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Temperature-Dependent Micellization in Aqueous Block Copolymer Solutions

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ABSTRACT: The temperature-dependent micellization of Pluronic F127 (EO_{99}–PO_{65}–EO_{99}, EO and PO being ethylene oxide and propylene oxide, respectively) was investigated experimentally and theoretically. While experiments involved the determination of the temperature dependence of the critical micellization concentration (cmc) and the fraction of polymer molecules in micellar form, the theoretical results were obtained through a self-consistent lattice theory for multicomponent mixtures of copolymers with internal states in heterogeneous systems. Comparison between theoretical and experimental findings shows qualitative agreement regarding the decrease in the cmc and the increase in the average aggregation number, the micellar size, and the fraction of polymer molecules in micellar form, all with increasing temperature. Furthermore, details about the temperature-dependent micellization, obtained from the model calculations, are discussed.

Introduction

The Pluronic diols, i.e., block copolymers of the PEO–PPO–PEO type [PEO and PPO being poly(ethylene oxide) and poly(propylene oxide), respectively], constitute a class of polymers which has received increasing attention during the last few years.[1–14] The reason for this, apart from the intriguing complexity of these systems, involving both micelle and mesophase formation as in many other block copolymer solutions,[15] is the importance of these systems in a wide range of applications. In particular, the "gels" formed in many of these systems at high polymer concentrations and intermediate temperatures have been extensively utilized in different pharmaceutical applications, since they are capable of solubilizing both water-soluble and oil-soluble solutes.[16,17] Another interesting feature of the Pluronic block copolymers is their ability to adsorb at a variety of interfaces. Due to their amphiphilic nature, these polymers can adsorb both extensively and strongly, and at the same time provide a good steric stabilization to colloidal dispersions, which is usually not the case with homopolymers.[18] Consequently, they are widely used as stabilizers, not the least in pharmaceutical applications, due to their relatively low toxicity.[1]

Undoubtedly, one of the most conspicuous features of polymers and surfactants containing ethylene oxide and similar groups is the strong inverse temperature dependence of a wide range of properties.[19] Consequently, much effort has been directed to the understanding of the mechanisms underlying this anomalous behavior. Over the years, three different models have emerged, discussing the reversed temperature dependence in terms of solute–solute,[20] solute–solvent,[21] and solvent–solvent[22] interactions, respectively.

We have adopted the first of these models for both experimental and theoretical reasons. From quantum mechanical calculations,[23] the conformations of ethylene oxide groups are divided into two classes, one being polar, having a low energy and a low statistical weight, and one being less polar, having a higher energy and a high statistical weight. This subdivision is further supported by, e.g., ^{13}C chemical shift measurements.[24] At low temperatures, the former class of states dominates and the interaction between the polymer and the solvent is favorable, whereas at higher temperatures, the latter class of states dominates, rendering the solute–solvent interaction less favorable. Furthermore, the effective solute–solvent interaction becomes more unfavorable as the polymer concentration increases.

Previously, the Flory–Huggins theory[25] and the theory of Scheutjens and Fleer[26] were extended to treat the adsorption of block copolymers possessing internal states.[27] By means of this approach, the adsorption of different Pluronic block copolymers at hydrophobic and hydrophilic silica surfaces was modeled.[28,29] In particular, the model predicted a strong increase in the adsorbed amount just prior to solution phase separation, which was also found experimentally. This was interpreted as an incipient phase separation in the surface region, presumably resulting in multilayer adsorption.

