Self-Assembly

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Micelle and Vesicle Formation of Amphiphilic Nanoparticles**

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Amphiphilic molecules such as surfactants or lipids spontaneously self-assemble into micelles or vesicles. This self-assembly principle has been shown to be generally applicable to organic molecules, as it can also be used with amphiphilic polymers,[1,2] dendrimers,[3] and fullerenes.[4] Amphiphilicity as a self-assembling principle can, in theory, be also applied to inorganic particles to provide a new and simple route for a controlled self-assembly of such particles into one-, two-, and three-dimensional structures. In the particular case of inorganic nanoparticles, controlled self-assembly in solution has so far been possible only by the attachment of template molecules such as DNA,[5] proteins,[6] or specific polymers.[7–9]

The structures that result from the amphiphilic self-assembly of amphiphilic molecules are determined by the interfacial energy of the hydrophilic–hydrophobic interface and the repulsive energy of the hydrophilic groups. When considering amphiphilic particles, the most general design rules for self-assembly are twofold: 1) the hydrophobic and hydrophilic parts should be of comparable volumes in order to balance interfacial and repulsive energy and 2) the amphiphilic particles should have some structural flexibility so that they can adjust to the different geometries of the superstructures. These requirements can be met by using amphiphilic nanoparticles consisting of a hydrophobic, that is, water-insoluble, inorganic core, together with a brushlike layer of hydrophilic polymer chains. The number and length of the chains can be adjusted so that the hydrophilic volume is comparable to the volume of the hydrophobic nanoparticle. In this simple picture, the nanoparticle–polymer conjugate acts as an integral unit capable of self-assembling into different superstructures.

The structures that result from amphiphilic self-assembly can be rationalized in terms of the packing parameter P, which is defined as $P=\frac{V}{AL}$, where V is the volume and L the length of the hydrophobic part of the amphiphile, and A the hydrophobic–hydrophilic interfacial area.[5,6] As the value of P increases, spherical ($P=1/3$), cylindrical ($P=1/2$), and planar structures ($P=1$) are formed. At intermediate values of $1/2<P<1$, saddle-type interfaces can occur by the development of Y junctions between cylinders, and lead to the formation of cylinder networks.[7] For amphiphilic nanoparticles, V and R correspond to the volume and the radius of the particle. The shape of the self-assembled structure for a given nanoparticle is then solely determined by the surface area per hydrophilic polymer chain A, which is inversely proportional to the surface density of the chains.

We investigated the self-assembly of CdSe/CdS core–shell nanoparticles with a brushlike layer of polyethylene oxide (PEO) chains. The PEO chains have amino ligands at their chain end that bind to the nanoparticle surface. The PEO chains are bound to the nanoparticles by a ligand exchange reaction in which the hydrophobic trioctylphosphine/trioctylphosphine oxide (TOP/TOPO) ligands that result from the synthesis of the nanoparticles are exchanged for the PEO chains (details of the procedure are given in the Supporting Information).[8] The procedure allows the variation of the polymer-chain surface density through the ratio r_{pm} of the number of polymer chains to the number of nanoparticles employed during the ligand exchange process, and also the binding strength of the ligand. The r_{pm} value was varied between 100 and 1200, which resulted in approximately 50–200 bound polymer chains per nanoparticle as estimated from TEM images of nanoparticle monolayers (see the Supporting Information). Three different ligands with either three (diethylentriamine, PEO–N3), six (pentaethylenehexamine, PEO–N6), or ten (branched polyethyleneimine, PEO–PEI) amine groups were investigated, which bind more strongly to the nanoparticle surface as the number of amine groups increases.

