

Interfacial Reactivity of Block Copolymers: Understanding the Amphiphile-to-Hydrophile Transition

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Block copolymers offer an interesting platform to study chemically triggered transitions in self-assembled structures. We have previously reported the oxidative degradation of vesicles made of poly(propylene sulfide)–poly(ethylene glycol) (PPS–PEG) copolymers. Here we propose a mechanism for vesicle degradation deduced from copolymer conformational changes occurring at the air/water interface in a Langmuir trough together with a reactive subphase. The hydrophobic PPS block is converted into hydrophilic poly(propylene sulfoxide) and poly(propylene sulfone) by oxidation upon exposure to 1% aqueous H₂O₂ subphase. As a result, a dramatic increase in area per molecule at constant surface pressure (Π) was observed, followed by an apparent decrease (recorded as decrease in area at constant Π) due to copolymer dissolution. For monolayers at the air/water surface, the large interfacial tensions present suppress increases in local curvature for alleviating the increased hydrophilicity of the copolymer chains. By contrast, vesicles can potentially rearrange molecules in their bilayers to accommodate a changing hydrophilic–lipophilic balance (HLB). Similar time scales for monolayer rearrangement and vesicle degradation imply a common copolymer chain solubilization mechanism, which in vesicles lead to an eventual transition to aggregates of higher curvature, such as cylindrical and spherical micelles. Subtle differences in response to the applied surface pressure for the diblock compared to the triblock suggest an effect of the different chain mobility.

Introduction

Stimulus-responsive macroamphiphiles represent a rich set of molecular building blocks for a variety of colloidal aggregates, making them uniquely suited for applications in nanostructured materials.^{1–3} Although synthetic chemists continue to create a wealth of novel macroamphiphiles,^{4–8} the most common and well-studied architectures thus far are the linear AB diblock and ABA triblock copolymers. Depending on the polymer interaction parameters, chain lengths, and compositions, these macroamphiphiles can, either spontaneously or with some energetic input (such as mechanical and/or thermal), self-assemble in aqueous media into ordered structures such as vesicles, wormlike micelles, and spherical micelles.^{9–17}

Much of the appeal of amphiphilic block copolymers in colloidal systems stems from the ability to almost infinitely tune the hydrophilic/hydrophobic ratio of the macromolecule, without changing the chemistry, by simply adjusting the lengths and organization of the blocks. In this straightforward yet labor-intensive fashion, the phase behavior of such materials is typically mapped. Additionally, it is known that selective chemical modification of block copolymers has dramatic consequences on microdomain segregation.¹⁸ Here we examine a system where the relevant interaction parameter of a macroamphiphile in water can be changed by means of a chemical reaction without altering chain length or integrity. This conversion should allow a novel means to induce and study the transition between microphases in aqueous media.

We have previously reported the synthesis of block copolymers of propylene sulfide and ethylene oxide and their lyotropic behavior in water.^{19,20} Notably, the oxidative sensitivity of thioethers in the hydrophobic block can be used to destabilize self-assembled vesicles formed by these copolymers.^{21,22} Here we focus on the destabilization process using a monolayer approach to reveal key features

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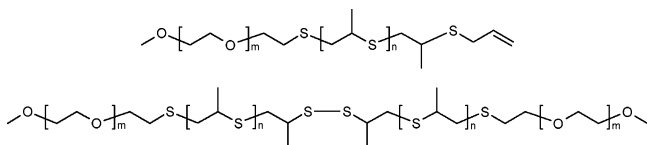


Figure 1. AB diblock and respective symmetric triblock AB–BA triblock copolymers, $\text{EO}_{16}\text{PS}_{25}$ and $\text{EO}_{16}\text{PS}_{50}\text{EO}_{16}$ ($m = 16$ and $n = 25$).

of the mechanism of the amphiphile-to-hydrophile transition. The dependence of kinetics on surface pressure is discussed in terms of copolymer conformation at the air/water interface and the relevant energetic factors. We find the use of a reactive subphase in a Langmuir trough to be an effective way to study transitions of responsive amphiphilic block copolymers.

Experimental Section

Materials and Methods. The synthesis and characterization of the block copolymers under study have been reported elsewhere.¹⁹ In Figure 1, the structure of the block copolymers is presented. The block copolymers have an average molecular weight of 2630 and 5300 g/mol for the diblock and triblock, respectively, and both have a polydispersity index between 1.2 and 1.3. The diblock was obtained by end-capping the sulfide-terminated poly(propylene sulfide) living chain (PPS) with allyl bromide, whereas the triblock represents the symmetric dimer of the diblock resulting from the formation of a disulfide bridge in absence of end-capping agent and upon exposure to air.

