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Vesicles Formed from a Poly(ethylene oxide)−Poly(propylene oxide)−Poly(ethylene oxide) Triblock Copolymer in Dilute Aqueous Solution

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Micelle formation of block copolymers in selective solvents (organic solvent or water) has been studied for many years.[1−3] The morphology of polymeric micelles has been the subject of more recent investigations both theoretically and experimentally.[4−8] Diblock copolymers with a long soluble block compared to the nonsoluble block may self-assemble into micelles of a starlike structure while copolymers with a short soluble block often form so-called crew-cut micelles.[3,9]

One class of water-soluble block copolymers that has attracted great interest in the literature is the triblock copolymers of poly(ethylene oxide) (PEO) and poly(propylene oxide) (PPO), often abbreviated as PEO−PPO−PEO or $EO_a-PO_b-EO_a$. These copolymers exist in a wide range of different compositions and display a rich phase behavior in water depending on their relative block lengths.[10,11] It is well established that the more hydrophilic copolymers associate into micelles, composed of a PPO core and a PEO corona, with a spherical or rodlike shape depending on temperature.[7,12−14]

The present work focuses on the investigation of one of the most hydrophobic PEO−PPO−PEO copolymers (L121) in dilute water solutions. New interesting structures found in the L121/water system are presented and visualized by the cryogenic transmission electron microscopy (cryo-TEM) technique. For the first time, to our knowledge, unilamellar vesicles are shown to exist in a triblock copolymer system of this type. Vesicles of branched PEO−PPO block copolymers in water have only been predicted as a metastable state in earlier model calculations.[15]

There are only a few reports in the literature on vesicle formation of diblock and multiblock copolymers in dilute solutions of selective solvents.[16−21] Vesicles were one among several different crew-cut aggregates found in polystyrene−poly(acrylic acid) (PS−PAA) and PS−PEO diblock copolymer aqueous systems.[9] These vesicular aggregates were prepared by a dialysis method. Both copolymers form so-called glassy vesicles, which are preserved in water since the water-insoluble PS block is in a glassy state at ambient temperatures. However, a recent study on a polybutadiene−PAA (PBD−PAA) copolymer/water system has concluded that the vesicular morphology is not controlled by the glass temperature of the nonsoluble block.[22] Other publications have reported the existence of multilamellar block copolymer vesicles in a homopolymer-rich matrix as a selective solvent and in a concentrated ternary block copolymer system exposed to a shear flow.[23−27]

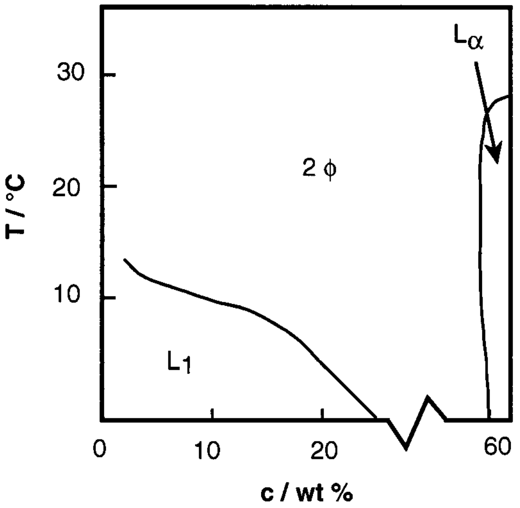

Figure 1. Schematic phase diagram of L121 in water. The vesicles were prepared in the two-phase region (2ϕ) at 25 °C from aqueous L121 solutions with concentrations of 0.2, 0.4, 0.6, and 1.2 wt %.

This communication presents a different and new preparation procedure of block copolymer vesicles than described in earlier work. The method uses an extrusion method often utilized for the preparation of single-tailed and double-tailed surfactant (or lipid) vesicles, during which the dispersed bilayers close into a spherical structure with a water interior.[28] The formation of unilamellar surfactant vesicles normally requires the input of energy by extrusion, ultrasonication, or dialysis, although it has been suggested that they may form spontaneously in some mixed cationic and anionic surfactant systems.[29]

The PEO−PPO−PEO triblock copolymer, denoted Pluronic L121, was a gift from BASF corporation and used without further purification. It has a nominal molecular weight of 4400 g/mol, and the average composition is $EO_5PO_{68}EO_5$, which corresponds to 10 wt % of PEO. L121 copolymers do not form micelles. At low concentrations and temperatures, unimers (individual copolymer chains) coexist with larger unimer aggregates (an L_1 phase). The hydrodynamic radii (R_H) of the unimers and the aggregates, obtained using dynamic light scattering (DLS) at 10 °C, are 1.9 and 44 nm, respectively. Figure 1 displays one part of the binary phase diagram of L121 in water.

