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Communications to the Editor

Vesicle Membrane Thickness in Aqueous Dispersions of Block Copolymer Blends

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Amphiphilic block copolymers are known to self-assemble into various geometries when placed into a selective solvent, including bilayered vesicles, wormlike micelles, and spherical micelles.[1−4] While each of these morphologies has received interest for biomedical applications (e.g., drug delivery, medical imaging),[5−7] vesicles in particular are exciting due to their ability to incorporate both hydrophilic and hydrophobic moieties in the hollow solvent-filled core and the membrane wall, respectively.[8−11] In addition, the ability to conjugate bioactive structures, such as peptides, to the hydrophilic corona chain offers a window to bioselective delivery applications.[12] It is not unreasonable to expect the binding efficiency of these peptide conjugated materials to depend on the extent to which the peptide ligand extends beyond the corona brush. With this in mind, it may be beneficial to design a vesicle with two distinct corona chain lengths, with the peptide conjugated to the larger of the two. This can be accomplished by blending a high and low molecular weight block copolymer of similar chemical composition. Since the addition of a peptide to the system would increase the complexity, it is important to understand the behavior of binary blends of nonconjugated vesicle forming block copolymers in aqueous solution so that abnormal behavior can be isolated. While dispersions of copolymer blends have been investigated elsewhere, these studies often concern highly asymmetric blend compositions,[13−15] chemically dissimilar polymers,[16,17] or differing molecular architecture.[18] Here, the focus is on two chemically and compositionally similar diblock copolymers of differing molecular weights that form vesicles when dispersed in water. To probe this behavior, the well-studied system of poly(ethylene oxide)−poly(1,2-butadiene) (OB)[15] was chosen. One parameter certain to vary with blend composition is vesicle membrane thickness, which is an important constraint in designing embeddable hydrophobes for various applications.[20,21] Membrane thickness has been reported in many studies to vary as a power law with hydrophobic core block molecular weight for pure block copolymers, although there is some debate as to the correct scaling exponent.[22−24]

The OB block copolymers used in this study were synthesized using a two-step living anionic polymerization scheme described in detail elsewhere.[25] This resulted in two polymer products: OB3 (M_n = 5.0 kDa, PDI = 1.08, w_{eo} = 0.26) and OB14 (M_n = 18.0 kDa, PDI = 1.03, w_{eo} = 0.25), both expected to fall within the window of vesicle formation on the OB phase diagram. Molecular weights and weight fractions were determined by ^{1}H NMR spectroscopy. Aqueous blend samples were prepared using a premixing procedure in which specific amounts of OB3 and OB14 were dissolved in dichloromethane and the solvent removed, resulting in a thin film of mixed block copolymer. After annealing in a vacuum oven at 40 °C for 12−16 h, samples were hydrated to 1 wt % solutions with HPLC grade water and stirred at 45 °C for 2 weeks. This method of preparation ensures a uniform population of polymer micelles.[15] Characteristics of the blend samples used in this study are given in Table 1. Aqueous solutions were characterized by cryogenic transmission electron microscopy (cryo-TEM) on a JEOL 1210 microscope operating at 120 kV, allowing a direct visualization of the morphological behavior of the blend samples. As illustrated in Figure 1a,b, cryo-TEM confirms the formation of vesicles for both OB3 and OB14, with the higher molecular weight OB14 naturally having a thicker membrane. Interestingly, cryo-TEM of aqueous blend samples prepared from these two vesicle forming block copolymers reveals a mixture of vesicles and cylindrical micelles (Figure 1c,d). While polymorphism is not uncommon in block copolymer surfactant systems, the effect appears to be exacerbated by the inherent polydispersity induced by the blending of two narrow PDI block copolymers despite keeping the overall weight fraction of each block constant. A full discussion of this effect is outside the scope of this study; it should be noted, however, that the number of cylindrical