One of the most interesting properties of aqueous Pluronic solutions is a temperature-dependent micellization. Not surprisingly, this has been studied extensively during the last few years with a variety of methods.[2–14] The obtainable parameters of interest are the critical micellization concentration (cmc), the fraction of polymer molecules in micellar form, and the size and the aggregation number of the micelles, as well as the temperature dependence of these parameters. Starting with the average aggregation number, it has been shown by a number of groups, using, e.g., static light scattering and fluorescence quenching, that this increases strongly with temperature, although the absolute values vary between different systems, and even between different batches. Furthermore, the size of the micelles generally increases with increasing temperature, although the extent of the increase varies between systems. Perhaps the parameter of largest fundamental value is the cmc. Unfortunately, the values reported in the literature differ substantially. However, as we hope to show below, and as has previously been observed as well, the cmc decreases with increasing temperature.[7–9,12,13] Thus, the lack of sufficient temperature control, in conjunction with batch-to-batch variations, seems to be responsible for the observed variations. It is further interesting to compare the micellization of Pluronic block copolymers to that of C_mE_n low molecular weight surfactants, which has been more widely studied.[30] In the latter systems, it is found that the cmc decreases and that the micellar size increases strongly, both with increasing temperature. Thus, in these respects, the analogy between these two classes of systems seems valid.

Although a knowledge of the details of the temperature-dependent micellization is slowly beginning to emerge from

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numerous experimental studies, much remains to be done. In particular, no study so far has compared experimental findings with theoretical predictions. We therefore decided to investigate how far the present model and some simple experiments could take us toward a better understanding of these systems. Indeed, as will be shown below, a comparison between theoretical and experimental findings shows the existence of a qualitative agreement regarding the decrease in the critical micellization concentration (cmc) and the increase in the average aggregation number, the micellar size, and the fraction of polymer molecules in micellar form, all with increasing temperature. Furthermore, details beyond those experimentally accessible to date are obtained from the model calculations as well.

Experimental Section

Methods. For the gel permeation chromatography (GPC) experiments, a Superose 6 column was used, with a LKB 2142 differential refractometer as the detector. The flow rate was 0.20 mL/min, and the initial polymer concentration was 1 wt %. No dependence on the flow rate was observed. All solutions were filtered through a Millipore filter (5.0 μm) before injection. The use of a differential refractometer implied that the peak intensity was directly proportional to the polymer concentration, at least at the low polymer concentrations used. Furthermore, since the refractive index increments of PEO and PPO are very similar, effects due to possible composition heterogeneity and preferential micellization were likely to be of minor importance, and thus the evaluation of the CPC data became straightforward.

Critical micellization concentrations were determined by standard surface tension measurements where the cmc was identified as the (often extrapolated) break point in the surface tension versus polymer concentration curve. We used a standard drop-volume technique, which has been discussed previously.[31] Analogously, the ellipsometrically determined cmc was obtained by identifying the break point in the adsorbed amount versus temperature curve at a constant polymer concentration (see ref 29).

Material. In the experiments we used a specially purified sample of Pluronic F127, which was kindly supplied by BASF Wyandotte, USA. The polymer has a total molecular weight of 12 500, and consists of approximately 70 wt % PEO. NMR spectra confirm that the ratio PEO/PPO is approximately 70/30. No impurities were observed in the NMR spectra. The water content of the dried sample is estimated to be less than 3 wt %.

Theoretical Modeling

Background. The Flory–Huggins lattice theory of homogeneous polymer solutions[25] has been extended to describe polymer solutions in heterogeneous systems.[26] This extension makes it possible to treat polymers at solid surfaces as well as self-aggregation in solution. So far, most applications have dealt with adsorption at solid surfaces, but the use of the heterogeneous lattice theory for describing self-aggregation is nevertheless of significant importance. The first step toward a description of self-aggregation was taken by Leermakers et al.,[32] who considered the formation of a membrane from A_9B_2 amphiphiles. Later, Leermakers et al.[33] and Lent and Schutjens[34] extended the procedure to micellar systems, where the translational entropy of the aggregate has to be taken into account.

