Distribution and Dynamics of a Low-Molecular-Weight Solute in the Shell of a Polymer Micelle As Studied by Nuclear Magnetic Resonance

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Distribution and dynamics of methyl methacrylate (MMA) in contact with polystyrene-block-poly(methacrylic acid) micelles under the conditions of its full solubility in D2O (2 g/L) were studied by 1H NMR methods, in particular pulsed-gradient-stimulated echo (PGSE), transverse relaxation, and rotating-frame relaxation, under varying intensity of the spin-lock field. It was found that MMA can penetrate into the micellar core after many hours at 300 K. In a freshly prepared system, MMA resides almost exclusively in the micellar shell. Its radial distribution there can be described by a Gaussian function with a maximum at the core-shell interface and a mean scatter of about 1.66 × R, where R is the radius of the core. Although it is fairly stable during the rotational and translational diffusion of the micelle as a whole, this distribution has an internal dynamics. According to the combined results of NMR, individual MMA molecules exchange their residence sites with an average correlation time of about 5 × 10⁻³ s. Transient sorption of MMA molecules to methacrylic acid units is discussed as a probable explanation of this dynamics.

Introduction

In two recent papers,1,2 polymerization of methyl methacrylate (MMA) in the shell of polystyrene-block-poly(methacrylic acid) micelles was investigated using nuclear magnetic resonance1 and small-angle neutron scattering3 (SANS). A part of the subject was the distribution of MMA before polymerization. Because of its diffuse nature, this distribution was beyond the reach of SANS or any other scattering method but could be approached by NMR. The problem of sorption of a dissolved low-molecular-weight solute by the shell of a polymer micelle could be interesting as such. According to the convincing evidence in the previous study,1 the solute resides almost exclusively in the shell area of the micelle (and not in the surrounding water), but moves there in a Brownian way. These conclusions were obtained mostly indirectly, by fitting a number of parameters, including those of the MMA radial distribution, the asymmetric inhomogeneity broadening, and the symmetrization/narrowing effect of the Brownian motion on its NMR signal. The model used was consistent both internally and externally (with the experimental signal shape) but had a drawback in many adjustable parameters. The author found that the dynamics of the solute, interesting for its own sake, is experimentally attainable by NMR relaxation and pulsed-gradient-stimulated-echo (PGSE) methods. This study presents the results of these observations and reexamines the theory of NMR signal shape using a somewhat better-founded physical model. Methyl methacrylate in an interaction of the mentioned type of micelles is examined again, mainly because MMA offers a reasonable solubility in water and well-separated NMR signals. However, analogous interesting behavior probably could be observed with a number of other low-molecular-weight solutes.

Experimental Section

The preparations of 0.5% micellar solutions of polystyrene-block-poly(acrylic acid) (PS–PAA) in D2O, as well as of 0.1% solutions of MMA in the PS–PAA, have been described previously.1 1H NMR spectra were measured at the resonance frequency 300.13 MHz with a Bruker Avance DXP300 spectrometer. Longitudinal and transverse relaxations were measured using the conventional inversion–recovery and Carr–Purcell–Meiboom–Gill (CPMG) sequences. For T2 measurements, a pulsed spin-lock (pulsedelay being 1/3) was used. Pulsed gradient stimulated echo PGSE self-diffusion measurements were performed with a Bruker z-gradient inversion probehead using a constant-diffusion delay, as well as constant length of a rectangular gradient pulse and variable gradient strength from 7.35 to 46.55 G cm⁻¹. In the series of PGSE experiments, the diffusion delay was varied from 3 to 50 ms. The lower limit was given by the necessary recovery after a gradient pulse and the sensitivity of measurement at the attainable gradient strength; the upper one was given by the fast transverse relaxation of MMA in the given system.

Results and Discussion

1. NMR: Model, Measurements, and Interpretation. Figure 1 shows the vinyl proton regions of the 1H NMR spectra of MMA (1 = cis, 2 = trans vinyl proton) dissolved in D2O and in a 0.5% D2O/buffer solution of PS–PMA micelles. In the second case, the system was measured 2 days after mixing so that separate signals of MMA absorbed by the micellar core (1c and 2c) could be detected, along with those of MMA in the micellar shell (1s, 2s). All signals of MMA in the shell have the same shift as those of MMA in water. As was already stated in the previous study,1 the primary reason for the broadening of the signals 1s and 2s is an additional inhomogeneous magnetic field, \( B(r, \theta) \).

\[
B(r, \theta) = \frac{4}{3} \pi (3 \cos^2 \theta - 1)(\chi_1 - \chi_2)B_0 (R/r)^3
\]  

(1)

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The shape of the function in eq 2 was shown to produce the broadening effect. There are two main contributions to such averaging: (1) isotropic tumbling of the whole micelle and (2) Brownian self-diffusion of the solute.

