Zhiyong Li,[†] He Cheng,^{*,†} Junyu Li,[†] Jinkun Hao,[†] Li Zhang,[‡] Boualem Hammouda,[§] and Charles C. Han^{*,†}

⁺State Key Laboratory of Polymer Physics and Chemistry, Joint Laboratory of Polymer Science and Materials, Beijing National Laboratory for Molecular Sciences, Institute of Chemistry, CAS, Beijing 100190, P. R. China

^{*}Neutron Scattering Laboratory, China Institute of Atomic Energy, Beijing, 102413, China

^{\$}National Institute of Standard and Technology Center for Neutron Research, Gaithersburg, Maryland 20899-8562, United States

ABSTRACT: Author: Because of the closed-loop phase diagram of tetrahydrofuran (THF)—water mixture, THF aqueous solution naturally exhibits concentration fluctuations near the phase boundary. Besides the fast mode induced by concentration fluctuations, the 4.5% mole fraction THF aqueous solution is also characterized by a slow mode. The existence of a trace amount of butylhydroxytoluene (BHT) antioxidant in commercial THF strongly influences the slow mode in 4.5% mole fraction THF aqueous solution. A core—shell structure with a BHT core and a shell made from THF-rich THF—D₂O mixture was identified by the combination of dynamic laser light scattering (DLS) and small-angle neutron scattering (SANS). BHT is hydrophobic, stabilized by a THF-rich domain in THF aqueous solution and acts as a tracer to make the large-scale structure (slow mode) "visible" through SANS because of its larger contrast with the solvent. In contrast, this large-scale structure was almost not detectable by SANS when BHT was removed from the THF—D₂O mixture. Combined UV—vis, DLS, and static light scattering (SLS) indicated that slow-



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moving objects do exist and that their sizes almost do not change, but their concentration decreases to a small but nonzero value at the infinite dilution limit. The origin of the elusive large-scale structure at zero BHT concentration is still not clear, but it might be associated with some hydrophobic impurities or nanobubbles. However, a polydisperse sphere model of ~8.5% mole fraction THF-D₂O mixture can fit the structure with a radius of ~100 nm, which gives the temperature-dependent low-*q* SANS profiles of 4.5% mole fraction THF aqueous solution at zero BHT concentration.

1. INTRODUCTION

As an amphipathic molecule, THF displays both electrophilic and hydrophobic type of hydration. It is a popular solvent because it offers an environment for assembling amphiphilic macromolecules.^{1–9} Lange's Chemistry Handbook clearly shows that THF is water-miscible¹⁰ and the unhindered oxygen atom of THF molecule carries two unshared pairs of electrons that favor the formation of coordination complexes and the solvation of cations. However, previous dynamic light scattering (DLS) measurements suggested that the mixture of water and THF is not microscopically homogeneous and that there seems to exist some large-scale structure (microscopically imperfect mixing).¹¹ We also found that a translucent mixture of THF/D₂O can be observed when 4.5% mole fraction of HPLC grade commercial THF was mixed with water, as shown in the insert photo in Figure 1.

Water—organic solvent mixtures are theoretically important because they are considered as hydrophilic—hydrophobic hydration model systems that occur in complex biological systems.^{12,13} Fourier transform infrared spectrometer, nuclear magnetic resonance spectroscopy, small-angle neutron diffraction, and largeangle X-ray scattering have been used to study the structure of THF—water mixtures.^{13–15} However, this research effort focused on the small-scale structure in THF-water mixtures, whereas, the existence of large-scale structure has been neglected.

In DLS, there are two modes in a 4.5% mole fraction THF aqueous solution even without BHT addition, but the slow mode is not the origin of the turbidity when we mix HPLC grade commercial 4.5% mole fraction THF with water, as will be demonstrated later. The existence of a slow mode in a variety of pure water—organic mixtures has been observed and considered to be a universal phenomenon by some authors.^{16,17} These mixtures include urea—water, ethanol—water, sugar—water, and so on. Jin et al. attributed the slow mode to the formation of nanobubbles, which are stabilized by small organic molecules absorbed at the gas/water interface.^{16,17} Sedlak found that the slow mode is caused by loose associates (giant clusters, aggregates) of organic molecules.^{18,19} We found the existence of a trace amount of antioxidant, which may help clarify this question. The slow mode (upturn at low q) almost completely disappears when BHT is removed but can be clearly observed when a trace amount of BHT antioxidant exists in the THF/D₂O

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Figure 1. Direct UV–vis spectra of THF and various THF–D₂O mixtures: time dependence, ultracentrifuge, ultrasonic, and the influence of BHT. The insert includes the photos of D₂O and freshly prepared 4.5% mole fraction THF–D₂O mixture with BHT. Here the temperature was controlled at 24 °C.

mixture. This clearly indicates that BHT participated in the structure formed in the THF $-D_2O$ mixture that gives the low q upturn in the SANS measurements. (BHT is the commonly used antioxidant and is also named 2,6-di-*tert*-butyl-4-methyl-phenol with molecular formula $C_{15}H_{24}O$.)

