ASSOCIATION OF GRAFT COPOLYMERS OF ALKYL METHACRYLATES WITH α-METHYL-ω-HYDROXY-POLY(OXYETHYLENE) METHACRYLATES

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Dedicated to Dr Blahoslav Sedlacek on the occasion of his 70th birthday.

Solution properties of the statistical copolymers of alkyl methacrylates (AMA) with α-methyl-ω-hydroxy-poly(oxyethylene) methacrylates (MPOEMA) (nonionic polysoaps) were studied using static and dynamic ligh scattering as a function of monomer composition and concentration in aqueous and methyl cellosolve solutions. The solubility of the copolymers in water was found to be dependent on molar contant of AMA. While copolymers with low content of hexyl methacrylate (HMA) (0 and 20 mole %) were directly soluble in water, forming true solutions with a low content of large swollen aggregates, copolymers with a higher content of HMA or lauryl methacrylate (LMA) were not directly dispersable in water. A special procedure, the stepwise dialysis from methyl cellosolve solutions against water, had to be used to prepare them in the pseudomicellar form. The copolymers were directly soluble in methyl cellosolve and its water solution containing up to 60 vol.% of water. Nevertheless, the light scattering experiments were dominated by light scattering of swollen particles of aggregated copolymer molecules. The copolymers were not soluble in the mixtures containing 70–100 vol.% of water. Paramaters of aggregates in the mixture with 60 vol.% of water and in pure water were found to be very similar.

Block copolymers associate and form micelles in selective solvents (i.e., good solvents for one block and precipitants for the other). Micellization of block copolymers has been shown to obey the model of closed association[1,2]. There has been tremendous progress over the past decade in the theory of block copolymer micelle formation[3–8]. Recently, interest in the formation of water-soluble micelles with hydrophobic cores and hydrophilic shells from hydrophobic/hydrophilic diblock and triblock copolymers has rapidly increased[9–15]. The motivation of this activity, besides an effort to understand the structure, thermodynamics of micellar equilibria, and kinetics of micelle formation, as well as other properties, has been the application of micelles in the

controlled release of hydrophobic substances into aqueous media[12,16]. In spite of an easier preparation of graft copolymers[17], their micellization has received less attention from theorists and experimental scientists; these copolymers, however, are believed to gain tremendous commercial significance and engineering interest.

A particularly interesting class of water-soluble polymers are the polysoaps[18–29], having both hydrophobic and hydrophilic pendant groups (side chains) distributed along the backbone. They can be visualized as a large number of surfactant moieties attached as side chains to the polymer backbone. Both ionic and nonionic polysoaps has been reviewed by several authors[18,27–29]. Aqueous solutions of such polymers are characterized by low viscosity and high solubilization capacity[20,30]. These properties reflect an aggregation (association) of the surfactant side chains providing hydrophobic microdomains called "polymeric micelles". The detailed structure of these "polymeric micelles" is still subject to discussion. Two major models have been proposed which have been referred to as "local micelles"[30–32] and "molar micelles"[33–35]. The "local micelle" assumes the intermolecular aggregate of limited number of neighbouring surfactant side chains. The model of the "molecular micelle" assumes the formation of at least monomolecular micelles by aggregation of all side chains of a given macromolecule into one aggregate. This model was recently treated theoretically[36,37]. As only few experimental data are available, none of the polysoap models can be rejected. Fluorescence quenching and neutron scattering studies support the "local micelle" model[38], whereas theoretical treatments favour the "molecular micelle" model[36,37].

In order to address the issue, statistical copolymers of alkyl methacrylates (AMA) with α-methyl-ω-hydroxy-poly(oxyethylene) methacrylates (MPOEMA), which can be regarded as graft copolymers AMA-*graft*-MPOE (nonionic polysoaps) were studied using static (SLS) and dynamic (DLS) light scattering methods as a function of monomer composition and concentration in aqueous and methyl cellosolve solutions. These graft copolymers were originally suggested as compounds which produce poly(oxyethylene)-rich surfaces on hydrophobic medical materials[25,26] by a simple coating treatment. Such modified surfaces are effective in decreasing protein adsorption and cell adhesion. The graft copolymers similar to block copolymer surfactants, such as pluronic[39], are suitable as drug delivery systems. These AMA-*graft*-MPOE copolymers were selected for this study because of the possibility of the tailor-made synthesis of the copolymers with various compositions permitting a systematic evaluation of the relationship between their structure and properties. The objective of this study was to find the relation between monomer composition of the graft copolymers and their solubility and/or association in water, methyl cellosolve and water/methyl cellosolve mixtures.

EXPERIMENTAL

Monomers and Chemicals

α-Methyl-ω-hydroxy-poly(oxyethylene) methacrylate with the molar mass of starting POE of 1 900 g/mol (MPOEMA-1900) and 4 000 g/mol (MPOEMA-4000) were prepared by the procedure described in our previous paper[25].

Methyl methacrylate (MMA), hexyl methacrylate (HMA) and lauryl methacrylate (LMA) (Polyscience) were freshly distilled under reduced pressure before use.

2,2′-Azobisisobutyronitrile (AIBN, Aldrich) was purified by recrystallization from methanol and used as an initiator for polymerization.

