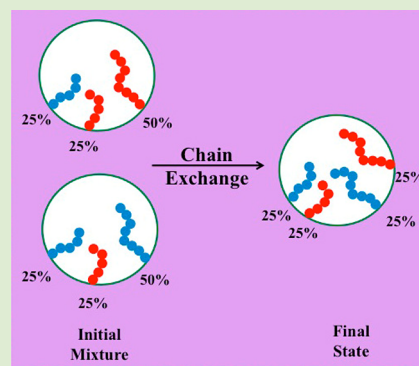


Chain Exchange in Binary Copolymer Micelles at Equilibrium: Confirmation of the Independent Chain Hypothesis

J. Lu,[†] F. S. Bates,^{*,†} and T. P. Lodge^{*,†,‡}

[†]Department of Chemical Engineering and Materials Science and [‡]Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455, United States

ABSTRACT: The mechanism of chain exchange in block polymer micelles at equilibrium is investigated using time-resolved small-angle neutron scattering (TR-SANS). The binary micelles are formed from blends of two poly(styrene-*b*-ethylene-*alt*-propylene) (PS-PEP) copolymers with different PS core block lengths, only one of which is contrast-matched with the solvent, squalane, so that the monitored scattering intensity only reflects the other species. Micelles prepared with an excess of deuterated PS chains (of the visible species) and those with the equivalent protonated PS chains are blended (“postmixed”) at room temperature, where the exchange of chains is suppressed. At several elevated temperatures these samples were monitored by TR-SANS, in which mixing of isotope-labeled visible species gives systematic reduction of scattering signals with time and provides a quantitative way to characterize the micelle exchange kinetics. Within experimental error, the results for each labeled chain (i.e., longer or shorter) in the binary micelles are identical to those recently reported for the same labeled chains in the corresponding single block copolymer component micelles, thus proving that chain exchange in these micelles involves independent chain motion. This reinforces the important conclusions that the single-chain exchange mechanism dominates in the studied micelle solutions and that micelle fusion or fission events are rare.



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Block copolymer micelles are aggregates formed by self-assembly of amphiphilic copolymers dispersed in a selective solvent, driven by unfavorable interactions between the solvent and the core-forming block.^{1,2} Due to the relatively long chains being subject to additional thermodynamic and dynamic constraints (e.g., entanglements, crystallinity, vitrification), block copolymer micelles exhibit significantly slower equilibration kinetics than small molecule surfactants.^{3–5} As a result, unlike the exchange kinetics between small molecule surfactant micelles that has been intensively studied decades ago,^{6,7} certain details of the mechanism(s) of equilibration in block copolymer micelles remain unclear.⁸ Understanding the block copolymer molecular exchange process represents a critical step in establishing a unified approach to dealing with self-assembly of amphiphiles of all sizes, from classical small surfactants⁹ and lipids¹⁰ progressing up in molecular weight through the enormous parameter space afforded by macromolecular architectures.¹¹ The work summarized here not only provides better insight into micelle structure but also will facilitate a host of applications such as drug delivery,^{12,13} viscosity modification,^{5,14} and colloidal and polymer blend stabilization.^{15,16} The observation of kinetically frozen block copolymer micelles, also known as path-dependent or non-ergodic micelles,^{3,17,18,28} implies that kinetics plays an important role in determining micelle properties such as aggregation number and stability. This is important to understand for both reproducible micelle preparation and prediction of long-term performance.

Two primary mechanisms have been considered for micelle exchange kinetics: unimer exchange or single-chain expulsion–diffusion and micelle fusion/fission. The former was described by Aniansson and Wall^{6,19,20} in the context of dilute low molecular weight surfactants. Halperin and Alexander (H&A)²¹ later examined the exchange kinetics of block copolymer micelles and concluded that, due to the unfavorable interactions between micelle coronas, the Aniansson–Wall process should dominate in the case of macromolecular micelles at equilibrium. Dormidontova²² studied the kinetics of micelle evolution in block copolymer micelles using a scaling approach and also concluded that single-chain exchange is favored over micelle fusion/fission when the system is close to its equilibrium state. Furthermore, micelle equilibration rates in several different systems have been experimentally observed to be largely independent of micelle concentration within the dilute regime,^{23–26} suggesting that micelle fusion/fission is insignificant. By assuming single-chain exchange, fitting models have been established and successfully described the relaxation kinetics in block copolymer micelles.^{25,26} In agreement with this, a recent fluorescence study²⁷ found that the micelle fusion/fission rate is 10^6 times slower than chain expulsion–insertion in symmetric triblock copolymer (poly(ethylene oxide-*b*-propylene oxide-*b*-ethylene oxide)) micelle solutions.

