Micellar Structure and Dynamics in Aqueous Solutions of PEO-PPO-PEO Block Copolymers

by

Isabella Goldmints

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Abstract

In Part I of this thesis, the structure and dynamics of micelles in aqueous solutions of poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO) triblock copolymers were investigated. The structure of micelles was studied using small-angle neutron scattering (SANS). A model-independent contrast variation method was used to obtain the aggregation number in solutions at lower concentrations, when the Guinier approximation can be used. To determine the structure of the micelles (core and corona radii), a number of spherical core-corona models were explored. It was found that a model allowing for different water contents in the core and corona described the experimental data well for all temperatures and concentrations. However, at lower concentrations the model fits were non-unique, and equally good fits could be obtained for widely varying core and corona water contents. At higher concentrations, steric interactions between micelles are present. These interactions were described using a hard sphere interaction potential with the assumption that the interaction radius is equal to the corona radius. Only with this constraint did the model become sufficiently sensitive to the fitted parameters to allow us to extract meaningful information on the water content in the core and the corona. It was conjectured that these conclusions could be extrapolated to lower concentrations. However, the details of the internal structure could not be determined because the scattering length densities (SLD) of PEO and PPO are very close, making it impossible to distinguish experimentally between the PPO and PEO regions within the micelle. To verify the model and obtain information on the internal structure of the micelles, a copolymer with deuterated PEO blocks was used. The different SLDs of the d-PEO and PPO blocks make it possible to distinguish between these blocks. By using a range of D<sub>2</sub>O to H<sub>2</sub>O ratios in the solvent to highlight different regions of the micelle, PPO and PEO regions can be studied independently. The assumption of equality of the corona and the hard-sphere interaction radii was not required. We used only dilute solutions for which the contributions from the structure factor to the scattering were negligible. The size of the PPO core was obtained directly from the form factor, which is very sensitive to the core radius. An analysis of the sensitivity
of the model to all fitting parameters was performed. It was found that the model is very sensitive to the aggregation number and the core radius, and less sensitive to the corona radius. The effect of micelle polydispersity was studied. It was shown that the standard deviation of the aggregation number is at most 25%. The results of the experiments were used to verify the validity of the previously developed core-corona model for lower concentrations. The average aggregation number was found to increase with increasing temperature with a corresponding decrease in the micellar water content. The number density of the micelles was found to decrease with temperature at higher concentrations. Now that the validity of the model has been established, it can be used to describe the micelle structure of commercial protonated copolymers.

The dynamics of block-copolymer micelle rearrangements were determined by following the relaxation from one equilibrium state to another after creating a temperature perturbation using a 2 μs iodine laser pulse. The relaxation of the system was monitored by measuring the change in intensity of scattered light at 90°. For many polymers, two time scales were identified. The first, fast relaxation process was accompanied by an increase in the light scattering intensity, while the second, slow relaxation process was accompanied by a decrease in the light scattering signal at temperatures close to the CMT (critical micellization temperature). The second relaxation process was detected only in a certain concentration and temperature range. The Aniansson-Wall theory of stepwise micellization was used to interpret the experimental results. A numerical solution of the Aniansson-Wall equations was obtained for the first time with experimentally measured initial conditions. The numerical solution of the Aniansson-Wall equations agrees with experimental data and suggests the mechanisms associated with the two time constants. The first time scale, in the tens of microseconds range, is attributed to monomer insertion into the micelles. The second time scale, in the millisecond range, is associated with the rearrangement of the micelle size distribution accompanied by a decrease in the micelle number density. For the second process, the Aniansson-Wall theory predicts a negative amplitude of the light scattering signal in the certain concentration and temperature range, and it explains the lack of it at other conditions.

In Part II of the thesis, the process of spontaneous vesicle formation in mixtures of cationic and anionic surfactants was studied. It was found that aggregate growth during the first three hours after mixing the initial solutions is independent of the presence of mixed micelles in the initial solutions and of added salt concentration. Viscosity and dynamic light scattering measurements suggest that the intermediate aggregates are nearly neutral and are non-equilibrium vesicles or mixture of vesicles and disk-like structures. Vesicles formed in the mixture were imaged by cryo-TEM.
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Part I

Micellar Structure and Dynamics in Aqueous Solutions of Block Copolymers
Chapter 1

Introduction

Amphiphilic molecules which consist of hydrophobic and hydrophilic parts form a variety of microstructures in water, a selective solvent for these molecules. The self-assembled microstructures, such as micelles, vesicles, and bilayers, can be viewed as microphase separations. The phase separation occurs on the microscopic scale while macroscopically the solution remains homogeneous. The formation of microscopic hydrophobic regions with extremely high surface to volume ratios within macroscopically homogeneous aqueous phases results in systems with unique physical chemical properties and an endless list of applications.

1.1 Motivation

The focus of this thesis is the understanding of equilibrium and dynamic properties of microstructures formed by amphiphilic block copolymers. They can also self assemble in a selective solvent, which is a good solvent for one block and a poor solvent for the other. Although many features of the self assembly process of block copolymers are similar to those of short chain surfactants, there are a few differences resulting from such properties as high molecular weight, polydispersity, variable length and composition of copolymers. This puts them in a separate class of amphiphilic molecules which is of specific interest from a fundamental point of view, as well as from the point of view of applications.
The PEO-PPO-PEO triblock copolymers have been chosen for this study for a variety of reasons. Poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) (PEO-PPO-PEO) triblock copolymers are commercially available nonionic macromolecular surfactants often known by trade names such as Pluronic® (BASF) and Synperonic® (ICI). The ability to vary molecular weight and the ratio of the hydrophilic (PEO) to hydrophobic (PPO) block lengths allows the production of PEO-PPO-PEO copolymers with desired properties for a variety of applications. As a result, PEO-PPO-PEO triblock copolymers are used for many applications including detergency, foaming, and emulsification [1], separation [2] and solubilization of organics in aqueous solutions [3], sustained release of perfume compounds [4], corrosion protection [5], and production of porous and composite materials [6], as well as some applications arising from the low toxicity of PEO-PPO-PEO, like protection of microorganisms from damage in bioprocessing [7], and drug solubilization [8] and controlled release [9, 10, 11].

PEO-PPO-PEO block copolymers form micelles in aqueous solutions. The process of micellization can be induced by increasing the solution concentration to be above the CMC (critical micellization concentration) and/or adjusting the temperature to exceed the CMT (critical micellization temperature). Above the CMT there is an equilibrium region of width 10-15°C, referred to as the unimer-to-micelle transition region, where significant amounts of both free and associated copolymer molecules coexist. Above the transition region most copolymer molecules are in micelles. The micelles can have different shapes and aggregation numbers and can be arranged into different ordered structures at higher concentrations and/or temperatures.

Many applications of PEO-PPO-PEO block copolymer solutions are based on the solubilization of hydrophobic compounds in aqueous solutions by placing them in the micellar hydrophobic core. In these cases, a knowledge of the structural characteristics of the micelles and their dependence on the solution conditions is vital. In many of these applications, the system is not in equilibrium. For example, in the case of controlled drug release, the hydrophobic drug is solubilized in the micelle. When introduced into the body, the solution undergoes dilution and/or a temperature change,
and the drug is released upon the breakup of the micelles. Even under equilibrium
the micellar solution is a dynamic system, so an exchange of surfactant molecules
between micelles and the solution, and micelle formation and break-up are present
all the time. Thus, a knowledge of the dynamics of these systems is necessary for the
best designed applications.

There have been numerous attempts to design drug delivery systems with con-
trolled release of the drug based on PEO-PPO-PEO block copolymers. Both dilute
and concentrated solutions have been studied. In the case of concentrated solutions,
a PEO-PPO-PEO gel usually forms. There is a possibility of solubilizing hydrophobic
drug molecules in the hydrophobic PPO core or entrapping hydrophilic drug molecules
in the extended hydrophilic PEO corona [12, 13, 14, 15, 16]. Although the process of
gelation attracted scientific attention [17, 18, 19, 20, 21] due to measurable effects on
the drug release process, there is still a lack of understanding of the mechanism of the
release, the structure of the gel, and the change in the gel structure upon introduction
of the solute and upon changing solution conditions (temperature, copolymer or salt
concentration).

In dilute solutions, a hydrophobic drug molecule is solubilized in the PPO core
of PEO-PPO-PEO micelles. The micellar solution is then introduced to the body
fluid, and the drug is released upon dilution of the micellar solution. In this case
there is also a measurable effect of extended and enhanced delivery to the targeted
areas [22, 23, 24, 25]. The structural changes in the micelles upon dilution as well
as the mechanism of such changes and of solute release are not understood. Studies
of micelle structure, its dependence on the solution conditions, and the dynamics of
micellar solutions are important steps in replacing the trial-and-error approach which
has dominated the design of applications of PEO-PPO-PEO systems.
1.2 Related Work in Micellar Dynamics

1.2.1 Theory

The dynamics associated with self-assembly of surfactant molecules has been studied both theoretically and experimentally. According to the Aniansson-Wall theory [26] there are two relaxation times, one associated with single surfactant molecules entering or exiting a micelle, and the other associated with micelle formation or dissolution. The theory assumes that micelle rearrangement following a perturbation in solution conditions proceeds stepwise as surfactant molecules are added one by one to the growing micelle. The relaxation times have been obtained from an approximate analytical solution of the linearized equations. The numerical solutions of the full non-linear equations [27] are in a good agreement with the analytical solution of the linearized equations for very small deviations from equilibrium. Some other cases of equilibrium perturbation have also been investigated using numerical solution [27]. The Aniansson-Wall theory has been extended to account for the effects of concentration, temperature, hydrophobic tail length, and counter-ion on relaxation times [28]. Extension to this theory was provided [29] to include the predictions of observed amplitudes and the fission/fusion of micelles in non-ionic surfactant systems or in ionic surfactant systems at high salt concentrations [30]. This model will be discussed in more detail in Chapter 4.

1.2.2 Experimental Studies

The Aniansson-Wall theory has been confirmed by a number of experimental studies in which the two relaxation times, $\tau_1$ and $\tau_2$, were detected by various experimental techniques. The experiments have been performed with short chain non-polymeric ionic surfactants. The fast process ($\tau_1$ on the order of microseconds) has been detected by means of temperature jump, ultrasonic absorption and shock tube methods. The slow process ($\tau_2$ ranging from milliseconds to seconds) has been detected by pressure and/or temperature jump experiments [28, 31, 32]. The effect of temperature, sur-
factant and salt concentrations on the dynamic behavior of ionic surfactant systems has been studied [28]. It has been found that the experimental results agree well with Aniansson-Wall predictions. A comparison has been made between the micellar systems consisting of single and double chain surfactants [33]. For most of these systems two relaxation times could be observed and the results have been explained in terms of the Aniansson-Wall theory. The kinetics of micelle formation in formamide has also been studied [34]. It has been shown that the kinetic mechanism is the same as the corresponding process in water.

Experimental investigation of non-ionic surfactant systems using temperature jump and pressure jump methods with fluorescence detection has also revealed two relaxation times. The time scale and amplitude of the first, fast relaxation and the amplitude of the second, slow process agreed well with theoretical predictions for non-ionic systems, while the second time scale and its concentration dependence showed considerable discrepancy with the proposed theory (Aniansson-Wall with micellar fission/fusion correction) [35]. The results of ultrasonic relaxation and volumetric studies of monomer exchange are in good agreement with the Aniansson-Wall theory [36].

1.3 Related work on PEO-PPO-PEO Block Copolymers

1.3.1 Equilibrium Properties

PEO-PPO-PEO block copolymer aqueous solutions exhibit an array of different phases depending on the concentration and composition of the copolymer and the temperature of the solution [37, 38, 39].

Properties near micellization region. Below the CMC (critical micellization concentration) and the CMT (critical micellization temperature) there are only unimers (single copolymer chains) in solution. The process of micellization can be induced
by increasing the solution concentration to be above the CMC (critical micellization concentration) and/or adjusting the temperature to exceed the CMT (critical micellization temperature). Above the CMT there is an equilibrium region of width 10-15°C, referred to as the unimer-to-micelle transition region, where significant amounts of both free and associated copolymer molecules coexist. Above the transition region most copolymer molecules are in micelles. Various techniques have been used to detect this region, which is characterized by rapid changes in such variables as hydrophobicity, partial specific volume, heat capacity, light scattering intensity and solubilization capacity; on either side of this region the changes in these property values are smaller [40, 41, 42, 39, 43, 44, 45]. The number density of unimers decreases rapidly throughout the transition region as they are incorporated into micelles. The largest change in the intensity of scattered light with temperature is observed in the transition region due to the formation and growth of micelles. This makes it possible to study dynamic properties of the system using temperature jump techniques, by following the scattered light intensity as the system relaxes to a new equilibrium state following a small, but rapid, increase in temperature [46]. In order to interpret such dynamic experiments fully, the micelle structure within the transition region should be understood. To date, however, there are very few studies of the micelle structure in this region [39], although small angle X-ray scattering (SAXS) has revealed the changes in the internal structure of micelles in the transition region [42].

**Properties above the unimer-to-micelle transition region.** There are several studies of the structural characteristics of micelles above the unimer-to-micelle transition region [39, 47]. Conventional methods such as light scattering and time-resolved fluorescence quenching (TRFQ) are not suitable for determination of aggregation numbers in this system: dynamic light scattering because of unknown water content in the micelle, and TRFQ because of slow quenching [48, 49, 50, 51, 52]. Small-angle neutron scattering (SANS) has been employed successfully to probe the structure of PEO-PPO-PEO micelles. Above the unimer-to-micelle transition region, the micelles are spherical and consist of a PPO core with no water and a strongly hydrated PEO
corona [39, 42, 53]. Mortensen and Pedersen [39] obtained aggregation numbers for P85 micelles above the transition region using SANS, showing that in this region the aggregation numbers are independent of concentration, but increase with temperature, from 37 at 20°C to 78 at 40°C. The hard sphere interaction radius reported is in the range of 50 to 70 Å and the core radius is in the range of 30 to 50 Å [39]. They also demonstrated that for one temperature in the transition region (C=4%, T=26.8°C) the micelles have a spherical shape and are relatively monodisperse [39]. The micelle radius at this temperature is approximately 50 Å. The aggregation number for P85 ($M_w = 4500$) at 40°C obtained by Brown et al. [17] using static light scattering and extrapolation to zero concentration is 30.

**Properties at high concentrations and/or temperatures.** As the concentration of copolymer and/or the temperature increases, the micelle shape can change to elongated, rod-like. This transition can be detected by measuring translational and rotational diffusion using dynamic light scattering [53] or by small angle neutron scattering [39, 54]. These rod-like micelles can assemble in hexagonal arrays.

The spherical micelles at higher concentrations and/or temperatures can form a variety of cubic crystalline structures [37, 38, 55]. These ordered cubic structures can undergo thermally or shear induced transitions from one type of lattice to another [37, 56, 57].

**Effect of additives.** The effects of additives and composition of block copolymer on the equilibrium properties of the solution have also been studied. The addition of several salts to the block copolymer solution lowers the CMT/CMC and the cloud point of the solution [21, 58, 59] while addition of KCNS resulted in an increase in the cloud point temperature [60]. Urea has been shown to increase the CMT of the block copolymer solutions [61], and some additives increase the cloud point temperature of solutions [62]. While no detailed study has been performed to elucidate the structure of the aggregates formed in the presence of salt, it is reasonable to assume that the structure is the same as in the solution without salt at the same deviation from the
CMT/CMC, since the addition of salt may result only in a change in the CMT/CMC without a qualitative change in the solution behavior at the same deviation from the CMT/CMC.

**Effect of copolymer composition.** The effect of copolymer composition on aggregation behavior (CMT, CMC, aggregation number and shape of the aggregates) has been studied [40, 41, 43, 63, 64, 65, 66, 67, 68]. The CMT/CMC decreases with increasing size of the PPO block, and only slightly increases with increasing size of the PEO blocks if the PPO block size is kept constant. A correlation for the estimation of the CMT and the CMC of PEO-PPO-PEO block copolymers has been developed [69]. The aggregation number is lower for copolymers with longer PEO blocks and the same PPO blocks due to steric interactions between the PEO blocks.

**Theory.** Self consistent mean field theory predictions of the effect of temperature, concentration and molecular weight of the copolymer are in a good qualitative agreement with experimental data [70, 71, 72]. The theory yields water and segment density profiles, predicts smaller micellar core, lower aggregation number, and more extended PEO corona for the copolymers with longer PEO blocks and the same PPO block. According to the theory, the micellar core consists of PPO blocks and some water, and the corona consists of strongly hydrated PEO blocks. There is no sharp interface between the core and corona regions.

### 1.3.2 Dynamic Properties

**Theory.** A theory of polymeric micelle relaxation kinetics has been developed by Halperin and Alexander [73] who analyzed the behavior of diblock copolymers in a selective solvent. Two mechanisms have been considered: the Aniansson-Wall mechanism in which aggregates are allowed to interact only with unimers, and the fission-fusion mechanism in which interaction between pairs of aggregates is allowed. The Aniansson-Wall mechanism has been found to have the lower activation free energy suggesting that it should be the preferred route by which perturbed micellar solutions
relax to their new equilibrium states.

The simulation studies have included Monte Carlo simulations of the self-assembly of the $A_{10}B_{10}$ diblock copolymer [74] and stochastic dynamic simulations of the model amphiphile $A_2B_2$ [75]. It was concluded in the latter study that the response of the system to a small perturbation can be successfully described by the Aniansson-Wall theory. The agreement with theory was excellent for the fast process while deviations from the theory at longer times were explained by the errors in estimating the dissociation rate and number density of aggregates in the micelle-depleted zone, i.e. that portion of the frequency vs. aggregation number curve in which the frequency is very low.

**Experimental studies.** Experimental dynamics studies of PEO-PPO-PEO block copolymer micelles are still rare and give inconsistent results. It has been concluded from gel permeation chromatography that the residence time of a copolymer molecule in a micelle is of the order of hours [76]. In contrast, NMR results suggested that the lifetime of a molecule in a micelle is less than 3 ms [77]. Temperature jump experiments with Joule heating [46] gave a single relaxation time in the millisecond range. A disadvantage of this method is that it requires the addition of salt as a third component in the system. In a more recent study two relaxation times have been detected for the copolymer L64 [78]. The experimental results have been explained in the framework of the Aniansson-Wall theory. In a different study of the dynamics of L64 three relaxation times have been reported [79], although it is unclear whether all three correspond to separate processes since a maximum of two relaxation processes have been observed in any single experiment.