A series of TEM images of the structures that are spontaneously formed by 3.4 nm CdSe/CdS nanoparticles with bound PEO–N3 chains when the r_{pm} value is decreased from 1200 to 150 are shown in Figure 1. At a high ratio of $r_{pm}=1200$, that is, high polymer surface densities, single nanoparticles are observed. At a ratio of $r_{pm}=600$, the mean distance between the nanoparticles still decreases, with a tendency to form dimers and trimers. At an even lower ratio of $r_{pm}=300$, a considerable number of string-type or cylindrical aggregates with up to ten nanoparticles are formed, while single nanoparticles are still present. At $r_{pm}=150$, all nanoparticles are aggregated and form extended wormlike strings with occasional Y junctions that connect them into a network. An overview of the network structure can be seen in Figure 1e and in cryoTEM images of the same samples in Figures 1 f–h. The formation of vesicles is observed at the

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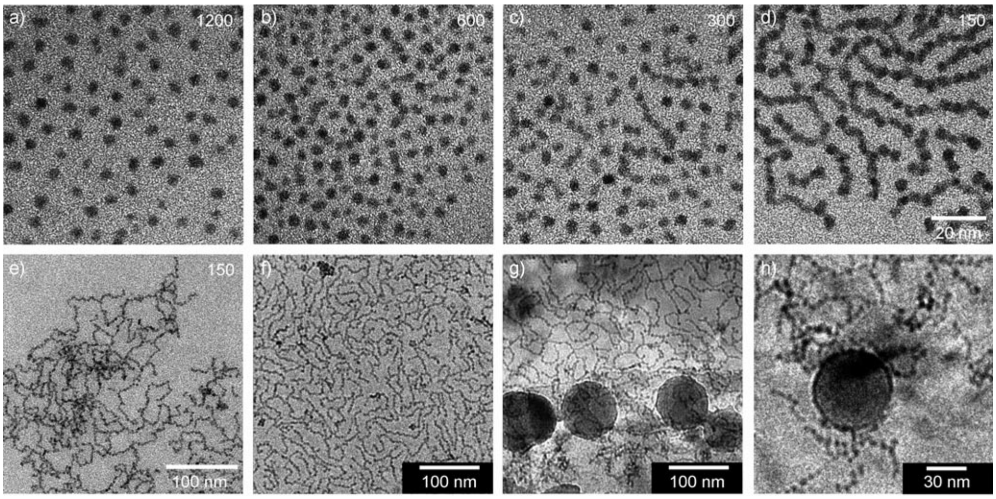

Figure 1. Series of TEM (a–e) and cryoTEM (f–h) images of structures formed by spontaneous self-assembly of amphiphilic CdSe/CdS nanoparticles with bound PEO-N3 chains. Polymer/nanoparticle ratios are given in the top-right corner of the images. As the polymer/nanoparticle ratio is decreased, the formation of short cylinders, networks, and vesicles is observed.

lowest ratios (Figures 1 g,h). The vesicles have diameters of 70–80 nm and consist of a monolayer of nanoparticles. Wormlike structures extrude from the vesicles at several locations, which is very similar to the structures of block-copolymer vesicles.[7] Confocal microscopy (CLSM) images of giant nanoparticle vesicles formed by two different PEO–PEI-stabilized CdSe/CdS nanoparticles are shown in Figure 2.

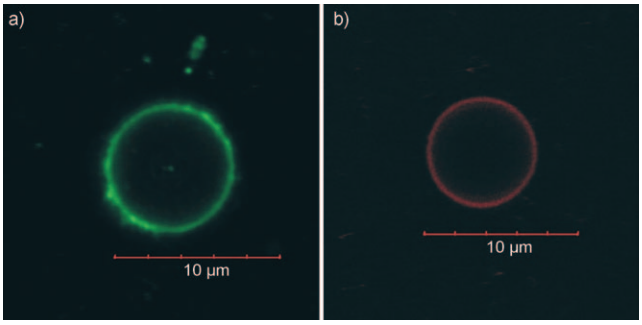

Figure 2. Confocal laser scanning microscopy (CLSM) images of vesicles formed by spontaneous self-assembly of a) 2.6 nm and b) 3.1 nm CdSe/CdS core–shell nanoparticles stabilized by PEO–PEI ligands at polymer/nanoparticle ratios of 375 (a) and 400 (b). The fluorescence of the vesicle walls can be clearly observed.