Langmuir Balance Experiments. Samples were applied to the water subphase (Millipore, 18.2 m Ω) from an approximately 1 mg/mL copolymer solution in dichloromethane (Fluka, Buchs Switzerland) using a Hamilton gastight microsyringe. For oxidation studies, a 30 vol % hydrogen peroxide solution (Fluka, Buchs Switzerland) was diluted with Millipore water to reach a final concentration of 1 vol % and used as the subphase.

Isotherms and area-versus-time curves at constant surface pressure (i.e., isobars) were acquired on a Lauda FW-2 trough at a temperature of 25.0 ± 0.5 °C, with a maximum trough area of 927 cm². The compression speed for the isotherms was set to 50 cm²/min. A feedback loop between the force transducer and trough barrier was used to maintain constant surface pressure and also give a readout of the total area. The initial barrier position (for a given surface pressure) was estimated from previously acquired isotherms and copolymer solution subsequently added onto the subphase (either 1% H_2O_2 or water). The films were allowed to equilibrate for at least 5 min before starting measurements. As a control for the oxidation experiment, area versus time was monitored using water as the subphase.

Optical Microscopy. From a 1 wt % solution in water of $\text{EO}_{16}\text{PS}_{25}$, 20 μL were applied to a glass slide and covered with a cover slip. Subsequently, 10 μL of a 30 vol % H_2O_2 solution were applied at the edge of the slide and introduced in the vesicle suspension by capillarity, thus forming a film of only several micrometers in thickness. Observations of single giant vesicle collapse were performed using a Zeiss Axiovert 135 inverted microscope equipped with a 20 \times objective under bright-field illumination using a Hamamatsu camera interfaced with a D/A converter attached to a PC. Movies were recorded with a VCR attached to the analogue output of the converter and transferred to a Mac G4 using a Pinnacle external A/D video converter.

Results and Discussion

This study is partly motivated by previous studies that have shown vesicles of PEG–PPS to be sensitive to an oxidative environment, initially transforming into micellar structures and, eventually, disappearing altogether.²¹ However, physical details at the molecular level of the vesicle “degradation” are unclear from our initial work. On the other hand, the chemical changes resulting from oxidation are fairly well understood: the sensitivity to oxidation of the thioethers in the hydrophobic block stems

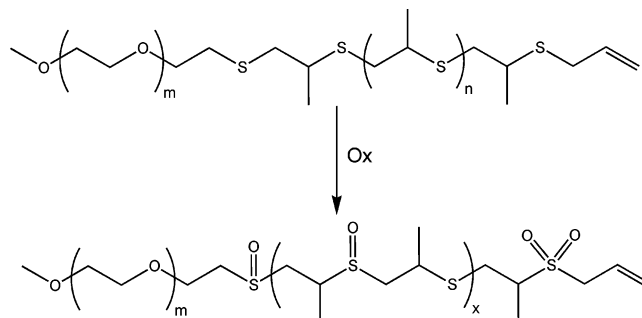


Figure 2. Schematic for the oxidation of the diblock with one possible intermediate product ($x = n/2$) is shown. While the formation of the sulfoxide is kinetically favored, sulfone groups can form by further oxidation of the sulfoxide moieties.

from the strong nucleophilic character of sulfur. Depending on the extent of reaction, sulfoxides and sulfones can be created, most readily to the sulfoxide and subsequently to the sulfone.^{23,24} Although in some cases oxidation of sulfoxides into sulfones needs a catalytic pathway,²⁵ we observed sulfone stretching bands in IR spectra of oxidized PPS upon exposure to stoichiometric excesses of H_2O_2 .²¹ Similar coexistence of SO and SO_2 moieties has been reported when insoluble crystalline poly(ethylene sulfide) is treated at room temperature with strong oxidants.²⁶

Conversion of thioethers in PEG–PPS copolymers to hydrophilic sulfoxides and sulfones groups has two consequences: first, it shifts the hydrophilic–lipophilic balance (HLB) to favor the formation of aggregates of higher interfacial curvature and, hence, area (i.e., cylindrical and spherical micelles),²¹ and second, it increases the solubility in water of the PPS block, which leads in a later stage to the gradual disappearance of the energetic factors maintaining the self-assembly. With a monolayer-based approach, we can carefully control the geometry and chemical environment of the system by means of the applied surface pressure Π and the composition of the subphase, respectively. Furthermore, as opposed to cryo-TEM methods, we can also monitor changes with time as they occur.