Experimental studies on the kinetics of other block copolymer micelle formation and dissociation have been carried out using temperature jump and stopped-flow techniques [80, 81]. For most of those studies, however, the initial condition lay in the unimer-only region and the final condition in the micelle region. In such jumps, significant numbers of dimers and trimers are formed during the initial stages and these then interact with each other in a manner not accounted for in the stepwise
association model of Aniansson and Wall.

1.4 Contributions

The goal of this thesis is to explore the structure and dynamics of micelles formed by PEO-PPO-PEO triblock copolymers.

The structure of micelles was studied using small angle neutron scattering (SANS). A model-independent contrast variation method was used to obtain the aggregation number in solutions at lower concentrations, where the Guinier approximation can be used. The results were in a good agreement with those obtained by the model fitting. The model fitting approach provided more details on the internal structure and must be used at higher concentrations. The model was verified and the additional information on segment distribution was obtained in SANS experiments using copolymer with deuterated blocks. These experiments also allowed for the direct determination of the micellar core size. The temperature and concentration dependence of the micellar structure was obtained from SANS experiments.

The dynamics of block copolymer micelle rearrangements were determined by following the relaxation from one equilibrium state to another after creating a temperature perturbation using a 2 µs iodine laser pulse. This technique does not require the addition of a third compound to the system and is preferred to the Joule heating temperature jump technique. For many polymers, two time scales were identified. The first, fast relaxation process was accompanied by an increase in the light scattering intensity, while the second, slow relaxation process was accompanied by a decrease in the light scattering signal. The second relaxation process was detected only in a certain concentration and temperature range.

The Aniansson-Wall theory of stepwise micellization was used to interpret the experimental results. A numerical solution of the full Aniansson-Wall equations was, for the first time, used with the experimental initial conditions for PEO-PPO-PEO micelles to explain the temperature jump results. The initial conditions were obtained from the SANS experiments. The numerical solution of the Aniansson-Wall equations
agrees with experimental data and suggests the mechanisms associated with the two time constants. The first time scale, in the tens of microseconds range, is attributed to monomer insertion into the micelles. The second time scale, in the millisecond range, is associated with the rearrangement of the micelle size distribution accompanied by a decrease in the micelle number density. For the second process, the Aniansson-Wall theory predicts negative amplitude of the light scattering signal in a certain concentration and temperature range, and it explains the lack of it at the other conditions.
Bibliography


Chapter 2

Micellar Structure in the
Unimer-to-Micelle Transition Region

2.1 Introduction

The focus of this chapter is on the determination of the equilibrium PEO-PPO-PEO micelle structure in the unimer-to-micelle transition region. As noted in Chapter 1, there are three regions near the CMT (critical micellization temperature). Below the CMT all of the unimers (single polymer chains) are unassociated in the solution. Above the CMT there is an equilibrium region of width 10-15°C, referred to as the unimer-to-micelle transition region, where significant amounts of both free and associated copolymer molecules coexist. Above the transition region most copolymer molecules are in micelles. The unimer-to-micelle transition region is characterized by rapid changes in such variables as hydrophobicity, partial specific volume, heat capacity, light scattering intensity and solubilization capacity; on either side of this region the changes in these property values are smaller [1, 2, 3, 4, 5, 6, 7]. The large change in the intensity of scattered light with temperature in the transition region due to the formation and growth of micelles makes it possible to study dynamic properties
of the system using temperature jump techniques, by following the scattered light intensity as the system relaxes to a new equilibrium state after a small, but rapid, increase in temperature [8]. Knowledge of the equilibrium micellar structure in this region is essential for the interpretation of such experiments and the understanding of the dynamic behavior of the system.

Although there have been several studies of the structural characteristics of micelles above the unimer-to-micelle transition region [3, 4, 9, 10, 11], almost no studies have been made of the transition region itself.

Goals. The goal of this Chapter is to determine the micelle structure in the unimer-to-micelle transition region. The model-independent approach which provides several characteristics of the micellar structure is compared to the model fitting approach which provides more information on the internal structure of the micelle.

2.2 Methods for Determination of Equilibrium Structure

Several methods are traditionally used for the determination of an aggregation number, one of the important equilibrium characteristics of the micellar structure. Conventional methods such as light scattering and time-resolved fluorescence quenching (TRFQ) are not suitable for the determination of the aggregation numbers in the PEO-PPO-PEO micellar system. Dynamic light scattering measurements give the hydrodynamic radius of a micelle, but because of the unknown water content in the micelle it is impossible to determine the aggregation number. TRFQ cannot be used in this system because of slow quenching due to high viscosity in the polymeric micellar core and its relatively large dimension [12, 13, 14, 15, 16]. Small-angle neutron scattering (SANS) has been employed successfully to probe the structure of PEO-PPO-PEO micelles above the transition region.
2.3 Description of Experiments

The triblock copolymer EO26PO46EO26 (Pluronic® P85, $M_w = 4600$) was obtained from BASF Corp. and used without further purification. The copolymer was dissolved in water with different D2O to H2O ratios at room temperature to form homogeneous transparent solutions, which were filtered through 0.22 μm Millipore filters. The mixtures of D2O and H2O were prepared from deuterium oxide (D2O, 99.9 atom% D) obtained from Aldrich Chemical Company, Inc. (Milwaukee, WI) and Milli-Q H2O. Samples were then transferred into 1-mm thick quartz containers for SANS measurements.

2.3.1 SANS

Small-angle neutron scattering experiments were performed at the National Institute of Standards and Technology, Gaithersburg, MD. The neutron wavelength in these experiments was 6Å with a neutron wavelength resolution $\Delta \lambda/\lambda = 0.11$. The range of scattering vectors $|q| = q = (4\pi/\lambda)(\sin \theta)$ covered by the experiments was from 0.01 to 0.15Å⁻¹. The scattering data were corrected for scattering from solvent, the quartz container, and other sources. To correct for the scattering from unimers in the solution, the scattering curves for unimers at a concentration equal to the CMC at the temperature of the experiments were subtracted from the scattering data. The effect of this correction was negligible at all temperatures except the lowest one. The smearing induced by the instrumental setup had practically no effect on the scattering data [17] and was not included in the analysis. The scattering patterns were azimuthally isotropic. The scattering intensity was therefore averaged over all directions for the same absolute value of $q$, resulting in a one-dimensional scattering function $I(q)$.

2.3.2 Light scattering

Static light scattering measurements were performed using Photon Technology International equipment with a xenon light source. The intensity of scattered light at 356
nm was measured at a scattering angle of 90°.

2.3.3 Partial specific volume measurements

Density measurements were performed using a Mettler/Paar Calculating Digital Density Meter DMA-45. The partial specific volume of the copolymer was obtained as the tangent to plots of the volume of the solution containing 1 kilogram of solvent vs. concentration in kilograms of polymer per kilograms of solvent.

2.4 SANS Contrast Variation Method

2.4.1 Method Description

The small angle neutron scattering intensity from a monodisperse system can be described as:

\[ I(q) = N P(q) S(q), \]

(2.1)

where \( N \) is the number density of scattering centers (colloidal particles), \( P(q) \) is the intraparticle form factor, and \( S(q) \) is the interparticle structure factor. For dilute solutions in which the interactions between particles are negligible, the structure factor \( S(q) = 1 \). The form factor, \( P(q) \) is

\[ P(q) = |F(q)|^2, \]

(2.2)

for a solution of identical colloidal particles. For each particle

\[ F_j(q) = \int_{\text{j-th particle}} (\rho_j(r) - \rho_s) \exp(iq \cdot r) d^3r, \]

(2.3)

where \( \rho_j(r) \) is the scattering length density (SLD) of the \( j \)-th particle, and \( \rho_s \) is the SLD of the solvent. It is assumed that the solvent molecules are small compared to the colloidal particles and the solvent can be treated as a continuum with a constant SLD. Expansion of equation (2.2) in the small \( q \) range \( (qR_g < 1) \) gives intensity \( I(q) \)
in this range \[18\]:

\[ I(q) = (C - CMC)N_{agg}(b_m - V_m \rho_s)^2 \exp(-q^2R_g^2/3) \] (2.4)

where \( N_{agg} \) is the average aggregation number, \( b_m \) is the sum of scattering lengths of nuclei in the unimer (single copolymer molecule), \( V_m \) is the volume of the unimer, and \( R_g \) is the radius of gyration of the micelle (colloidal particle) defined by

\[
R_g^2 = \frac{\int s^2(\rho(r) - \rho_s)d^3r}{\int(\rho(r) - \rho_s)d^3r} . \tag{2.5}
\]

The value of the solvent SLD, \( \rho_s \), may be changed by varying the ratio of \( D_2O \) to \( H_2O \) in the solvent. A Guinier plot \((\ln I(q) \text{ vs. } q^2)\) of eq.(2.4) yields a straight line with slope \(-R_g^2/3\) and intercept \(\ln I(0)\), where

\[ I(0) = (C - CMC)N_{agg}(b_m - V_m \rho_s)^2 \] (2.6)

A plot of \(-\sqrt{I(0)/(C - CMC)} \text{ vs } \rho_s \text{ (or } % \text{ D}_2\text{O in the solvent)}\) gives the volume of the copolymer molecule \(V_m\) \((V_m = b_m/\rho_s \text{ at } I(0) = 0)\) and, from the slope, the aggregation number \(N_{agg}\) [18].

### 2.4.2 Assumptions

The contrast variation method described above involves several assumptions which are discussed in this section. The method assumes no interaction between micelles \((S(q) = 1)\). The characteristic scattering pattern for different concentrations of P85 at a deviation from the CMT of approximately 9°C is shown in Figure 2-1. The CMT (critical micellization temperature) of PEO-PPO-PEO block copolymer solutions depends on concentration [1], so it is convenient to compare properties of solutions of different concentrations at the same deviation from the CMT \((T-CMT)\) rather than at the same temperature. At high concentrations \((5\%)\), \(I(q)\) initially increases and then passes through a maximum before decreasing; this behavior is characteristic of micellar systems in which there are significant correlations between micelles. The 1%
curve does not show this behavior, decreasing monotonically with increasing $q$. The lack of interactions between micelles at this lower concentration is confirmed by the linear nature of the Guinier plot ($\ln I(q)$ vs. $q^2$) at low $q$ values (Figure 2-2).

The scattering intensity from the 1% solution at different temperatures is shown in Figure 2-3. Although the absolute intensity increases with temperature, the shape of the curve does not change, as attested to by the fact that the curves are essentially identical when normalized by their respective highest intensity values (at the lowest $q$). Micelles above the transition region have been shown by dynamic light scattering to be nearly monodisperse [5]. More importantly, Mortensen and Pedersen [4] concluded that for 4% P85 solution at 26.8°C, which lies within the transition region, micelles have very low polydispersity. It will therefore be assumed in the analyses here that all micelle populations are monodisperse. We will also assume no interactions between micelles when analyzing data for the 1% solution.

The contrast variation approach involves an additional assumption: the behavior
Figure 2-2: Guinier plots of \( \ln I \) vs. \( q^2 \) for 1% P85 in 100% D\(_2\)O.

Figure 2-3: Scattering curves for a 1% solution of P85 (CMT=30\(^\circ\)C) in D\(_2\)O at different temperatures.
of the system is the same in H₂O as in D₂O. To test this assumption we performed static light scattering measurements in the transition region (Figure 2-4). The scattering intensity shown in Figure 2-4 is normalized with respect to the value at the highest measured temperature. The behavior of P85 in H₂O and D₂O is very similar; the difference being close to the experimental error.

### 2.4.3 Results

Figure 2-5 shows a plot of $\pm \sqrt{I(0)/(C - CMC)}$ vs. % D₂O for different temperatures. The mean polymer volume $V_m$ extracted from the plot is $6400 \pm 200\text{Å}^3$. The aggregation numbers (Figure 2-6) vary linearly with temperature from 29 at $T=33.3^\circ\text{C}$ to 52 at $T=42.9^\circ\text{C}$. The polymer volume obtained from solution density measurements is $6900 \pm 100\text{Å}^3$ which is higher than that obtained from neutron scattering experiments but is the same for polymer in D₂O and H₂O as shown in Figure 2-7.

Polymer volume depends on temperature [6, 7, 9] but, for the modest temperature
Figure 2-5: Linear fit to plots of $\pm(I(0)/(C - CMC))^{1/2}$ vs. % D$_2$O in the solvent at different temperatures for 1% solutions of P85.

Figure 2-6: The effect of temperature on micelle aggregation numbers obtained using the contrast variation method for a 1% solution of P85 (CMT=30°C).
Figure 2-7: Partial specific volume measurements for P85 in H₂O (circles) and D₂O (squares) at two temperatures: 27°C (open symbols) and 37°C (filled symbols). The partial specific volume determined as the tangent to the plots is 0.898 l/kg.
range of interest, this dependence is within experimental error. Using the contrast variation method we cannot draw any conclusions about water content in the micelle because the SLD of water within the micelle is the same as that of water in the bulk and therefore does not contribute to the observed scattering [19].

2.5 Model Fitting Approach

2.5.1 Models

To obtain information about micelle structure (water content and water distribution within the micelle) we need to develop appropriate models and fit the models to the data. The scattering function for a monodisperse system of particles can be written as

\[ I(q) = NP(q)S(q) \]

where \( N \) is the number density of scattering centers \( N = (C - CMC)/N_{agg} \), \( P(q) \) is the particle form factor, and \( S(q) \) is the structure factor describing particle interactions. As shown earlier there are no interactions in the dilute 1% solution, and thus \( S(q) = 1 \). It has been shown that P85 micelles formed in aqueous solutions at temperatures and concentrations above the transition region are spherical [3, 4], and therefore it is reasonable to assume that micelles in the transition region are also spherical. We propose four different models with different form factors.

In Model 1 we assume there is no water in the micelle (either in the core or in the corona). The form factor for this model is just that for spherical particles,

\[ P(q) = \left[ \frac{3}{(qR)^3} \left( \sin(qR) - qR \cos(qR) \right) \right]^2 \left( \frac{4\pi}{3} R^3 \right)^2 (\Delta\rho)^2 \]

where \((\Delta\rho)^2\) is the contrast \((\rho_s - \rho)^2\), \(\rho\) is the particle SLD, and \(R\), the radius of the micelle, is the only fitting parameter in this model. This model was unable to fit the shape of the curve and the absolute intensity at the same time and is not considered further. Since the absolute maximum intensity depends mostly on the
aggregation number, and the curvature of the scattering function depends on the micelle geometry, indications are that there is water in the micelle, so the micelle can have a larger radius with the same copolymer aggregation number. Including micelle size distribution (polydispersity) in the model did not improve the fit. The influence of polydispersity in the model is discussed in greater detail in Chapter 3.

Models 2, 3, and 4 allow for various degrees of solvation within the spherical micelle.

In Model 2 the water is assumed to be evenly distributed in both the core and the corona of the micelle. The form factor is the same as in Model 1 (eq. 2.8), but because there could be water in the micelle, the contrast factor will be \((\rho_s - \rho_{\text{micelle}})^2\), with \(\rho_{\text{micelle}} = a\rho_m + (1 - a)\rho_s\), where \(a\) is the volume fraction of polymer in the micelle, and \(\rho_m = b_m/V_m\).

Model 3 does not allow for water in the core, but allows for uniformly distributed water in the corona of the micelle. Model 4 allows for different amounts of uniformly distributed water in the core and corona. For Models 3 and 4 it is known that [18]:

\[
P(q) = \left[ \frac{4\pi}{3} R_1^3 (\rho_1 - \rho_2) \frac{3j_1(qR_1)}{qR_1} + \frac{4\pi}{3} R_2^3 (\rho_2 - \rho_s) \frac{3j_1(qR_2)}{qR_2} \right]^2
\]

where \(R_1\) and \(R_2\) are the core and corona radii, respectively, \(\rho_1\) and \(\rho_2\) are the SLDs of the core and corona on the basis of total core or corona volume, and \(j_1(x) = (\sin x - x \cos x)/x^2\) is the first order spherical Bessel function. For Model 3, \(\rho_1\) is just the SLD of PPO, for Model 4 \(\rho_1 = a_1\rho_{\text{PPO}} + (1 - a_1)\rho_s\), where \(a_1\) is volume fraction of PPO in the micelle core, and for both Models 3 and 4, \(\rho_2 = a_2\rho_{\text{PEO}} + (1 - a_2)\rho_s\), where \(a_2\) is volume fraction of PEO in the corona of the micelle. It is assumed here that there is only PPO (and maybe water) in the micellar core. In fact there could also be some PEO in the core, but because the SLD of PO and EO are very close to each other we cannot experimentally distinguish between PO and EO, and the models are valid even if there is PEO in the core. The fact that the SLD of PO \((\rho_{\text{PO}} = b_{\text{PO}}/V_{\text{PO}})\) and EO \((\rho_{\text{EO}} = b_{\text{EO}}/V_{\text{EO}})\) are very close to each other, and the difference between them is not experimentally detectable \((\rho_m \approx \rho_{\text{PO}} \approx \rho_{\text{EO}})\) is confirmed by an invariance of
Table 2.1: Apparent micelle radius of gyration, $R_g$, (in Å) in solvents with different D$_2$O content.

<table>
<thead>
<tr>
<th>T, °C</th>
<th>100% D$_2$O</th>
<th>80% D$_2$O</th>
<th>60% D$_2$O</th>
<th>40% D$_2$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>33.3</td>
<td>41.5</td>
<td>41.7</td>
<td>41.5</td>
<td>41.2</td>
</tr>
<tr>
<td>39.1</td>
<td>39.2</td>
<td>38.8</td>
<td>39.4</td>
<td>38.8</td>
</tr>
</tbody>
</table>

$R_g$ (obtained from the Guinier plots) at different $\rho_s$ (Table 2.1). The largest error was ±0.7Å.