In this manuscript, a combination of DLS and SANS measurement is used to study the origin of this particular DLS slow mode in commercial 4.5% mole fraction THF aqueous solution. DLS and SANS are powerful tools to study this question because both can monitor the structure variation of a mixed solvent system in real time. On one hand, DLS can easily obtain the basic structure variation of an object when it is close to the size limit of SANS $(\sim 100 \text{ nm})$ and provides more information for understanding the SANS data. On the other hand, SANS can eliminate the influence of dust on the slow mode and cover a length scale from 1 to 100 nm, which is not possible by static light scattering (SLS). In our study, UV-vis experiments were first used to give a visual representation of the existence of trace amounts of antioxidantinduced large structure. DLS was then used to confirm that this large structure has a Brownian characteristic (most probably spherical in shape) in a heating-cooling-heating cycle with a length scale of ~100 nm. SANS measurements were finally used to prove that this spherical shape large structure has a core-shell morphology, with a core made from BHT and a shell made from \sim (7 to 10)% mole fraction THF-rich THF-D₂O mixture. The contrast between BHT and THF-D2O mixture makes the core-shell structure "visible" through SANS. Therefore, SANS was used together with DLS and UV-vis for this study of the large-scale core-shell structure of THF-D2O mixture with trace amount of BHT.

2. EXPERIMENTAL SECTION

2.1. Sample Preparation. HPLC grade THF (\geq 99.5%, product number: 9440–03) containing ~0.01% BHT (according to the supplier) as a preservative stabilizer was bought from J. T. Baker. In this work, total BHT concentration in this commercial THF was measured to be 30.8 μ g/g (UV–visible spectrometer) and was used as received unless stated otherwise. When we studied the BHT dependence of 4.5% mole fraction THT–water mixture, THF was distilled to purify it (remove the antioxidant stabilizer), and different amounts of BHT were added to get a





Figure 2. (a) Temperature dependence of UV–vis transmittance spectra of 4.5% mole fraction THF aqueous solutions with (solid lines) and without BHT (dashed lines) (upper plot) and (b) the corresponding temperature dependence of BHT concentration calculated based on Beer–Lambert's law and the fitted line ($\sim 2.3 \ \mu g/g$) (lower plot). All measurements were carried out after 48 h of aging.

series of mixtures with different concentrations of $c_{\rm BHT}$. Deuterated water was bought from Cambridge Isotope and used as received. In all of our experiments, THF concentration was fixed at 4.5% mole fraction, and the fraction of BHT in the mixture was $\varphi_{\rm BHT} = 2.3 \ \mu g/g$ calculated according to UV-visible results (shown in Figure 2b). All solutions utilized in laser light scattering (LLS) measurements were filtered through 0.45 μ m Millipore PTFE filters.

2.2. UV–Visible Spectrometer. Optical transmittance spectra were made on an ultraviolet–visible (UV–vis) spectrophotometer (Varian Cary 50 Series) with 1 nm optical resolution over the range of 200–600 nm.

2.3. Laser Light Scattering. A commercial LLS spectrometer (ALV/DLS/SLS-5022F) equipped with a cylindrical 22 mW He—Ne laser (Uniphase, at $\lambda = 632.8$ nm) was used. The spectrometer has a high coherence factor of $\beta \approx 0.95$ because of a novel single-mode fiber optics coupled to an efficient avalanche photodiode. The LLS cell was held in a thermostat refractive index matching vat filled with purified and dust-free toluene. In SLS, the angular dependence of the excess time-averaged scattered intensity was acquired. In DLS, the intensity—intensity correlation function ($G^{(2)}(\tau,q)$) was acquired with an ALV-5000 multitau digital time correlator; a line-width distribution $f(\tau)$ was obtained by Laplace inversion.^{20,22} For a pure diffusive relaxation, τ_i is related to the translational diffusion coefficient D_i by $\tau_i = 1/\Gamma_i$ and $D_i = \Gamma_i/q^2$ ($q \rightarrow 0, c \rightarrow 0$) or to a hydrodynamic radius $R_{\rm h} = k_{\rm B}T/6\pi\eta D$, with $k_{\rm B}$, T, and η as the



Figure 3. (a) Intensity–intensity time correlation function $(G^{(2)}(\tau,q))$ of 4.5% mole fraction THF aqueous solution at different temperatures (with BHT) (upper plot) and (b) the corresponding relaxation time spectra obtained from CONTIN (lower plot). The scattering angle is $\theta = 20^{\circ}$.