Because of the short hydrophilic PEO chains, and therefore the small headgroup area, the copolymers can easily pack into a lamellar phase (L_α) which appears at higher copolymer concentrations (>55 wt %). The lamellar phase boundaries, as preliminary determined by small-angle X-ray scattering (SAXS), are also indicated in the figure. At low concentrations and at ambient temperatures, the system phase separates, and the phase separation curve determined by visual inspection is shown in Figure 1. The two-phase region is an equilibrium between the lamellar phase and the L_1 phase. The L121 block copolymer vesicles were prepared at 25 °C from dilute block copolymer solutions in this L_1/L_α two-phase regime by repeated extrusion of the

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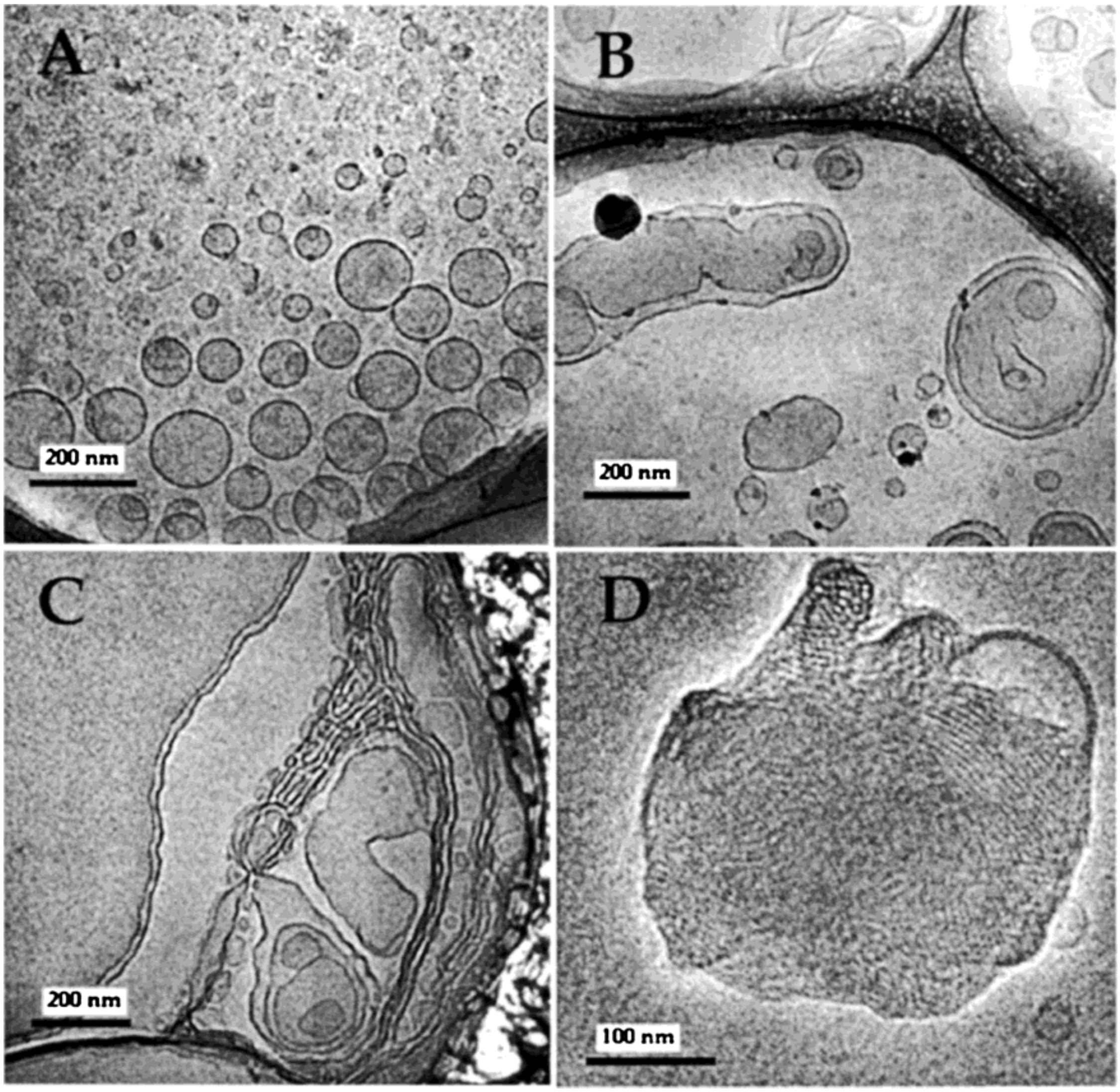