In Models 2 and 3 there are two fitting parameters, namely the radius of the micelle ($R_2$) and the aggregation number ($N_{agg}$). In Model 4, three parameters are to be fitted, the core ($R_1$) and corona ($R_2$) radii and the micelle aggregation number ($N_{agg}$). The water contents in the core (1-$a_1$) and corona (1-$a_2$) regions are not independent parameters because they can be expressed in terms of the three fitting parameters ($R_1$, $R_2$ and $N_{agg}$):

$$1 - a_1 = 1 - \frac{3N_{agg}V_{PPO}}{4\pi R_1^3} \quad \text{and} \quad 1 - a_2 = 1 - \frac{3N_{agg}V_{PEO}}{4\pi (R_2^3 - R_1^3)}$$

where $V_{PPO}$ and $V_{PEO}$ are volumes of the PPO and the two PEO blocks respectively.

The models are summarized in Table 2.2.

### 2.5.2 Dilute Solutions

Three models (2, 3, and 4) fit the data equally well for the 1% solution of P85 at all temperatures in the transition region, as demonstrated by the fits in Figure 2-8, where the three models are not resolvable. All three models give the same aggregation numbers (within the error bars) as were obtained using the contrast variation approach described in section 2.4. These models assume a monodisperse system. Polydispersity was included in the model by assuming a Gaussian distribution about the mean micelle size. Incorporation of the additional fitting parameter, the variance of the distribution, did not improve the model fit, and the aggregation number and mean micelle size obtained were unchanged from those estimated for the monodisperse sys-
Table 2.2: Models description and goodness of fit.

<table>
<thead>
<tr>
<th>Model #</th>
<th>Model description</th>
<th># of fitting parameters</th>
<th>fits 1% data</th>
<th>fits 5% data at low temp.</th>
<th>fits 5% data at high temp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1</td>
<td>no water in core and corona</td>
<td>1</td>
<td>no</td>
<td>no</td>
<td>no</td>
</tr>
<tr>
<td>Model 2</td>
<td>even distribution of water in core &amp; corona</td>
<td>2</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Model 3</td>
<td>no water in core, even distribution of water in corona</td>
<td>2</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>Model 4</td>
<td>different concentrations of water in core and corona</td>
<td>3</td>
<td>yes</td>
<td>yes</td>
<td>yes</td>
</tr>
</tbody>
</table>

Figure 2-8: Models fits for the P85 1% solution data \((S(q) = 1)\).
tem. The maximum variance in the micelle size distribution obtained by fitting was 20% of the mean micelle size. Therefore, the assumption of monodisperse micelles in the system was used in all model fitting. The radii are slightly different for these models since the form factor $P(q)$ is not sufficiently sensitive to the dimension of the particle to distinguish between the models. On the other hand, the structure factor $S(q)$ which describes interactions between micelles is very sensitive to the micelle size and, when included in the analysis, discriminates between the three proposed models for the data taken at concentrations at which $S(q)$ is significantly different from unity.

### 2.5.3 More Concentrated Solutions

It is clear from the scattering functions in Figure 2-1 that there are interactions in the P85 5% solution, since $I(q)$ exhibits a maximum at low $q$. $S(q)$ is not equal to 1 in this case. We describe the steric interactions between micelles based on a hard-sphere interaction potential, characterized by micelle radius $R_{mic}$, assumed to be equal to $R_2$ used in the form factor $P(q)$. In this case [4],

$$S(q) = \frac{1}{1 + 24\phi G(2qR_{mic}, \phi)/(2qR_{mic})} \quad (2.10)$$

where $G$ is a function of $x = 2qR_{mic}$ and micelle volume fraction $\phi (\phi = \frac{(C-CMC)4\pi R_{mic}^3}{3N_{egg}})$:

$$G(x, \phi) = (\alpha(\phi)/x^2)[\sin x - x \cos x] + (\beta(\phi)/x^3)[2x \sin x + (2 - x^2) \cos x - 2] + (\gamma(\phi)/x^5)[-x^4 \cos x + 4(3x^2 - 6) \cos x + (x^3 - 6x) \sin x + 6] \quad (2.11)$$

where $\alpha$, $\beta$, and $\gamma$ are

$$\alpha = (1 + 2\phi)^2/(1 - \phi)^4$$

$$\beta = -6\phi(1 + \phi/2)^2/(1 - \phi)^4$$

$$\gamma = (\phi/2)(1 + 2\phi)^2/(1 - \phi)^4$$

Figure 2-9 shows the best fits of these models at two different temperatures,
Figure 2-9: Fits of the three models to the P85 5% solution data \( S(q) \neq 1 \) at temperatures \( 31.4^\circ C \) and \( 40.0^\circ C \) (CMT=25°C).

Figure 2-10: Fit of the three models to the P85 5% solution data \( S(q) \neq 1 \) at temperatures \( 34.3^\circ C \) and \( 37.2^\circ C \) (CMT=25°C).
Figure 2-11: Micelle core water content, aggregation number and diameter for the P85 5% solution obtained by fitting Model 4 to the scattering profiles.

\( T = 31.4^\circ C \) and \( T = 40.0^\circ C \). Models 2 and 4 give a satisfactory fit at the lower temperature, while Model 3 does not fit the data. At the higher temperature Models 3 and 4 fit the data well, while Model 2 does not. Only Model 4 fits the data at all temperatures. (The fits at intermediate temperatures are shown in Figure 2-10.) The calculated water content in the core of the micelle from Model 4 is shown in Figure 2-11. At \( 31.4^\circ C \) the water content in the micellar core is about 60%, about the same as in the corona. In this case Model 4 can be approximated by Model 2, in which water content in the core and the corona is the same. Figure 2-9 shows that Model 2 fits as well as Model 4 at lower temperature. At \( 40.0^\circ C \) the water content in the core is about 10%, and the core consists mostly of PPO. For higher temperatures Model 4 can be approximated by Model 3, in which there is no water in the core, but there is water in the corona, hence Model 3 fits almost as well as Model 4. Model 3 is the same as that used by Mortensen and Pedersen [4] and has been shown to fit the data at temperatures and concentrations above the unimer-to-micelle transition region.
Figure 2-12: Micelle aggregation number for the P85 1% and 5% solutions as a function of deviation from the CMT (T-CMT).

Aggregation numbers were obtained by fitting Model 4 to the data at different temperatures. The aggregation number information for 1% and 5% P85 is summarized in the Tables 2.3 and 2.4. When expressed in terms of T-CMT, the data for these two concentrations are found to fall on the same curve (Figure 2-12), indicating that it is the departure from the CMT that determines the structure of the micelles in the transition region. The micellar core radius extracted from the model fit is constant (40 ± 1Å) in the transition region, while the aggregation number increases with temperature. This implies that water in the micelle is replaced by polymer as temperature is increased. The micelle diameter is in the range of 10 to 12 nm. The largest error in the estimated micelle diameter is at the lowest temperature because the maximum in the structure factor is not very well defined under these conditions.
Table 2.3: Aggregation numbers for 1% solution of P85 (CMT=30°C).

<table>
<thead>
<tr>
<th>T-CMT, °C</th>
<th>1% P85 (from contr. var.) ( V_m = 6400 \text{Å}^3 )</th>
<th>1% P85 (from Model 4 fit) ( V_m = 6400 \text{Å}^3 )</th>
<th>1% P85 (from Model 4 fit) ( V_m = 6900 \text{Å}^3 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.3</td>
<td>29</td>
<td>28</td>
<td>25</td>
</tr>
<tr>
<td>6.3</td>
<td>35</td>
<td>34</td>
<td>30</td>
</tr>
<tr>
<td>9.1</td>
<td>43</td>
<td>42</td>
<td>37</td>
</tr>
<tr>
<td>12.9</td>
<td>52</td>
<td>51</td>
<td>45</td>
</tr>
</tbody>
</table>

Table 2.4: Aggregation numbers for 5% solution of P85 (CMT=25°C). The aggregation numbers marked by * were obtained by fitting only the form factor \( S(q) = 1 \) because no clear maximum in the scattering intensity was observed and the fitted \( S(q) \) was very close to unity. Since the temperature is very close to the CMT and the aggregation number is very low there is a concern about the micelle shape.

<table>
<thead>
<tr>
<th>T-CMT, °C</th>
<th>5% P85 (from Model 4 fit) ( V_m = 6400 \text{Å}^3 )</th>
<th>5% P85 (from Model 4 fit) ( V_m = 6900 \text{Å}^3 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.3</td>
<td>11*</td>
<td>9*</td>
</tr>
<tr>
<td>6.4</td>
<td>35</td>
<td>31</td>
</tr>
<tr>
<td>9.3</td>
<td>47</td>
<td>41</td>
</tr>
<tr>
<td>12.2</td>
<td>55</td>
<td>49</td>
</tr>
<tr>
<td>15</td>
<td>62</td>
<td>55</td>
</tr>
</tbody>
</table>
2.5.4 Comparison with Other Results

The aggregation numbers obtained in this study (37 for 1% solution and 55 for 5% at 40°C) are higher than the value of 30 at 40°C obtained by Brown et al. [9] using static light scattering, but they are consistent with the value of 78 at 40°C reported by Mortensen and Pedersen [4] for concentrations above the transition region. At 40°C the 1% solution is well within the transition region (aggregation number of 37) while the 5% solution at the same temperature is almost at the end of this region (aggregation number of 55). Above the transition region we expect aggregation numbers to be higher, approaching that reported by Mortensen and Pedersen. The micelle hard sphere radius obtained by our analysis varies from 50 to 64Å. For comparison, the hydrodynamic radius of the micelles obtained by NMR varies from 71 to 90Å [9], and that obtained by dynamic light scattering is 80Å [9].

2.6 Conclusions

Information on the structure of P85 micelles in the unimer-to-micelle transition region was obtained using small-angle neutron scattering. It was found that the micellar core contains water (up to 60%) at the beginning of the transition region, which is gradually replaced by polymer as the temperature is increased. Above the transition region the core is nearly anhydrous. Aggregation numbers for P85 1% solution obtained by the contrast variation method and model fitting are the same. The aggregation number increases with increasing temperature while the micellar core radius is constant. Information on the internal structure of the micelles was obtained for more concentrated solutions (5%) when hard sphere interactions were present. The internal structure of the micelles for dilute solutions (1%) can be deduced from the structure of micelles in the more concentrated solutions at the same deviation from the CMT. It was not possible to determine the internal structure of the micelles in the dilute solution directly, nor was it possible to distinguish experimentally between PO and EO, and therefore the PO and EO distributions within the micelle were not included in the analysis.
Bibliography


Chapter 3

Model Verification

3.1 Introduction

Small-angle neutron scattering (SANS) has proved to be a powerful technique for investigating the structure of PEO-PPO-PEO block copolymer micelles and has been used recently to infer certain micelle properties in the unimer-to-micelle transition region [1]. In this Chapter we make use of the unique opportunity that SANS offers to study the details of the internal micelle structure with a minimum of a priori assumptions. Nature made a gift to researchers by giving hydrogen and deuterium very different scattering lengths. Molecules, or parts of molecules, in which hydrogen is substituted with deuterium have very similar physical and chemical properties, but very different scattering length densities (SLDs). Scattering from a particulate system depends on the contrast between the particles and the solvent. If the scattering length density of the particle is the same as that of the solvent, the scattering from such a system will be the same as from the pure solvent. It is possible to change the SLD of one of the regions in the particle and to adjust the SLD of the solvent to match it. Then the only region contributing to the scattering (after solvent scattering subtraction) will be the one in which the SLD is different from that of the solvent. In this way we can “look” at different parts of the molecule or different regions in the aggregates formed by these molecules. This approach also eliminates difficulties arising from the fact that scattering length densities of different parts of a molecule
can be similar, and it is impossible to distinguish between them experimentally.

Goals. The goals of this Chapter are to justify the need for model verification, to verify the model, to analyze the model sensitivity to the fitted parameters and to the polydispersity, and to compare it to the existing models.

3.2 Need for Model Verification

In the previous Chapter we found that the spherical core-corona model which allowed for different water contents in the core and corona was able to describe the experimental data well at all temperatures and concentrations in this region, although at lower concentrations the model fits were non-unique, equally good fits being obtained for widely varying core and corona water contents. This is explained by the fact that the form factor for these models is not very sensitive to the micelle radius $R_2$ as discussed in Section 3.6 and can be illustrated by the following example. Let us assume that our model fit provides the correct aggregation number since our model is very sensitive to this parameter. In this case, if we assume too low value for the water content in the core, the radius of the core $R_1$ will also be too low. This affects the form factor (eq. 2.9) and shifts the curve to higher $q$ values. But the compensation of this effect is possible by increasing the corona radius $R_2$ because the SLD of protonated PEO is very close to the SLD of PPO. The larger, more extended hydrated PEO corona affects the form factor by shifting the curve to the lower $q$ values, thus compensating for the smaller core and resulting in non-unique fits. An additional restriction on the corona radius is needed.

At higher concentrations micelle-micelle interactions are present. At these concentrations hard-sphere interactions (with the hard sphere radius assumed to be equal to the corona radius) are included in the analysis providing an additional restriction on the corona radius. Only with this assumption was the model sufficiently sensitive to the fitted parameters to allow one to extract meaningful information on the water content in the core and the corona. It was then conjectured that these conclusions
could be extrapolated to lower concentrations. In neither case, however, could the
details of the internal structure (PPO and PEO distribution within the micelle) be
determined because the scattering length densities (SLD) of PEO and PPO are very
close, making it impossible to distinguish experimentally between the PPO and PEO
regions within the micelle.

In this Chapter, the model used in the Chapter 2 and reported in our recent
paper [1] on the structure of PEO-PPO-PEO triblock copolymer micelles in the tran-
sition region is verified using a copolymer with deuterated PEO blocks. The different
scattering length densities of the d-PEO and PPO blocks allow for easy discrimination
between these blocks, which was not possible in the earlier analysis using conventional
protonated block copolymers. In particular, by using a range of D$_2$O to H$_2$O ratios in
the solvent to highlight different regions of the micelle, we have focused independently
on the PPO core and PEO corona regions, respectively. This approach provides more
direct information on the size and structure of the micelle core. The size of the PPO
core can be obtained directly from the form factor which is very sensitive to the core
dimension. In this case the assumption of equality of the corona and the hard-sphere
interaction radii is not necessary, the model can be directly verified for the lower
concentration solutions, and the important micelle characteristics such as core and
corona radii and water contents, and micelle aggregation numbers can be obtained
directly for dilute solutions with no interactions between the micelles.

### 3.3 Experimental Details

#### 3.3.1 Deuterated Polymer

The triblock copolymer was prepared by Dr. Ga-er Yu, University of Manchester,
and deuterated monomer (ethylene oxide). Samples were characterized by $^{13}$C
and $^1$H NMR to determine average composition and degree of deuteration of EO
groups and by gel permeation chromatography (GPC) to determine the width of
Table 3.1: Critical micellization temperatures (CMTs) for aqueous solutions of (d-EO)$_{23}$(PO)$_{34}$(d-EO)$_{23}$ as a function of copolymer concentration.

<table>
<thead>
<tr>
<th>Concentration, %</th>
<th>0.075</th>
<th>0.1</th>
<th>0.125</th>
<th>0.25</th>
<th>0.5</th>
<th>1</th>
<th>2.5</th>
<th>5</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMT, °C</td>
<td>49</td>
<td>47</td>
<td>45.5</td>
<td>41.5</td>
<td>39</td>
<td>37.5</td>
<td>33.5</td>
<td>31</td>
</tr>
</tbody>
</table>

The average composition of the block copolymer was (d-EO)$_{23}$(PO)$_{34}$(d-EO)$_{23}$. The distribution was relatively narrow ($M_w/M_n=1.06$) and the d-PEO blocks were (within experimental error) completely deuterated.

The copolymer was dissolved at room temperature in water with different D$_2$O to H$_2$O ratios to form homogeneous transparent solutions, which were filtered through 0.22 μm Millipore filters before being transferred to 1-mm thick quartz containers for SANS measurements. The CMTs of the solutions of different concentrations were determined using static light scattering measurements. The results are summarized in Table 3.1.

### 3.3.2 SANS

Small-angle neutron scattering experiments were performed at the National Institute of Standards and Technology, Gaithersburg, MD. The neutron wavelength used in these experiments was 5Å with a neutron wavelength resolution, $\Delta \lambda/\lambda$, of 0.15. The range of scattering vectors $|\vec{q}| = q = (4\pi/\lambda)(\sin \theta)$ covered by the experiments was from 0.009 to 0.19Å$^{-1}$. The scattering data were corrected for scattering from the solvent, the quartz container, and other sources. To correct for the scattering from unimers in solution, the scattering curves for unimers at a concentration equal to the CMC at the temperatures of the experiments were subtracted from the scattering data. The effect of this correction was negligible. The scattering patterns were azimuthally isotropic. The scattering intensity was therefore averaged over all directions for the same absolute value of $q$, resulting in a one-dimensional scattering function $I(q)$. The smearing induced by the instrumental setup was included in the analysis of the scattering data [3].
3.3.3 Light Scattering

Static light scattering measurements were performed using Photon Technology International equipment with a xenon light source. The intensity of scattered light at 356 nm was measured at a scattering angle of 90°.

Dynamic light scattering measurements for the estimation of micelle diffusion coefficients, and thus hydrodynamic radii, were performed on a Brookhaven Model BI-200SM laser light scattering system (Brookhaven Instrument Corp.) at a scattering angle of 90° and wavelength of 514 nm.

3.3.4 Partial Specific Volume Measurements

A Mettler/Paar Calculating Digital Density Meter DMA-45 was used for density measurements. The partial specific volume of the polymer was obtained as the tangent to plots of the volume of the solution containing 1 kilogram of solvent vs. concentration expressed as kilograms of polymer per kilograms of solvent.