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Time-resolved small-angle neutron scattering (TR-SANS) has recently drawn attention as a clean and quantitative way of investigating micelle kinetics. Separately prepared deuterated core and protonated core micelles are “postmixed” in a solvent of intermediate scattering length density. As chain exchange proceeds, the average core becomes contrast-matched to the solvent, and the scattered intensity decays to the background. Micelles prepared with previously blended deuterated and protonated chains (a “premixed” sample) provide a reference for the fully exchanged limit. Applying this technique, Richter and co-workers^{23,24,26,28–30} reported studies on several systems and defined a dimensionless molecular relaxation function $R(t)$ that quantifies the extent of chain exchange

$$R(t) = \left(\frac{I(t) - I(\infty)}{I(0) - I(\infty)} \right)^{1/2} \quad (1)$$

Here $I(0)$ and $I(\infty)$ are the scattering intensities of the postmixed and premixed samples, respectively. Following their work, we have investigated the chain exchange mechanisms in poly(styrene-*b*-ethylene-*alt*-propylene) (PS-PEP) micelles in squalane, a selective solvent for the PEP block, in both dilute^{25,31} and concentrated solutions.³² Since the rate of chain exchange in dilute solutions was observed to be largely independent of polymer concentration (from 0.5% to 2% by volume), a single-chain expulsion mechanism was inferred. According to H&A,²¹ $R(t)$ should adopt a single exponential form. However, both the pioneering work by Lund et al.^{23,24,29,30} and our results^{25,31,32} show a much broader, almost logarithmic relaxation instead. We were able to show that this is almost entirely attributable to core block dispersity, and a fitting model that accounts for the dramatic sensitivity of the molecular exchange dynamics to core block dispersity was proposed²⁵

$$R(t) = \int_0^\infty P(N_i)K(t, N_i)dN_i \quad (2)$$

In this expression, $P(N_i)$ is the Schulz–Zimm distribution function for the core block length, N_i , and $K(t, N_i)$ is the core block extraction relaxation function of an individual polymer chain. The latter was expressed as $K(t, N_i) = \exp(-t/\tau(N_i))$, where $\tau(N_i) = \tau_{\text{Rouse}}(N_i) \times \exp(E_a(N_i)/kT)$, and τ_{Rouse} is the longest relaxation time. This model is an extension of the detailed model of H&A but utilizes a linear N_{core} dependence ($E_a \sim N_{\text{core}}$) in the extraction barrier, rather than the $N_{\text{core}}^{2/3}$ in H&A. By accounting for polydispersity, the equilibrium kinetics in a variety of block copolymer micelles was successfully described.^{25,31,32} In particular, we investigated the influence of core block size distribution on chain exchange kinetics directly by blending copolymer chains of two different average PS block lengths in one binary micelle; the PS core block molecular weights differed by a factor of 1.6.³¹ The measured relaxation curve was quantitatively accounted for by summing the weighted relaxation functions obtained from micelles formed by the individual components, consistent with the previously published model. These results complement the reported work of Zinn et al.²⁶ on spherical micelles with poly(ethylene oxide) corona polymers and hydrophobic *n*-alkyl head groups in the core, as these strictly monodisperse core segments yielded single exponential exchange rates. Thus, it can be inferred that chain exchange is an independent, chain-by-chain event, and the barrier for one chain is not influenced by the length of the

other chains in the same core; this also supports the single-chain extraction hypothesis.