Boltzmann constant, the absolute temperature, and the solvent viscosity, respectively. The details of LLS instrumentation and theory can be found elsewhere.^{22–25}

2.4. Small-Angle Neutron Scattering. SANS is the main tool in our approach. It was performed at the National Institute of Standard and Technology, Center for Neutron Research (NCNR). The angular dependence of excess scattering was measured in the angular range of $0.2-24^{\circ}$. In SANS, the essential measurement length scale is the reciprocal of the scattering vector q,²¹ that is, 1/q, with $q = (4\pi)/\lambda \sin \theta/2$, where $\lambda = 0.6$ nm is the neutron wavelength, and θ is the scattering angle; q is in the range of $(0.04 \text{ to } 5) \text{ nm}^{-1}$ in our measurements.

3. RESULTS AND DISCUSSION

3.1. UV-vis Determination of the Existence of Trace Amounts of BHT-Induced Large Structure. Figure 1 shows the UV-vis spectra of various THF-D₂O mixtures with or without BHT and compared with pure THF. We found that there is a large absorption peak at $\bar{\lambda}^* = 279$ nm in 4.5% mole fraction THF aqueous solution containing BHT, and the band does not exist in both pure THF and 4.5% mole fraction pure THF aqueous solution. This band is due to the characteristic absorption of BHT, which corresponds to a nonbond orbital to an antibonding orbital transition $(n-\pi^*)$.²⁶ As we can see from the insert photos, 4.5% mole fraction THF (with BHT) aqueous solution is not clear when it is freshly prepared. As time goes by, the solution becomes clear, and its transmittance increases. After ultracentrifugation, the system turns even clearer because the density of BHT (ρ_{BHT} = 1.05 g/mL) is slightly lower than that of pure 4.5% mole fraction THF aqueous solution ($\rho_{THF-D,O,20^{\circ}C}$ = 1.07 g/mL), and ultracentrifugation must have separated out this part of BHT. In addition, if we subject this solution to an ultrasonic treatment, then the absorbance of BHT becomes

larger, which means that the optical transparency of the system becomes worse, but the system is not yet visually translucent. A trace amount of small-molecule antioxidant, BHT, should never produce such a huge turbidity change by itself if it is truly dissolved and dispersed in the mixed THF $-D_2O$ solvent. It must have combined to form structures with other components in the system.

Figure 2a shows the temperature dependence of the UV-vis spectra of 4.5% mole fraction THF aqueous solutions with and without BHT. Note that all measurements were performed after 48 h of equilibration. It clearly shows that the spectrum has almost no temperature dependence, and there is no absorption peak at $\lambda^* = 279$ nm if there is no BHT. However, when trace amounts of BHT exist, the characteristic absorption peak does not shift with temperature; its amplitude keeps constant, but the bandwidth decreases with temperature. The concentration of BHT in the complex structure $c_{BHT,large}$ can be calculated from Lambert-Beer's law, as shown in Figure 2b. We found that the concentration of BHT, c_{BHT,large}, in 4.5% mole fraction THF aqueous solution, is almost constant with temperature at ~ 2.3 ppm, which may suggest that the concentration of the BHTinduced structure did not change with temperature. The narrower trend of the BHT characteristic absorbance bandwidth with temperature implies that the distribution of the large-scale structure becomes more and more homogeneous.

3.2. Dynamic Light Scattering Determination of the Variation of the Large Structure. DLS was used to monitor the variation of the BHT-induced structure with temperature. Figure 3a,b show examples of intensity-intensity time correlation function and the corresponding relaxation time spectra at various temperatures. It clearly indicates that there are two modes in THF-D₂O mixture with BHT. Previously, we studied the phase behavior of pure THF aqueous solution by SANS and concluded that the THF-D₂O mixture has an LCST-type phase diagram at constant pressure,²⁰ and its concentration fluctuation corresponds to the fast mode in DLS that has been investigated for various temperatures. Here the slow mode is the focus of the present manuscript. Yang et al. studied the dynamics of THF-D₂O mixture by LLS and concluded that large-scale structure with a dynamic correlation length of (200 to 600) nm exists in all THF content.¹¹ However, they did not remove BHT before their LLS measurements. The existence of trace amounts of antioxidant, BHT, overwhelmingly influences the structure of THF-D₂O mixture. As demonstrated in our previous paper, large-scale structure does not exist anymore when THF content is >10% mole fraction in pure THF aqueous solution but is observed in 4.5% mole fraction pure THF aqueous solution. In the present case, trace amount of BHT makes the large-scale structure visible in SANS and DLS of 4.5% mole fraction THF aqueous solution. The basic shape of the large-scale structure can be estimated by the examination of the relationship between the average characteristic line width ($<\Gamma_{slow}>$) and the scattering vector (q^2) .

Figure 4 shows that for the slow relaxation mode (and its $\langle \Gamma_{\text{slow}} \rangle$ obtained from each measured time correlation function) is a linear function with respect to q^2 , and the extrapolation to $q \rightarrow 0$ passes through the origin, which is an indication of a characteristic diffusive motion. Because spherical structure has the lowest surface free energy, the large-scale structure is most probably spherical in shape. The temperature dependence of the apparent hydrodynamic radius $R_{\rm h}$ distribution based on the Stokes–Einstein equation is shown in Figure 5. It suggests that



Figure 4. Scattering vector (q^2) dependence of average characteristic line width of large-scale structure ($\langle \Gamma_{slow} \rangle$) in 4.5% mole fraction THF aqueous solution (with BHT) at different temperatures.