3.4 Model Fit

As was discussed in Chapter 2, the internal structure of PEO-PPO-PEO micelles in aqueous solutions at higher temperatures is usually well described by the core-corona model in which a spherical core composed only of PPO is surrounded by a corona composed only of the strongly hydrated PEO [4]. At lower temperatures, just above the CMT, this model does not give good agreement with experimental data. It was suggested that either some PEO or some water must be present in the core at these temperatures [1, 5]. To probe the internal structure of the micelle in this temperature region, we used the contrast variation method for a block copolymer with deuterated PEO blocks and a protonated PPO block. By changing the scattering length density (SLD) of the solvent, it is possible to change the relative contributions of PEO and PPO to the scattering curve and therefore to discriminate between the core and corona regions. The SLD of the solvent can also be matched to the SLD of PPO (14% D₂O
in the solvent), in which case only the PEO corona contributes to scattering.

### 3.4.1 Assumptions

In order to use the contrast variation method we need to assume that the properties of the micelles are independent of the D$_2$O/H$_2$O ratio in the solvent. To check this assumption, static light scattering measurements were performed in the temperature region of interest.

Figure 3-1 shows normalized static light scattering curves for 0.5% solution of the copolymer in 100% and 14% D$_2$O. CMTs of these two solutions are within 1°C of each other. The difference between the light scattering curves is small and is close to the experimental error. It will therefore be assumed that properties of the micelles are the same in solvents with different proportions of D$_2$O at the same temperature.

Another important assumption is the absence of interactions between the micelles (structure factor $S(q) = 1$) in both 0.5% and 1% solutions. Normalized neutron
scattering curves for 0.5% and 1% solutions at the same deviation from the CMT (T-CMT≈10.6°C) are shown in Figure 3-2. They are self-similar, an indication that the form and structure factors are the same for both curves. They do not exhibit a maximum at lower $q$ values, which is an indication that there are no hard sphere interactions between the micelles.

### 3.4.2 Three-Parameter Model Fit

The scattering intensity from a monodisperse system is described by

$$I(q) = NP(q)S(q)$$  \hspace{1cm} (3.1)$$

where $N$ is the number density of scattering centers ($N = (C - CMC)/N_{agg}$, $C$ is the total concentration of copolymer and $N_{agg}$ is the aggregation number), $P(q)$ is the intraparticle form factor, and $S(q)$ is the interparticle structure factor, which is assumed to be unity in our case.
Figure 3-3: Three parameter model fit for 0.5% solutions at 49.5°C (CMT=39°C). For clarity, curves for 50% and 60% D₂O are omitted.

Figure 3-4: Three parameter model fit for 0.5% solutions at 49.5°C (CMT=39°C) for 50% and 60% D₂O omitted in Figure 3-3. The curves are shown on the same scale as in Figure 3-3.
Figure 3-3 shows scattering curves for 0.5% solutions in solvents with different $D_2O$ to $H_2O$ ratios at a temperature of 49.5°C. To obtain information on the internal structure of the micelle, such as aggregation number and water contents in the core and corona, we fit the curves simultaneously using a spherical core-corona model which allows for different water contents in a core composed of PPO blocks and a corona composed of PEO blocks. It has been shown previously that micelles are spherical if the temperature is more than a few degrees above the CMT [4] and that polydispersity of the micellar size is low in this region [6].

Recall that the model is described by eq.(3.1) with $S(q) = 1$ and the form factor described in Chapter 2:

$$P(q) = \left[ \frac{4\pi}{3} R_1^3 (\rho_1 - \rho_2) \frac{3j_1(qR_1)}{qR_1} + \frac{4\pi}{3} R_2^3 (\rho_2 - \rho_s) \frac{3j_1(qR_2)}{qR_2} \right]^2$$ (3.2)

where $\rho_s$ is the SLD of the solvent, $R_1$ and $R_2$ are the core and corona radii, respectively, $\rho_1$ and $\rho_2$ are the respective SLDs of the core and corona on the basis of total core or corona volume, and $j_1(x) = (\sin x - x \cos x)/x^2$ is the first order spherical Bessel function. For our model $\rho_1 = a_1 \rho_{PPO} + (1 - a_1) \rho_s$, where $a_1$ is volume fraction of PPO in the micelle core, and $\rho_2 = a_2 \rho_{PEO} + (1 - a_2) \rho_s$, where $a_2$ is volume fraction of PEO in the corona of the micelle. The SLDs ($\rho_m = \sum b_i/V_m$, where $\sum b_i$ is the sum of scattering lengths of all nuclei in the molecule and $V_m$ is the volume of this molecule) were calculated based on bulk density measurement for PPO polymer ($d_{PPO} = 1.01g/cm^3$) and partial specific volume measurements for PEO polymer ($d_{PEO} = 1.18g/cm^3$) at 40°C. For seven curves corresponding to different values of $\rho_s$, three independent parameters were fit simultaneously: the core and corona radii ($R_1$ and $R_2$) and the micelle aggregation number ($N_{agg}$). Five of the seven curves are shown in Figure 3-3, where the symbols correspond to experimental data, and the solid lines are the model fits. Two curves, omitted for clarity in Figure 3-3, are shown in Figure 3-4 on the same scale. The resulting values of $R_1 = 37.2 \pm 1.0 \text{Å}$, $R_2 = 60 \pm 3 \text{Å}$, and $N_{agg} = 34 \pm 1$ show that PPO content in the core is 51%, and PEO content in the corona is 14% by volume. The hydrodynamic radius of the micelle at
Figure 3-5: Two parameter model fit for 0.5% solutions at 49.5°C (CMT=39°C). As in Figure 3-3, curves for 50% and 60% D$_2$O have been omitted.

The same temperature measured by dynamic light scattering is 60±2Å, which is in excellent agreement with the SANS result.

### 3.4.3 Two-Parameter Model Fit

The best fit of a spherical core-corona model which allows no water in the core of the micelle is shown in Figure 3-5. The symbols are experimental data and the solid lines are the best model fits. There are two independent fitting parameters in this model: these were taken to be the aggregation number and the micelle radius, $R_2$. With this selection and because the water content of the core has been assumed to be zero, the core radius $R_1$ was not an independent parameter in this case ($R_1 = (3N_{agg} V_{PPO}/4\pi)^{1/3}$). The values of the two independent parameters in this fit are $N_{agg} = 28.8$ and $R_2 = 55.6$Å. The value of $R_1$ is 28.1Å and the PEO content in the corona is 13%. The fits are satisfactory for 14% and 30% D$_2$O solutions. In these cases the SLD of the core is equal or close to the solvent SLD and only the
PEO corona contributes significantly to the scattering curve. The shape of the curve is determined mainly by $R_2$. The absolute intensity is determined largely by the aggregation number. The curves for 14% and 30% solutions show that, because the PPO core of the micelle does not contribute substantially to the scattering, the model is able to predict the outer radius of the micelle and the aggregation number with rather good agreement for both the shape of the curve and the absolute intensity. On the other hand, in the solutions with 80% and 70% D$_2$O, the largest contribution to the scattering is from the PPO core, since the SLD of the hydrated PEO corona is close to the SLD of the solvent. In this case the model was not able to fit both the shape of the curve and the absolute intensity simultaneously. The prediction for absolute intensity is nearly correct at low $q$, but the model underestimates the radius of the core (the model curves are shifted to higher $q$ values). Thus the aggregation number is approximately correct, but the core requires a larger volume. This leads to the conclusion that the core cannot be composed of PPO only.

In connection with this conclusion we need to note that the model accounts for both the water bound to the EO or PO segments and for free water. The highest hydration number for EO in P85 which has been obtained using a spin probe technique is 3.3 H$_2$O/EO [7]. This result corresponds to water molecules which are directly bound to EO. The radius of the micelle calculated considering only this hydration would be much smaller (>4nm) than the hydrodynamic radius measured using dynamic light scattering (8nm) [8], and it therefore follows that most of the water in the corona is free.

### 3.4.4 Temperature Dependence of Micelle Structure

To obtain the temperature dependence of the internal structure of the micelles just above the CMT, model fits at different temperatures in the transition region were done for 1% solutions in solvents with five different D$_2$O to H$_2$O ratios (100%, 80%, 60%, 40%, and 14% D$_2$O). The model fit for 1% solutions in all five solvents at 48.2°C is shown in Figure 3-6. The model with three independent parameters is fit simultaneously to these five curves. It is very sensitive to two parameters ($N_{agg}$ and
Figure 3-6: Three parameter model fit for 1% solution at 48.2°C (CMT=37.5°C).

$R_1$) and slightly less sensitive to $R_2$ which results in higher error bars for $R_2$ values. The model sensitivity to the fitting parameters is discussed in Section 3.5. The model used in this study is simplified because the micelles are assumed to be monodisperse and the scattering length density is assumed to be uniform in both the core and the corona. Despite this simplification, the model was able to fit experimental data quite well. The fits for 100% $D_2O$ solution at temperatures of 41.9°C, 43.7°C, 45.5°C, and 48.2°C are shown in Figure 3-7, from which it is clear that the model can describe the experimental data for all temperatures in the transition region.

The temperature dependence of the internal structure of the micelle is shown in Figure 3-8. The PPO content in the core and the aggregation number increase with temperature, while the corona radius is essentially constant and is virtually indistinguishable from the hydrodynamic radius measured by dynamic light scattering. The parameters obtained from the fit are summarized in Table 3.2 and the results of the dynamic light scattering experiments are summarized in Table 3.3.
Figure 3-7: Three parameter model fit for 1% solutions at different temperatures. Five curves with different $p_s$ (100%, 80%, 60%, 40%, and 14% D$_2$O in the solvent) were fitted simultaneously at all temperatures. Only 100% D$_2$O results are shown for clarity.

Table 3.2: The values of parameters for 1% solution (CMT=37.5°C)

<table>
<thead>
<tr>
<th>Temperature, °C</th>
<th>$N_{agg}$</th>
<th>$R_1$, Å</th>
<th>$R_2$, Å</th>
<th>%PPO in the core</th>
</tr>
</thead>
<tbody>
<tr>
<td>41.9</td>
<td>21±1</td>
<td>35.4±1.0</td>
<td>56±3</td>
<td>37±7</td>
</tr>
<tr>
<td>43.7</td>
<td>26±1</td>
<td>35.7±1.0</td>
<td>57±3</td>
<td>45±7</td>
</tr>
<tr>
<td>45.5</td>
<td>30±1</td>
<td>35.8±1.0</td>
<td>57±3</td>
<td>51±7</td>
</tr>
<tr>
<td>48.2</td>
<td>35±1</td>
<td>35.7±1.0</td>
<td>57±3</td>
<td>60±7</td>
</tr>
</tbody>
</table>

Table 3.3: Hydrodynamic radius of the micelle in 1% solution measured by dynamic light scattering.

<table>
<thead>
<tr>
<th>Temperature °C</th>
<th>41.0</th>
<th>44.0</th>
<th>46.1</th>
<th>47.8</th>
<th>50.6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrodynamic radius, Å</td>
<td>56±2</td>
<td>59±2</td>
<td>60±2</td>
<td>60±2</td>
<td>61±2</td>
</tr>
</tbody>
</table>
Figure 3-8: Temperature dependence of the micellar properties for 1% solution (CMT=37.5°C). The filled triangles are hydrodynamic diameter, measured using dynamic light scattering, the open triangles are the micelle diameter from model fitting (both in nm). The error bars on the hydrodynamic diameter, micelle diameter and core diameter are smaller than the symbol size. The filled squares are % PPO in the core for 5% P85 solution (CMT=25°C) from Chapter 2.
3.4.5 Discussion

It is intriguing that the volume of water lost during micelle dehydration with increasing temperature is just compensated for by an increase in the micelle aggregation number such that, within experimental limits, the micelle size remains essentially constant. Similar behavior has been observed in dynamic light scattering studies at temperatures well above the transition region where the micelle cores are already dehydrated [9, 10]. In this case, it is dehydration of the micelle corona that is accompanied by an increase in micelle aggregation number to ensure a constant micelle hydrodynamic size with increasing temperature.

The deuterated polymer used in this study, \((d-\text{EO})_{23}(\text{PO})_{34}(d-\text{EO})_{23}\), has a lower molecular weight than the P85 copolymer, \((\text{EO})_{26}(\text{PO})_{40}(\text{EO})_{26}\), used in our earlier analysis [1], and thus we might expect that we cannot make a direct comparison between the two sets of results. In fact, it is generally recognized that the small physico-chemical differences between deuterated and non-deuterated surfactants can lead to slight differences in micellar properties, manifested particularly in differences in the CMTs for the two systems. For the PEO-PPO-PEO copolymers, however, it is often possible to 'normalize' the results by plotting them in terms of the temperature deviation from the CMT, i.e., in terms of T-CMT. In Figure 3-8, we show that, when expressed in this manner, the core PPO/water contents determined for the P85 micelles in our earlier SANS study show remarkably good agreement with the results for the deuterated copolymer despite the differences in molecular weight, concentration (1% for deuterated vs. 5% for protonated copolymer), and CMT (37.5°C for deuterated copolymer vs. 25°C for protonated P85) between the two systems. (The micelle aggregation number and overall dimensions are larger for the higher molecular weight P85, as expected because of the differences in molecular size.) The agreement in terms of the core water contents is reasonable, as it is the dehydration of the copolymers that drives the micellization process, and one might expect similar structures for micelles formed by copolymers with similar compositions (the deuterated polymer and P85 have approximately the same PPO/PEO block length ratio) at similar stages in
their growth, i.e., at similar deviations from the CMT. The consistency between the two sets of results validates our earlier study detailed in Chapter 2, and gives added credence to the model used in that study. In particular, our present verification of the core-corona model in which the core contains only PPO and water, and the corona is comprised only of the PEO and water, justifies a posteriori its use in our earlier study.

We emphasize again that high surfactant concentrations were required in our earlier studies to ensure micelle-micelle interactions (modeled as hard sphere interactions) because, in their absence, the SANS spectra were not sufficiently rich in structure to provide unambiguous determination of the core radius and water content in the context of the core-corona model. In the present case, since contrast matching provided the sensitivity needed to probe the micelle core directly, we were able to obtain the core radius and water content even at low surfactant concentrations at which micelle-micelle interactions were negligible. Based on these comparisons, it would appear that a detailed examination of the micelle properties in the transition region can be undertaken for other protonated block copolymers in this series using the core-corona model, provided the experiments are performed at sufficiently high concentrations that micelle-micelle interactions are present. For any given surfactant, then, we should be able to extrapolate such results to lower concentrations by invoking the similarity of the properties when expressed in terms of T-CMT rather than temperature itself.

### 3.5 Model Sensitivity

The model sensitivity to the fitted parameters can be examined by performing simulations of scattering from the micelles when two out of three parameters are fixed and one is varied. Figure 3-9 shows the simulated SANS intensities of the \((d\text{-EO})_{23}(PO)_{34}(d\text{-EO})_{23}\) micellar system. The smearing that would be induced by the real experimental setup was included in these simulations. In this case two parameters in the model, the aggregation number \((N_{agg}=30)\) and the corona radius
Figure 3-9: The simulated SANS intensity from the model system. Two parameters are fixed, $N_{agg}=30$, $R_2=55\text{Å}$, one parameter $R_1$ is varied. D$_2$O content in the solvent is 100%.

$(R_2=55\text{Å})$, are fixed. The third parameter, the micellar core radius $R_1$, is varied. The concentration of D$_2$O in the solvent is 100%, since at this concentration the contrast of the core to the solvent reaches its maximum together with the sensitivity of the model to the varied parameter. It can be seen from Figure 3-9 that the model is very sensitive to the core radius. It can also be seen that the core radius affects mainly the shape of the scattering curve.

The sensitivity of the model to the aggregation number is shown in Figure 3-10. In this case the core radius $(R_1=35\text{Å})$ and the corona radius $(R_2=55\text{Å})$ are fixed and the aggregation number is varied. The concentration of D$_2$O in the solvent is again 100%. It should be noted that for the varied aggregation number, either 14% D$_2$O or 100% D$_2$O in the solvent serve well, because the former provides good contrast for the corona and the latter provides good contrast for the core. Figure 3-10 shows that the model is sensitive to the variations in the aggregation number of the micelle because it determines the absolute intensity of the scattering signal.
Figure 3-10: The simulated SANS intensity from the model system. Two parameters are fixed, $R_1=35$, $R_2=55\text{Å}$, one parameter $N_{agg}$ is varied. D$_2$O content in the solvent is 100%.
Figure 3-11 shows the model sensitivity to the corona radius $R_2$ which is varied in this simulation while the other two parameters are fixed ($N_{agg}=30$, $R_1=35\text{Å}$). The concentration of D$_2$O in the solvent is 14%. In this case the solvent SLD matches the SLD of PPO in the core and only PEO contributes to the scattering. Although the sensitivity to the corona radius is the highest in this case, it can easily be seen from Figure 3-11 that the model is not as sensitive to the corona radius variations as it is to the other two parameters. As a result the error in determining the corona radius is higher. The reason for the lower sensitivity to the corona radius is that the PEO corona is strongly hydrated thus providing lower overall contrast to the solvent.

**Polydispersity effect.** The effect of polydispersity was investigated. Note that, if polydispersity were admitted, there would be a variance associated with each of the fitted parameters with an attendant increase in the number of disposable parameters: mean values of the aggregation number, the core and corona radii, and the variances.
Figure 3-12: Scattering data and the simulated SANS intensity from the model system with the Gaussian distribution of aggregation number. Standard deviation is fixed in each case. D$_2$O content in the solvent is 14%.

of the respective distributions. The quality of the experimental data together with the model sensitivity to all six parameters does not allow us to obtain any meaningful information on polydispersity in this case. Simulations to check for the effect of polydispersity in the aggregation number only, assuming constant water content in the core and corona, indicated that the standard deviation of the aggregation number is at most 25%. The polydispersity mainly affects the sharp features in the scattering curve causing the effective smearing of the curve. This effect can be best seen at the first minimum in the scattering curve. Figure 3-12 shows the scattering data and the model intensity in the case of the Gaussian distribution of the aggregation number with the fixed standard deviation for each case. It can be seen that for the standard deviation of 20% the fit is practically as good as for the monodisperse system. For a standard deviation of 40% the smearing of the scattering curve is overestimated. The overall quality of the fit is not particularly sensitive to polydispersity over the range of 0 to 25%, and the mean parameters extracted using the monodisperse assumption.
are therefore believed to be reliable.