These experiments demonstrate that amphiphilic nanoparticles undergo surfactant-like self-assembly. When the polymer/nanoparticle ratio is decreased, that is, the surface area A is increased, a structural sequence of spheres→ cylinders→networks→vesicles is observed, which exactly parallels the behavior known for surfactants and lipids, except that the vesicle wall consists of a nanoparticle monolayer instead of the bilayer structure known for liposomes. The observed nanoparticle self-assembly does not require anisometric molecular shapes as in the case of amphiphilic surfactants, lipids, polymers, or dendrons. In this respect it parallels the behavior reported for vesicle-forming fullerenes.[4]

The mechanism for the formation of string-type and vesicular aggregates is shown schematically in Figure 3. For high surface densities (Figure 3 a), that is, at high r_{pm} values, the polymer chains form a dense spherical brush that provides steric stabilization. If the surface density is lowered (Figure 3 b), the nanoparticles aggregate into stringlike structures where the polymer chains reorganize to form a dense cylindrical brush that prevents further aggregation. The formation of vesicles occurs by coplanar aggregation of the nanoparticles with the formation of planar brushes.

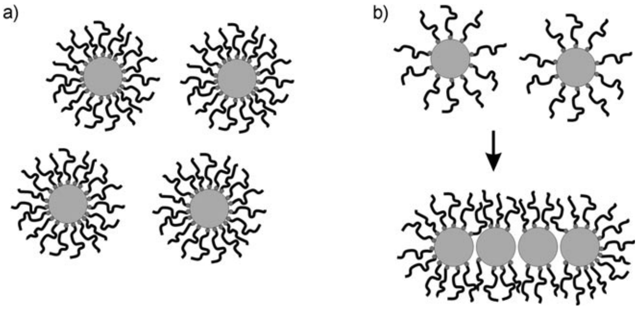

Figure 3. Schematic representation of the spontaneous self-assembly of amphiphilic nanoparticles consisting of a hydrophobic core with bound hydrophilic polymer chains. a) A high surface density of bound polymer chains prevents aggregation whereas lower surface densities lead b) to association into stringlike structures. Reorganization of the polymer chains into a cylindrical brush increases the surface density and prevents further aggregation.

The aggregation process shown in Figure 3 b requires a reorganization of the polymer chains, specifically, a depletion of polymer chains between adjacent nanoparticles. In order to determine the proximity of adjacent nanoparticles in a stringlike aggregate, we performed high-resolution TEM experiments. The arrangement of 3.4 nm nanoparticles within a stringlike aggregate is shown in Figure 4. In many instances, near-surface contact between adjacent nanoparticles is observed (see the expansion in Figure 4 b), which indicates a considerable relocalization of polymer chains from the contact area between adjacent nanoparticles to the surface of the stringlike aggregate. This structural flexibility is an important requirement for the formation of cylindrical and vesicular structures.

In summary, we have demonstrated that amphiphilic nanoparticles consisting of a hydrophobic nanoparticle and a

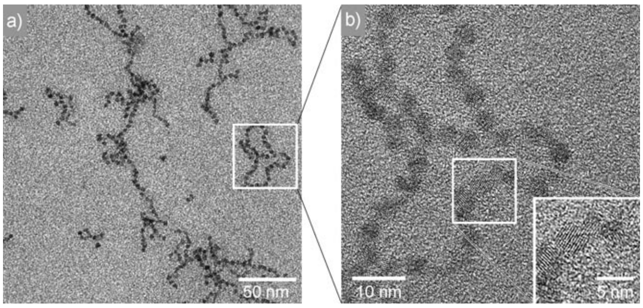

Figure 4. Local arrangement of nanoparticles within stringlike aggregates. a) TEM and b) HRTEM images showing adjacent nanoparticles with near-surface contact.

brushlike hydrophilic polymer shell can self-assemble into spherical, cylindrical, and vesicular structures in dilute solution. The self-assembly can be driven by the surface density of bound polymer chains. It parallels the known self-assembly behavior of surfactants and lipids and provides a new and simple route for the controlled spatial assembly of nanoparticles and polymers. Immediate possibilities involve the preparation of nanoparticle hybrid vesicles that provide encapsulation and imaging contrast for therapeutic and diagnostic applications, and the formation of ordered lyotropic phases for the preparation of nanostructured hybrid materials.

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