Figure 5. Hydrodynamic radius distribution of large-scale structure in 4.5% mole fraction THF aqueous solution (with BHT) at different temperatures. The scattering angle is $\theta = 20^\circ$. The solid lines and dashed lines show Gaussian and Schultz distribution fitted results, respectively.

the size of the large-scale structure is large and widely distributed at 14 $^{\circ}$ C. It becomes smaller and more narrowly distributed with temperature increase, which is consistent with our UV—vis results. The variation of the slow mode size can be fitted by a Gaussian or Schultz polydispersity distribution. The normalized Gaussian distribution is expressed as

$$f_{\text{Gaussian}}(R) = \frac{1}{\sigma\sqrt{2\pi}} \exp\left[-\frac{1}{2\sigma^2}(R-\overline{R})^2\right]$$
(1)

where \overline{R} is the average radius of particles, and σ is the standard deviation. The normalized Schultz distribution is expressed as

$$f_{Schultz}(R) = (z+1)^{z+1} \zeta^{z} \frac{1}{\overline{R}\Gamma(z+1)} \exp[-(z+1)\zeta]$$
 (2)

Here ζ is the scaled variable, $\zeta = R/\overline{R}$, and z is the width parameter $z = (\overline{R}/\sigma)^2 - 1$ and is related to the polydispersity index (μ) by $\mu = 1/(z+1)^{1/2}$. Gaussian and Schultz distribution models are both presented and applied for analysis because of the ease in analytical computation, and they do represent most common polydisperse systems. All of the fitted results are displayed in Table 1. We found that both models fit the size variation of the large-scale structure well, but the Schultz model is better with smaller standard deviations. In the following SANS discussion, we will use the Schultz model to estimate

Table 1. Temperature Dependence of the Average Radius \overline{R} and the Standard Deviation σ of the Large-Scale Structure in 4.5% mole fraction THF Aqeuous Solution Calculated through Schultz and Gaussian Distribution Fitted Results

| | Gaussian Distribution | | Schultz Distribution | |
|------|-----------------------|-------------------|----------------------|-------------------|
| T/°C | \overline{R}/nm | $\sigma/{\rm nm}$ | \overline{R}/nm | $\sigma/{\rm nm}$ |
| 14 | 200 ± 7 | 83 ± 22 | 213 ± 4 | 42 ± 4 |
| 24 | 181 ± 6 | 81 ± 19 | 202 ± 4 | 42 ± 4 |
| 34 | 148 ± 2 | 42 ± 6 | 154 ± 2 | 13 ± 1 |
| 44 | 137 ± 1 | 35 ± 2 | 141 ± 1 | 10 ± 0 |
| 54 | 113 ± 1 | 22 ± 2 | 114 ± 0 | 5 ± 0 |
| 39 | 113 ± 0 | 22 ± 1 | 136 ± 1 | 8 ± 0 |
| 29 | 134 ± 1 | 32 ± 1 | 172 ± 2 | 31 ± 2 |
| 19 | 152 ± 3 | 65 ± 6 | 187 ± 1 | 38 ± 1 |
| 12 | 194 ± 4 | 83 ± 8 | 217 ± 2 | 41 ± 2 |
| 39 | 157 ± 2 | 60 ± 5 | 170 ± 1 | 26 ± 1 |



Figure 6. SANS from reversible process of scattering profiles for 4.5% mole fraction THF aqueous solution at different temperatures (with BHT). The solid lines are the best fits of polydisperse core—shell model with BHT at core.

the polydispersity index from the fitting process of scattering profiles.

3.3. SANS Determination of Large-Scale Structure. *a.* BHT Influence on THF– D_2O Structure. To clarify the structure variation of the BHT-induced large structure, we made SANS measurements. A heating—cooling—heating cycle was conducted (error bars correspond to one standard deviation), as shown in Figure 6. Consistent with our DLS results, there are two modes observed. The high-q small-scale structure is due to concentration fluctuation of pure THF– D_2O mixture. The size and amplitude of this fluctuation increase with temperature as it is getting close to the phase boundary.²⁰ This temperature-dependent



Figure 7. Fitted results of different models at 14 and 54 °C of 4.5% mole fraction THF aqueous solutions (with BHT).

high-q concentration fluctuation can be expressed by Ornstein-Zernike (O-Z) equation

$$I(q) = \frac{C}{1 + (qL)^2} + B$$
(3)

Here *L* is the static correlation length and *C* and *B* are *q*-independent constants obtained from $I(q \rightarrow 0) = C + B$ and $I(q \rightarrow 0) = B$. The first term on the right is characteristic of the thermodynamics (I(0), susceptibility), and the second term is incoherent background.^{20,21} The low-*q* upturn comes from the BHT-induced large-scale spherical structure.