AMA-MPOEMA Copolymers

The copolymers were prepared by radical polymerization of monomers in toluene at 50 °C for 45 h (Table I).

A polymerization mixture, containing 14.0 wt.% of monomer, 0.6 wt.% of AIBN and 85.4 wt.% toluene, was bubbled with nitrogen for 15 min and then sealed in an ampoule. After the polymerization was finished, polymers were precipitated into cool diethyl ether, washed and dried. To remove non-polymerized macromonomer (about 10–20%, as determined by GCP) the polymers containing POE-1900 were dialyzed for 3 days in a Visking dialysis tubing (molar mass cut-off, 6 000–8 000 g/mol). The polymers containing POE-4000 were purified by using ultrafiltration (Amicon, membrane PM-30) and isolated by lyophilization. The yields of polymers were 60–70%. Monomer composition and molecular characteristics of the copolymers prepared and investigated are summarized in Table I and their structure is shown in Scheme 1.

TABLE I
α-Methyl-ω-hydroxy-poly(oxyethylene) methacrylate–alkyl methacrylate copolymers: monomer composition (mole %)

Copolymer	MPOEMA-1900	MPOEMA-4000	MMA	HMA	LMA
1[a]	80	–	20	–	–
2[b]	80	–	–	20	–
3	40	–	20	40	–
4	25	–	20	55	–
5	20	–	20	60	–
6	25	–	20	–	55
7	–	20	20	60	–
8	–	20	20	–	60
9	–	10	20	–	70

[a] M_{wu} 1 900, M_{wu}/M_{nu} 2.5; [b] M_{wu} 2 000, M_{wu}/M_{nu} 2.4 (M_{wu} and M_{nu}, mass- and number-average molar masses of unimers; M_{wu}/M_{nu} determined by GPC)

As most of the copolymers were not soluble in water (Table I, copolymers 3–9), a special procedure introduced in refs[11,25] was used for preparation of aqueous solutions for light scattering measurements. Copolymer was first dissolved in methyl cellosolve at ≈ 100 °C and the solution was dialyzed against water/methyl cellosolve mixtures. Five mixtures with water contents successively increasing by 20% were used and the last dialysis was against water. Typical concentration of copolymer used for dialysis was 1–2 . 10^{-3} g ml^{-1}. The solutions were diluted to the concentrations needed.

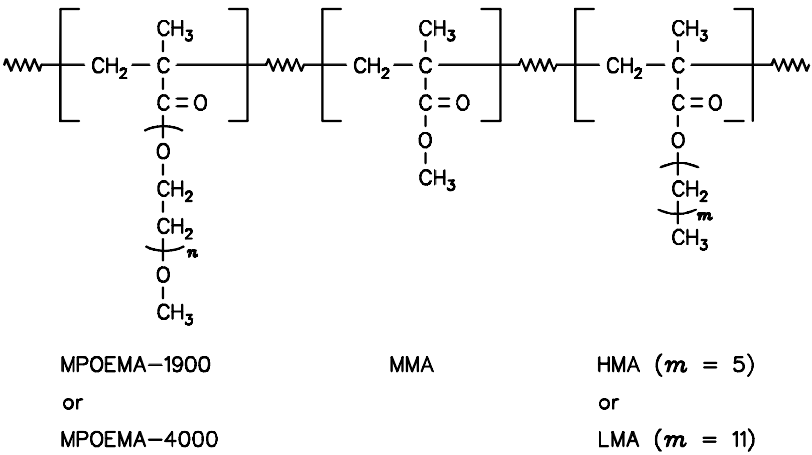
Copolymers 1 and 2 were analyzed on a 1.6 × 80 cm column packed with Sepharose 4B and 6B (1 : 1) and eluted with 0.05 M Tris buffer pH 8.0, which was 0.5 M in NaCl. Molar mass averages were estimated using PEG standards (molar mass 2 000–22 000 g mol^{-1}).

Static Light Scattering (SLS)

Static light scattering measurements were performed with a Sofica instrument, equipped with a He-Ne laser (vertically polarized, λ = 633 nm) in the angular range 30–150 °C. The processed data are represented (unless otherwise noted) as

$$Kc/\Delta R(0) = 1/M_w + 2A_2c \ , \qquad (1)$$

where M_w is the mass-average molar mass, K is the optical constant which includes the square of the refractive index increment, $\Delta R(0)$ is the excess Rayleigh ratio, proportional to the intensity of light scattered from the copolymer particles, extrapolated to zero angle of measurement, A_2 is the second virial coefficient, and c is the copolymer concentration in g ml^{-1}. Refractive index increment of copolymer solutions in water and methyl cellosolve, $(dn/dc)_\mu$, was measured with a Brice–Phoenix differential refractometer after equilibrium dialysis of copolymer solutions against corresponding solvents, as described elsewhere[40]. For the aqueous solutions of copolymers effective value of $(dn/dc)_\mu$ lay in the range 0.125–0.136. For solutions in methyl cellosolve $(dn/dc)_\mu$ were about 0.073 ± 0.002.