(1) The effect of collective motions of the whole micelle depends on the degree of their correlation with the motions of the solute. Let us assume that the solute behaves as an integral part of the micellar shell. From the Debye expression for the rotational diffusion correlation time \( \tau_{rd} = 4\pi M \eta / 3kT \), \( M \) being the radius of the whole micelle (4.7 \times 10^{-8} m) and \( \eta \) the viscosity of the medium (7.98 \times 10^{-4} Pa s), we obtain (for 300 K) \( \tau_{rd} = 0.837 \times 10^{-4} s \), which corresponds to a rotational frequency of about 1.9 kHz. As the isotropic tumbling drives the chemical shift, \( \omega \), to 1/3, most of the shielding anisotropy, given by eq 1, is removed by collective motions of the micelle in this case. Hence, NMR detects its mere residues, and the radial-angular dependence of the magnetic shielding, expressed in the chemical shift, will be

\[
\omega(r, \theta) = \omega_0 + \kappa \gamma B(r, \theta) = \omega_0 + \left(\delta/2 \right) (3 \cos^2 \theta - 1)(R/r)^3
\]

where \( \delta \) is the residual chemical shift for \( \theta = 0 \) and \( r = R \). As will be shown below, even such a residue offers valuable information on both the distribution and dynamics of the absorbed solute.

(2) Even if it is being fully absorbed by the shell, the solute can be expected to move about in a Brownian way either by free diffusion or by discrete jumps between different adsorption sites. In principle, both types of motions can be investigated by PGSE experiments that take into account the collective micellar motions described in the preceding paragraph. According to the Einstein-Stokes relation \( D_{sd} = kT / 6\pi \eta M \), the translation diffusion coefficient of the whole micelle is approximately 5.85 \times 10^{-12} m^2 s^{-1}. During the time \( t_d \), the micelle transverses the diffusion length \( L_d = (6D_{sd}t_d)^{1/2} \). For a typical measurement time, \( t_d = 10^{-2} s \), \( L_d = 2.42 \times 10^{-7} m \), i.e., more than 5 times the micellar radius \( R_m \). Collective translation diffusion of the whole micelle can thus be detected (see below). In the case of the low-molecular-weight solute, the translation motion is coupled with rotational motion of the type (1) and the PGSE response is modulated by \( \cos(2\gamma B t_d) \). However, if \( t_d \) is held constant and the gradient is incremented, this modulation does not interfere with measurement.

In a good approximation warranted by a large difference between \( t_d \) (typically 100 ms) and \( \delta \) (typically 1 ms), the stimulated echo response in a PGSE experiment can be expressed as

\[
M_s(g) = M_s(0) \exp(-2\gamma T_2) \exp(-D_{sd}g^2 \delta^2 \gamma t_d)
\]

where \( g \) and \( \gamma \) are the length of the gradient pulse and the corresponding field gradient, respectively; \( T_2 \) is the delay between the gradient pulses (or diffusion time); and \( 2\gamma T_2 \) is the delay between the first hard pulse and the echo.

In an example, Figure 2 compares the exponential decays (\( t_d = 100 \) ms) corresponding to a linearly increased \( g \) for MMA dissolved in D_2O, absorbed in the micellar shell and...
in the micellar core. In the last case, the decay reflects the translation of the whole micelle (there is evidently no fast exchange of MMA between the core and the shell, as the signals are well-separated and their widths are different). In principle, \( \alpha \)-methyl signals of the PMA shell could also be used. In the last study,\(^7\) they were believed to be broadened beyond detection. As found in the meantime, their broadening is not extreme and their invisibility is only relative to the water-suppressing pulse sequence used. However, their fast transverse relaxation (\( R_{\perp} \approx 10 \text{ s}^{-1} \)) precludes their utilization under the attainable conditions. The values of \( D_{\perp} \) fitted to eq 4 are indicated in the figure.

Let us name \( D_M \) and \( D_S \) the diffusion coefficients corresponding to the whole micelle and to MMA in the shell, respectively. When the same PGSE experiment is repeated with various values of \( t_d \), \( D_M \) remains approximately constant \( (6.7 \times 10^{-12} \text{ cm}^2 \text{s}^{-1} \) from DLS), but \( D_S \) apparently decreases with increasing \( t_d \). Denoting the respective diffusion lengths \( \lambda_M \) and \( \lambda_S \), it is easy to see that the relative diffusion length

\[
\lambda_{rel} = \lambda_S - \lambda_M = (D_M t_d)^{1/2} (\alpha^{1/2} - 1) \tag{5a}
\]

or

\[
\alpha^{1/2} = \left( \frac{\lambda_{rel}}{D_M^{1/2}} \right) t_d^{-1/2} + 1 \tag{5b}
\]

where \( \alpha = D_M/D_S \). Figure 3 shows that the dependence of \( \alpha^{1/2} \) on \( t_d^{-1/2} \) is almost linear except for very short \( t_d \), i.e., the slope \( \lambda_{rel}/D_M^{1/2} \) is approximately constant. Because \( D_M \) is constant in the whole range of \( t_d \), \( \lambda_{rel} \) must be also constant except for very short \( t_d \).