This argument for independent chain motion, although reasonable, still lacks direct proof. Here we report a TR-SANS study that quantitatively confirms the underlying assumption of independent, single-chain exchange, independent of fitting parameters. Taking advantage of the TR-SANS technique and contrast matching strategy, we designed a micelle exchange system so that the same two PS-PEP diblock copolymers with different core block lengths are involved, but with separate observation of exchange kinetics of one species (i.e., either “long” or “short” chains are visible). Normal (hPS-PEP-1 and hPS-PEP-2) and selectively deuterated (dPS-PEP-1 and dPS-PEP-2) diblocks with relatively narrow distribution ($\bar{D} \leq 1.1$) (Table 1) were synthesized by sequential anionic polymer-

Table 1. Diblock Copolymer Characteristics, Reproduced from Reference 25

polymer	N_{PS}^a	N_{PEP}^b	\bar{D}
hPS-PEP-1	250	970	1.04
dPS-PEP-1	260	985	1.10
hPS-PEP-2	400	880	1.05
dPS-PEP-2	423	926	1.10

^aNumber of PS repeat units. ^bNumber of PEP repeat units.

ization of styrene and isoprene, as previously described.³³ The poly(isoprene) blocks were then saturated with deuterium using a homogeneous Ni/Al catalyst. The average degrees of polymerization of the two PS blocks were $\langle N_{\text{PS}} \rangle \cong 255$ (“short”) and 412 (“long”), while the PEP blocks of all four polymers are comparable.

Micelle solutions (1 vol %) were prepared using a cosolvent method. The polymers were dissolved in squalane with dichloromethane as a neutral cosolvent, and then the cosolvent was removed by evaporation, leading to the formation of spherical micelles. The micelle solutions were annealed at 190 °C for 30 min to allow full chain exchange and thus equilibrated micelle structures.³³ Figure 1 illustrates the contrast-matching strategy and includes the representations of “long-chain visible” micelles before and after exchange. For the premixed samples, all four types of polymers (d-, h-PS-PEP-1, d-, h-PS-PEP-2) were codissolved in squalane and dichloromethane. The isotopic composition of the squalane (42 vol % normal squalane and 58 vol % perdeuterated squalane; Sigma-Aldrich and C/D/N Isotopes, respectively) was selected to contrast-match the premixed micellar cores. The postmixed solutions, on the other hand, contain blends of separately prepared protonated micelles and deuterated micelles at room temperature, where PS chain extraction is suppressed ($T_{\text{g,PS core}} \approx 70$ °C in squalane³⁴). To keep track of the exchange of PS-PEP-1 and PS-PEP-2 polymers individually in micelles containing both, it is necessary to prepare two different batches of postmixed solutions: the long-chain visible and the short-chain visible. The long-chain visible postmixed samples, as depicted in Figure 1, contain micelles formed by precontrast-matched short chains (hPS-PEP-1 and dPS-PEP-1) and exclusively either deuterated long chains (dPS-PEP-2) or protonated long chains (hPS-PEP-2). Consequently, exchange of PS-PEP-1 molecules, i.e., the short chains, between the long-chain visible micelles cannot be detected in TR-SANS, and only exchange of PS-PEP-2 chains is tracked. Similarly, the short-chain visible postmixed solutions contain precontrast-matched long chains and are