SCHEME 1

Dynamic Light Scattering (DLS)

Polarized DLS measurements were made using the apparatus and technique described previously[41]. An argon ion laser (λ_0 = 514.5 nm) was the light source. An ALV 5000, multibit, multi-tau autocorrelator was operated with 32 simultaneous sampling times covering approximately 12 decades in delay time. The samples were thermostatted in a refractive index matching liquid (*m*-xylene).

Two different methods were used to analyze the multi-tau autocorrelation functions:

(*1*) The inverse Laplace transformation using the REPES method[42] of constrained regularization, which is similar in many respects to the inversion routine[43] CONTIN, to obtain a distribution $\tau A(\tau)$ of decay timer τ, according to

$$g^2(t) - 1 = [\int_0^\infty A(\tau)\exp(-t/\tau)\mathrm{d}\tau]^2 \quad , \tag{2}$$

where $g^2(t)$ is the measured normalized autocorrelation function of scattered light. REPES directly minimizes the sum of the squared differences between the experimental and calculated intensity time correlation functions using nonlinear programming. This method uses an equidistant logarithmic grid with fixed components (here a grid of 10 components per decade) and determines their amplitudes, $\tau A(\tau)$.

(*2*) The forced fit of experimental correlation functions to functions calculated under the assumption that the distribution of the relaxation times can be described by the Pearson V distribution:

$$A(\tau) = \tau_0^p \, \tau^{-(p+1)} \exp(-\tau_0/\tau)/\Gamma(p) \quad , \tag{3}$$

where τ_0 determines the position of the distribution on the τ axis and p its width; Γ is the gamma function. The results of iteration procedure are parameters of distribution τ_0 and p.

From characteristic decay times τ_i (peak positions of $\tau A(\tau)$) of dynamic modes (i = f, fast or s, slow), apparent diffusion coefficients, D_{ai}, were obtained from the equation

$$D_{ai}(q) = 1/\tau_i q^2 \quad , \tag{4}$$

where q is the length of scattering vector ($q = 4\pi n_0 \sin(\theta/2)/\lambda_0$), where n_0 is the refractive index of the solvent and λ_0 the wavelength of used light (514.5 nm). The diffusion coefficients, D_i, were obtained by extrapolating D_{ai} to zero scattering angle and zero copolymer concentration.

RESULTS AND DISCUSSION

Graft copolymers used in this study were prepared by radical copolymerization of hydrophobic monomers (MMA, HMA or LMA) with a hydrophilic macromonomer (α-methyl-ω-hydroxy-poly(oxyethylene) methacrylate). Consequently, the copolymer molecules under study have different chemical composition. The compositional heterogeneity is generally the higher, the larger the difference in copolymerization parameters is. Both the conventional monomers and the macromonomers used in this study are methacrylates with various alkyl ester groups. As polar effects of alkyl ester parts

do not differ substantially and the lengths of macromonomer side chains used in this study should not have a pronounced effect on the macromonomer reactivity[44], the copolymerization parameters should be similar for all combinations of monomers used. The discussion of the structure–solution properties relationship in this paper is based on the composition of the monomer mixture. We are aware that the real copolymer composition is slightly different from the starting one used in Table I.

The solubility of AMA-*graft*-MPOE copolymers in water was found to be a function of molar content of conventional hydrophobic comonomers. While copolymers 1 and 2 with low content of HMA (0 and 20 mole %) were soluble in water, forming true solutions with a low content of large swollen aggregates (see Fig. 1), copolymers with higher contents of HMA or LMA were not dispersable in water. A special procedure had to be used to prepared them in the pseudomicellar form in water. Thus, the proper hydrophilic/hydrophobic balance in these copolymers seems be the decisive factor in determining their solution properties.

The solution properties of water-soluble AMA-*graft*-MPOE copolymers (1 and 2) are complex. This is demonstrated in Fig. 1, where the decay time distribution functions $\tau A(\tau)$, obtained by the inverse Laplace transformation of multisampling time correlation functions, are plotted for an aqueous solution of the copolymer 2. The decay time distribution functions are bimodal. The two well-separated bands are ascribed to the fast decay time, τ_f, and the slow decay time, τ_s. The dynamic processes (fast and slow), characterized by τ_f and τ_s, have diffusive character (reciprocal values of τ_f and τ_s are q^2-dependent). Hence, it was possible to introduce two diffusion coefficients, D_f and D_s. The existence of two diffusion coefficients in dilute solutions generally points to the occurrence of two types of scatterers in the system with different hydrodynamic radii. Since R_{hf} is small and practically the same for both discussed copolymers, the fast mode was ascribed to polymer coil diffusion. The fairly broad distribution of this mode