Figure 6 shows that the low-q scattered intensity becomes lower with increasing temperature and increases again when we decrease the temperature. Although this agrees with our DLS observation (e.g., the size of large-scale structure is decreasing with temperature), we still cannot explain why the BHT concentration keeps constant in the whole process. Some models were used to analyze the detailed BHT-induced spherical structure variation. There are three possible sphere-like models, homogeneous BHT nondraining sphere, core-shell structure with BHT nondraining shell, and core-shell structure with BHT nondraining core, and THF-D₂O (THF-rich) mixture shell. Here the sphere model expresses a spherical domain of radius R with uniform density, whereas the second model is represented by a sphere with an inner spherical core of THF and D₂O covered with an outer nondraining BHT shell. The third model described above is a sphere with an inner spherical core of BHT covered with an outer THF-D₂O shell. In the case of coreshell model, three regions can be defined as the inner core, the outer shell and the surrounding solvent. Figure 7 shows the best fitting results at 14 and 54 °C in THF aqueous solution. Here we note that the scattering length densities of BHT, D₂O, 4.5% mole fraction, and 10% mole fraction THF-D₂O mixture are 4.30×10^{-7} , 6.38×10^{-6} , 6.10×10^{-6} , and 5.75×10^{-6} Å⁻², respectively.

The form factor for a nondraining hard-sphere is given by the following function 27

$$P(q) = \left[\frac{3J_1(qR)}{qR}\right]^2 \tag{4}$$

Here *R* is the characteristic size of the particle and $J_1(qR)$ is the spherical Bessel function. In our case, $R \approx 150$ nm at 14 °C,

then $qR \gg 1$; therefore

$$P(q) \propto \frac{1}{q^4 R^4}$$
 (5)

As we can find in Figure 7, the low-q exponent of the SANS profile for 4.5% mole fraction THF aqueous solution at 14 °C is ~3.0, which is much smaller than 4.0, and indicates that the nondraining polydisperse sphere model cannot be used here.

1

The normalized form factor of a core—shell sphere by the total particle volume is calculated from^{21,27,28}

$$P(q) = \frac{\varphi}{V_{\text{core-shell}}} \left\{ V_{\text{core}}(\rho_{\text{core}} - \rho_{\text{solvent}}) \frac{3J_1(qR_{\text{core}})}{qR_{\text{core}}} + (\rho_{\text{shell}} - \rho_{\text{solvent}}) \left[V_{\text{core-shell}} \frac{3J_1(qR_{\text{core-shell}})}{qR_{\text{core-shell}}} - V_{\text{core}} \frac{3J_1(qR_{\text{core}})}{qR_{\text{core}}} \right] \right\}^2$$

$$(6)$$

Here φ is the particle volume fraction; $R_{\text{core-shell}} = R_{\text{core}} + d_{\text{shell}}$ is the radius of core-shell structure, with d_{shell} the shell thickness; $V_{\text{core}} = 4\pi R_{\text{core}}^3/3$ and $V_{\text{core-shell}} = 4\pi R_{\text{core-shell}}^3/3$ are the volume of core and core-shell structures, respectively. In the case of the Schultz distribution, the form factor is integrated

$$P_{\text{Schultz}}(q) = \int_0^\infty dR f_{\text{Schultz}}(R) P_{\text{single}}(q)$$
(7)

Nonlinear regression process was conducted with Igor software with seven variables in the fitting process. We fix three of them, that is, $\rho_{\text{solvent}} = \rho_{\text{D},\text{O}} = 6.38 \times 10^{-6} \text{ Å}^{-2}$, ρ_{core} or $\rho_{\text{shell}} = \rho_{\text{BHT}} = 4.30 \times 10^{-7} \text{ Å}^{-2}$, and the polydispersity index μ from Schulz fitted results of DLS relaxation spectra, constrain one of them, that is, $R_{\text{core-shell}} \approx R_{\text{h,slow}}$ from DLS measurements, and fit the other three parameters, that is, particle volume fraction φ_{large} , core size R_{core} , and scattering length density of THF-rich domain ρ_{core} or ρ_{shell} . Figure 7 clearly demonstrates that nondraining BHT as both the core and the shell can fit 14 °C SANS data quite well. Note that eq 6 shows that the scattered intensity of the core-shell model comes from two parts: the contrast between core and solvent, and the contrast between shell and solvent, respectively. Although both models fit low-temperature SANS data well, the BHT shell model has difficulty in explaining high-temperature SANS data. As we can see from Figures 6 and 7, low-q scattered intensity decreases with temperature and is characterized by a "Guinier region" when q is <0.005 Å⁻¹ at 54 °C. However, DLS shows that $R_{\rm core-shell}$ is still \sim 100 nm and $qR_{\rm core-shell}$ is still much larger than 1. If BHT is in the shell, then the contribution from the shell-solvent contrast is overwhelming when $qR_{core-shell} \gg 1$, and we can never see the so-called "Guinier region" in Figures 6 and 7 at high temperature. On the contrary, if BHT is in the core and the nondraining BHT core size is smaller, for example, \sim 300 Å, we can indeed see the so-called "Guinier region". Although $qR_{\rm core-shell}$ is still much larger than 1 because the contrast between shell and solvent $(\rho_{\text{shell}} - \rho_{\text{solvent}})$ is too small, the shell intensity contribution to our SANS observation can be negligible.