Figure 2. Cryo-TEM images of aqueous solutions of L121 block copolymer extruded through a 100 nm diameter filter: (a) spherical unilamellar vesicles, (b) elongated two-lamellar vesicles, (c) multilamellar structures, (d) L121 aggregate with a lamellar structure. Block copolymer concentrations: (a, b) 0.2 wt %, (c) 1.2 wt %, (d) 0.6 wt %. The vitrified samples were prepared at about half an hour after extrusion.

solutions through a 100 nm diameter membrane filter. Water solutions of L121 with concentrations of 0.2, 0.4, 0.6, and 1.2 wt % were individually prepared and kept at 25 °C for 1−2 days before the extrusion. This equilibration time is of great importance. For instance, no vesicles were formed when the extrusion was carried out on freshly mixed block copolymer solutions. This indicates that the dispersed L121 lamellar flakes need to have a minimum equilibrium size in order to be able to close into a vesicular structure. The amount of input energy is also crucial. The use of ultrasound instead of extrusion did not result in vesicle formation. Since an external input of energy is necessary for vesicles to form, they are nonequilibrium (or metastable) structures. As will be shown, they are flexible and may adopt nonspherical shapes.

Cryo-TEM is now a well-established technique for direct imaging of the original microstructures present in dilute liquid systems by the use of rapid vitrification of the samples. It is relatively free from artifacts that are normally found when using staining methods and is described elsewhere.[30] The vitrified samples were examined in a Philips CM 120 BioTWIN electron microscope, and the electron micrographs were recorded digitally.

Figure 2 shows four different examples of structures found in the vitrified samples of the extruded PEO−PPO−PEO triblock copolymer solutions.

Extrusion of lowest L121 concentrations (0.2 and 0.4 wt %) resulted in spherical and unilamellar vesicular structures, seen as dark rings in Figure 2a. The triblock copolymer vesicle consists of a polymer layer, with a PPO interior shielded by PEO layers on each side, that encloses a water compartment.[31] Due to the similar electron density of PEO and PPO, it is difficult to distinguish the thin PEO corona layer from the PPO core region of the vesicles in the images. DLS measurements on freshly prepared dilute vesicle solutions indicate an apparent vesicle R_H of 57 nm, which corresponds well with the mean radius of the vesicles in Figure 2a. A few two-lamellar or multilamellar vesicles were found, the shape and size of which varied substantially within one dispersion (Figure 2b).

Only rarely were aggregated vesicles observed (data not shown). Multivesicular aggregates or large compound vesicles (LCV) have recently been shown to exist

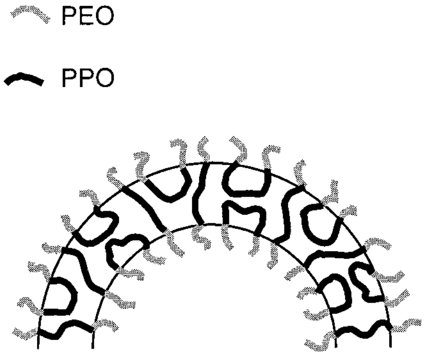

Figure 3. A schematic picture of a PEO−PPO−PEO vesicle wall. The relative length scale of the polymer chains and the vesicle curvature are not representative.

in PS−PAA, PS−PEO, and polyisoprene−poly(2-cinnamoylethyl methacrylate) systems.[18,32−34] The morphology of the LCV's has been described as resembling aggregated soap bubbles, which agrees well with the aggregated vesicles observed in this system. However, it is not clear whether they are of the same stable nature as the LCV's found in the PS−PAA/water systems. According to Eisenberg et al., the LCV's form spontaneously when collisions between vesicles are more frequent than the fusion process and when the repulsion between the coronal layers of the vesicles is weak.[9,33] This may also be true for the PEO−PPO−PEO vesicles discussed here. It is expected that the formation of aggregated vesicles is facilitated at higher L121 concentrations. Within these aggregates, the vesicles start to fuse to create a less curved vesicle wall, and finally structures such as those shown in Figure 2c are formed. The system tends to revert to its initial state as a dispersed L_α phase in equilibrium with an L_1 phase, which is confirmed by the turbidity results discussed below.