Another important step was taken by Evers et al.[35] who extended the general lattice theory for heterogeneous systems to general multicomponent systems. This formulation has furthermore been generalized to the case where the block copolymer segments possess internal degrees of freedom.[27] The latter extension provides means of modeling effective segment–segment interaction parameters which are temperature as well as concentration dependent. This polymer model was originally devised to describe the existence of a lower consolute point in homogeneous aqueous PEO solutions,[20] but has been extended to heterogeneous systems of homopolymers.[36] The basis of the PEO model is that the distribution of conformations of a segment depends on temperature, and that different conformations interact differently with adjacent polymer segments and solvent molecules. The conformations of the OCCO segment are divided into two classes or states, one being polar and having a low energy and a low statistical weight, and one being less polar or nonpolar and having a higher energy and a higher statistical weight. At low temperature the former state is dominating, and thus a more favorable polymer–water interaction is obtained, whereas at elevated temperatures, the latter state becomes progressively more important, which results in a more unfavorable polymer–water interaction.

Table I
Internal State Parameters U_{AB} (Energy) and g_{AB} (Statistical Weight) and Flory–Huggins Interaction Parameters $\chi_{BB'}$ (Energies in kJ mol^{-1})

species	state	state no.	U_{AB}	g_{AB}
water		1	0	1
EO	polar	2	0[a]	1[a]
	nonpolar	3	5.086[a]	8[a]
PO	polar	4	0[b]	1[b]
	nonpolar	5	11.5[b]	60[b]

$kT\chi_{BB'}$

state no.	2	3	4	5
1	0.6508[a]	5.568[a]	1.7[b]	8.5[b]
2		1.266[a]	0[c]	1.3[d]
3			1.3[d]	0[c]
4				1.4[b]

[a] From fit to the experimental PEO–water phase diagram.[20,27] In the original work[20] the energy parameters were given to four figures, of which probably two are significant. In order to be consistent with this work,[20] we have refrained from truncating these parameters. [b] From fit to the experimental PPO–water phase diagram.[27] [c] Taken to be equal. [d] Taken to be equal.

It should be pointed out that the model contains only temperature- and concentration-*in*dependent interaction parameters among the segments in *given* states. The temperature and concentration dependence of the *effective* (averaged over the states) segment–solvent and segment–segment interactions arises from the fact that the equilibrium between the states depends on temperature (as discussed) as well as on concentration (since the probability of a state also depends on its interaction with the neighbors, cf. eq 6 in ref 27). The virtue of the two-state model is that it introduces the temperature and concentration dependence of the interaction in a simple and physically reasonable manner and uses parameters which all have clear physical interpretations. The most obvious alternative to the two-state model would be to assume an explicit functional form of χ's dependence on temperature and concentration. Such an approach would be of less value, since the mechanism of the dependence will not be explained and the fitting parameters will not have clear interpretations.

Model Calculations. On the basis of the molecular weight and the fraction of ethylene oxide, Pluronic F127 is modeled as EO_{99}–PO_{65}–EO_{99}. Since aqueous solutions of both PEO and PPO display a lower consolute point,[37] both EO and PO segments are modeled with two internal states, one polar and one nonpolar. The interaction parameters are given in Table I and are the same as those used in our previous studies of the adsorption of Pluronic block copolymers at solid surfaces,[28,29] when applicable.

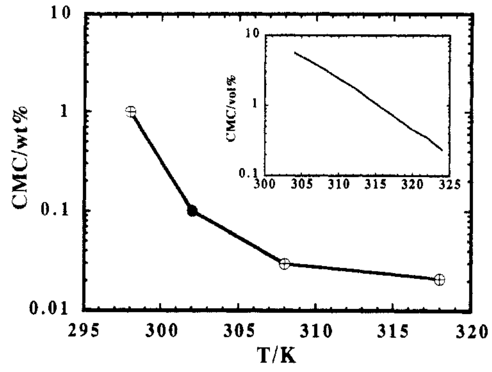

Figure 1. Critical micellar concentration (cmc) versus temperature (*T*) from surface tension (crossed circles) and ellipsometry (filled circle) measurements. The inset shows the results from model calculations. The uncertainty in the experimental cmc is estimated to be less than a factor of 2.