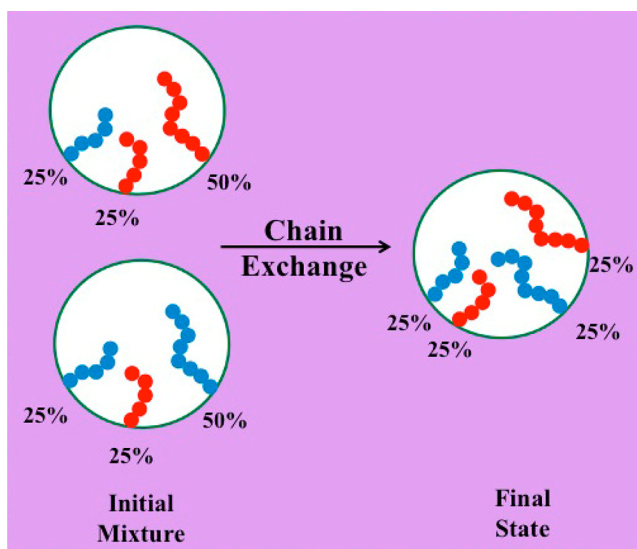


Figure 1. Chain exchange in a long-chain visible postmixed micelle solution. Micelles with protonated (blue) and deuterated (red) core blocks are blended, both containing 50 vol % contrast-matched short chains (hPS-PEP-1 and dPS-PEP-1) and 50 vol % long chains (hPS-PEP-2 or dPS-PEP-2, respectively) (the “initial mixture”). After complete chain exchange, mixed core micelles with 25% of each type by volume (the “final state”) are obtained. A partially deuterated solvent is chosen (purple), to match the contrast of final-state micelle cores.

monitored to characterize short-chain exchange separately. In both cases, complete chain exchange leads to binary micelles, in which the four types of polymers are evenly redistributed. The premixed samples approximate this scenario.

TR-SANS experiments were performed with the CG-2 General-Purpose SANS instrument at the High Flux Isotope Reactor (HFIR) facility of the Oak Ridge National Laboratory (ORNL) in Oak Ridge, Tennessee. The identical instrument configurations and temperature control techniques as in the previous study were used.³¹ On the basis of past experience with PS-PEP micelle equilibration kinetics, two temperatures were selected for each type of postmixed solution (i.e., long- or short-chain visible). The 2-D scattering patterns were acquired at 5 min intervals and were reduced and normalized using the Igor package provided by ORNL to give absolute intensities. Figure 2 shows a set of representative TR-SANS results, obtained with the premixed solution and a long-chain visible postmixed sample at 140 °C.

As the solvent squalane contrast matches the mixed cores, the mixing of isotope-labeled chains can be signaled by scattering intensity reduction with exposure time at appropriate temperatures. The relaxation function $R(t)$ (see eq 1) is then calculated from each set of measurements at a certain temperature. To minimize experimental uncertainties, integrated intensities over a range of wave vector q (0.01–0.03 Å⁻¹ in this reported work) were used instead of that for a particular value of q . (The partially contrast-matched micelles lead to a reduction of scattering intensity as compared to our previous SANS studies and therefore a larger uncertainty in the calculated $R(t, T)$). $R(t, T)$ traces for both the long-chain and short-chain visible cases, each at two different temperatures, are plotted in Figure 3. The first point of each trace, which corresponds to scattering during the first 5 min exposure, was removed due to the time-dependent temperature.

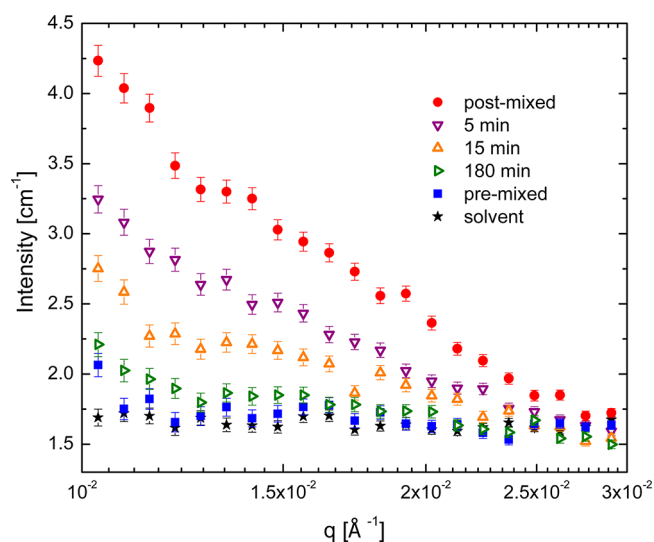


Figure 2. Representative TR-SANS patterns recorded in 5 min increments during molecular exchange of PS-PEP in a long-chain visible postmixed solution at 140 °C.