Figure 2d exemplifies a highly ordered lamellar aggregate found at higher L121 concentrations. The thickness of a lamella within the aggregate has the same magnitude of thickness as the vesicle wall; see Figure 2a. Similar lamellar aggregates have also been observed, using TEM, in a PS−PAA/water system.[17] From the mass thickness contrast in the cryo-TEM images, the apparent wall thickness of the L121 vesicles was estimated to be 3−5 nm, which is comparable to the wall thickness of a lipid vesicle.[35] The PS−PAA, PS−PEO, and PBD−PAA diblock copolymer vesicles have a much greater wall thickness (about 25 nm).[22,33,34]

A slice of a triblock copolymer vesicle wall is schematically depicted in Figure 3. The picture suggests the possibility that the copolymer chains can fold, still keeping the hydrophobic PPO block away from the water outside of and inside the vesicle and with the hydrophilic PEO blocks protruding out from the wall on both sides. Packing arguments may predict that the amount of folded copolymers is lower toward the interior of the vesicle. Noolandi and Linse have suggested that there is an increased probability of finding both PEO end segments on the same side of the PPO domain with an increased hydrophobic domain size of a block copolymer lamellar phase.[36,37] Here, the apparent wall thickness is about 5 times smaller than a completely zigzag stretched hydrophobic block of 68 PO units (ca. 24 nm)[38] which would make it possible for a majority of the polymer chains to span the vesicle wall.

The time stability of the L121 vesicles at 25 °C was investigated by turbidity (τ) measurements performed on a Perkin-Elmer Lambda 14 UV−vis double-beam spectrophotometer at a wavelength of 633 nm with a simultaneous subtraction of the background using pure water ($\tau = A \ln 10$, where A is the absorbance). The absorbance recording started immediately after extrusion of a 0.2 wt % L121 solution of dispersed lamellar phase and continued over a time period of 3.5 h (Figure 4).

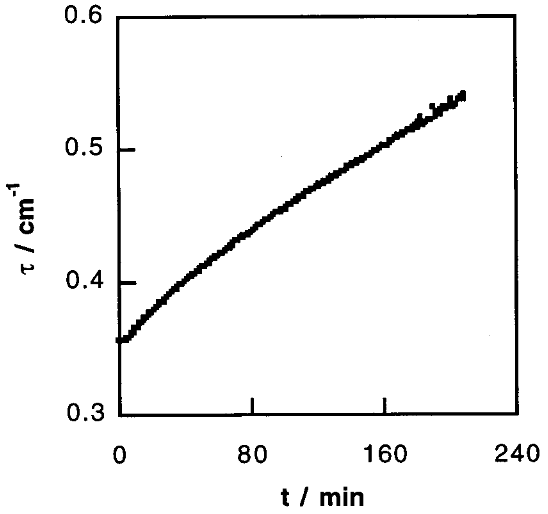

Figure 4. Turbidity (τ) at 633 nm of L121 block copolymer vesicles in water as a function of time. The measurements started directly after extrusion of a 0.2 wt % L121 solution.

It may be noted that the turbidity increases by approximately 50% within the chosen time interval, which shows that these vesicles are not thermodynamically stable. The increase may be due vesicle aggregation and/or the breakup of the vesicles with subsequent formation of aggregated flakes such as those shown in Figure 2c,d. Preliminary DLS measurements show a continuous broadening of the size distribution already half an hour after extrusion. It is concluded that, after a sufficiently long time, the vesicle solution eventually reverts to its original state as a dispersed lamellar phase in equilibrium with an L_1 phase. A fuller investigation of the effect of additives on the stability of these and other triblock copolymer vesicles will be reported in a future publication.[39]

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