### 3.6 Analysis of Other Models

Several other models have been proposed to describe the PEO-PPO-PEO micelles. All of these models were used at higher temperatures and/or concentrations, outside the unimer-to-micelle transition region. The fact that the micelle corona is strongly hydrated and therefore does not provide sufficient contrast to the solvent and does not contribute significantly to the form factor in the case of protonated copolymer in D$_2$O, has been noted by Mortensen and Pedersen [4] who have not included the corona in their form factor at all, and only considered its size in the structure factor. This model can only be used for concentrated solutions when the contribution from the structure factor is significant. Using the assumption of a dehydrated core at high temperatures they also overspecified the number of parameters used in their model (aggregation number, or core radius, micelle radius and volume fraction of the micelles). One of the parameters is not independent, as was discussed in Section 3.4. The Model 3 described in the previous chapter as well as in the current chapter (two-parameter model) resembles the Mortensen-Pedersen model except that the former includes a contribution from the corona to the form factor. We showed that the Mortensen-Pedersen model cannot be used in the unimer-to-micelle transition region and that in the case of different scattering length densities (SLDs) for PEO and PPO and different contrast to the solvent, the contribution from the corona should be included in the analysis.

The other model, known as the cap-and-gown model, investigated in the literature has five fitting parameters and included the distribution of the PEO in the corona and sticky spheres interaction potential [11]. The five parameters are aggregation number, number of water molecules attached to the polymer chain, stickiness, micelle diameter, and polymer volume fraction in the core. Although the attempt to include the distribution of PEO in the corona is entirely justified by general physical considerations, the Gaussian distribution of PEO in the corona introduced by the
authors with the purpose of elimination of the abrupt boundary between the polymer chains and the solvent is only the first step in introducing a distribution of PEO, since the abrupt boundary between the PPO and PEO, or the core and the corona in the micelle, still exists in their model. The difficulties in calculation of the hydration number (the number of water molecules per polymer chain) are also recognized. In order to calculate the hydration number the cut-off distance from the center of the micelle should be set because the physical limit of the fully extended chain is not realistic and will lead to the overestimated hydration number. This consideration brings back the issue of establishment of a sharp boundary between the polymer and the solvent. The boundary was established at a micelle radius which is lower than the interaction radius from the structure factor (for example, for P84 copolymer at 35°C the interaction diameter was 12.0 nm, while the cut-off diameter from the mass balance was 10.5 nm). Unfortunately, due to the fact that a molecular volume of 72.4Å³ was used for EO unit in the model fitting it is difficult to compare results to the ones obtained using other models and a molecular volume of 60.9Å³ (the molecular weight of EO unit is 44 and PEO density is 1.2 g/ml). The authors have noted that one of the two less sensitive parameters is the polymer fraction in the core. While in our model we use the same representation of the core as in cap-and-gown model, the use of deuterated copolymer significantly improves sensitivity to the core radius, or volume fraction of the polymer in the core, as was shown in Section 3.5. Since a model with a uniform distribution of PEO in the corona fits the data well at different contrasts to the solvent and at different concentrations and temperatures, we believe that a more complicated model with more parameters cannot be justified.

3.7 Conclusions

In this Chapter we have obtained the internal structure of PEO-PPO-PEO micelles using small angle neutron scattering from aqueous solutions of a selectively deuterated PEO-PPO-PEO block copolymer. A global three-parameter model was fit to either five or seven SANS curves obtained with solvents having different SLDs to give the
core and corona radii and the aggregation number. It was shown that, at temperatures close to the CMT, the micelle core cannot be composed of PPO only, but must contain significant quantities of water. The aggregation number and PPO content in the core increase with temperature in this region, the core radius remains constant, and, consistent with dynamic light scattering measurements, the corona radius is also essentially constant. This validation of the core-corona model reinforces the conclusions drawn in the earlier SANS study in which the internal structure was determined indirectly. The use of deuterated copolymer combined with varied SLD of the solvent provided a sensitivity to the core radius which cannot be achieved otherwise.
Bibliography


Chapter 4

Micellar Dynamics

4.1 Introduction

The dynamics of PEO-PPO-PEO triblock copolymer micelle systems are of interest for a variety of reasons. These copolymers are commercially available nonionic macromolecular surfactants which are used in a wide range of applications due to their availability in a variety of molecular weights and ratios of the hydrophilic (PEO) to hydrophobic (PPO) block lengths. Some applications such as sustained release of perfume compounds [1], drug solubilization [2] and controlled release [3, 4, 5] require knowledge of dynamic processes in the system. In the solutions used in these applications, the hydrophobic solute is dissolved in the micellar core. Changes in solution conditions (copolymer or salt concentration, or temperature) result in the breakup of the micelles and the release of the solute. The system is not in equilibrium in this case and knowledge of the dynamic processes is very important. Even when the system is in equilibrium, it is a dynamic equilibrium. There is an exchange of unimers between the micelles and the solution, micelles form and break up.

Goals. The goals of this Chapter are to determine the time scale of the dynamic processes in the system, to propose a dynamic model which would explain the system behavior and to compare the model predictions to the experimental data.
Short chain surfactants. The dynamics associated with self-assembly of surfactant molecules has been studied both theoretically and experimentally. According to the Aniansson-Wall theory [6] there are two relaxation times, one associated with single surfactant molecules entering or exiting a micelle, and the other associated with micelle formation or dissolution. This theory assumes that micelle rearrangement following a perturbation in solution conditions proceeds stepwise as surfactant molecules are added one by one to the growing micelle. The theory has been confirmed by a number of experimental studies in which the two relaxation times, $\tau_1$ and $\tau_2$, were detected by a variety of experimental techniques. The fast process ($\tau_1$ on the order of microseconds) has been detected by means of temperature jump, ultrasonic absorption and shock tube methods. The slow process ($\tau_2$ ranging from milliseconds to seconds) has been detected by pressure and/or temperature jump experiments [7, 8, 9, 10]. These experiments have been performed with short chain non-polymeric surfactants.

Polymeric surfactants. A theory of polymeric micelle relaxation kinetics was developed by Halperin and Alexander [11] who analyzed the behavior of diblock copolymers in a selective solvent. Two mechanisms were considered: the Aniansson-Wall mechanism in which aggregates are allowed to interact only with unimers, and the fission-fusion mechanism in which interaction between pairs of aggregates is allowed. The Aniansson-Wall mechanism has been found to have the lower activation free energy suggesting that this should be the preferred route by which perturbed micellar solutions relax to their new equilibrium states.

Experimental techniques. The experimental framework for investigating the dynamics of PEO-PPO-PEO micellar systems is the same as for the non-polymeric surfactants. The small deviation from equilibrium is created by the temperature jump method, and the relaxation to the new equilibrium state is observed by measuring the intensity of scattered light as a function of time. The largest change in the intensity of scattered light with temperature is observed in the unimer-to-micelle
transition region due to the formation and growth of micelles. This and the presence of significant amounts of free unimers in this region provide favorable conditions for performing the temperature jump experiments in this region.

Experimental dynamics studies of PEO-PPO-PEO block copolymer micelles using gel permeation chromatography [12] or NMR [13] techniques gave inconsistent results for the lifetime of a molecule in a micelle ranging from less than 3 milliseconds (NMR) to hours (GPC). The temperature jump technique therefore became more popular for studying PEO-PPO-PEO micellar dynamics. Temperature jump experiments with Joule heating [14] gave one relaxation time in the millisecond range. A disadvantage of the Joule heating method is that it requires the addition of salt as a third component in the system.

In our study, an iodine laser pulse was used to create the desired temperature jump. This approach does not have the limitations of the Joule heating temperature jump method, since it does not require the addition of a third component (salt) to the solution; and thus it is unnecessary to decouple salt effects from the system dynamics and structural properties. We were able to describe the behavior of the system in terms of the full Aniansson-Wall model, which allows analysis of the temperature jump data using equilibrium structural information at the start and end points of the dynamics experiment. This success permits us to propose the mechanisms associated with the observed relaxation processes.

More recently, after the research described in this Chapter was completed, other investigators detected two relaxation times for the copolymer L64 [15] following the temperature jump created by Joule heating. The experimental results were explained in the framework of the linearized Aniansson-Wall theory. In yet a different study of the dynamics of L64 three relaxation times were reported [16], although it was unclear whether all three correspond to separate physical processes since a maximum of two relaxation processes were observed for any given condition.
Table 4.1: Properties of Copolymers Used in Dynamics Study.

<table>
<thead>
<tr>
<th>Polymer</th>
<th>MW</th>
<th>PPO block wt</th>
<th>Number of PO units</th>
<th>Number of EO units</th>
</tr>
</thead>
<tbody>
<tr>
<td>P84</td>
<td>4200</td>
<td>2520</td>
<td>43</td>
<td>2×19</td>
</tr>
<tr>
<td>P85</td>
<td>4600</td>
<td>2300</td>
<td>40</td>
<td>2×26</td>
</tr>
<tr>
<td>P103</td>
<td>4950</td>
<td>3465</td>
<td>60</td>
<td>2×17</td>
</tr>
<tr>
<td>P104</td>
<td>5900</td>
<td>3540</td>
<td>61</td>
<td>2×27</td>
</tr>
<tr>
<td>F108</td>
<td>14600</td>
<td>2920</td>
<td>50</td>
<td>2×132</td>
</tr>
</tbody>
</table>

4.2 Experimental Details

PEO-PPO-PEO triblock copolymers were obtained from BASF Corp. (Parsippany, NJ) and used without further purification. The properties of the copolymers used in this work are listed in Table 4.1. Each copolymer was dissolved in Milli-Q water at room temperature to form a homogeneous solution. The experiments were performed within a few days of the solution preparation.

Temperature jump experiments were carried out using the iodine laser temperature jump apparatus described by Holzwarth et al. [17]. All experiments were conducted in the unimer-to-micelle transition region as shown in Figure 4-1, which shows the intensity of scattered light for an equilibrated system as a function of temperature. Following rapid heating, the solution will relax to a new equilibrium state at $T_{\text{final}}$ for which the final value of scattered light intensity is higher than that in the initial equilibrium state at $T_{\text{initial}}$; it is the relaxation path which is the subject of the current work.

In each experiment the solution was placed in a cuvette and thermostated for at least 20 minutes before being heated rapidly. The fast temperature increase was created by an iodine laser pulse whose photons, emitted at $\lambda=1315\,\text{nm}$, are absorbed by the rotational-vibrational states of water. The temperature rise has been shown to be quite uniform for thicknesses of up to 3 mm [17]. The solution temperature rise was always 1°C with a heating time of 2.4 μs. The solution relaxation to the new equilibrium state was monitored by measuring the change in the intensity of scattered light at 90° at a wavelength of 330 nm. The light source was a Xe/Hg 200 W arc lamp. Each experiment was repeated at least four times and the results were
Figure 4-1: Scattered light intensity as a function of temperature showing the unimer-to-micelle transition region and a typical temperature jump experiment. $\Delta T$ is exaggerated for clarity.
averaged. Experiments with solutions for which the relaxation time was expected to be smaller, and therefore the experimental error to be larger, were performed several times and on different days to ensure the stable performance of the experimental setup. Cooling of the solution was detectable after 1.5 s, imposing an upper limit on the time scales that may be investigated.

Dynamic light scattering measurements for estimation of unimer diffusion coefficients were made using the Brookhaven Model BI-200SM laser light scattering system (Brookhaven Instrument Corp.) at a scattering angle of 90° and wavelength of 514 nm.

4.3 Results

The intensity of the light scattered from the unit volume of the micellar solution \( I_s \) relative to the intensity of the incident light \( I_0 \) is [18]:

\[
\frac{I_s}{I_0} = \frac{2\pi^2[n dn/dc]^2 c}{N_A r^2 \lambda^4 (1/M + 2Bc)} (1 + \cos^2 \theta)
\]

(4.1)

where \( n \) is the refractive index of the solution, \( c \) is the solution concentration in units of weight per volume, \( N_A \) is the Avogadro number, \( r \) is the distance to the detector, \( \lambda \) is the incident light wavelength, \( \theta \) is the scattering angle, \( M \) is the molecular weight of the scattering particle, and \( B \) is the second virial coefficient. The change in refractive index of the solution with temperature is very small and the gradient (dn/dc) is constant as shown in Figure 4-2. The gradient (dn/dc) is equal to \((1.494\pm0.004) \times 10^{-4}\) l/g for five sets of data at different temperatures in the temperature range between 24°C and 32°C. The scattering intensity for a dilute solution, in which both \( c \) and \( B \) are very small and when measured at constant wavelength, scattering angle and distance to the detector, satisfies the proportionality:

\[
I_s \propto c M = AM^2
\]

(4.2)
Figure 4-2: Refractive index of P85 solution as a function of temperature and concentration. The slope (dn/dc) does not change with temperature.

where $A$ is the number density of the particles in mole per volume units ($A = c/M$). The molecular weight of the scattering particle (micelle) is proportional to the aggregation number of the micelle. Then for polydisperse micellar systems the intensity of scattered light is

$$I_s \propto \sum_s A_s s^2$$  \hspace{1cm} (4.3)$$

where $A_s$ is the number density of micelles of aggregation number $s$. Thus, the measured scattered light intensity is sensitive to both the aggregation number and the number density of micelles, both of which can change during the temperature jump experiment. Care must therefore be exercised in the interpretation of the relaxation curves.

A typical response curve for the iodine laser temperature jump experiment is shown in Figure 4-3. Two processes are observed: the first, fast process is accompanied by an increase in the scattered light intensity, while the second, slow process is accompanied by a reduction in light intensity. Relaxation times for each process,
Figure 4-3: A typical response curve for the temperature jump experiment showing two different time scales for the relaxation process following a 1°C temperature jump.

\( \tau_1 \) and \( \tau_2 \), were obtained from exponential fits. This behavior was observed only in the transition region. The first relaxation process was detected at all concentrations studied (0.25% to 5%) and at all temperatures in the transition region. The second process was observed only at concentrations of 2.5% and higher, and only for polymers P85, P84 and P103 at temperatures in the middle of the transition region.

Both relaxation times were found to depend on temperature, solution concentration and molecular weight of the polymer. Since the CMT of PEO-PPO-PEO block copolymer solutions depends on concentration and copolymer structure, it is useful to compare the properties of different copolymer solutions at the same deviation from the CMT, i.e., at the same values of T-CMT, where T is the final equilibrium temperature. The values of the CMT for solutions at different concentrations for all copolymers were obtained from the literature [19].

The first relaxation time, \( \tau_1 \), decreases with increasing temperature and concentration as shown in Figure 4-4. The same behavior was observed in other copolymer solutions as shown in Figures 4-5 and 4-6. The first relaxation time depends on
polymer size, increasing with the molecular weight of the polymer (Figure 4-7).

The second relaxation time, $\tau_2$, increases with temperature. Both $\tau_1$ and $\tau_2$ for a single copolymer (P85) are shown in Figure 4-8. The second relaxation time also depends on the size of the copolymer, as is clear from the temperature dependence of $\tau_2$ for 2.5% solutions of P85 and P84 shown in Figure 4-9. Although the difference between the molecular weights of P85 and P84 is not significant the difference between the slow relaxation times is relatively large. This indicates that not only the molecular weight but also the structure of the aggregates formed by the copolymers can be important in the second relaxation process.
Figure 4-5: The first relaxation time for P104 as a function of temperature and concentration.

Figure 4-6: The first relaxation time for F108 as a function of temperature and concentration.
Figure 4-7: The effect of temperature on the first relaxation time for different copolymers at a concentration of 1%.

Figure 4-8: The temperature dependence of the two relaxation times for a 2.5% solution of P85.
Figure 4-9: The temperature dependence of the second relaxation time for 2.5% solutions of P84 and P85.

4.4 Discussion

4.4.1 Aniansson-Wall Model

To interpret the behavior of the system we have used the Aniansson-Wall theory [6], according to which the micellization proceeds stepwise:

\[ A_1 + A_{s-1} \xrightleftharpoons[k_s^-]{k_s^+} A_s \]  \hspace{1cm} (4.4)

where \( A_s \) is an aggregate of size \( s \), and \( k_s^+ \) and \( k_s^- \) are the association and dissociation rate constants respectively. If the concentration of aggregates of size \( s \) is also denoted as \( \tilde{A}_s \) and the corresponding equilibrium concentration as \( \bar{A}_s \) the relative deviation from equilibrium is:

\[ \xi_s = (A_s - \bar{A}_s)/\bar{A}_s \]  \hspace{1cm} (4.5)
The forward rate of the micellization process is equal to $k_+^sA_1A_{s-1}$ and the reverse rate is $k^-_sA_s$. Using the fact that

$$k^+_sA_1A_{s-1} = k^-_sA_s$$  \hspace{1cm} (4.6)

we can write

$$A_s \frac{d\xi_s}{dt} = k^-_{s+1}A_{s+1}(\xi_{s+1} - \xi_s(1 + \xi_1) - \xi_1)_s - k^-_sA_s(\xi_s - \xi_{s-1}(1 + \xi_1) - \xi_1); \quad s \geq 2$$  \hspace{1cm} (4.7)

and for $s=1$

$$A_1 \frac{d\xi_1}{dt} = 2k^-_2A_2(\xi_2 - 2\xi_1 - \xi_1^2) + \sum_{s=3}^{\infty} k^-_sA_s(\xi_s - \xi_{s-1}(1 + \xi_1) - \xi_1)$$  \hspace{1cm} (4.8)

The flux of aggregates from $(s-1)$ to $s$ is then

$$J_s = -k^-_sA_s(\xi_s - \xi_{s-1}(1 + \xi_1) - \xi_1)$$  \hspace{1cm} (4.9)

and the rate of change of $A_s$ is

$$\frac{dA_s}{dt} = \tilde{A}_s \frac{d\xi_s}{dt} = J_s - J_{s+1}; \quad s \geq 2$$  \hspace{1cm} (4.10)

By solving the system of differential equations (4.10 and 4.8) with initial conditions $\xi_s$ at $t = 0$ corresponding to the system of interest, we can obtain information on the time-dependent behavior of the system. Since we are interested only in the qualitative behavior and since time scales with $k^-$, we do not need to know the actual value of $k^-$, but only its functional form. In this work, $k^-$ is treated as a constant. Equation (4.8) is replaced by the mass conservation equation. The numerical method used for time integration was a fourth order Runge-Kutta method.