This dynamic aspect in the colloidal system is manifested by PEG–PPS monolayers in the presence of H_2O_2 , which undergo a dramatic increase in area per molecule, eventually reaching a maximum. This is subsequently followed by a decrease that continues past the capabilities of our experimental apparatus (Figure 3). The area increase/decrease was initially surprising, given that vesicles become smaller and eventually disappear after oxidation.²¹ However, the qualitative trend holds for the entire range of surface pressures examined, and control experiments with water exclude any effect of atmospheric oxygen. The area increase is caused by the oxidation reaction at the interface, which increases the amount of SO_x groups in the initially hydrophobic PPS block. Thus, the number of contacts between the PPS chain and the subphase increases, possibly inducing chain flattening. The repulsion between the hydrophobic and hydrophilic segments arising from their chemical incompatibility therefore competes with attraction of hydrophobic seg-

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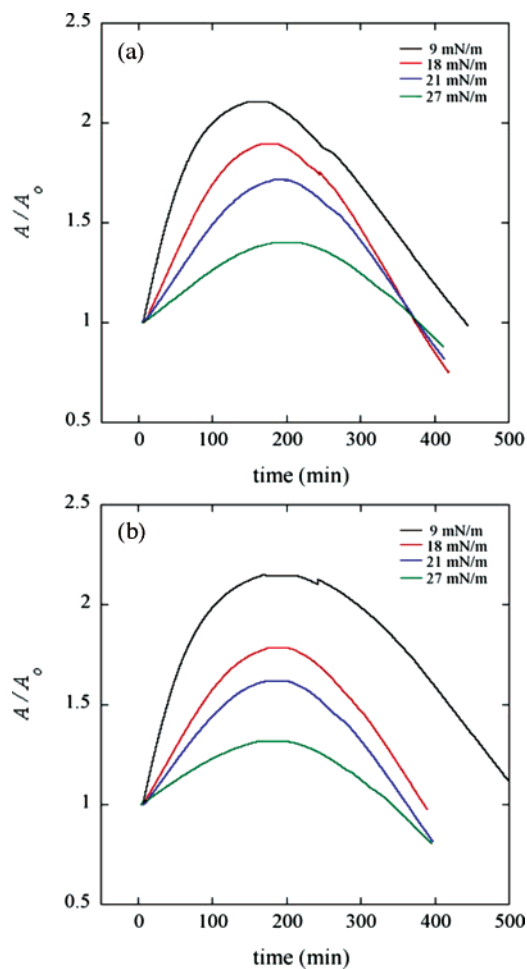


Figure 3. Monolayer areas versus time at different surface pressures on a H_2O_2 1 vol % subphase. Data are normalized with respect to A_0 , the initial minimum area. Data sets are the averages of at least two measurements. (a) $\text{EO}_{16}\text{PS}_{25}$ diblock and (b) $\text{EO}_{16}\text{PS}_{50}\text{EO}_{16}$ triblock. Control experiments with H_2O did not show any area change in the same time interval. Local sudden changes in slope or spikes have no physical meaning and were associated to vibrations or changes in the air temperature (overnight experiments).

ments toward the interface, driven by the oxidation reaction. Irrespective of the mechanisms, simple chain rearrangements restricted to the interface would result in the area per molecule eventually reaching a limiting (equilibrium) value. Instead, we see a decrease in area at later times, providing strong evidence that the chains in the monolayer are becoming solubilized into the subphase over time. We should note that the instrument measures the total monolayer area for a given surface pressure and that the area per molecule refers to the initial number of molecules. Thus if molecules leave the interface, the instrument can maintain the initial surface pressure by moving the barrier and compressing the monolayer.

A schematic of the proposed process is depicted in Figure 4.