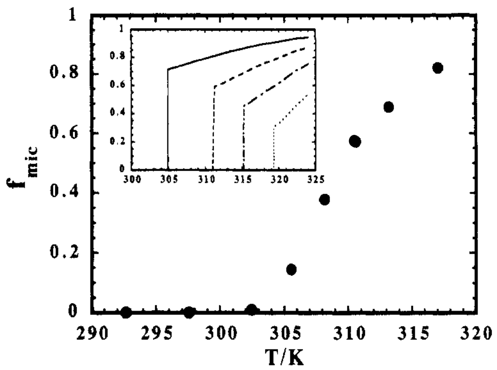

Figure 2. Fraction of polymers in micelles (f_{mic}) versus temperature (*T*) from GPC measurements. The inset shows the results from model calculations at polymer volume fractions of 0.005 (dotted line), 0.010 (dashed-dotted line), 0.020 (dashed line), and 0.050 (solid line).

The calculations were performed using a spherical lattice.[34] The space is divided into shells by concentrically placed spheres with increasing radii. The width of the shells is constant; it corresponds to the lattice size in planar geometry, and is taken to be equal to the size of the polymer segment. Moreover, each shell (or layer as it later will be referred to) is divided into lattice cells which are able to contain one polymer segment or a solvent molecule. The random-mixing (mean-field) approximation employed in the Flory–Huggins theory is applied to each layer *separately*, and thus we are able to describe radial concentration profiles of the different species.

The computation involves a self-consistent determination of the volume fractions of all species (EO and PO segments and water molecules) and state distributions of the EO and PO segments in each layer of the model system.[27] As a result a single Pluronic micelle *is* formed in the center of the lattice at a specified bulk polymer concentration (or chemical potential) *if* it is stable with respect to a homogeneous solution. Given the distributions of volume fractions and states, the free energy of forming the micelle at a fixed position may be calculated.[38] At equilibrium, this free energy is balanced by the favorable translational entropy of the micelle. This requirement makes it possible to evaluate the micellar concentration, the average polymer concentration of the model system, and the aggregation number of the micelle. A description of the relevant equations for calculating the micellar concentration etc. is given in ref 34. It should be mentioned that in order to evaluate whether the micelle is globally stable or not, other types of aggregates, such as rods and membranes, have to be considered as well. This, however, is out of the scope of the present investigation.

Results and Discussion

Considering the strong temperature dependence displayed by ethylene oxide-containing polymers and surfactants in general,[19] and the effects of temperature on the micellization of, e.g., C_mE_n surfactants in particular,[30] it is of obvious interest to investigate the temperature dependence of the micellization in the Pluronic systems. As can be seen in Figure 1, the experimentally obtained cmc decreases strongly with increasing temperature, as has also been found previously.[7-9,12,13] This behavior is analogous to that of, e.g., C_mE_n systems.[30] Furthermore, model calculations agree reasonably well with the experimental findings (Figure 1, inset). Note that although the shape of the decrease and the absolute values of the temperature and the polymer concentration are somewhat different in the two cases, the model appears to capture the major features of the experimental data.

By performing GPC experiments at different temperatures, it is possible to follow the temperature dependence of the micellization process in detail. The reason for this is that the micelles formed are long-lived, which means that the micelle fraction appears as a separate peak in the chromatogram. (Similar conclusions have been reached previously.[39,40]) By comparison of the peak areas, it is thus possible to follow the temperature dependence of the fraction of polymer molecules in micellar form. As can be seen in Figure 2, this parameter increases strongly with increasing temperature, which is consistent with a decrease of the cmc with increasing temperature. Again, the model calculations agree qualitatively with the experimental fidings (Figure 2, inset). The origin of the discontinuity in the former case is that the model displays a discontinuity in the micellar *concentration* at the cmc. That is, as the polymer concentration exceeds the cmc from below, micelles occur at a finite concentration with a concomitant reduction of the free polymer concentration (see Figure 3 in ref 34).