On the basis of the discussions above, a combination of O-Z with polydisperse core—shell model is used to explain the variation of the BHT induced spherical structure with temperature; note that the interparticle correlation was neglected. The



Figure 8. (a) Scattering length density of shell (ρ_{shell}) and (b) volume fraction of large-scale structure (φ_{large}) and the ratio of the volume of core and large-scale structure $V_{\text{core}}/V_{\text{large}}$ and (c) the observed amount of BHT (c_{BHT}) in 4.5% mole fraction THF aqueous solution (with BHT) with temperature. The statistical error bars correspond to one standard deviation. All results were obtained from polydisperse core—shell model.

Table 2. Fitted Results of the Core-Shell Structure (BHT in Core) in 4.5% Mole Fraction THF Ageuous Solution

| $T/^{\circ}C$ | $10^5 \ \varphi_{\text{large}}$ | $R_{\rm core}/{\rm \AA}$ | $d_{\rm shell}/{\rm \AA}$ | $10^6~\rho_{shell}/\text{\AA}^{-2}$ |
|---------------|---------------------------------|--------------------------|---------------------------|-------------------------------------|
| 14 | 10.6 ± 0.5 | 428.4 ± 5.8 | 803.7 ± 23.1 | 5.76 ± 0.02 |
| 24 | 7.8 ± 0.5 | 424.0 ± 7.8 | 722.8 ± 30.9 | 5.88 ± 0.02 |
| 34 | 4.8 ± 0.2 | 416.1 ± 9.1 | 591.8 ± 22.7 | 5.89 ± 0.02 |
| 44 | 3.0 ± 0.3 | 408.0 ± 14.6 | 518.9 ± 43.4 | 6.00 ± 0.05 |
| 54 | 1.2 ± 0.2 | 250.0 ± 19.7 | 308.2 ± 15.0 | 5.54 ± 0.11 |
| 39 | 3.6 ± 0.3 | 462.3 ± 12.3 | 619.3 ± 41.2 | 5.99 ± 0.04 |
| 29 | 4.0 ± 0.2 | 403.5 ± 21.8 | 526.9 ± 34.9 | 5.78 ± 0.07 |
| 19 | 4.7 ± 0.4 | 447.7 ± 22.5 | 602.5 ± 45.2 | 5.80 ± 0.06 |
| 12 | 4.9 ± 0.3 | 448.8 ± 18.8 | 623.0 ± 39.3 | 5.79 ± 0.05 |
| 48 | 1.6 ± 0.2 | 374.0 ± 20.9 | 431.8 ± 51.6 | 6.00 ± 0.10 |
| 51 | 1.6 ± 0.3 | 358.3 ± 25.1 | 426.2 ± 62.8 | $\boldsymbol{6.00 \pm 0.11}$ |
| 56 | 1.0 ± 0.6 | 338.4 ± 49.4 | 301.1 ± 148.0 | 6.00 ± 0.38 |

concentration of BHT in the system can be calculated through

$$c_{\rm BHT, \, large} = \frac{\rho_{\rm BHT}}{\rho_{\rm solution}} \varphi_{\rm large} \frac{R_{\rm core}^3}{\left(R_{\rm core} + d_{\rm shell}\right)^3} \tag{8}$$

Here φ_{large} is the volume fraction of large-scale structure, and ρ_{solution} is the density of THF-D₂O mixture. The fitted results are all shown in Figure 8 and listed in Table 2. Figure 8a demonstrates that the scattering length density of the shell is \sim (5.75 to 6.00) $\times 10^{-6}$ Å⁻², smaller than that of pure D₂O (6.38 $\times 10^{-6}$ Å⁻²) or 4.5% mole fraction THF-D₂O mixture (6.10 $\times 10^{-6}$ Å⁻²), which means that the shell is composed



Figure 9. (a) UV–vis absorbance (A_{λ}) , (b) diffusion coefficient of the slow mode $(D_{\text{slow}}, \text{ from DLS})$, and (c) zero-angle scattered light intensity $(I_{\text{SLS}}(0), I(q) \text{ extrapolated to } q = 0, \text{ from SLS})$ as a function of c_{BHT} of 4.5% mole fraction THF aqueous solution. Here the insert shows the semilogrithmatic plot of $I_{\text{SLS}}(0)$ to c_{BHT} .