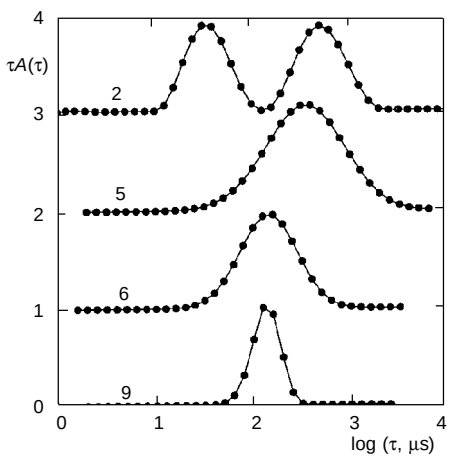


FIG. 1
Relaxation time distribution, $\tau A(\tau)$, from DLS data for the copolymers in water (for numbers of copolymers, see Table I)

reflects the polydispersity of a copolymer sample prepared by free radical copolymerization. Well-defined slow modes with a rather broad distribution can be related to diffusion of large scatterers which are probably formed by the association of copolymer molecules. Since the aggregates were found to be unstable at low concentrations (see below), the hydrodynamic radii of aggregates, R_{hs}, were calculated from the values of diffusion coefficients for infinite dilution (D_s) obtained by linear extrapolation of D_{as} (Eq. (*4*)) values for the higher concentration range only to $c = 0$ and they are shown in Table II.

In order to estimate the molar mass of aggregates, static light scattering measurement were performed. The total molar masses (M_{wt}) values shown in Table II were obtained by extrapolation of $Kc/\Delta R(0)$ values to $c = 0$ from the higher concentration range only. M_{wt} consists of the contribution of both aggregates, M_{wa}, and copolymer (unimer) molecules, M_{wu}

$$M_{wt} = w_a M_{wa} + w_u M_{wu} \ , \qquad (5)$$

where w_a and w_u are the mass fractions of aggregates and unimer, respectively. Since we do not know the mass fraction of aggregates and copolymer molecules in solution, the molar mass of aggregates cannot be determined accurately. It can only be stated that

TABLE II
Characteristics of copolymers particles in water

Copolymer	$M_{wt} \cdot 10^{-5}$, g mol^{-1}	R_{hs}, nm	$\rho_a \cdot 10^4$, g ml^{-1}	$\Delta\log\tau$
1	3.3	68[a]	4.2[b]	–
2	8.6	109[c]	2.6[d]	–
3	2.0[e]	60	3.7[e]	0.6
4	64	65	92	0.45
5	8.3[e]	96	3.7[e]	0.42
6	8.0	21	330	0.32
7	2.9[e]	21	120[e]	0.30
8	3.5[e]	16.2	310[e]	0.17
9	6.6[e]	17.3	510[e]	0.16

M_{wt}, total mass-average molar mass (micelles + unimers); R_{hf}, hydrodynamic radius of unimers; R_{hs}, hydrodynamic radius of aggregates; ρ_a, the average segmental density in micelles ($\rho_a = 3M_{wt}/4\pi R_{hs}^3 N_A$); $\Delta\log\tau$, the halfwidth at the half height of the distribution of relaxation times.
[a] R_{hf} 4.0 nm; [b] ρ_u 0.12 g ml^{-1}; [c] R_{hf} 4.3 nm; [d] ρ_u 0.10 g ml^{-1}; [e] $\Delta R(0)/Kc$ for $c \approx 2 \cdot 10^{-3}$ g ml^{-1}.

the molar mass of aggregates, M_{wa} is actually higher than the experimental value of M_{wt}. In the case of copolymers 1 and 2, where the relative scattering amplitudes for fast (A_f) and slow (A_s) modes are comparable (Fig. 1), w_a should be several times lower than w_u.

Copolymers with higher contents of hydrophobic AMA comonomers (No. 3–9) were not easily soluble in water and a special dialysis procedure had to be used to dissolve them. The light scattering of aqueous solutions of these copolymers is dominated by

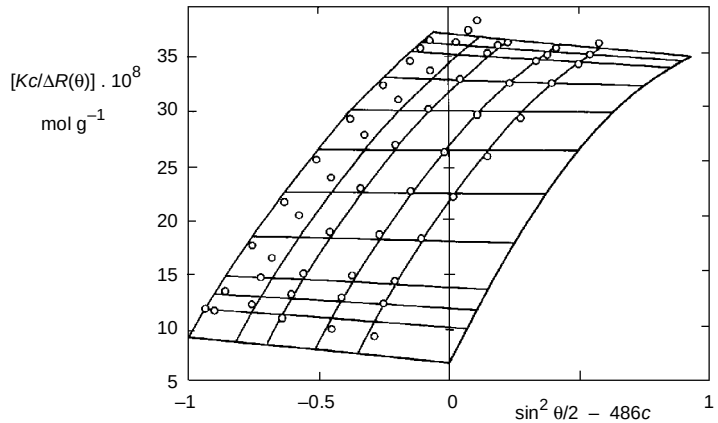


FIG. 2
Zimm plot for copolymer 4 in water; c is in g ml^{-1}

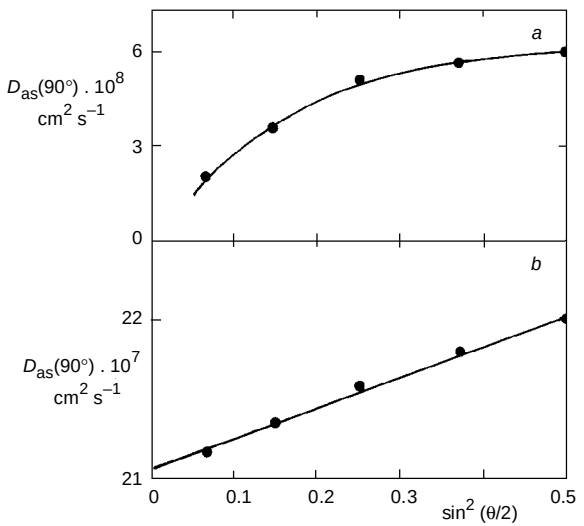


FIG. 3
Scattering angle dependence of the apparent diffusion coefficient of the slow mode, $D_{as}(90°)$, as obtained from DLS data for copolymers 4 (*a*) and 9 (*b*)