Simple energetic considerations show that the high interfacial tension of the air/water interface ($\gamma = 72$ mN/m) opposes all but the longest wavelength deformations of the monolayer, even when reduced by the surface activity of the copolymer and the applied surface pressure Π . Therefore, after a critical extent of oxidation, solubilization into the subphase is the primary mechanism to alleviate the increased hydrophilicity of the copolymer chains. The possibility of aggregates forming in the subphase, either by cooperative association of single chains

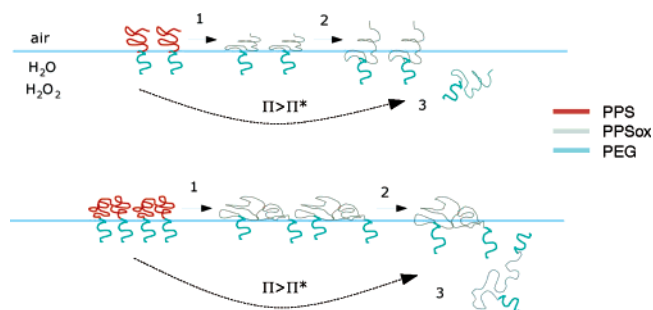


Figure 4. Schematic of proposed transition induced by the oxidation of the hydrophobic PPS block in the diblock (above) and the triblock (below). Initial increases in the area per molecule are caused by flattening of chains (i.e., contacts with the interface). Subsequent insertion (possibly tethered to the interface) and solubilization (leaving the interface into the subphase) of the resulting hydrophilic poly(sulfoxide/sulfone) block contribute to the decrease in area per molecule. For surface pressures above a critical value Π^* , insertion may be favored over the flattening process resulting in lower maximum expansion areas.

or by direct migration of surface micelles, is unlikely to occur, even given the low critical micellar concentration (CMC) of the non-oxidized polymers:²¹ assuming the entire applied copolymer sample transfers into the subphase, the total concentration is still at least 2 orders of magnitude below the CMC of the non-oxidized copolymer. Furthermore, oxidation of the poly(propylene sulfide) will reduce the amphiphilic character of the copolymer, effectively raising the CMC.

In contrast to monolayers, vesicles are closed surfaces, and thus there is no lateral tension in the membrane. Moreover, curvature is set by the bending rigidity $k_c \sim \gamma d^2$ for a membrane of thickness d . The interfacial tension γ is dictated by the effective interaction parameter χ among PEG, PPS, and water, which is reduced as oxidation progresses, thereby lowering k_c and allowing evolution of more highly curved surfaces. On a molecular level, this curvature effect can be expressed by a decrease in the packing parameter $\nu/A l_c$, as the molecular area A increases with time, assuming the ratio between volume ν and length l_c remains constant.²⁷

Experiments with giant vesicles of diblock PEG-PPS show a strong increase in surface fluctuations upon exposure to a large excess of H_2O_2 , indicative of increases in membrane area (analogous to increases in monolayer area in the Langmuir trough). Thus, simply monitoring the vesicle radius would not reveal the initial response to H_2O_2 . The process is later characterized by sudden shrinkage, indicative of material expulsion (Figure 5) and the presence of local transient defects (indicated in Figure 5 with a black arrow).

For vesicles exposed to an oxidative environment, one can now imagine a two-step mechanism: (i) copolymer solubilization, as discussed above for monolayers and (ii) reassembly into aggregates of higher curvature, such as micelles. The second step requires polymer concentration at or above the CMC, as previously seen with cryo-TEM.²¹

The monolayer response provides additional clues to molecular rearrangements. The most dramatic effect of surface pressure is seen in the rates of area change dA/dt as well as the maximal area A_{max} . From Figure 6a, A_{max} decreases with increasing surface pressure for both diblock and triblock macroamphiphiles. This trend is not surprising, since higher surface pressures will act to reduce

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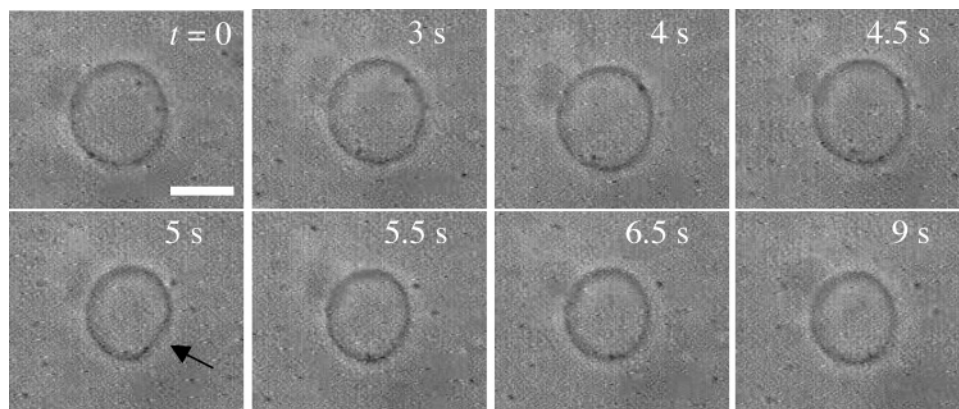


Figure 5. Bright-field optical micrographs of a $\text{EO}_{16}\text{PS}_{25}$ giant vesicle exposed to a large excess of H_2O_2 . The total exposure time was about 15 min before this sequence was recorded. Between $t = 4.5$ and 5 s, sudden shrinkage of the vesicle occurs. The local defect in the membrane (indicated by the black arrow) apparently reseals in the following seconds. The change in vesicle diameter induced by the oxidation of the PEG–PPS chains in the membrane is apparent (bar represents $20\ \mu\text{m}$).