of ~(7 to 10) % mole fraction THF-rich THF-D₂O mixture. Figure 8b shows that φ_{large} decreases from ~1.0 × 10⁻⁴ to ~1.0 × 10⁻⁵, d_{shell} decreases from ~800 Å to ~300 Å, and $V_{\text{core}}/V_{\text{large}}$ increases from 0.05 to 0.1 when temperature is varied. Figure 8c concludes that the BHT concentration in the system stays almost the same (or decreases a little) with temperature according to eq 8, that is, in the range of (1.5 to 4.0) μ g/g, which is consistent with UV-vis measurement (~2.3 μ g/g). It indicates that the concentration fluctuation amplitude increases with temperature, and the mixed solvent of THF and water becomes more and more hydrophobic, and hence fewer THF-rich domains are needed to stabilize the hydrophobic BHT core at higher temperature so that the shell thickness decreases with temperature.

b. SANS Profiles for Pure 4.5% Mole Fraction THF Aqueous Solution (No BHT). In the previous section, we found that the hydrophobic BHT core surrounded by a THF-rich THF-D₂O shell is thermodynamically stable and that the existence of a THF-rich shell is formed to stabilize the BHT core in aqueous solution. Then, the question arises as to what will happen if there is no antioxidant in THF aqueous solution. To verify the effect of BHT, various 4.5% mole fraction THF aqueous solutions with different BHT amounts were prepared. Figure 9 shows the BHT concentration dependence of (a) absorbance at $\lambda = 279$ nm, A_{λ} , from UV-vis, (b) the diffusion coefficient of the slow mode, D_{slow} , from DLS, and (c) zero-angle scattered light intensity, $I_{SLS}(0)$, from SLS at room temperature, where $I_{SLS}(0)$ was obtained from the extrapolation of the Guinier relation between the scattered intensity I(q) and scattering vector (q) to zero angle. The linear relation between A_{2} and the BHT concentration through the origin means that the Beer-Lambert's law fits our system quite well in all of the BHT concentration range. The



Figure 10. Relaxation time spectra at different BHT concentrations (c_{BHT}) of 4.5% mole fraction THF aqueous solution. The insert figure shows that the c_{BHT} dependence of the ratio of scattering from the slow mode to the fast mode (A_s/A_f). The scattering angle is $\theta = 20^{\circ}$.

basic spherical shape of the large-scale objects (core-shell structure with a BHT core) does not vary, but its concentration decreases with decreasing BHT concentration. Figure 9b demonstrates that the size of the core-shell structure almost does not change when the BHT concentration is close to zero. Assuming that the mass of the core-shell object is proportional to the cube of its size, its mass also does not change when the BHT concentration is close to zero. Besides, the zero-angle scattered light intensity, $I_{SLS}(0)$, linearly decreases with decreasing BHT concentration when $c_{BHT} \rightarrow 0$, as shown in Figure 9c. Because $I(0) \approx cM^2$ and the mass may also be a constant, the linear decrease in $I_{SLS}(0)$ with decreasing BHT concentration means that the concentration of the core-shell object decreases linearly with the BHT concentration when $c_{BHT} \rightarrow 0$, which is consistent with UV-visible observation, as shown in Figure 9a. Note that the extrapolated $I_{SLS}(0)$ at $c_{BHT} = 0$ in a semilogrithmatic plot is not zero; it is larger than that of pure D_2O but smaller than that of pure THF, as demonstrated in the insert of Figure 9c. Although it is difficult to conclude about the exact concentration of the large-scale structure at zero BHT concentration, the semilog extrapolation in the insert of Figure 9c may indicate that the large-scale structure exists when there is no BHT in pure 4.5% mole fraction THF aqueous solution.

DLS measurements show the same trends as the SLS results. Figure 10 shows the relaxation time spectra for 4.5% mole fraction THF aqueous solution with different BHT concentrations (c_{BHT}) , and the insert figure shows the corresponding normalized peak area of the slow mode (A_s) to the fast mode $(A_{\rm f})$, that is, $A_{\rm s}/A_{\rm f}$. Here the fast mode corresponds to concentration fluctuation, and the slow mode comes from the Brownian motion of the large-scale structure. It clearly indicates that the size scale of the slow mode is almost unchanged when $c_{BHT} \rightarrow 0$ (also indicated in Figure 9b), and the contribution from the fast mode increases with decreasing $c_{\rm BHT}$. Because the fast mode comes only from temperature-dependent concentration fluctuation and should be independent of c_{BHT} , its amplitude can be used as a reference to study whether the large-scale structure exists when there is no BHT. It clearly demonstrates that the ratio of the slow mode to the fast mode (A_s/A_f) decreases with decreasing BHT concentration, and $A_s/A_f \approx 4$ when $c_{BHT} = 0$, so that the large-scale mode does exist if there is no BHT.