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Table 1. Characteristics of the OB14/OB3 Blends

blend	x_{OB14}[a]	d (nm)[b]	$2R_c$ (nm)[c,d]	PDI[e]
OB3	0	12.0 ± 0.6		1.08
14_3_10	0.10	15.0 ± 1.0	28.7 ± 0.9	1.44
14_3_20	0.20	19.5 ± 1.1	34.0 ± 2.0	1.52
14_3_30	0.30	21.8 ± 1.5	41.7 ± 1.5	1.50
14_3_40	0.40	24.5 ± 0.7	43.1 ± 1.8	1.44
14_3_50	0.51	24.6 ± 1.4	45.3 ± 1.9	1.36
14_3_60	0.59	25.3 ± 1.0	44.9 ± 1.5	1.29
14_3_70	0.68	25.9 ± 1.3	47.6 ± 1.0	1.23
14_3_80	0.82	28.3 ± 0.9	49.7 ± 0.4	1.14
14_3_90	0.87	28.7 ± 1.0	51.3 ± 0.9	1.10
OB14	1	29.2 ± 1.4		1.03

[a] Mole fraction of OB14 in the blend. [b] Vesicle membrane thickness as determined using cryo-TEM. [c] Cylindrical micelle core diameter as determined using cryo-TEM. [d] As cylinders are the less prevalent morphology, fewer measurements were taken than for vesicles. [e] Polydispersity index for pure block copolymers determined by size exclusion chromatography. Polydispersity index for blends was calculated from measured OB3 and OB14 values.

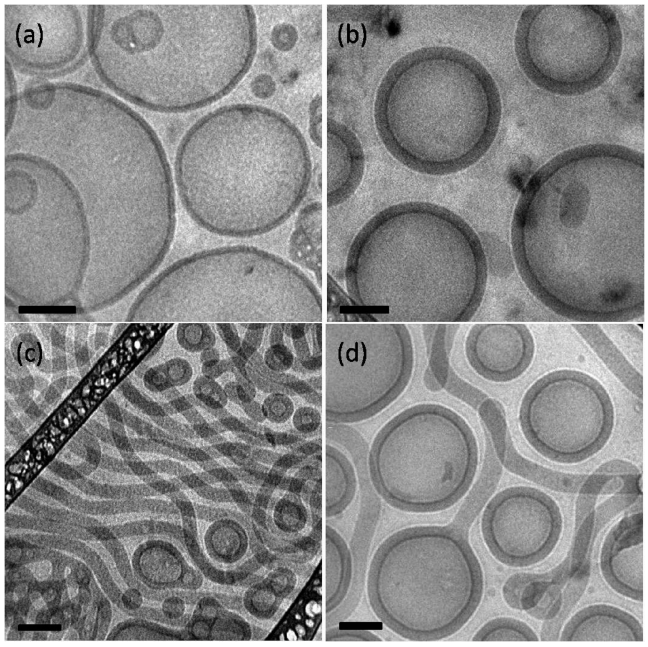

Figure 1. Cryo-TEM images of 1 wt % aqueous dispersions of (a) OB14, (b) OB3, (c) 14_3_20, and (d) 14_3_60. Both block copolymers form vesicles in water due to their low weight fraction of hydrophilic poly(ethylene oxide), while the blend samples show a mixture of vesicles and cylindrical micelles. Cylindrical micelles were less prevalent in the lower PDI samples. Scale bars indicate 100 nm.

micelles observed appears to be directly correlated to the calculated PDI values of the blends, as presented in Table 1. Similar behavior has been predicted elsewhere in simulated systems.[26]

The average values of the vesicle membrane thickness (d) in each blend sample are reported in Table 1. Details on the measurement procedure can be found in the Supporting Information. Although the average degree of polymerization of the poly(butadiene) increases linearly in the blends, the membrane thickness does not follow a simple power law scaling, as would be seen with pure block copolymers. Rather, the membrane thickness increased sharply upon addition of higher MW OB14 to OB3 before leveling off at higher OB14 contents, as shown in Figure 2. We can explain this behavior using the arguments previously presented by Court and Hashimoto,[27] who used the Birshtein, Zhulina, and Lyatskaya (BZL) model[28,29] to describe their experimental results of strongly segregated diblock copolymer blends that form a lamellar morphology in the bulk.