A plausible explanation of this phenomenon is that MMA is fluctuating rapidly within the area of the micellar shell but is prevented by a rather high barrier from diffusing into the surrounding water. Such behavior can be seen approximately as a molecule fluctuating in a potential well, described by a damped Langevin equation\(^7\)

\[
f \frac{d\delta x(t)}{dt} + \gamma \delta x(t) = F(t) \tag{6}
\]

where \( \delta x \) is a small fluctuation, \( F(t) \) is a rapidly fluctuating force, \( \gamma \) is the force constant of the well, and \( f \) is the friction factor, \( f = \gamma \tau_d \) (\( \tau_d \) being the correlation time of this fluctuation). As was recently shown by Schurr and co-workers,\(^7\) the autocorrelation function for Gaussian variables can be expressed as

\[
\langle \delta x(0) \delta x(t) \rangle = \langle \delta x(0) \rangle^2 \exp (-t/\tau_d) \tag{7}
\]

and also, for pseudolinear behavior at small intervals, \( \langle \delta x(0) \delta x(t) \rangle = \delta^2 \exp (-t/\tau_d) \), where \( \delta^2 = \langle \delta x(0) \delta x(0) \rangle \), the quadratic scatter of the chemical shift. Under such conditions, transverse magnetization obeys the relation

\[
\langle M_x(0) M_y(t) \rangle = \langle (\alpha^{1/2} / 8) \exp [-i\omega_0 + R_2^{0.9}] \exp [-\delta^2 \tau_d^2 (t/\tau_d - 1 + e^{-\theta_{12}})] \rangle \tag{7}
\]

The shape of the function given by eq 5 deviates markedly from an exponential one for \( \tau_d > 10^{-3} \text{ s} \). Figure 4 shows transverse magnetization time decays for MMA in \( D_2O \), micellar shell, and core. Although the decay for the micellar shell reflects much faster transverse relaxation, it is almost exponential, too. Careful fitting gives the values \( \tau_d = 4.5 \times 10^{-4} \text{ s} \), \( \phi_{12} = 48.2 \text{ Hz} \).

These values can be checked using rotating frame relaxation. For the \( j \)th site exchanging with a number of sites having different magnetic shielding, we can write\(^8\)

\[
\langle M_x(0) M_y(t) \rangle = \langle (\alpha^{1/2} / 8) \exp [-i\omega_0 + R_2^{0.9}] \exp [-\delta^2 \tau_d^2 (t/\tau_d - 1 + e^{-\theta_{12}})] \rangle \tag{7}
\]

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\[(T_{1p})^{-1} = (T_{1p}) \exp^{-1} - T_{1}^{-1} = \sum_{k \in j} \frac{\Delta \omega_{jk}^2}{4} \frac{\tau_{jk}}{1 + \omega_1^2 \tau_{jk}^2} \quad (8)\]

from which, using the mean values \[^2\langle \Delta \omega^2 \rangle\] and \(\tau_{\text{cf}}\) of \(\Delta \omega_{jk}^2\) and \(\tau_{jk}\), respectively,

\[\langle T_{1p} \rangle = \frac{4}{\langle \Delta \omega^2 \rangle} + \omega_1^2 \frac{4\tau_{\text{cf}}}{\langle \Delta \omega^2 \rangle} \quad (9)\]

where \(\omega_1\) is the intensity of the applied spin–lock field (in rad/s). Figure 5 shows the measured dependence of \(T_{1p}\) on \(\omega_1\). Fitting gives \(\tau_{\text{cf}} = 4.73 \times 10^{-4}\) s and \(\langle \Delta \omega^2 \rangle = 9.673 \times 10^2\) rad\(^2\)s\(^2\), i.e., \(\delta_{\text{int}} = 49.5\) Hz. Both values are in a rather good agreement with those obtained from transverse relaxation. Converting \(\tau_{\text{cf}}\) to \(D_{\text{cf}}\) in the geometry of the micellar shell, one gets \(D_{\text{cf}} = 2.86 \times 10^{-11}\) m\(^2\)s\(^{-1}\), whereas the value of the same quantity obtained from PGSE by extrapolation to \(t_0 \to 0\) is \(2.26 \times 10^{-11}\) m\(^2\)s\(^{-1}\), which again is in a reasonable agreement. Thus, we see that approximately the same diffusion mobility of the solute within the micellar shell can be obtained from three independent measurements (PGSE as well as laboratory-frame and rotating-frame transverse relaxation). The corresponding correlation time, \(\tau_{\text{cf}}\), or correlated diffusion coefficient, \(D_{\text{cf}}\), is fully consistent with the outlined physical model, i.e., motional averaging (relative symmetrization) and relaxation broadening. It should be emphasized again that fast diffusion throughout the area of local field inhomogeneity is the only mechanism able to both broaden and symmetrize the signal: as there is no shift difference relative to water solution, fast exchange with a substantial portion of the solute residing outside the micelle could not boost transverse relaxation but would diminish the influence of inhomogeneity, producing thus a symmetrical and narrowed signal.