stable aggregates and the scattering of molecularly dissolved copolymer molecules was undetectable in DLS experiments. Therefore, the multisampling time correlation functions were analyzed by the forced fit (method 2) which provides more realistic information on the distribution widths of relaxation times, $\Delta \log \tau$. As demonstrated in Fig. 1, the distribution width decreases with increasing hydrophobicity of AMA units. Thus, copolymers containing LMA units have better defined aggregates than those containing comparable amounts of HMA (cf. copolymers 5 and 6 in Fig. 1). The use of the hydro-

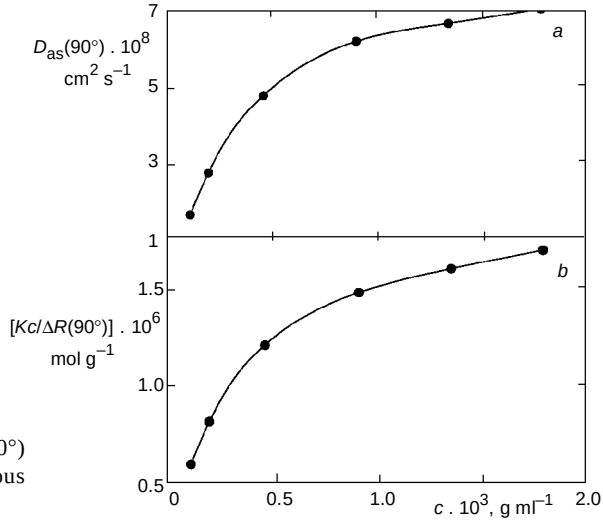


FIG. 4
Concentration dependence of $D_{as}(90°)$ (*a*) and $Kc/\Delta R(90°)$ (*b*) for aqueous solutions of copolymer 4

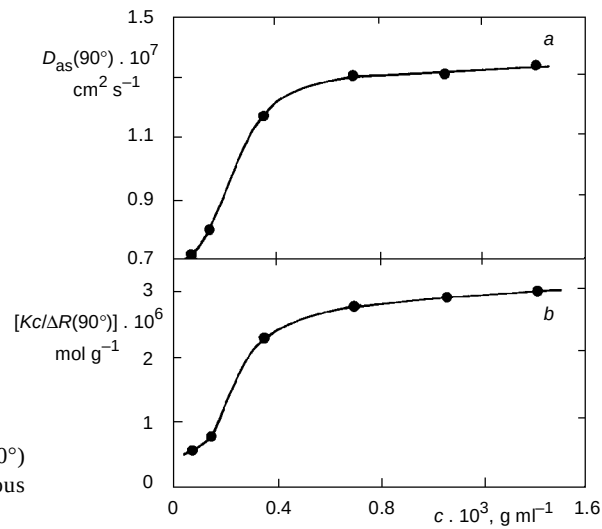


FIG. 5
Concentration dependence of $D_{as}(90°)$ (*a*) and $Kc/\Delta R(90°)$ (*b*) for aqueous solutions of copolymer 6

philic macromonomer with molar mass 4 000 unambiguously enhances the formation of small, well-defined particles (cf. copolymer 9 in Fig. 1). Thus, the hydrophilic/hydrophobic "polarity" of copolymers is a dominant factor in determining their aggregation (association) properties.

The very high polydispersity of aggregates complicates evaluation of light scattering data. Practically all $\sin^2(\theta/2)$-dependences of $Kc/\Delta R(\theta)$ (see Zimm plot in Fig. 2) have shown a deviation from linear dependences, a steep decrease at small scattering angles. Similar deviations were observed even in the plots of $D_{as}(\theta)$ versus $\sin^2(\theta/2)$ for copolymers containing HMA units (see Fig. 3*a*). The copolymers from MPOEMA-4000 macromonomers provide generally better results than those from MPOEMA-1900 (see Fig. 3*b*). Therefore, $Kc/\Delta R(0)$ and $D_{as}(0)$ values obtained by linear extrapolation from only back scattering angles were used for the evaluation of M_{wt} and R_{hs}. Another factor which complicated analysis of light scattering data was the instability of aggregates upon dilution as demonstrated in Figs 4 and 5 for copolymers 4 and 6, respectively. The decrease in $D_{as}(90°)$ of samples 4 (Fig. 4*a*) and 6 (Fig. 5*a*) with decreasing concentration coincides with the decrease in $Kc/\Delta R(90°)$ (Figs 4*b* and 5*b*). All these changes may be explained by an increase in the molar mass and size of the aggreagates upon dilution. This behaviour of aggregates is similar to the behaviour observed for micellar systems of block copolymers just above the critical micelle concentration, CMC, named "anomalous micellization"[45–47]. By analogy, critical aggregate concentration, CAC, can be introduced for aqueous solutions of graft copolymers under study. This effect was explained in the case of block copolymers by the presence of homopolymers identical to the core-forming block[47] or by the presence of copolymer molecules with a high mass fraction of the core-forming blocks due to compositional heterogeneity[45]. The latter explanation could be adopted for the system under study because large compositional heterogeneity can be assumed in the graft copolymers used. In analogy to block copolymers, the anomalous behaviour can be ascribed to a fraction of graft copolymers with a higher content of hydrophobic units which would form large aggregates even below CAC of the major component of the graft copolymer. It is worth mentioning that the copolymer aggregates seem to be in dynamic equilibrium with unimers while the bulk copolymers are insoluble in water.