To obtain a wider time scale in the relaxation function $R(t, T)$, the time–temperature superposition principle³⁵ (well-known for its application in rheological studies³⁶) was applied, and the individual $R(t, T)$ traces were shifted along the horizontal axis until they visually overlap. An empirical shift factor a_T for a certain reference temperature T_{ref} is calculated according to $R(t/a_T, T_{ref}) = R(t, T)$. Figure 4a shows the $R(t)$ master curve from shifting individual traces measured at different temperatures (Figure 3) using shift factors shown in Figure 4b, at a reference temperature of 125 °C. Reassuringly, within the uncertainty the shift factors (filled symbols) match those associated with single-component micelle equilibration reported previously (straight line²⁵) and those determined for binary polymer blends (open squares³¹) as well. This observation also confirms that having a different species of chains presented does not alter the micelle equilibrium mechanism.

Figure 4a compares the kinetics of PS-PEP block copolymer chains in the binary micelles with that of a single component. Two sets of filled symbols represent the shifted $R(t/a_T, T_{ref})$ data obtained with short-chain visible (in light and dark blue) and long-chain visible (in light and dark red) solutions, respectively. The dashed lines are model fits reproduced from the previous publication²⁵ in which single component PS-PEP micelles were investigated. The blue curve represents short-chain (PS-PEP-1) micelles and the red one long-chain (PS-PEP-2) micelles. The observation that the blue symbols fall right on the blue curve thus indicates that having long chains together in the binary micelle does not affect the exchange kinetics of the short chains. Similarly, the overlap of the red symbols and red curve implies that the long-chain kinetics is independent of the presence of the short chains. These results unequivocally demonstrate that molecular exchange in block copolymer micelles is an independent event, which is consistent with the single-chain expulsion mechanism predicted originally by Halperin and Alexander.²¹ All the summarized earlier results suggested, but did not explicitly exclude, the possibility of micelle fission/fusion. For example, if the fission/fusion mechanism operated in parallel with single-chain exchange, there might not be a strong micelle concentration dependence

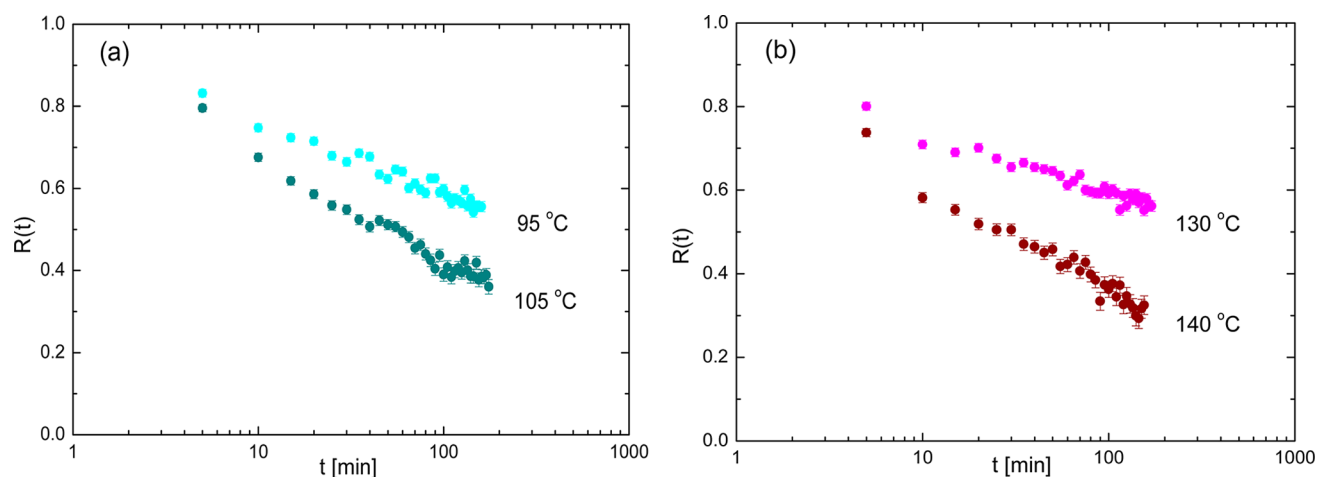


Figure 3. $R(t, T)$ traces determined by TR-SANS, with (a) short-chain visible postmixed solutions and (b) long-chain visible postmixed solutions, at two temperatures each.