According to the model checked with the use of the above-described experiments, fluctuations between different sites in the micellar shell expand the signal frequency, assigned to the instant point \((r, \theta)\) by eq 2, into a distribution

\[g(r, \theta, \omega) = \frac{1}{\delta \sqrt{2\pi}} \exp\{-[\omega - \omega(r, \theta)]^2/2\delta^2\} \quad (10)\]

Because of fast exchange, the corresponding frequency \(\omega_{\text{es}}(r, \theta)\) is

\[\omega_{\text{es}}(r, \theta) = \int_{\omega_0 - \delta}^{\omega_0 + \delta} g(r, \theta, \omega) d\omega \quad (11)\]

The collective signal then has the form

\[l(\omega) = \int_0^\infty \int_0^{2\pi} G(r, \theta) w/[w^2 + (\omega_{\text{es}}(r, \theta) - \omega)^2] dr d\theta \quad (12)\]

where \(w = R_2 + \delta^2 \tau_{\text{cf}}\). The assumption implicit in eq 12, that the signal is a collection of Lorentzians, is not fully justified. However, the observed signal has a predominantly (slightly asymmetric) Lorentzian shape. The most probable reason is that the signal envelope is given by fast relaxation, which is almost totally exponential.

Assuming now for simplicity a Gaussian radial distribution of the solute

\[g(r') = \frac{1}{b \sqrt{2\pi}} \exp\{-(r' - 1)^2/2b^2\} \quad (13)\]

where \(r' = r/R\), the parameter \(b\) can be fitted to the experimental shape of the signal. The result with \(b = 1.66\), achieved for the best-resolved signal 1s, is shown in Figure 6. The same value is consistent with the simulated shapes of the remaining signals, which were not used for fitting because of their overlap with other signals. The radial \(G(r)\) and volume \(G(r)\) distribution is illustrated in Figure 7. As can be seen, the distribution is rather diffuse but converges to zero near the outer rim of the micellar shell. The resulting distribution is almost identical to that achieved in the previous work. In contrast to a fitting of a multiparameter model function to the experimental signal shape, the distribution was obtained here using the translation–diffusion correlation time and the correlated mean shift difference (obtained by three independent experimental methods) as fixed parameters, leaving only the radial distribution adjustable.

**2. General Discussion.** The present study offers two important results: (1) the solute is distributed diffusely in the micellar shell, its statistical density being highest near the core–shell interface, and (2) its molecules enact translation diffusion motions or jumps with the correlation time \(\tau_{\text{cf}}\) of about \(5 \times 10^{-4}\) s. These motions are apparently uncorrelated but conserve the overall distribution, i.e., the molecules are loosely trapped in the shell. Given that the system is under conditions of full solubility of the solute in water, such trapping can be due only to adsorption of
the solute molecules on the poly(methacrylic acid) chains of the shell. This conclusion is strongly supported by the value of \( \lambda \), which is many orders of magnitude higher than that of an unhindered diffusion motion.

It must be pointed out that no sorption comparable with that described here was observed in polymer micelles having poly(acrylic acid) or poly(ethylene oxide) in their shells, except for cases of an extremely low solubility of the solute (such as chlorobenzene).\(^{10}\) The reason for such special behavior of poly(methacrylic acid) is probably in its intrinsically amphiphilic nature given by the combination of a hydrophilic carboxyl and a hydrophobic \( \alpha \)-methyl group. The predominance of hydrophilicity or hydrophobicity of a methacrylic acid unit is given, among other factors, by the ionization of the carboxyl group. In the present study, the micelles were dissolved in a buffer solution (pH = 10) so that ionization of the carboxyl groups could be expected. However, strong evidence\(^{11-13}\) exists for suppressed ionization and increased hydrophobicity of poly(methacrylic acid) in the interior of a micellar shell because of its crowding near the core–shell interface. This peculiar behavior plausibly explains why the solute is not distributed evenly along the poly(methacrylic acid) chains in the present case but tends to accumulate as near the core–shell interface as the actual free volume there allows.

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