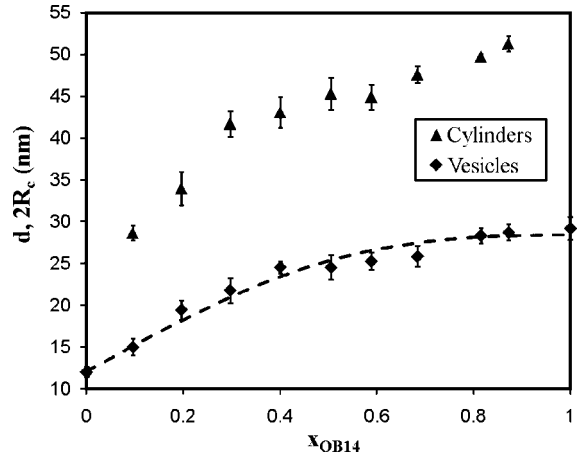

Figure 2. Thickness of the poly(butadiene) core of vesicles and cylindrical micelles as a function of blend composition. The similar behavior of the coexisting morphologies indicates a lack of chain partitioning between domains. The dashed curve represents the BZL theoretical prediction of vesicle membrane thickness.

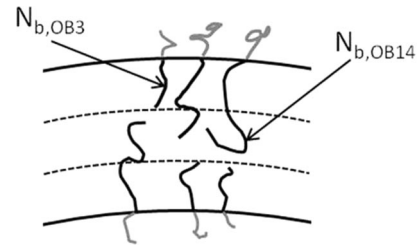

Figure 3. Schematic of the poly(butadiene) chain organization within the vesicle membrane as described by the BZL model. The longer OB14 chains extend beyond the OB3 chains, filling a subdomain. The relative sizes of the subdomains vary upon changing blend composition.

Specifically, the following equation adapted from the work of Court and Hashimoto was used to model the thickness of the PB membrane in our aqueous blend samples:

$$d = d_0\left[1 + x_{OB14}\left(\frac{N_{b,OB14}}{N_{b,OB3}} - 1\right)\right] \times \left[1 + x_{OB14}^3\left(\frac{N_{b,OB14}}{N_{b,OB3}} - 1\right)\right]^{-1/3} \quad (1)$$

where d_0 is the experimentally measured thickness of the OB3 vesicles, $N_{b,OB14}$ and $N_{b,OB3}$ are the degrees of polymerization of the PB block in each block copolymer, and x_{OB14} is the mole fraction of OB14 in the blend. The BZL theoretical prediction is compared to the experimental data in Figure 2. There is strikingly good agreement between the data and theory, suggesting that the long and short PB chains in the blended vesicle membranes are organized in a similar manner as those in lamellar domains formed in binary bulk blends. The model considers polydisperse diblock copolymer chains as a mixture of two sets of monodisperse chains of differing lengths; this approach naturally mirrors experimentally prepared binary blends of monodisperse block copolymers. Two major differences exist between the treatment of the aqueous vesicle system and the previously studied bulk lamellar system. Whereas the BZL model considers both A and B domains in the lamellar A−B diblock copolymer blends, here it is used solely to describe the bilayered PB membrane; this approach is illustrated in Figure 3. This is not a significant difference, as chains A and B are assumed to occupy the same molecular volume and have the same Kuhn length in the BZL model for simplicity. More

importantly, the BZL model assumes a flat interface between A and B domains that is not characteristic of block copolymer vesicles. The presence of curvature in the experimental system likely introduces some error into the theoretical prediction. Nevertheless, the fit of the BZL model to the experimental results is instructive as a first approximation.

A similar approach was carried out for the cylindrical micelles in the blend samples. The average diameter of the PB core was measured for each sample, the results of which are presented in Table 1. The core diameter was systematically larger than the corresponding vesicle membrane; this is consistent with previous reports for OB block copolymers.[2,15] Although the values of micelle diameter for the higher molecular weight blends (specifically 14_3_80 and 14_3_90) are likely less accurate due to a smaller sample population of cylindrical micelles (the aforementioned polydispersity effect), the general trend is clear. As with the vesicles, a strong initial increase in diameter occurs upon addition of the larger OB14 block copolymer before again stabilizing as the blend composition becomes OB14 rich. The strong similarity between the behavior of the vesicles and cylinders, presented visually in Figure 2, indicates that the parent block copolymers are distributed evenly between the two geometries and that the coexistence of morphologies is not due to chain partitioning.

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Supporting Information Available: Figure S1 and the cryo-TEM experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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