**Initial conditions.** To obtain the initial relative deviation from equilibrium, $\xi_s$, we need to know the equilibrium size distributions at the start and end points of the temperature jump. Equilibrium data in the transition region are available only for
Figure 4-10: The effect of temperature on micelle number density in two P85 solutions as determined by SANS.

P85 [20], so we solved the Aniansson-Wall equations (4.10 and 4.8) for this copolymer. It has been shown that, in the unimer-to-micelle transition region (at T-CMT>2-3°C), the micelles are relatively monodisperse [21]; so that only unimers and micelles with a relatively narrow size distribution are present. It will be assumed that the concentration of unimers is the same as the CMC at the particular temperature of interest.

The number density of micelles calculated based on the average aggregation number obtained from SANS measurements [20] is shown in Figure 4-10. Within experimental error the number density of micelles is constant throughout the transition region for the 1% P85 solution, but decreases with temperature for the 5% P85 solution. We do not have exact information on the standard deviation of the size distribution, but there are indications that it does not change significantly and is within 20% of the mean aggregation number as discussed in the Chapters 2 and 3. Thus, we will assume a Gaussian distribution around the measured mean aggregation number with a standard deviation of ~ 20%. The distribution of aggregates with small aggregation
number $s$ is chosen to be represented by an exponential, so that the concentration of dimers and trimers is negligible compared to the concentration of unimers. The entire distribution, including the “valley” between unimers and proper micelles, is modeled by the sum of these two distributions. A schematic picture of the size distribution is shown in Figure 4-11. It has been shown that the sum of an exponential and a Gaussian distributions fit well the data obtained from the simulations for the $A_2B_2$ model system [22]. The ratio of the total number density of micelles to the number density of unimers corresponds to experimental values obtained for P85.

4.4.2 Solutions of Aniansson-Wall Equations

**Temperatures close to the CMT.** The solution of equations (4.10 and 4.8) for a temperature jump of $1^\circ C$ (from $28^\circ C$ to $29^\circ C$) in 5% P85 aqueous solution is shown in Figure 4-12. The first, fast process involves a shift in the mean aggregation number which brings it close to the final value while the number density of micelles remains practically unchanged. The second, slow process involves rearrangement of the size
I I I I

First, fast process

Second, slow process

Figure 4-12: Solution of the Aniansson-Wall equations showing the relaxation in micelle size distribution following a temperature perturbation in 5% P85 solution at 28°C. The dashed line represents the final equilibrium distribution.
distribution with a decrease in the number density of micelles to the final equilibrium value. The change in light scattering intensity with time (eq. 4.3) calculated from the solution of the Aniansson-Wall equations (in arbitrary units) using \( k^- = 2 \times 10^5 \text{ s}^{-1} \) is shown in Figure 4-13. This value of \( k^- \) was selected to provide qualitative matching of the behavior of the first relaxation region of the Aniansson-Wall model solution to the experimental observations on the real time scale (Figure 4-14). The time scale of the second relaxation depends on the product of \( k^- \) and concentration of the aggregates in the “valley”, \( A_v \). There is no information available on the distribution of aggregates in this region, and we model it in a simplified way. Although the solution of the Aniansson-Wall model is in qualitative agreement with the experiment; i.e., it predicts the shape of the light scattering signal and the decrease in the scattering intensity during the second relaxation process, the lack of information on \( A_v \) in the “valley” does not allow us to make quantitative theoretical predictions about the time scale of the second process.

The concentration of free, non-associated copolymer molecules (unimers) obtained from the numerical solution of Aniansson-Wall equations is shown in Figure 4-15. The concentration of unimers decreases to a value below the final equilibrium value during the first relaxation process while the free molecules are being incorporated in the existing micelles during their growth. During the second process which involves dissolution of the micelles with a decrease in their number density, the unimer concentration increases, eventually reaching the equilibrium value. This result is consistent with simulation results [22] which also showed a small overshoot in the free surfactant concentration after the first relaxation.

The numerical solution of the non-linear equations was compared to the analytical solution of the linearized equations. The values of the two time scales (\( \tau_1 \) and \( \tau_2 \)) were calculated using the same final size distribution of the aggregation number as in the numerical solution. For the linearized equations [6, 7]:

\[
\frac{1}{\tau_1} = \frac{k^-}{\sigma^2} + \frac{k^-}{m} a
\]  

(4.11)
Figure 4-13: Light scattering intensity changes observed experimentally for a temperature jump of 1°C (from 28°C to 29°C) in a 5% solution of P85.

\[ \frac{1}{\tau_2} \approx \frac{m^2}{A_1 R} \left( 1 + \frac{\sigma^2}{m} \right)^{-1} \]  

(4.12)

where \( \sigma \) is the standard deviation of the size distribution curve, \( m \) is the mean aggregation number, and

\[ a = \frac{\sum_s s A_s - \bar{A}_1}{\bar{A}_1} \]  

(4.13)

\[ R = \sum_{valley} \frac{1}{k_s A_s} \]  

(4.14)

The calculated values of \( \tau_1 \) and \( \tau_2 \) (9.8 \( \mu s \) and 4.4 ms respectively) compare well with the values obtained from the numerical solution (10.4 \( \mu s \) and 4.3 ms respectively). This implies that the non-linear term in the equations is not very important for our initial conditions.

**Higher temperatures.** The behavior is different for lower concentrations of unimers in solution. This situation exists at higher temperatures in the transition region. The temperature dependence of unimer and micelle concentration for 5% P85 solution is
Figure 4-14: Light scattering intensity change for the solution of the Aniansson-Wall equations for a 1°C jump (from 28°C to 29°C) in a 5% solution of P85.

Figure 4-15: Concentration of free copolymer following a temperature perturbation in 5% P85 solution at 28°C.
Figure 4-16: Temperature dependence of the unimer and micelle concentration in the transition region for a 5% solution of P85 (CMT=25°C). The arrows show the starting temperature in temperature jump experiments and numerical solutions; (1) corresponds to Figures 4-12 to 4-14, (2) corresponds to Figures 4-17 to 4-19.
Figure 4-17: Solution of the Aniansson-Wall equations showing the relaxation in micelle size distribution following a temperature perturbation in 5% P85 solution at 37.2°C. The dashed line represents the distribution after the first, fast relaxation process.
shown in Figure 4-16. The unimer concentrations, assumed to be equal to the CMCs at the particular temperatures, are taken from the literature [19], the micelle concentrations are the same as in Figure 4-10. If there are not enough unimers to attain the equilibrium aggregation number, the size distribution shifts rapidly to some intermediate mean aggregation number, which is far from the equilibrium aggregation number, practically without changing the number density of aggregates. Then the size distribution slowly rearranges to the final equilibrium value with an increase in aggregation number and a decrease in number density (Figure 4-17). The process of unimer insertion into the micelle at this second stage is slow because it is now limited by dissociation of existing micelles. In this case, no overshoot in scattering intensity is observed. Instead, the second, slow process, which involves net dissolution of the smaller micelles with a corresponding decrease in their number density and a simultaneous growth of the rest of the micelles, results in an increase in light scattering intensity as shown in Figures 4-18 and 4-19. The change in the free copolymer concentration for these conditions is shown in Figure 4-20. During the first, fast process the unimers are incorporated in the micelles. But the aggregation number does not change significantly due to the low initial concentration of unimers. Then there is a region in which the concentration of the unimers is practically constant, all the unimers resulting from the breakup of the micelles are incorporated by existing growing micelles. Finally, the unimer concentration reaches the equilibrium value.

**Low concentrations.** The fact that the second process, accompanied by a decrease in scattered light intensity, is observed experimentally only at the concentrations of 2.5% and higher can be explained by the temperature dependence of the number density of the micelles in the transition region (Figure 4-10). There is a significant decrease in the number density of the micelles at higher concentrations (5%) while for low concentration (1%) it is constant within experimental error in this region. Since the decrease in intensity in the second process is due to a decrease in number density of micelles, it does not, within the experimental error, occur for low block copolymer concentrations.
Figure 4-18: Light scattering intensity change for the solution of the Aniansson-Wall equations for a 1°C jump (from 37.2°C) in a 5% solution of P85 as a function of time on a log scale.
Figure 4-19: Light scattering intensity change for the solution of the Aniansson-Wall equations for a 1°C jump (from 37.2°C) in a 5% solution of P85 as a function of time on a linear scale.

Figure 4-20: Concentration of free copolymer following a temperature perturbation in 5% P85 solution at 37.2°C.

\[ T_{\text{initial}} = 37.2^\circ C \]
4.4.3 Discussion of Two Relaxation Times

Second relaxation time. The temperature dependence of $\tau_2$ is a direct result of $\tau_2$ being determined by the product of $k_-$ and $\bar{A}_s$ (i.e. the concentration of aggregates in the “valley” between unimers and proper micelles). In general, we anticipate that $\bar{A}_s$ and $k_-$ decrease with temperature due to the fact that the micelle formation is favored by increasing temperature; thus it should be expected that $\tau_2$ would increase with temperature, as observed experimentally.

First relaxation time. The first relaxation time $\tau_1$ for P85 is on the order of tens of microseconds. The diffusion coefficient for single P85 chains in water is on the order of $10^{-6}$ cm$^2$/s as measured by dynamic light scattering. The characteristic unimer diffusion length in water, equal to half the distance between two micelles, can be estimated from equilibrium properties such as aggregation number and micelle diameter. The diffusion time is on the order of one microsecond, which is ten times smaller than $\tau_1$. Although the dependence of $\tau_1$ on concentration ($\tau_1$ increases four fold as the diffusion length of the unimer in water doubles) may suggest that diffusion in water is the main process in the first relaxation, the time scale of the first process is different from that for pure diffusion in water. Thus, other factors such as diffusion through the micellar corona must play a significant role in the first process.

The increase in the first relaxation time for different polymers (P85→P104→F108) is difficult to interpret quantitatively since equilibrium information is not available for P104 and F108. The diffusion coefficient of a single chain in water is of the same order of magnitude for all of these copolymers, but the structure of the aggregates may be different and may play a significant role. In particular, since F108 micelles have thicker coronae, diffusion through the corona may be the rate limiting step.

4.4.4 Comparison with Other Results

The first relaxation time had been reported earlier for different copolymers (F88, P123 and F127) by Hecht and Hoffmann [14]. Their results show the same temperature
and concentration behavior as those reported here. However, they were not able to
detect the second relaxation process, a failure which they attributed to polydispersity
of the block copolymer. We have shown that the second relaxation exists, but can be
detected only in certain temperature and concentration ranges.

The second relaxation process for L64 was detected by two different groups [15, 16]
after the research described in this Chapter was completed. In the first case [15] only
the decrease in scattering intensity was detected during the second relaxation, but
Kositza et al. [16] reported a decrease in light scattering intensity during the second
relaxation for the lower temperatures and an increase for higher temperatures. While
the authors attributed the increase in scattering intensity to a third relaxation process,
we showed that it is possible to observe an increase in scattering intensity even if the
mechanism of the relaxation is described by the Aniansson-Wall model, as when
unimers are in short supply.

4.4.5 Discussion of Fission-Fusion Model

Although Halperin and Alexander [11] have shown that the Aniansson-Wall mech-
anism has the lower activation free energy than the fission-fusion mechanism in
which interaction between pairs of aggregates is allowed, it is worth examining the
fission-fusion mechanism as well. In this exercise we use the linearized version of the
Aniansson-Wall model [7], according to which

\[
\frac{1}{\tau_{2}^{AW}} \simeq \frac{m^2}{A_1 R} \left( 1 + \frac{\sigma^2}{m} \right)^{-1}
\]  

(4.15)

where \(\sigma\) is the standard deviation of the size distribution curve, \(m\) is the mean ag-
gregation number, and

\[
a = \frac{\sum s s A_s - \bar{A}_1}{A_1} \quad \text{and} \quad R = \sum_{\text{valley}} \frac{1}{k_s A_s}
\]
According to the fission-fusion model

\[
\frac{1}{\tau_2} = \beta m a \left( 1 + \frac{\sigma^2}{m} \right)^{-1}
\]  

(4.16)

where \( \beta \) is the mean dissociation rate constant of the fission reaction. When two processes compete it is convenient to express the apparent second relaxation time dependence on the concentration as

\[
\frac{1}{\tau_2} = \left( \frac{m^2}{\tilde{A}_1 R} + \beta m a \right) \left( 1 + \frac{\sigma^2}{m} \right)^{-1}
\]  

(4.17)

This means that if \( m^2/(\tilde{A}_1 R) \) is much larger than \( \beta m a \), the predominant mechanism of the micellar growth is the unimer stepwise incorporation. If \( \beta m a \) is much larger than \( m^2/(\tilde{A}_1 R) \) the main mechanism is the coagulation of the submicellar aggregates. Unfortunately there are too many unknown parameters in these terms: \( \beta \) is usually determined by fitting the experimental data with the assumption that the fission-fusion mechanism is the main one, and \( \tilde{A}_s \) in the “valley” between the unimers and proper micelles is impossible to determine experimentally. It is often assumed that if \( 1/\tau_2 \) increases with the dimensionless concentration \( a \) and then reaches a plateau that the micellar growth proceeds via a fission-fusion mechanism, if it decreases than the mechanism of growth is described by a stepwise Aniansson-Wall model [23, 24]. While the former statement is true, the latter is not. Provided that \( m \) and \( \tilde{A}_1 \) do not change with concentration significantly, \( 1/\tau_2 \) depends on the product of \( (1 + \frac{\sigma^2}{m} a)^{-1} \) which decreases with concentration and \( 1/R \) which increases with concentration. So the product can increase with concentration, decrease or pass through a maximum [7]. This behavior depends on the shape of the size distribution. Without a detailed knowledge of the micelle size distribution it cannot be concluded based only on the \( 1/\tau_2 \) dependence on concentration whether the predominant mechanism is the fission-fusion or the stepwise growth. Because the detailed information on the size distribution is not available, we favor the Aniansson-Wall mechanism as the one with the lower activation free energy [11].
4.5 Conclusions

Two relaxation processes have been observed in PEO-PPO-PEO micellar solutions in the unimer-to-micelle transition region when using temperature-jump experiments with light scattering detection. The first process had been observed before for PEO-PPO-PEO copolymers [14]. In this Chapter we report the presence of a second relaxation process in this system. Depending on the copolymer, the first relaxation time, \( \tau_1 \), ranges from tens of microseconds to about ten milliseconds while the second relaxation time, \( \tau_2 \), is in the range of one to one hundred milliseconds. \( \tau_1 \) decreases with increasing temperature and concentration, and increases with molecular weight of copolymer. The relaxation time \( \tau_2 \) increases with temperature. The second relaxation, which was measured close to the CMT, was accompanied by a decrease in scattered light intensity and occurred only in the transition region and only for concentrations above 2%. The Aniansson-Wall equations were solved using equilibrium information obtained from SANS experiments. The solution of the Aniansson-Wall equations predicts qualitatively that the second relaxation will be accompanied by a decrease in scattered light intensity at the lower temperatures in the transition region which is in agreement with experimental data. It also predicts the increase in scattering intensity during the second relaxation at higher temperatures. It also suggests a two-stage mechanism for the micellar relaxation processes, with unimer insertion into the micelle in the first stage, and size distribution rearrangement accompanied by a decrease in the number density of micelles during the second stage.
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Chapter 5

Conclusions and Future Directions

In Part I of the thesis the structure and dynamics of the micelles formed by amphiphilic block copolymers were studied. Poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymers were chosen as an experimental system.

In Chapter 2 the structure of the micelles formed by the block copolymer P85 in the unimer-to-micelle transition region was determined using small angle neutron scattering. Two approaches were used at low concentration: the model independent contrast variation method and model fitting. Aggregation numbers for P85 1% solution obtained using the contrast variation method and model fitting are the same. The details of the internal structure of the micelle could be obtained only by model fitting. At low concentrations the model fits were non-unique, equally good fits being obtained for three different models. Only at a higher concentration when hard sphere interactions were present was it possible to discriminate between the models. A model with different water contents in the core and the corona of the micelle was able to fit the data at all temperatures and concentrations in the transition region. The internal structure of the micelles for dilute solutions (1%) can be deduced from the structure of micelles in the more concentrated solutions at the same deviation from the CMT.

It was found that the micellar core contains water (up to 60%) at the beginning of the transition region, which is gradually replaced by polymer as the temperature is increased. Above the transition region the core is nearly anhydrous. The aggregation number increases with increasing temperature while the micellar core radius is
constant.

While a detailed study of the micelle structure of block copolymer P85 has now done, the effect of the block size and ratio of the block sizes in the copolymer molecule on the structure of the micelle remains to be explored. One can anticipate that, when the poly(ethylene oxide) blocks are very large compare to the poly(propylene oxide) block, the steric interactions of PEO in the corona reduce the aggregation number of the micelle significantly. At some point the assumption of spherical core and corona with a sharp boundary can no longer be valid and some other model should be developed to describe the micelle form factor.

In Chapter 3 we verified the model from Chapter 2 using a copolymer with deuterated PEO blocks. By changing the SLD of the solvent we were able to highlight the different regions in the micelle. This approach provided a sensitivity to the core radius which cannot be achieved otherwise. By using only dilute solutions in which contributions from the structure factor are negligible we were able to extract the internal structure of the micelles from the form factor only. The analysis of the model sensitivity to the fitted parameters showed that in the case of a deuterated copolymer the form factor is very sensitive to the core radius and the aggregation number, and less sensitive to the radius of the corona. A global three-parameter model was fit to either five or seven SANS curves obtained with solvents having different SLDs to give the core and corona radii and the aggregation number. It was shown that, at temperatures close to the CMT, the micelle core cannot be composed of PPO only, but must contain significant quantities of water. The aggregation number and PPO content in the core increase with temperature in this region, the core radius remains constant, and, consistent with dynamic light scattering measurements, the corona radius is also essentially constant.