In order to determine the characteristics of stable aggregates only, linear extrapolation from the higher concentration range only to $c = 0$ was again made to obtain molar masses and hydrodynamic radii of aggregates which, along with other parameters of copolymer aggregates are summarized in Table II. In extremely complicated cases only $\Delta R(0)/Kc$ values for $c = 2 \cdot 10^{-3}$ g ml^{-1} are given for the sake of comparison. The copolymers in Table II can be divided into two main groups according to molar masses of the hydrophilic macromonomers (MPOEMA-1900 and MPOEMA-4000); within these groups the samples are ordered according to the increasing hydrophobicity of AML units. The values for total molar mass, M_{wt}, and segmental density, ρ_a, increased

with the increasing content of HMA in graft copolymers with MPOEMA-1900 (copolymers 2, 3, 4, 5) indicating a higher tendency to aggregate formation. Contrary to this, the hydrodynamic radius, R_{hs}, changes only slightly. The graft copolymers of LMA with both the macromonomers (copolymers 6, 8 and 9) provide compact, dense and stable microparticles. Thus, besides very thin large polydispersed particles with $\rho_a << \rho_u$ (copolymers 1–5), small dense particles with $\rho_a \approx \rho_u$ are also formed from copolymers with the highest "polarity" (copolymers 6–9). It seems that these significant differences in properties of aggregates reflect their different structures. It is difficult to imagine that the structure of large aggregates is similar to that of normal micelles with the hydrophobic parts located in the spherical cores and hydrophilic POE chains in the shells. We propose the concept of a random association via attractive forces between hydrophobic HMA side chains, leading to a formation of aggregates through interpolymeric multiplets[48]. The existence of small interpolymeric multiplets was revealed several times by fluorescence spectroscopy[49,50] and light scattering methods[51,52] in aqueous solutions of hydrophilic copolymers containing hydrophobic side chains. As regards the small and compact particles ($R_{hs} \approx 20$ nm), we propose for them a quasimicellar structure with HMA or LMA hydrophobic side chains in geometrically unspecified cores and POE chains protecting the hydrophobic cores from further aggregation or even precipitation. Such a structure was recently proposed for hydrophobic/hydrophilic graft copolymers[36,37]. Because of the complexity of the graft copolymer system, only a qualitative verification of some theoretical implications has been possible on the basis of theoretical considerations. The theory predicts that the association number of micelles and, consequently, their molar mass increase with increasing length of the hydrophobic chains. This prediction could not be corroborated in our experimental results. Rather

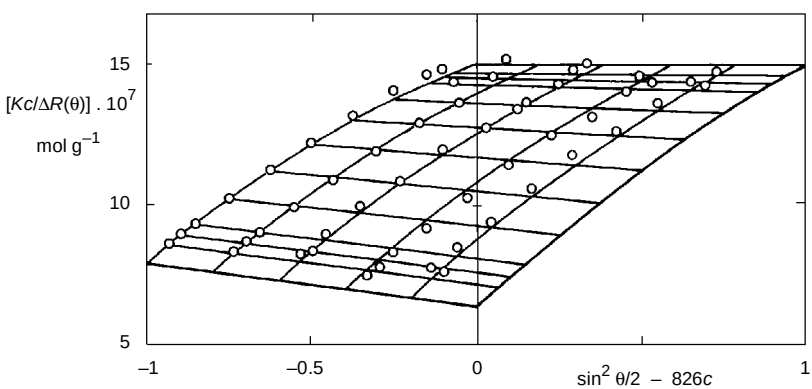


FIG. 6
Zimm plot for copolymer 4 in methyl cellosolve; c is in g ml^{-1}

than an increase of aggregate M_{wt} with a change in the number of carbon atoms in the hydrophobic side from five for HMA to eleven for LMA, a decrease in aggregate sizes due to the growing density of aggregates was observed (cf. characteristics of the copolymer 4 with 6, and 7 with 8). Unfortunately, the effect of copolymer composition has not been theoretically discussed yet.

The above experimental observation gave rise to a question whether the aggregates were formed during the preparation (stepwise dialysis). In order to elucidate this problem, solution properties of graft copolymers were also measured in methyl cellosolve.