The aggregation number of the Pluronic micelles is another parameter of large interest. This can be obtained, e.g., by static light scattering or fluorescence quenching measurements. Although the light scattering of block copolymers is generally quite complex, the optical similarity between PEO and PPO allows a straightforward evaluation of the average molecular weight, and hence of the aggregation number. Fluorescence quenching, on the other hand, relies on the determination of the number of micelles, which, in conjunction with the total amount of material, gives the aggregation number.

Although the experimental values obtained for the aggregation number vary quite strongly, it is clear that an increase in temperature results in a strong increase in the aggregation number.[2-6,8-14] As can be seen in Figure 3, this result is obtained also from model calculations. The model calculations predict aggregation numbers (N_{agg}) in the range of 7–9 for different temperatures at the cmc which are within the experimental range for Pluronic F127 at the cmc [(N_{agg}, t/°C) = (3.2, 35), (9.4, 40), (12.0, 45),[11] (N_{agg}, t/°C) = (6, 10), (15, 30), (20, 35), (44, 40),[12] and (N_{agg}, t/°C) = (30, 25)[14]]. A more detailed comparison is hampered by the spread of the experimental data due to uncertainty of the temperature dependence of the micellization, and by the often very gradual micellization behavior displayed by these somewhat polydisperse and heterogeneous systems. An interesting feature predicted from the model calculations is that, at the cmc, the

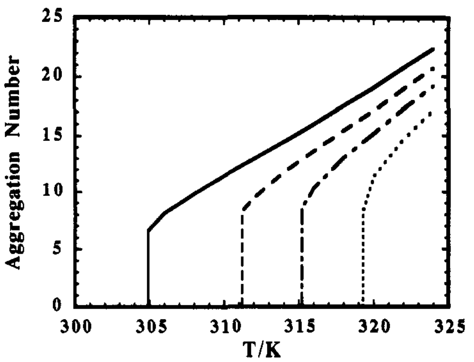

Figure 3. Calculated micellar aggregation numbers versus temperature (*T*) at polymer volume fractions of 0.005 (dotted line), 0.010 (dashed-dotted line), 0.020 (dashed line), and 0.050 (solid line).

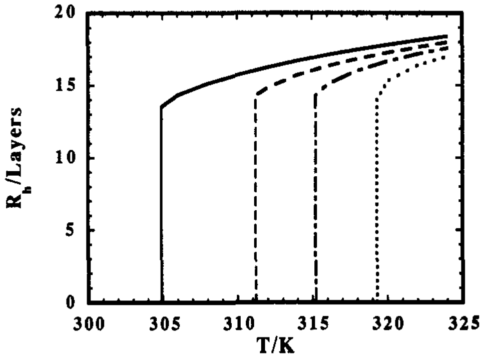

Figure 4. Calculated hydrodynamic radius of the micelles (R_h) versus temperature (*T*) at polymer volume fractions of 0.005 (dotted line), 0.010 (dashed-dotted line), 0.020 (dashed line), and 0.050 (solid line).

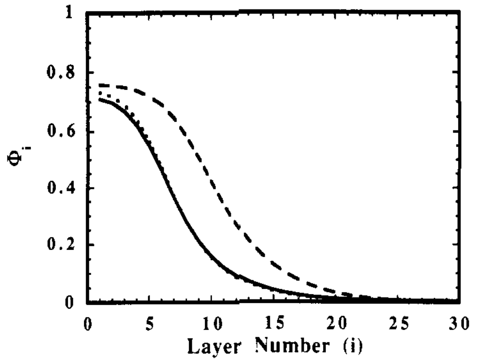

Figure 5. Calculated total volume fraction (Φ_i) of polymer versus layer number (*i*) at polymer volume fractions of 0.005 at T = 319.3 K (at the cmc, dotted line), 0.050 at T = 304.9 (at the cmc, solid line), and 0.050 at T = 324 K (above the cmc, dashed line).