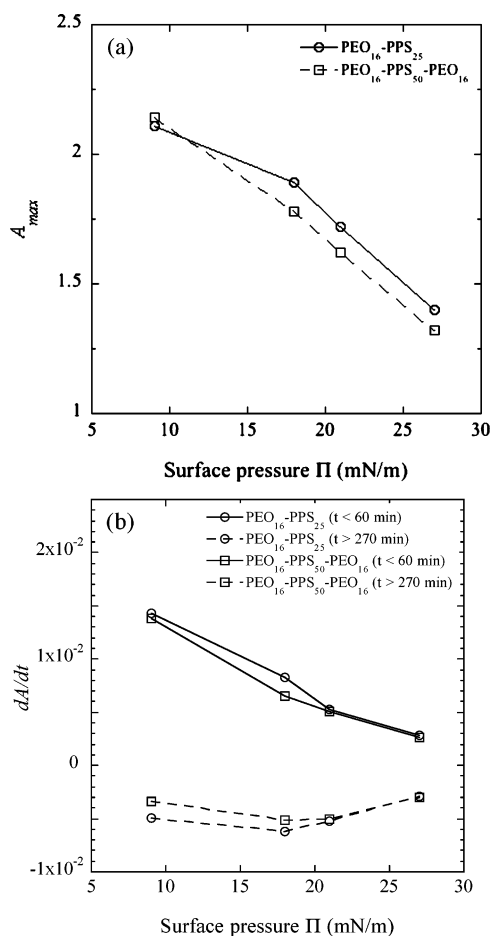


Figure 6. (a) Maximal area A_{max} and (b) rates of area change dA/dt (initial: $t < 60$ min; final: $t > 270$ min) for both $\text{EO}_{16}\text{PS}_{25}$ and $\text{EO}_{16}\text{PS}_{50}\text{EO}_{16}$ at different surface pressures. Lines interconnecting points are just drawn to as guides to distinguish between different datasets.

interfacial area and stretch the chains away (normal) from the interface. Thus, for sufficiently high surface pressures, chain insertion occurs at a lower degree of oxidation. Close to the monolayer collapse pressure, we would expect little or no increase in A/A_0 . In contrast, extrapolating to zero pressure suggests an almost 3-fold increase in the area per molecule. Such dramatic increases are not likely to be observed in vesicular systems, as the membrane integrity would be compromised by the dramatic change in the HLB.

The initial rate of area expansion is also affected by

increasing surface pressure, understood as a reduction of the interfacial thioether concentration (lateral compression causing out-of-plane extension of the PPS),²⁸ thereby slowing the kinetics of oxidation (Figure 6b). This is not the case for later times ($t > 270$ min), where the rate is only minimally affected by pressure, possibly due to favorable solubilization of what are largely hydrophilic molecules. This statement is rationalized by estimates of hydrophilicity for the various species, determined from calculated values of the oil/water partition coefficient (clogP).²⁹ The poly(propylene sulfoxide)₂₅ has a $\text{clogP} = -26$, which is substantially more hydrophilic than the value of 26 for the starting PPS_{25} and even more negative than the value of -4 for PEG_{16} . These findings suggest that the hydrophilic nature of the oxidized PPS block will not greatly depend on the ratio of SO/SO_2 created during the reaction.

Given that our ABA triblock is the symmetric analogue of the AB diblock, we would initially expect similar behavior if thermodynamic factors were dominant. Such an interpretation is based on results from melts, which show the architecture of analogous copolymers to have only a small effect on the order–disorder and order–order transitions.^{30,31} Indeed we see only minor differences in A_{max} and dA/dt for both copolymers, well within experimental error.