TABLE III
Characteristics of copolymers particles in methyl cellosolve

Copolymer	$(dn/dc)_\mu$	$M_{wt} \cdot 10^{-5}$ g mol^{-1}	R_g, nm	R_{hs}, nm	$\rho_a \cdot 10^3$ g ml^{-1}	$\Delta\log\tau$
3	0.071	3.5	35	40	2.2	0.35
4	0.073	6.1	63	53	1.7	0.38
5	0.072	8.0	138	155	0.085	0.44
6	0.072	5.1	39	31	7.0	0.38
7	0.078	1.4	37	29	2.4	0.43
8	0.075	1.4	36	14.4	19	0.37
9	0.074	9.0	195	14.7	110	0.23

For the meaning of symbols, see Table II.

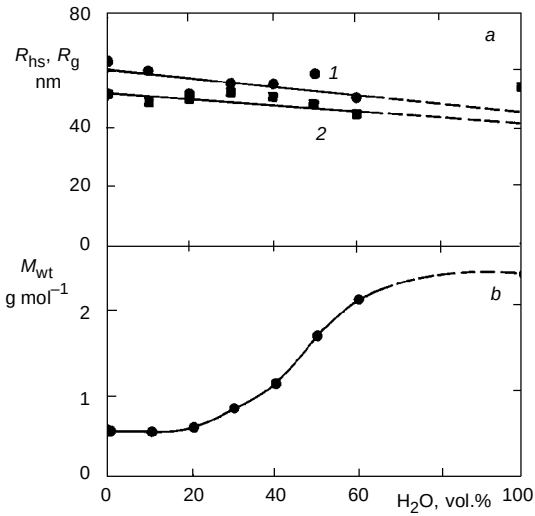


FIG. 7
Plot of *a* the geometric (*1*) and hydrodynamic (*2*) radii and *b* the total mass-average molar mass (M_{wt}) as a function of water/methyl cellosolve mixture composition

Contrary to aqueous solutions, the scatterers are better defined in methyl cellosolve solutions so that the usual Zimm plot analysis could be successfully used. This is demonstrated in Fig. 6 where the Zimm plot is shown for copolymer 4. The characteristics of scatterers are given in Table III. Since R_{hs} values in Table III are more than one order of magnitude higher than those of R_{hf} for unimer molecules in Table II, its appears that the light scattering experiments are again dominated by light scattering of loosely aggregated copolymer molecules. Comparing particle characteristics in Tables II and III it is evident that M_{wt} values for particles in methyl cellosolve are systematically smaller than those in water, whereas the particle sizes remain essentially the same. This means that the average segmental density in methyl cellosolve is smaller than in water. It can be assumed that the formation of denser and heavier aggregates takes place somewhere in water/methyl cellosolve mixtures during the dialysis procedure. Therefore, we started a detailed investigation of solution properties of the copolymers in water/methyl cellosolve mixtures. It was found that the copolymers are soluble in the mixed solvent system up to the 60 vol.% water content. As demonstrated in Fig. 7 for copolymer 4, M_{wt} increases in the mixed solvents between 20 and 60 vol.% of water and R_{hs} is practically constant as expected. The copolymers are not soluble in the mixtures with 70–100 vol.% of water. Parameters of aggregates in the mixture with 60 vol.% of water and in pure water are practically the same (Fig. 7) which means that no significant changes of particles take place in the course of dialysis in the latter region of mixed solvent. The same results were obtained with all the samples under study.

CONCLUSION

Aqueous solutions of graft copolymers containing variable amounts of hydrophilic (oxyethylene) and hydrophobic (alkyl methacrylate) units have been studied by static and dynamic light scattering. Generally, these copolymers were not soluble or dispersable in water but could be transferred into water from aqueous methyl cellosolve by a stepwise dialysis. Experimental results gave evidence of rather polydisperse multimolecular "pseudomicelles" which, unlike "regular" micelles of block copolymers with a concentric core/shell structure, have a very low segmental density.

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REFERENCES

1. Tuzar Z., Kratochvil P.: Adv. Colloid Interface Sci. *6*, 201 (1976).
2. Tuzar Z., Kratochvil P. in: *Surface and Colloid Science* (E. Matijevic, Ed.), p. 1. Plenum Press, New York 1993.