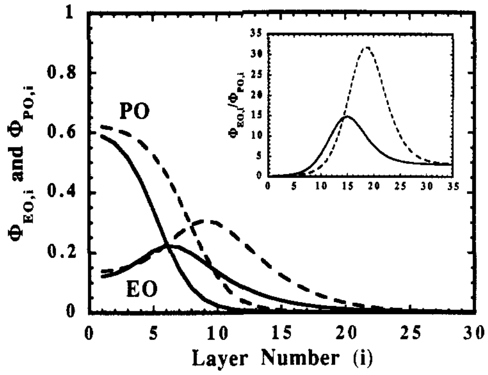

Figure 6. Calculated segment volume fraction ($\Phi_{EO,i}$ and $\Phi_{EO,i}$) versus layer number (*i*) at a polymer volume fraction of 0.050 at T = 304.9 K (at the cmc, solid lines) and at T = 324 K (above the cmc, dashed lines). The inset shows the volume fraction ratio ($\Phi_{EO,i}/\Phi_{PO,i}$) at 304.9 K (solid line) and 324 K (dashed line).

aggregation number is essentially independent of the polymer concentration. Simply speaking, this means that, with increasing temperature, the tendencies of (i) *increasing* the micellar size as a consequence of the more unfavorable solute-solvent interaction in the solution (at constant solute concentration) and (ii) *decreasing* the micellar size due to the lower solute concentration (chemical potential) to a large extent balance each other.

Another parameter describing the size of the micelles is their hydrodynamic radius. Experimentally, this parameter is obtained from diffusion experiments, using, e.g., NMR or photon correlation spectroscopy (PCS), and applying the Stokes-Einstein equation. From experiments, it has been found in several studies that, at micellization, the hydrodynamic radius increases. The magnitude of the increase, however, varies among studies.[2-6,8-11,13] In the model calculations, the hydrodynamic radius was obtained from the segment concentration distribution, according to the theory of Cohen Stuart et al.[41] As can be seen in Figure 4, the hydrodynamic radius is found to increase weakly with temperature, once micelles are formed, whereas an abrupt increase is observed at micellization. In regard to the absolute values of the theoretically obtained hydrodynamic radii, i.e., 15-20 layers, it is difficult to compare these directly with those obtained experimentally (100 Å at 32 °C and the cmc[11] and 110 Å at 25 °C and a concentration well above the cmc[14]). However, from previous adsorption studies of these and similar systems, we have found that a lattice size of roughly 4 Å gives a good agreement between experimental results and model predictions.[28,29] Using this value, we see that the theoretical values correspond to roughly 60-80 Å, in reasonable agreement with experimental findings, although somewhat too small. Note further that, as in the case of the aggregation number, the hydrodynamic radius of the micelles at the cmc is essentially independent of the polymer concentration.

So far, we have seen that the model gives a satisfactory agreement with experimental findings. With the model, however, we may go further to obtain more detailed information on the structure of the micelles. From Figure 5, showing the radial polymer volume fraction profile, we conclude that the micelles are rather diffuse objects on average. The polymer concentration decays continuously from about 70% to 80% at the center of the micelles, and reaches the free polymer concentration (to within 10%) at layer 30 (about 120 Å). In analogy with previous results, we find that the volume fraction profile at the cmc is essentially independent of the polymer concentration. Increasing the temperature once micelles are formed, however, results in larger micelles, as illustrated by the displacement of the entire volume fraction profile to larger distances with increasing temperature. This is analogous to the increase in the aggregation number with increasing temperature (Figure 3).