The only notable distinction between architectures is a difference in the time t_{max} corresponding to A_{max} . Whereas t_{max} for the triblock is only weakly dependent on the surface pressure, t_{max} for the diblock shifts to longer times with increasing pressure (Figure 3a,b). A tentative explanation for this shift is that the diblock can more easily adopt an extended state away from (i.e., normal to) the interface as compared to the triblock, which is entropically constrained by the central junction in the PPS block. Such an extended state effectively reduces the interfacial concentration of thioethers at intermediate times, increasing the time to reach A_{max} at high surface pressures. This difference is easily seen from the isotherms (Figure 7) where, at the relevant pressures, the triblock isotherm is not equivalent to the diblock isotherm simply shifted by a factor of 2. Additionally, it is known that chain architecture in melts plays a more important role in

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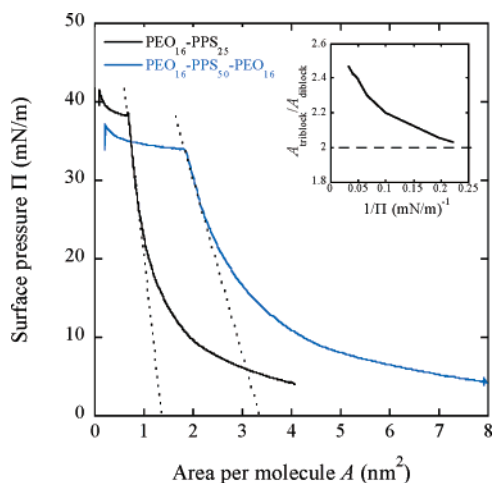


Figure 7. Pressure-area isotherms at 25 °C for the diblock and triblock. Some degree of chain extension normal to the interface is expected, since the nominal grafting distance $\Gamma \sim A^{0.5}$ is less than the end-to-end distance R for the PPS block (however, any extension is likely to be identical, as the two copolymers have the same PPS length per PEG chain, anchoring them to the interface). Differences in compression behavior become evident with increasing surface pressures, reflecting the effect of architecture (AB versus AB-BA). For example at $\Pi = 30$ mN/m, the corresponding A for the diblock is ~ 0.8 nm² and for the triblock ~ 2.0 nm², whereas in the absence of such effects one would expect $A \sim 1.6$ nm² for the triblock. The inset shows the deviation (from the ideal of 2) of the ratio $A_{\text{triblock}}/A_{\text{diblock}}$ vs $1/\Pi$.

dynamic responses, arising from bridging and looping conformational constraints.^{32,33} While this kinetic effect of architecture is subtle, it should be more dramatic in vesicular systems, where additional interactions across the bilayer are possible. Qualitative observations of diblock and triblock vesicle formation support this conclusion: kinetics of formation from thin films on glass fibers indicates significantly faster assembly for diblock compared to the analogous triblock.

Conclusions

PEG-PPS block copolymers offer an interesting platform to study chemically triggered transitions in self-

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assembled constructs. In the present work we focus on a fixed ratio of PEG to PPS (i.e., constant HLB), chosen for having the ability to form vesicles in dilute aqueous solutions. Upon exposure to oxidizing conditions, vesicles formed from these polymers undergo a transition to wormlike micelles, then spherical micelles, and finally unimolecular micelles and soluble polymer.²¹ We sought here to utilize a Langmuir trough with a reactive subphase to gain more insight into the transitions in the membrane. The large interfacial tensions present at the air-water interface prevent changes in local curvature, which by contrast are available to vesicles for alleviating increased hydrophilicity. The monolayers of two vesicle-forming copolymers were observed to first expand to keep Π constant, likely due to flattening of the PPS chain upon the subphase surface as it is oxidized. Subsequently, the monolayer contracted, due to dissolution of highly oxidized polymer into the bulk of the subphase. Observations of giant vesicles in oxidizing conditions suggest an analogous transition characterized by an area increase/decrease (fluctuations/shrinkage). Evidence for a common mechanism is further supported by similar time scales for monolayer rearrangement and vesicle degradation. The relative conformational flexibility of the diblock compared to the triblock is reflected in subtle differences in responses to the applied surface pressure. Such kinetic effects are likely to be magnified in vesicular systems, where additional interactions across the bilayer are possible, further slowing triblock responses. It is clear that the relative block lengths affect the interfacial behavior and response to oxidation, while the absolute lengths (or molecular weights) will also have a role in the characteristic times associated with chain, and therefore monolayer, rearrangement. Extending this work to include the dependence on chain lengths and compositions is likely to provide additional insights. Controlling the time scales, kinetic, and thermodynamic factors discussed here are also relevant for other potential applications, including surface functionalization and patterning in biosensing devices.

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