3. de Gennes P. G. in: *Solid State Physics* (J. Liebert, Ed.), Suppl. 14, p. 1. Academic Press, New York 1978.
4. Noolandi J., Hong M. H.: Macromolecules *16*, 1443 (1983).
5. Leibler L., Orland H., Wheeler J. C.: J. Chem. Phys. *79*, 3550 (1983).
6. Nagarajan R., Ganesh K.: J. Chem. Phys. *90*, 5843 (1989).
7. Munch M. R., Gasr A. P.: Macromolecules *21*, 1360 (1988).
8. Halperin A.: Macromolecules *20*, 2943 (1987).
9. Riess G., Rogez D.: Polym. Prepr. *23*(2), 19 (1982).
10. Zhou Z., Chu B.: Macromolecules *21*, 2548 (1988).
11. Tuzar Z., Webber S. E., Ramireddy C., Munk P.: Polym. Prepr. *31*(1), 525 (1991).
12. Cao T., Munk P., Ramireddy C., Tuzar Z., Webber S. E.: Macromolecules *24*, 6300 (1991).
13. Kiserow D., Prochazka K., Ramireddy C., Tuzar Z., Munk P., Webber S. E.: Macromolecules *25*, 461 (1992).
14. Prochazka K., Kiserow D., Ramireddy C., Tuzar Z., Munk P., Webber S. E.: Macromolecules *25*, 454 (1992).
15. Xu R., Winnik M. A., Riess G., Chu B., Croucher M. D.: Macromolecules *25*, 644 (1992).
16. Kotaoka K.: J. Macromol. Sci., Pure Appl. Chem. A *31*, 1759 (1994).
17. Battaerd H. A. J., Treager G. W.: *Graft Copolymers.* Wiley-Interscience, New York 1967.
18. Bekturov E. A., Bakauova Z. Kh.: *Synthetic Water-Soluble Polymers in Solution.* Huthig and Wepf, Basel 1986.
19. Strauss U. P., Jackson E. G.: J. Polym. Sci. *5*, 649 (1951).
20. Luhmann B., Finkelmann H., Rehage G.: Angew. Makromol. Chem. *123*, 217 (1984).
21. Shih L. B., Shen E. Y., Chen S. H.: Macromolecules *21*, 1387 (1988).
22. Schulz D. N., Kaladas J. J., Maurer J., Bock J., Pace S. J., Schulz W. W.: Polymer *28*, 2110 (1987).
23. Valint P. L., jr., Bock J.: Macromolecules *21*, 175 (1988).
24. Pietschmann N., Brezesinski G., Tschierske C., Zaschke H., Kuschel F.: Liq. Cryst. *5*, 1697 (1989).
25. Lee J. H., Kopeckova P., Kopecek J., Andrade J. D.: Biomaterials *11*, 455 (1990).
26. Lee J. H., Kopecek J., Andrade J. D.: J. Biomed. Mater. Res. *23*, 351 (1989).
27. *Polymers in Aqueous Media: Performance through Association.* Adv. Chem. Ser. *223* (1989).
28. McCormick C. L., Bock J., Schulz D. N. in: *Encyklopedia of Polymer Science and Engineering*, 2nd ed. (H. F. Mark, N. M. Bikales, C. G. Overberger, G. Menges and J. I. Kroschwitz, Eds), Vol. 17, p. 730. Wiley-Interscience, New York 1989.
29. Anron P., Koberle P., Laschewsky A.: Makromol. Chem. *194*, 1 (1993).
30. Nakagawa T., Inove H.: Kolloid-Z. Z. Polym. *195*, 93 (1964).
31. Dubin P. L., Strauss U. P. in: *Polyelectrolytes and Their Applications* (A. Rembaum and E. Selegny, Eds). D. Reidel, Dordrecht 1975.
32. Barbieri B. W., Strauss U. P.: Macromolecules *18*, 411 (1985).
33. Kammer V., Elias H. G.: Kolloid-Z. Z. Polym. *250*, 344 (1972).
34. Nagai K., Elias H. G.: Makromol. Chem. *188*, 1095 (1987).
35. Chen D. Y., Thomas J. K.: Macromolecules *24*, 2212 (1991).
36. Hamad E., Qutubuddin S.: Macromolecules *23*, 4185 (1990).
37. Hamad E., Qutubuddin S.: J. Chem. Phys. *96*, 6222 (1992).
38. Zdanowicz V. S., Strauss U. P.: Macromolecules *26*, 4770 (1993).
39. Kabanov A. V., Batrakova E. V., Melik-Nubarov N. S., Fedoseev N. A., Dorodnich T. Yu., Alakhov V. Yu., Chekhonin V. P., Nazarova I. R., Kabanov V. A.: J. Controlled Release *22*, 141 (1992).

40. Tuzar Z., Kratochvil P.: Collect. Czech. Chem. Commun. *32*, 3358 (1967).
41. Konak C., Stepanek P., Sedlacek B.: Czech J. Phys., A *34*, 497 (1984).
42. Stepanek P. in: *Dynamic Light Scattering: The Methods and Some Applications* (W. Brown, Ed.), p. 177. Clarendon Press, Oxford 1993.
43. Provencher S. W.: Makromol. Chem. *180*, 201 (1979).
44. Gnanou Y., Lutz P.: Makromol. Chem. *190*, 577 (1989).
45. Zhou Z., Chu B.: Macromolecules *21*, 2548 (1988).
46. Lally P., Price C.: Polymer *15*, 325 (1983).
47. Tuzar Z., Bahadur P., Kratochvil P.: Makromol. Chem. *182*, 1752 (1981).
48. Nyrkova I. A., Khokhlov A. R., Doi M.: Macromolecules *26*, 3601 (1993).
49. Ringsdorf H., Venzmer J., Winik F. M.: Macromolecules *24*, 1678 (1991).
50. Ringsdorf H., Simon J., Winik F. M.: Macromolecules *25*, 5353 (1992).
51. Konak C., Kopeckova P., Kopecek J.: Macromolecules *25*, 5451 (1992).
52. Konak C., Kopeckova P., Kopecek J.: J. Colloid Interface Sci. *168*, 235 (1994).