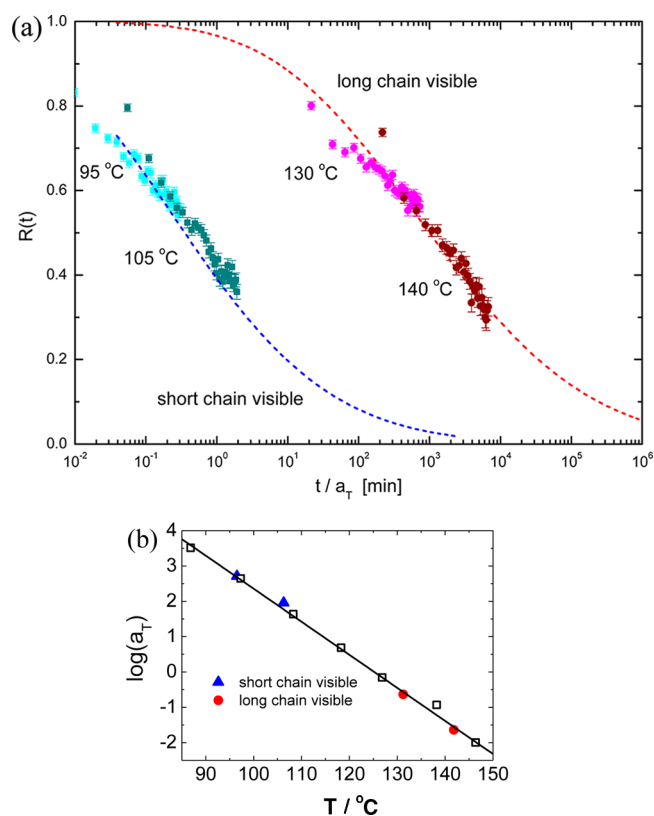


Figure 4. (a) Master curve for TR-SANS results shown in Figure 3, including a comparison with a previously reported model fit²⁵ (the dashed curves) for single-component micelles. (b) Temperature-dependent shift factors (blue triangles and red circles) extracted from the relaxation function in (a). Open symbols identify shift factors associated with a core block dispersity study³¹ with blends of PS-PEP copolymers in squalane. The solid line represents a linear regression of shift factors reported for single-component PS-PEP micelles.²⁵

to the overall rate, as reported. The work presented here addresses this problem by resolving the motion of shorter and longer chains, in micelles with equivalent coronas (and therefore comparable barriers to fusion). If the contribution of fission/fusion were significant, the long chains in mixed micelles should be able to exchange at a rate closer to that of

the short chains than in pure long chains, but no hint of such a trend can be discerned.

In this letter we investigated micelle equilibrium kinetics of PS-PEP block copolymers in squalane using TR-SANS. The micelles contain polymers with two different PS block lengths, one of which is precontrast-matched so that they are invisible to SANS. Consequently, the time-dependent scattering intensity signals only the mixing of the visible species. A relaxation function $R(t, T)$ is calculated for quantitative comparison to the situation where the corresponding visible species is the only component in the micelles. Within experimental error, the two match with each other quantitatively, proving that the mixing of isotope-labeled chains is an independent event, and thus the single-chain exchange mechanism dominates in the described micelle solution. These results also exclude the possibility of micelle fusion/fission. In neat block copolymer melts, and in concentrated spherical domains of diblock copolymers in homopolymers, diffusion of single diblock copolymers by “activated hopping”, i.e., core block extraction, has also been reported. The confirmation of the single-chain extraction mechanism for chain exchange between spherical diblock copolymer micelles presented here is thus in accordance with the interpretation of the reported diffusion mechanism in melts.^{37,38}

AUTHOR INFORMATION

Corresponding Author

*E-mail: bates001@umn.edu; lodge@umn.edu.

Notes

The authors declare no competing financial interest.

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