Finally, we should mention that the predicted water content of the core of the micelles is likely to be too high and that it should *not* be used as an indication of the presence of water in the Pluronic micelles. Previously, it has been demonstrated that this type of mean-field lattice theory exaggerates the water content in hydrophobic regions, e.g., in lecithin bilayers, which from experiments are known to be essentially free of water.[42]

Using the model, we may go one step further, which is illustrated in Figure 6. In this figure, the radial volume fraction profiles of EO and PO segments are shown at a polymer volume fraction of 0.050, both at the cmc and at a higher temperature. At both temperatures, the PO

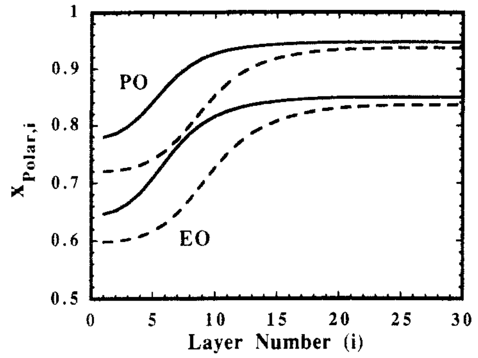

Figure 7. Calculated fraction of polar state ($x_{\mathrm{polar},i}$) versus layer number (i) at a polymer volume fraction of 0.050 at T = 304.9 K (at the cmc, solid lines) and at T = 324 K (above the cmc, dashed lines).

segments are preferentially located in the core of the micelles, whereas the EO segments are primarily located in the outer region of the micelles. This is what one would expect from solvency, since PPO is more hydrophobic than PEO. Note, however, that the segregation is far from complete, and that the volume fraction of EO in the core of the micelles is substantial (~15%). On increasing the temperature, the aggregation number and the hydrodynamic radius both increase, as discussed previously. This results in the segment concentration distributions of both EO and PO being displaced to larger distances. Furthermore, as is illustrated by the inset of Figure 6, the segregation of EO and PO groups increases with increasing temperature, which is analogous to the behavior of these polymers at hydrophobic surfaces with an increasing adsorbed amount.[28] Note, however, that there appears to be no dramatic dehydration of the micelles at higher temperature, as has previously been suggested (cf ref 14).

In Figure 7, we show the fraction of polar states (vide supra) as a function of the radial distance from the center of the micelles at two different temperatures. As can be seen in this figure, the fraction of polar states of both EO and PO groups decreases with decreasing distance to the center of the micelles, which is a result of conformational adaptation to the higher segment concentrations at smaller radii and to the PO/EO segregation. Thus, the model predicts a micelle consisting of a hydrophobic core surrounded by a more hydrophilic shell. (Note that $x_{\mathrm{PO},i} > x_{\mathrm{EO},i}$ should not be interpreted as PO being more hydrophilic than EO. Although the conformations of both PEO and PPO are subdivided into one polar and one nonpolar class of conformations, their interactions with water are quite different; cf. Table I.) On increasing the temperature, both the aggregation number and the micellar size increase, as discussed previously. From Figure 7, we see that this results in the hydrophobic core extending to larger radii at higher temperatures. This is primarily a consequence of the polymer concentration at a given radius being higher at a higher temperature, although the increase in temperature as such results in an overall decrease of the fraction of polar states as well (cf. Figure 7).

Conclusions

The present model is able to qualitatively reproduce a number of experimental findings on the temperature-dependent micellization of Pluronic block copolymers. These include the decrease in the cmc, the increase in the fraction of polymer molecules in micellar form, the increase in the average aggregation number, and the increase in the hydrodynamic radius, all with increasing temperature. Furthermore, the model directly provides information on the details of the micellization, e.g., the radial distributions of the different segments and the distribution of conformational states. Note that although the model contains a number of parameters, the present findings were obtained by using the same values of the parameters as those used in our previous studies of the adsorption of Pluronic block copolymers to solid surfaces. Moreover, these values were obtained from the binary PEO/water and PPO/water phase diagrams directly. Thus, the predictive capacity and the usefulness of the two-state model for describing polymers displaying a reversed temperature behavior, previously documented for homogeneous systems, appear to be good for heterogeneous systems as well.

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