The model described in Chapter 3 can be extended to include more details on the internal structure of the micelles. The distribution of EO segments in the corona or PO segments in the core can be obtained by using a copolymer in which only a few EO segments are deuterated. Selective deuteration of some segments at the end of the PEO block, then in the middle of the block, and then at the connecting
point with the PPO block, will provide the sensitivity to resolve the PEO density distribution in the corona. The same can be done for the PPO block. In this case one should use copolymers with higher molecular weight in order to obtain a reasonable SANS intensity. The use of the higher molecular weight copolymer with deuterated blocks can also help to incorporate the micelle polydispersity in the model. The issue of the micelle polydispersity was addressed in the Chapter 3. While we showed that the polydispersity is moderate, we were unable to obtain precise information on the standard deviation of the aggregation number distribution due to the fact that the overall scattered intensity and subsequently the signal to noise ratio at the first minimum were very low. The use of higher molecular weight copolymers should provide higher intensity and result in a better quality data in the same measurement time.

In Chapter 4 the dynamics of micellar rearrangements were studied. Two relaxation processes have been observed in PEO-PPO-PEO micellar solutions in the unimer-to-micelle transition region when using temperature-jump experiments with light scattering detection. The first process had been observed before for PEO-PPO-PEO copolymers. The second relaxation process was reported for the first time for this system. Depending on the copolymer, the first relaxation time, $\tau_1$, ranges from tens of microseconds to about ten milliseconds while the second relaxation time, $\tau_2$, is in the range of one to one hundred milliseconds. $\tau_1$ decreases with increasing temperature and concentration, and increases with molecular weight of copolymer. $\tau_2$ increases with temperature. The second relaxation which was measured close to the CMT was accompanied by a decrease in scattered light intensity and occurred only in the transition region and only for concentrations above 2%. The Aniansson-Wall equations were solved numerically using equilibrium information obtained from SANS experiments. The solution of the Aniansson-Wall equations predicts qualitatively that the second relaxation will be accompanied by a decrease in scattered light intensity at the lower temperatures in the transition region which is in agreement with experimental data. It also predicts an increase in scattering intensity during the second relaxation at higher temperatures. It also suggests a two-stage mechanism for
the micellar relaxation processes, with unimer insertion into the micelle in the first stage, and size distribution rearrangement accompanied by a decrease in the number density of micelles during the second stage.

The analysis in Chapter 4 showed that the Aniansson-Wall model is very sensitive to the initial conditions. The change in the size distribution using the addition of the copolymer of a different structure can lead to the change in the dynamic time scales and in the amplitudes of the light scattering signal. This can be additional proof of the Aniansson-Wall mechanism if it can predict this change based on the change in the initial condition. Or it can prove that the mechanism is different. An understanding of the dynamics of solute exchange is the ultimate goal which is directly connected to the applications of PEO-PPO-PEO block copolymer micelles as solute carriers.
Part II

Vesicle Formation in a Mixed Cationic/Anionic Surfactant System
Chapter 6

Vesicle Formation in a Mixed Cationic/Anionic Surfactant System

6.1 Introduction

Aqueous mixtures of cationic and anionic surfactants form a variety of microstructures in solution depending on the concentration and composition of the surfactant mixture [1]. The aggregates that are formed include mixed micelles of different shapes, vesicles, and a variety of lamellar phases. The vesicles are of particular interest because of a large number of potential applications. Although these systems are not biologically compatible, they can serve as models for biological membranes, and encapsulation devices for drug, flavor, or fragrance delivery and release. Vesicles can also be used as microreactors for formation of nanoparticles [2].

Goals. The goals of this Chapter are to investigate the kinetics of vesicle formation, to identify the intermediate aggregates formed, and to gain an understanding of the mechanism and the limiting steps of vesicle formation and growth.
Equilibrium properties of SOS/CTAB aqueous solutions. The surfactant pair used in this study is sodium octyl sulfate (SOS) and cetyltrimethylammonium bromide (CTAB). The phase diagram for this system has been produced recently [1]. The electrostatic effects on the phase behavior of this mixture have been studied and phase diagrams of SOS/CTAB mixtures have been mapped for different concentrations of added salt (sodium bromide) [3]. The structure and composition of the equilibrium vesicles have been studied experimentally using small-angle neutron scattering (SANS) with contrast variation and theoretically by developing a thermodynamic cell model [4]. The vesicles formed in the solution with a total surfactant concentration of 2% and a 3/7 weight ratio of CTAB/SOS (21/79 molar ratio) have been found to be composed of 45 molar % CTAB. The bilayer thickness was 22Å. The theoretical predictions were in a good agreement with experimental measurements.

Dynamic studies of vesicle systems. Although the catanionic vesicles are formed spontaneously, the process of formation and the attainment of equilibrium can take a very long time ranging from hours to months [1, 5]. An understanding of the mechanism of formation and growth of vesicles, and a knowledge of the time scale of such processes and of the characteristics of the intermediate metastable aggregates are of great interest. Kinetics studies of vesicle formation and growth are still rare. Cholesterol-lecithin vesicle growth has been studied using turbidity and light scattering measurements, and fluorescence probe encapsulation [6]. It has been concluded that vesicles grow by the transfer of lecithin and cholesterol via diffusion in the aqueous medium. The conclusion that vesicles are formed by unimer addition has been inferred from a stopped-flow study of vesicle formation in sodium xylenesulfonate/Laureth 4 aqueous solutions [7]. A SANS and dynamic light scattering studies of the bile salt-lecithin system have shown that the process of vesicle formation and growth takes hours and proceeds through a series of intermediate states [8, 9, 10]. The small angle neutron scattering technique has allowed the authors to identify the structures of the intermediate aggregates, suggesting that the growth proceeds through the following stages: formation of elongated micelles; growth of these micelles
into long, polymer-like aggregates; formation of metastable disks; and formation of non-equilibrium vesicles which then grow to the equilibrium size. The authors have shown that, at each step, a mixture of these structures rather than only one type of aggregate is present.

**Dynamics of SOS/CTAB vesicle system.** The dynamics of micelle to vesicle transition in SOS/CTAB system have been studied using static and dynamic light scattering [5]. The vesicles were formed by mixing two pure solutions of SOS and CTAB. Three time scales have been identified on the order of ten, one hundred and two thousand seconds respectively. It has been shown that the intensity of the scattered light during the slowest process was proportional to the square of the aggregate diameter, from which it has been concluded that the growth is two-dimensional. The proposed mechanism of the vesicle formation and growth suggests the following sequence of the events: formation of mixed micelles and their growth, followed by formation of small non-equilibrium vesicles, and growth of these vesicles to their equilibrium size. The proposed mechanism has been found to be consistent with the experimental observations.

### 6.2 Experimental Details

#### 6.2.1 Materials

Sodium octyl sulfate (SOS, 99%) was obtained from Lancaster Synthesis, Inc. (Windham, NH), cetyltrimethylammonium bromide (CTAB, >99%) from Sigma Chemical Co. (St. Louis, MO), 2,6-pyridinedicarboxylic acid (DPA, 99%) and terbium (III) chloride hexahydrate (99.9%) from Aldrich Chemical Company, Inc. (Milwaukee, WI), sodium bromide (NaBr, 99.5%) from Acros, NJ, calcium chloride dihydrate (99%) and ethylenediamine tetaacetic acid disodium salt, dihydrate (disodium EDTA, >99%) from EM Science (Gibbstown, NJ), deuterium oxide (D₂O, 99.9% D) from Cambridge Isotope Laboratories, Inc. (Andover, MA). All chemicals were used as received without further purification. It has been shown that the purified
surfactant displayed kinetics that were indistinguishable from those of the unpurified surfactant [5]. All surfactant solutions were prepared in Milli-Q water at room temperature and then stored at 25°C until used.

6.2.2 Fluorescence measurements

Fluorescence measurements can be used to provide an estimate of the volume fraction of water entrapped by the vesicles. The water soluble fluorophore is evenly distributed in the water of the initial surfactant solutions. After mixing and vesicle formation, the fluorophore should still be evenly distributed in water both inside and outside the vesicle. At a certain time after the two solutions are mixed, a quencher is added. The diffusion time of a quencher molecule through the vesicle bilayer wall is typically much larger than the measurement time. In this way the the fluorescence outside the vesicles is quenched while the molecules inside the vesicle are still fluorescent. This provides the measure of the volume of the water inside the vesicles (Appendix A). The fluorescence measurement method of estimating the volume fraction of the water inside the vesicles was developed by Akihisa Shioi.

In real systems the fluorescence can rarely be quenched completely. Some probe molecules remain fluorescent in the water outside the vesicle. (The existence of the residual fluorescence can be verified by performing quenching experiments in pure water to ensure that it is not caused by interactions with surfactant). In addition to residual fluorescence there is some contribution to the signal from the scattered light. A small portion of light at the emission wavelength can be present in the excitation light because the monochromator selects not a single wavelength, but a wavelength distribution. To account for the residual fluorescence after quenching, a sample with quencher added before mixing was used. This sample was used as a blank (reference) allowing us to take into account not only residual fluorescence but also the contribution from the growing scattering intensity. The volume fraction of
water in the vesicles was calculated using the formula:

\[ \phi_w = \frac{I_0 - I_{reference}}{I_q - I_{reference}} \]  \hspace{1cm} (6.1)

where \( I_0 \) is the fluorescence intensity before quenching, \( I_q \) is the fluorescence intensity after the quencher was added, and \( I_{reference} \) is the fluorescence intensity of the sample with quencher added before mixing.

Fluorescence measurements were performed using QuantaMaster Spectrophotometer (Photon Technology International Inc., London, Ontario). Fluorescence intensity was measured at an angle of 90° to the incident light. The fluorophore, \( \text{Tb}^{3+}\)-DPA, was dissolved in the surfactant solutions prior to mixing. \( \text{Tb}^{3+} \) is practically non-fluorescent by itself, as is DPA. The Tb-DPA complex has a fluorescence spectrum with three distinct emission peaks at 490 nm, 545 nm and 583 nm, when excited at 276 nm, and is frequently used as a fluorescent probe in biological systems [11, 12]. The highest intensity peak is the one at 545 nm. However we could not use this peak due to the fact that the incident light contains not only the 276 nm light, but also the double wavelength light (552 nm), which interferes with the 545 nm peak. The fluorescence intensity was measured at 490 nm. While the complex is fluorescent at different \( \text{Tb}^{3+}/\text{DPA} \) ratios, we are interested in the regime in which the intensity has a linear dependence on concentration. Figure 6-1 shows that this regime is achieved at ratios of \( \text{Tb}^{3+}/\text{DPA} \) greater than 1/3. Introduction of the high concentrations of the fluorescent probe and the quencher into the system can change the properties of the system. On the other hand, low concentrations result in much higher error in the estimation of the water volume fraction (Appendix A). The \( \text{Tb(DPA)}_3^{3-} \) concentration chosen for this study was 10\( \mu \)M. The dynamic light scattering measurements showed that there was no difference between hydrodynamic diameters of the aggregates formed in the solutions without any probes, with fluorescent probe only, or with the probe and the quencher. The fluorescence is quenched by EDTA disodium salt and CaCl\(_2\). The fluorescence is not quenched completely. The maximum error associated with measuring fluorescence intensity is 1.5%. The resulting error in volume
Figure 6-1: Fluorescence intensity of Tb-DPA per 1 μM of Tb$^{3+}$ at different Tb$^{3+}$ concentrations and Tb$^{3+}$/DPA ratios.

The volume fraction of water inside the vesicles was identical to the one obtained using EDTA and CaCl$_2$ as a quencher, but the experimental error was larger.

### 6.2.3 Viscosity Measurements

The kinematic viscosities of the solutions were measured using a Ubbelohde capillary viscometer. The viscometer was immersed in the circulating water bath with the temperature control up to ±0.01°C. The viscosity was obtained by multiplying the measured kinematic viscosity by the density of the solution.
6.2.4 Dynamic Light Scattering

Dynamic light scattering measurements for the estimation of particles diffusion coefficients, and thus hydrodynamic radii, were performed on a Brookhaven Model BI-200SM laser light scattering system (Brookhaven Instrument Corp.) at a scattering angle of 90° and wavelength of 514 nm. The hydrodynamic radii were obtained using cumulant analysis in case of a unimodal distribution, and using a biexponential fit in case of the bimodal distribution. The results obtained by both methods were compared to non-negative least square fits (NNLS). The results obtained by NNLS agreed well with the simpler methods.

6.3 Growth of the Aggregates

The phase diagram for SOS/CTAB aqueous mixtures is shown in Figure 6-2. The experiments are shown by dashed lines. In these experiments either two pure surfactant solutions were mixed with the resulting composition and total concentration of the surfactants in the vesicle region (point A), or mixed surfactant solutions were mixed to reach the same point on the phase diagram.

Mixing of pure SOS and CTAB solutions. While the pure micelles of SOS or CTAB are very small, the aggregates formed after mixing the solutions are relatively large and grow with time. The growth was monitored using dynamic light scattering. The increase of the apparent mean micellar hydrodynamic diameter with time after mixing equal amounts of 1.5% CTAB and 3.4% SOS (points B and C) is shown in Figure 6-3. The analysis of the size distribution showed that although there is some polydispersity in the aggregate size (relative variance 0.08±0.02), the distribution is closely described as a unimodal distribution. It has been argued that the mechanism of vesicle formation involves first the formation of mixed micelles and their growth, followed by the formation of some closed structures [5]. This is consistent with the overall two-dimensional growth.
Figure 6-2: Ternary phase diagram for SOS/CTAB/H₂O at 25°C.
Figure 6-3: Mean hydrodynamic diameter of the aggregates formed in the solution after mixing equal amounts of 3.4% SOS and 1.5% CTAB at 25°C. The final total concentration of the surfactant is 2.45%, the weight ratio of SOS/CTAB is 7/3. The characteristic error bars are shown in the Figure.
Starting from the mixed micelles. To check whether the formation and growth of mixed micelles limits the first stage of the growth, we performed an experiment in which we started with mixed micellar systems. The solution of 0.3% CTAB and 2.7% SOS (point E) was mixed with the solution of 0.17% SOS and 1.43% CTAB (point D) in the proportion to reach the same point on the phase diagram (point A). The dynamic light scattering measurements showed that small aggregates exist in the original mixtures. It is difficult to determine the exact hydrodynamic diameters of these aggregates because of the effects of electrostatic interactions on the apparent diffusion coefficients, but the apparent micelle hydrodynamic diameter in the SOS rich solution is about 5 nm, and the CTAB rich solution exhibits a bimodal distribution of the apparent hydrodynamic diameters (3 nm and 19 nm) which may indicate that the mixed micelles are rods. The apparent hydrodynamic diameters do not account for the electrostatic interactions and can only be used to estimate the order of magnitude of the micellar size. The growth of the aggregates formed from the mixing of these solutions is shown in Figure 6-4. No difference can be seen between the results for mixing pure surfactant solutions and solutions with preassembled mixed micelles. This observation leads to the conclusion that the formation of mixed micelles cannot significantly limit the vesicle growth time.

Starting from mixed aggregates and pure CTAB micelles. In a different experiment a solution of 2.2% SOS and 0.25% CTAB (point F) was mixed with pure 2.45% CTAB (point G) in the proportion to reach the same point in the vesicle phase (point A). The phase diagram shows that the initial point lies in the mixed micellar phase. But the solution was turbid and exhibited properties of a vesicle solution. Dynamic light scattering measurements showed that the mean hydrodynamic diameter of the aggregates was 76±2 nm with relatively low polydispersity (relative variance 0.09±0.03). The distribution was unimodal. It is highly improbable that finite disks of this size can exist in the solution because of the high energetic cost of the free edge. Mixing of this solution with the pure CTAB solution resulted in a bimodal distribution with one population growing from 20 nm to 40 nm over time and an-
Figure 6-4: Mean hydrodynamic diameter of the aggregates formed in the solution after mixing the solution of 0.3% CTAB and 2.7% SOS in the proportion of 3/2 with the solution of 0.17% SOS and 1.43% CTAB at 25°C. The final total concentration of the surfactant is 2.45%, the weight ratio of SOS/CTAB is 7/3. The characteristic error bars are shown in the Figure.
Figure 6-5: Mean hydrodynamic diameter of the two populations of the aggregates formed in the solution after mixing the solution of 0.25% CTAB and 2.2% SOS in the proportion of 7/2 with the solution of 2.45% CTAB at 25°C. The final total concentration of the surfactant is 2.45%, the weight ratio of SOS/CTAB is 7/3. The characteristic error bars are shown in the Figure.

other keeping essentially constant size (Figure 6-5). Although both distributions had some polydispersity, the biexponential fits of the autocorrelation function were very satisfactory. This indicates that the bimodal distribution is indeed present. The contribution of the small aggregates to the fit increases with time, suggesting that the number of small aggregates may be increasing, which would require a decrease in the number of large aggregates.

**Effect of added salt.** An increased salt concentration in the system had practically no effect on the aggregate growth. The change in the mean hydrodynamic diameter on mixing equal amounts of 3.4% SOS solution and 1.5% CTAB solution with varied NaBr concentration is shown in Figure 6-6. The size of the aggregates is independent of the salt concentration within the experimental error.
Figure 6-6: Mean hydrodynamic diameter of the aggregates formed in the solution after mixing of equal amounts of 3.4\% SOS and 1.5\% CTAB at 25^\circ C for different concentrations of NaBr. The final total concentration of the surfactant is 2.45\%, the weight ratio of SOS/CTAB is 7/3. NaBr concentrations shown in the Figure are the concentrations in the final mixture. The characteristic error bars are shown in the Figure.
6.4 Aggregates Volume Fraction

6.4.1 Dynamic Light Scattering and Viscosity Measurements

While the growth of the aggregates is obvious, dynamic light scattering provides no information about the nature of these aggregates, i.e. their shape and composition. It has been shown that the composition of the equilibrium vesicles at 2% total concentration of surfactant with the SOS/CTAB weight ratio of 7/3 is about 55 molar % SOS and 45 molar % CTAB [4]. This means that at this SOS/CTAB ratio in the total surfactant concentration the vesicles are nearly neutrally charged. In our experiments the total final concentration of surfactants is 2.45% with the weight ratio of SOS/CTAB of 7/3. We will assume that the aggregates in our case are also neutral, an assumption which will be confirmed later in this Chapter. We also assume that while the shape and aggregation number of the aggregates can change with time, the composition of the aggregates is constant throughout the growth process. We can obtain information on the shape of the aggregates by measuring the volume fraction of the aggregates using different experimental techniques assuming a particular shape and then checking the consistency between different techniques. It has been shown that the aggregates exhibit two-dimensional growth [5], and we therefore consider two shapes: vesicles (hollow spheres) and disks. The volume fraction of the aggregates was calculated using dynamic light scattering and viscosity measurements, as described below. These measurements also give us a possibility to check the assumption of nearly neutral aggregates as opposed to the other limiting case when all the surfactant molecules are incorporated in the aggregates by checking the consistency between the volume fractions obtained by these two methods.

