addition of MUL-modified AuNPs to an aqueous dispersion of preformed spherical or rod-shaped polymer micelles resulted in polymer assemblies coated with nanoparticles. This approach, however, was not applicable to polymersomes because nanoparticles cannot travel across the membrane of preformed polymersomes in water. Therefore, they decorate only the outer interface of polymersomes, which causes the deformation of membrane structure and macroscopic aggregation of polymers (Supporting Information).

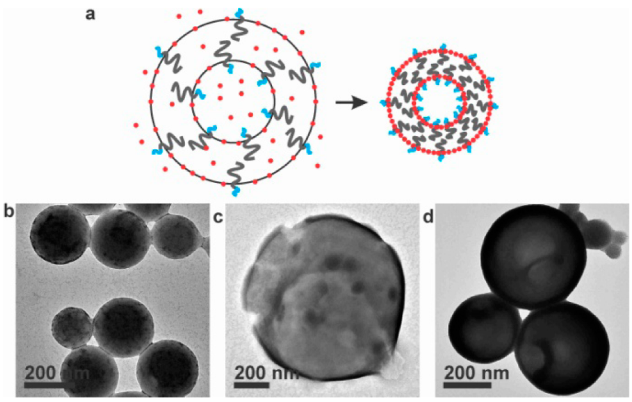

Figure 2. (a) Scheme showing the formation of AuNP-decorated polymersomes by the selective solvent method. (b–d) TEM images of binary self-assembly structures of AuNP and PS-*b*-PAA in water/THF mixtures at different water volume fractions, 48% (b), 73% (c), and 100% (d). The volume fraction of AuNP to polymer was 1.2%.

Interestingly, polymersomes with highly structured internal membranes were formed at high nanoparticle volume fractions (2.4 AuNP vol %), as shown in Figure 3. The nanoparticle-induced formation of these "multicompartment polymersomes" is highly reminiscent of how the binding of membrane proteins induces changes in the curvature and shape of biological cell membranes.[31] A different type of structured vesicles, called large compound vesicles, has been previously prepared by Eisenberg and co-workers[32] by the addition of acids (e.g., HCl) or ions (e.g., $CaCl_2$) during the self-assembly process of PS-*b*-PAA. In that, the formation of large compound vesicles was attributed to the agglomeration of small vesicles by the reduction of electrostatic repulsion of PAA chains. For

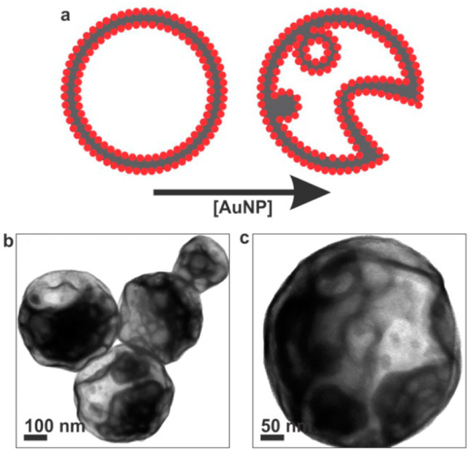

Figure 3. Formation of multicompartment polymersomes with AuNPs. (a) Scheme representing formation of multicompartment polymersomes at increased AuNP concentrations. (b,c) TEM images of coassembly of AuNPs and polymers at a AuNP volume fraction of 2.4%.

nanoparticle additives used in our study, a different mechanism appears to induce the formation of complex membrane structure of polymersomes. We hypothesize that the multicompartment polymersomes are formed at high nanoparticle volume fraction to accommodate the excess amount of nanoparticles at the PS/PAA interface, as multicompartment polymersomes with high local curvature possess a larger interfacial area than regular polymersomes. The relative volume change of the two polymer blocks by the addition of nanoparticles might also contribute to the morphology change. In this mechanism, the addition of nanoparticles increases the relative PAA volume fraction (f_{AA}) through the hydrogen bonding between MUL-modified nanoparticles and PAA chains, which favors the formation of high curvature structures. Previous thin-film studies showed similar phenomena where the addition of nanoparticles forming hydrogen bonds with one polymer block resulted in morphology changes from low curvature structures such as lamella to higher curvature structures such as cylindrical assemblies.[33,34]

This approach should be readily applicable to other types of amphiphilic polymers including biocompatible polymers. To demonstrate this capability, a widely used degradable polymer, poly(ethylene oxide)-*block*-poly(lactide) (PEO-*b*-PLA), was used for the binary self-assembly with MUL-capped AuNPs (Figure 4). Cryo TEM images revealed that nanoparticles and PEO_{45}-*b*-PLA_{83} assembled into well-defined polymersomes as expected (Figure 4). It is interesting to note that without nanoparticles PEO_{45}-*b*-PLA_{83} tends to form large irregular aggregates that precipitate out of solution when the same procedure was used for self-assembly (Supporting Information). This result indicates that MUL-modified AuNPs with an intermediate solubility can be used as an effective stabilizer for colloidal polymer assemblies.[35−37]

In summary, we demonstrated that the interfacial self-assembly of AuNPs can be used to prepare polymersomes loaded with nanoparticles. The addition of MUL-stabilized AuNPs was shown to stabilize colloidal polymer assemblies and prevent the formation of macroscopic polymer aggregates. We found that nanoparticles should be introduced in such a way that they can access both inner and outer interfaces of polymersome membranes for successful interfacial assembly. Furthermore, multicompartment polymersomes with complex internal structure were formed at high nanoparticle loading percents. The nanoparticle-induced morphology change was attributed to the large interfacial area created by the formation of high curvature internal structure, which can accommodate the excess amount of nanoparticles. This strategy should be applicable to various amphiphilic polymers and nanoparticles, providing a facile way to prepare and stabilize nanoparticle-loaded hollow polymer assemblies.

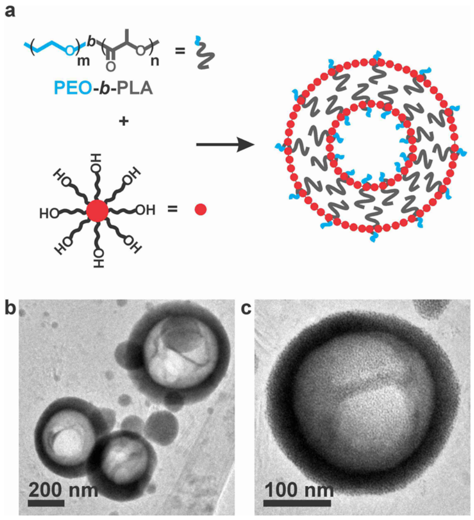

Figure 4. (a) Scheme depicting simultaneous self-assembly of AuNPs and PEO_{45}-PLA_{83} into polymersomes. (b, c) Cryo-TEM images of AuNP-decorated PEO_{45}-*b*-PLA_{85} polymersomes formed at AuNP volume fraction of 1.2%.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Detailed experimental procedures, additional TEM images, and dynamic light scattering data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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