As mentioned in the Introduction, there are two theoretical explanations about the origin of large-scale objects in



Figure 11. SANS scattering profiles for 4.5% mole fraction THF aqueous solutions at different temperatures (without BHT). The predicted lines are shown according to the polydisperse sphere model.

water—organic solvent mixtures, that is, loosely associated structures and nanobubbles, respectively. Unfortunately, the experimental parts above cannot unambiguously determine the origin. The associated structures explanation cannot theoretically explain why these can coexist with THF—D₂O concentration fluctuation domains, and the nanobubbles explanation cannot experimentally explain why we cannot observe the large-scale structure in pure 4.5% mole fraction THF aqueous solution by SANS because air has larger contrast than BHT when compared with D₂O. As far as this part is concerned, it is still an open question.

Figure 11 shows the typical SANS profiles for 4.5% mole fraction THF aqueous solution at various temperatures without BHT. In the case of THF aqueous solution without BHT, concentration fluctuations dominates the high-q scattering profiles, that is, the intensity increases with temperature when the system is close to the phase boundary.²⁰ However, it is difficult to say if there is low-q upturn or not because the error bars are too large (error bars correspond to one standard deviation), and the absolute scattered intensity is extremely low. It should be noted that the large-scale structures do exist here, as illustrated in DLS experiment in pure 4.5% mole fraction THF aqueous solution,²⁰ which points out possible spheres composed of THF-rich THF-D₂O mixture or core-shell structure with air-bubble core and THF-D₂O shell. The assumptions that the scattering length density of THF-rich domains $\rho = 5.85 \times 10^{-6} \text{ Å}^{-2}$ (8.5% mole fraction THF) is the same as in the previous discussion and R =Rhslow in pure aqueous solution DLS measurements are quite reasonable. We found that if the slow mode comes from homogeneous THF-rich THF-D₂O spheres, then the contrast between THF-rich domains and D₂O is quite low; although $qR \gg 1$, the intensity contribution to our SANS observation range is very small, and we can hardly find any low-q scattering profile in pure 4.5% mole fraction THF aqueous solution in SANS data. The latter assumption that the large-scale structure is composed of air bubbles core and THF-rich shell is not very reasonable, because the contrast between air bubbles and deuterated water is even larger than that between BHT and D_2O_1 , and if there is a trace amount of air bubbles inside, then the scattered intensity will be much larger than what we can see in BHT-THF-D₂O system.

3.4. Basic Model. Figure 12 is the possible model for the small-scale concentration fluctuations and large-scale nondraining core—shell structure in 4.5% mole fraction THF aqueous solution with BHT. It is shown that THF is well-dissolved in



Figure 12. Possible models for 4.5% mole fraction THF aqueous solutions (with BHT): The small-scale concentration fluctuation domains and large-scale core—shell structure.

deuterated water, and the concentration fluctuation domains are clearly observed. Because the BHT antioxidant is hydrophobic, it can enter into the THF-rich large-scale structure to keep stability. Pure BHT acts as droplets in the core of spherical structures, and the THF-rich (7% to 10% mole fraction) THF $-D_2O$ phase acts as shell enclosing the BHT core. Both BHT and THF concentration in the shell almost remain constant with temperature, but the shell size decreases, which means that the mixed solvent gets more and more hydrophobic with the increase in concentration fluctuation amplitude, and less THF-rich component is needed to stabilize hydrophobic BHT. Besides, the large-scale structure still exists in 4.5% mole fraction THF aqueous solution without BHT. It could be attributed to lose THF-rich associates with other organic residues or nanobubbles.

4. CONCLUSIONS

Trace amounts of BHT antioxidant in HPLC grade commercially THF solvent can influence the large-scale structure in THF-water mixtures. From UV-vis measurement, we have found a large absorbance peak at 279 nm, which comes from the characteristic absorption of BHT. BHT concentration does not vary with temperature. From DLS measurement, we found that the large-scale structure has a length scale of ${\sim}100$ nm, and the diffusive large-scale structure is probably spherical in shape. The SANS technique helped us detect the detailed structure of these objects. Various models were applied to fit the temperature dependence of the scattering profiles in THF aqueous solution, for example, polydisperse sphere, BHT-core, and BHT-shell polydisperse core-shell model. We found that the core-shell model with a BHT core and (7 to 10) % mole fraction THF-rich shell is the best fitting model. The size of this core-shell structure decreases with temperature because the shell becomes thinner, whereas the concentration of BHT core decreases a little $(\sim 2.3 \,\mu g/g)$ with temperature. Although in the present manuscript we could still not sort out the mechanism behind the formation of the DLS slow mode if no BHT exists, it is clear that a trace amount of BHT is very important for us to "see" the largescale structure in SANS, and SANS cannot monitor it in THF $-D_2O$ mixture (without BHT) because of the low contrast.

A polydisperse sphere model with THF-rich THF $-D_2O$ mixture can be used to fit the low-q SANS profiles of pure 4.5% mole fraction THF aqueous solution.

AUTHOR INFORMATION

Corresponding Author

*Tel: +86 010 82618089. Fax: +86 010 62521519. E-mail: c.c.han@iccas.ac.cn (C.C.H.); chenghe@iccas.ac.cn (H.C.).

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