The thickness of the vesicle wall or bilayer of 22Å was taken from the literature [4]. If we assume that all surfactant molecules are in the aggregates, we use the viscosity of pure water as the solvent viscosity η0. If the aggregates are assumed to be neutral and in equilibrium with the excess SOS in the surrounding solution, the viscosity of the SOS solution at the concentration of this SOS excess is used as the solvent viscosity. When calculating the volume fraction of the aggregates using dynamic light scattering
measurements with the assumption of hollow spherical shape the outer radius of the sphere is taken to be equal to the measured hydrodynamic radius. For disks or oblate ellipsoids, the radius of the disk $R_d$ is related to the measured hydrodynamic radius $R_h$ in the following way [13]:

$$R_h = \frac{r(f^2 - 1)^{1/2}}{\arctan((f^2 - 1)^{1/2})}$$  \hspace{1cm} (6.2)

$$f^2 = \frac{3R_d^2}{2r^2}$$  \hspace{1cm} (6.3)

where $r$ is the half-bilayer thickness.

The volume fraction of the aggregates can also be calculated from the viscosity measurements. The relative viscosity $\eta_r$ for dilute solutions depends on the volume fraction of the aggregates in the following way:

$$\eta_r = \frac{\eta}{\eta_0} = 1 + \nu \phi$$  \hspace{1cm} (6.4)

where $\eta$ is the viscosity of the solution, $\phi$ is the volume fraction of the aggregates, and $\nu$ is the shape factor which is equal to 2.5 for spheres [14]. For disks the shape factor is defined as [15]:

$$\nu = \frac{16f}{15 \arctan(f)}$$  \hspace{1cm} (6.5)

It has been shown that equation (6.4) is valid for volume fractions of neutral particles less than 10% [16, 17]. When particles are charged the viscosity is affected by the electroviscous effect [18, 14], which is accounted for by a second-order term. However, when salt is present in the solution the electroviscous effect becomes negligible. In our case, even if we assume that all of surfactant molecules are in the aggregates, there is salt (NaBr) in the surrounding solvent. Thus, we assume that the second-order term in equation (6.4) is negligible compared to the first-order term.

The volume fractions of the aggregates, when assumed to be vesicles, calculated using dynamic light scattering and viscosity measurements with two assumptions on the aggregate composition (neutral aggregates and the aggregates which include all
Figure 6-7: Volume fraction of the vesicles (hollow spheres) in the solution determined by dynamic light scattering (open symbols) and viscosity (filled symbols) measurements with two different assumptions: (1) nearly neutral aggregates are formed (squares), (2) all the surfactant molecules are incorporated in the aggregates (circles).

of the surfactants in the system) are shown in Figure 6-7. The results show that if the assumption that all the surfactant molecules are incorporated into the micelles is used, the volume fraction calculated from the light scattering measurements is inconsistent with the volume fraction calculated from the viscosity measurements. If the vesicles are assumed to be nearly neutral, the results of these experiments are in remarkable agreement. The volume fraction of the aggregates calculated assuming a disk-like shape is shown in Figure 6-8. The lines show the total volume fraction of neutral aggregates based on the total amount of aggregated material. The results do not agree well for any case. This can lead to the conclusion that either the aggregates are vesicles, or a mixture of disks and other aggregates is present.
Figure 6-8: Volume fraction of disk-like aggregates in the solution determined by dynamic light scattering and viscosity measurements with two different assumptions: (1) nearly neutral aggregates are formed (squares), (2) all the surfactant molecules are incorporated in the aggregates (circles).
1.5

Fluorescence

Dynamic light scattering

Figure 6-9: Comparison of the volume fraction of water inside vesicles obtained from the fluorescence quenching experiments and calculated using dynamic light scattering measurements with the assumption of nearly neutral vesicles.

6.4.2 Fluorescence Quenching Experiments

Fluorescence measurements were performed to provide independent measurement of the volume fraction of water entrapped by the vesicles. The volume fraction was estimated as described in section 6.2.2. The volume fraction of water entrapped by vesicles calculated from the fluorescence measurements is shown in Figure 6-9. The volume fraction obtained from the fluorescence quenching experiments is close to zero and is much smaller than the one obtained from dynamic light scattering or viscosity measurements with the assumption that all of the aggregates are vesicles. The disagreement between fluorescence and dynamic light scattering results can appear if the probe molecules are not evenly distributed in water both inside and outside the vesicle. Such uneven distribution can occur if the vesicles grow by coalescence during which the bilayer area is conserved and the volume of water inside the vesicle is adjusted via diffusion of water through the vesicle wall. Since diffusion of the water molecules is much faster than that of the fluorophore molecules, the concentration of
the fluorophore molecules inside the vesicle will be lower than outside.

This disagreement can also arise from the faster exchange of the vesicle contents with the external solution. This can happen if the holes in the vesicle bilayer are present, or if the probe or quencher disrupts the bilayer in such a way that the permeability of the bilayer is changed. Dynamic light scattering measurements showed that the size of the aggregates formed within the three hours after mixing is not affected by the fluorescent probe or quencher. The fluorescence intensity of the probe in the surfactant mixture was only slightly different from that in the pure water. The residual intensity after quenching however was significantly higher in the surfactant solution than in water. This may indicate that the quencher interacts with the surfactant molecules in the vesicle bilayer and probably causes a change in its properties. The possibility of existence of the holes in the vesicle wall is discussed in the next section.

6.4.3 Cryo-TEM

The existence of the vesicles in the solution within three hours of mixing can be confirmed by the cryo-TEM (transmission electron microscopy) experiments. The cryo-TEM images can also shed the light on the issue of the hole existence in the vesicle bilayer. Figures 6-10 to 6-12 show the cryo-TEM images of the aggregates formed from mixing 3.4% SOS solution with an equal amount of 1.5% solution 30 minutes and 60 minutes after mixing (courtesy of Mats Almgren). A broad distribution of vesicle sizes can be seen on a micrograph. The few larger size vesicles are found close to the wall of the hole in the polymer film where the water film filling the hole is thicker thus allowing the larger size vesicles to partition in this area (Figure 6-11). Some of the vesicles are not completely closed structures. The arrow in Figure 6-11 shows a hole in a vesicle. In this case the vesicle content can be leaking out thus explaining the lower volume fraction of water in the vesicles obtained by fluorescence measurements comparing to that obtained by dynamic light scattering or viscosity measurements. The micrographs do not show any objects other than vesicles. But the radiation damage seen on the micrographs (Figure 6-13) suggests the presence of
Vesicles formed 30 minutes after mixing 3.4\% SOS solution with equal amount of 1.5\% CTAB solution.

Vesicles formed 30 minutes after mixing 3.4\% SOS solution with equal amount of 1.5\% CTAB solution. The larger vesicles can be seen close to the wall of the hole filled with the water film. The arrow shows the hole in the vesicle wall.

hydrocarbon structures in the solution which were not resolved in this experiment.

6.4.4 SANS

In another experiment to resolve the shape of the aggregates we compared the radius of gyration $R_g$ obtained from small angle neutron scattering experiments (SANS) and the radius of gyration calculated from dynamic light scattering measurements with the assumption of a particular shape. The SANS data were kindly provided to us by Paul Huibers. The radius of gyration $R_g$ obtained from the Guinier plot (the method is described in Chapter 2) does not require the assumption of a particular shape of the aggregates. The Guinier plots ($\ln I$ vs $q^2$) for different times after mixing are shown in Figure 6-14. The 2\% solutions of SOS and CTAB in D$_2$O were mixed in the proportion of 7/3 at 25$^\circ$C. The radius of gyration as a function of time obtained from these plots is shown in Figure 6-15. The radius of gyration of the aggregates
Figure 6-12: Vesicles formed 60 minutes after mixing 3.4% SOS solution with equal amount of 1.5% CTAB solution.

Figure 6-13: Vesicles formed from mixing 3.4% SOS solution with equal amount of 1.5% CTAB solution. The micrograph (taken at later time, about 26 hours after mixing) contains the image of the radiation damage, which is an indication of the presence of the hydrocarbon structures.
can be calculated using the dynamic light scattering measurements and assuming the aggregate shape. For hollow spheres (vesicles) the radius of gyration is defined as:

$$R_g^2 = \frac{3(R_1^5 - R_2^5)}{5(R_1^3 - R_2^3)}$$  \hspace{1cm} (6.6)$$

where $R_1$ is equal to the measured hydrodynamic radius, and $R_2$ is equal to $R_1$ minus the bilayer thickness. For disks the radius of gyration is

$$R_g^2 = \frac{R_d^2}{2}$$  \hspace{1cm} (6.7)$$

where $R_d$ is the radius of the disk. The hydrodynamic radii of the aggregates were measured by DLS. We used the viscosity of the SOS solution in D$_2$O at the concentration of the SOS excess in equilibrium with neutral aggregates, as the solvent viscosity.

It can be seen that at earlier times the SANS results agree with the hypothesis of the disk-like aggregates. After approximately 30 minutes after mixing it is impossible to
Figure 6-15: Radius of gyration of aggregates formed after mixing of the pure 2% SOS solution in D$_2$O with the pure 2% CTAB solution in D$_2$O at the proportion of 7/3 at 25°C as a function of time. Squares show the results obtained from SANS using model independent Guinier approximation. Circles and triangles represent calculated radius of gyration obtained from the dynamic light scattering measurements assuming hollow sphere and disk shapes respectively.
determine which assumption would work better due to the high experimental error in the determination of the radius of gyration by both SANS and DLS. This shows that a definitive answer to the aggregate shape requires better resolution in size using SANS.

The earlier time (first 30 minutes) data show that the disk-like structures are more likely to be present in the solution than the vesicles. This disagrees with the results obtained by the dynamic light scattering and viscosity measurements. We can see several reasons for this disagreement. First, the total concentration of the surfactant is lower in the experiments described in this section than in the experiments described in the previous sections. Second, D$_2$O was used as a solvent to obtain good contrast in SANS experiments. It has been shown that the phase diagram is slightly different in D$_2$O [4] compared to H$_2$O. Because of these two conditions the equilibrium point in this experiment may be in a different area of phase diagram, and the results may not be directly comparable. The experiments with deuterated water are also complicated by the fact that the 2% CTAB solution in D$_2$O is supersaturated at 25°C and nucleation and precipitation can occur. The additional scattering from the small crystals can lead to the errors in the interpretation of the results.

### 6.5 Conclusions and Future Directions

**Conclusions.** Catanionic vesicles are formed spontaneously in the SOS/CTAB surfactant system. The process of vesicle formation and growth takes a very long time: from hours to weeks. The vesicle growth during the first three hours after mixing the initial solutions, when the change in the aggregate size is most significant, was studied. The growth of the aggregates was found to be independent of the presence of mixed micelles in the initial solutions and of the added salt concentration. The viscosity and the dynamic light scattering measurements suggest that the aggregates are nearly neutral, i.e. the molar ratio of SOS/CTAB in the vesicle bilayer is close to unity. They also suggest that the intermediate aggregates are vesicles or mixture of vesicles and disk-like structures. The volume fraction of water inside the vesicles
obtained from the fluorescence quenching experiments was much lower than that obtained from the dynamic light scattering measurements. This suggests that either some of the vesicles are not completely closed structures, or that the quencher affects the permeability of the vesicle bilayer. The cryo-TEM images supported the idea that some of the vesicles are not completely closed and showed that holes in the vesicle walls can be found. The effect of the quencher on the permeability of the membrane was not investigated. A comparison of the radii of gyration of the intermediate aggregates obtained from the model independent Guinier approximation using small angle neutron scattering data and from the dynamic light scattering data with the shape assumption, showed that both disks and vesicles can be present as the intermediate aggregates.

**Future directions.** To better understand the nature of the intermediate aggregates and the effect of the composition and total concentration of surfactant on the structure and kinetics of formation of such intermediates, more experiments should be performed following the framework described in this Chapter. Although other fluorophore-quencher pairs were explored during the experimental studies, the possibility of finding more effective pairs should be explored. The interaction of quencher with the surfactants in the system should be studied and accounted for. Cryo-TEM studies of vesicle formation from two mixed micelle solutions should be performed. The structures in the initial mixed micellar solutions should be imaged. The small angle neutron scattering experiments should be performed at lower $q$ range than the one used in this study. This and statistically better dynamic light scattering data will provide better resolution in the radii of gyration of the intermediate aggregates, and subsequently will allow the differences between proposed shapes of the aggregates to be distinguished. An understanding of the mechanism by which vesicles are formed and grow should also be the subject of future investigations.
Bibliography


Appendix A

Estimation of the Volume Fraction of Water Inside the Vesicles and Reliability of Such Estimate

Suppose the total volume of water inside the vesicle is $W$ and the total water volume is $V$. Then the probability of a fluorophore molecule ending up inside a vesicle is $p = W/V$. Let the total number of fluorophore molecules be $N$.

So the probability of having $k$ out of $N$ molecules inside vesicles is

$$P(p, k) = p^k(1 - p)^{N-k} \binom{N}{k}$$

where $\binom{N}{k} = \frac{N!}{(N-k)!k!}$. Suppose we observe that $k$ molecules are inside. We are trying to estimate $W$, or, equivalently, $p$. We do maximal likelihood estimation, that is, find $p$, such that for given $k$, $P(p, k)$ is maximal. Differentiating $P(p, k)$ with respect to $p$, we get

$$kp^{k-1}(1 - p)^{N-k} - (N - k)p^k(1 - p)^{N-k-1} = 0$$

with the solution $p = k/N$. This means that, whatever the number of fluorophore
molecules vs. the number of vesicles, the best estimate of the fraction of water inside the vesicles is $k/N$. In this estimate we assumed that the chances of the probe molecules ending up at any point in the water volume are the same.

Next, we want to find the reliability of such estimate. We assume that the volume fraction of the vesicles in the solution is low, so that $W/V << 1$. In this case $k << N$ and the distribution can be approximated by

$$P(p, k) \approx (Ne/k)^k p^k e^{-Np} = (p/p_0)^N p_0 e^{-N(p-p_0)}$$

for $p$ close to $p_0 = k/N$. Simplifying, we get

$$P(\epsilon, k) = ((1 + \epsilon)e^{-\epsilon})^k$$

with $\epsilon = (p - p_0)/p_0$. Further approximating, we get

$$P(\epsilon, k) \approx (1 - \epsilon^2)^k = e^{k \ln(1-\epsilon^2)} \approx e^{-k\epsilon^2}$$

Suppose we want to estimate the size $2\delta$ of the interval around $k/N$ such that the probability of $p$ being different from $k/N$ is less than some $r$.

We use the Bayes formula:

$$P(A_i|B) = \frac{P(A_i)P(B|A_i)}{\sum_i P(A_i)P(B|A_i)}$$

Suppose we have some hypotheses $A_i$ about some past event (in our case this is a continuous set, and the hypothesis $A_p$ is that $W/V$ is between $p$ and $p + dp$). We know that an event $B$ has occurred (we have observed that $k$ probe molecules are fluorescent). Then if we know the conditional probabilities $P(B|A_i)$ (probability of $B$ given $A_i$), and probabilities of each hypothesis $P(A_i)$, the Bayes formula gives us the conditional probability of $A_i$ given that $B$ has occurred. In our case, $P(A_i)$ are all equal to $dp$.

We get the probability of $\epsilon = (p - p_0)/p_0$ being in an interval $d\epsilon$ near the value $\epsilon_0$ to be approximately
\[
\frac{P(\epsilon_0, k)d\epsilon}{\int P(\epsilon, k)d\epsilon} = \frac{e^{-k\epsilon_0^2}d\epsilon}{\int e^{-k\epsilon^2}d\epsilon}
\]
with integration over all permissible values of \( \epsilon \). As \( 0 \leq p \leq 1 \) the interval for \( \epsilon \) is \(-1\) to \( \frac{1}{p_0} - 1 \). The actual limits of integration are not important for large \( k \), because most of the contribution comes from a narrow area around zero, so we can assume the integration to be over the whole real line:

\[
\int_{-\infty}^{+\infty} e^{-k\epsilon^2}d\epsilon = \int_{-\infty}^{+\infty} e^{-y^2} \frac{y}{\sqrt{k}} = \sqrt{\pi / k}
\]

where \( y = \sqrt{k}\epsilon \).

The probability of \( p \) being in the interval \([\frac{k}{N}(1-\delta), \frac{k}{N}(1+\delta)]\) is the same as probability of \( \epsilon \) to be in \([-\delta, \delta]\) and is approximately:

\[
\sqrt{\frac{k}{\pi}} \int_{-\delta}^{\delta} e^{-k\epsilon^2}d\epsilon = \sqrt{\frac{k}{\pi}} \int_{-\sqrt{k}\delta}^{\sqrt{k}\delta} e^{-y^2} \frac{y}{\sqrt{k}} = 2\sqrt{\frac{1}{\pi}} \int_{0}^{\sqrt{k}\delta} e^{-y^2}dy = \text{erf}(\sqrt{k}\delta)
\]

The condition for \( \epsilon \) to be in \([-\delta, \delta]\) with probability at least \( 1 - r \) is:

\[
\text{erf}(\sqrt{k}\delta) > 1 - r
\]

This means that for any given \( r \) the size of the error interval \( \delta \) is proportional to \( 1 / \sqrt{k} \).

The conclusion is that the ratio of fluorophore concentration/vesicle concentration does not affect the estimate of the volume fraction of water inside the vesicles. But the absolute number of the fluorophore molecules does affect the error of such an estimate.