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Multiple morphologies of aggregates from block copolymers containing glycopolymer segments

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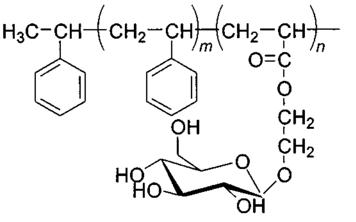
Multiple morphologies of aggregates (micelle-like spheres, vesicles, tubules) from well-defined polystyrene-*b*-poly[(2-β-D-glucopyranosyloxy)ethyl acrylate] (PS-*b*-PGEA) diblock copolymers in diluted aqueous solutions were observed by transmission electron microscopy.

Block copolymers have been investigated vigorously as building units for highly ordered molecular aggregates. It has been shown that when diblock copolymers are dissolved in a solvent which is selective for one of the blocks, colloidal size aggregates or micelles can form as a result of the association of the insoluble blocks.[1–3] Recent reports on rigid-coil diblock copolymers reveal that highly asymmetric diblock copolymers can self-assemble into highly ordered supramolecular architectures with special optical and electrical or encapsulation properties.[4,5] Ordered aggregates from other types of diblock copolymers have also been reported by Armes *et al.*[6] Amphiphilic AB block copolymers are a very important type of block copolymer that show various applications in which the combination of hydrophobic and hydrophilic properties of these materials may be utilized. It has been shown recently by Eisenberg *et al.* that special amphiphilic block copolymers can form stable aggregates of variable morphologies, namely, spheres, rods, vesicles *etc.*, in aqueous solution. Polystyrene (PS) based copolymers, PS-*b*-poly(acrylic acid) (PS-*b*-PAA), PS-*b*-poly(ethylene oxide) (PS-*b*-PEO) and PS-*b*-poly(4-vinylpyridine) (PS-*b*-P4VPy) with various compositions have been extensively investigated.[7] Several factors, including the copolymer composition, the initial copolymer concentration and the nature of the common solvent, have been found to be essential to control the aggregate morphologies. The morphologies are normally studied by observation with a transmission electron microscope (TEM).

In the recent past, increasing attention has been paid to synthetic polymers substituted with pendant saccharide moieties (so called glycopolymers) as biological recognition signals.[8–10] Studies on the synthesis of block copolymers containing glycopolymers as hydrophilic segments and the aggregates formed therefrom in aqueous media are few, especially for block copolymers with controlled molecular weight and narrow molecular weight distribution.[11–13] Recent developments in atom transfer radical polymerization (ATRP) have made it possible to synthesize well-defined block polymers very easily.[14] By using this initiation system, we have successfully synthesized a series of well-defined amphiphilic block copolymers with PS as the hydrophobic block and poly(2-β-D-glucopyranosyloxy)ethyl acrylate) as the hydrophilic one (PS-*b*-PGEA).[15]† The aim of our study is to use these amphiphilic copolymers to construct ordered molecular aggregates and then to use them as models for the study of cell–lectin interactions. Here, we report our preliminary results on the multiple morphologies formed from these amphiphilic block copolymers in aqueous media. The block copolymers used in this study are summarized in Table 1.



PS-*b*-PGEA

To study the aggregation behavior of these new block copolymers in water, a known amount of the completely dried block copolymer sample was dissolved in a common solvent of the two blocks, such as DMF, dioxane *etc.*, to obtain solutions with different concentrations (0.5–5 wt%). While vigorously stirring the solution, water was added at a rate of 0.2–0.3 wt% every 10 s. When *ca.* 6 wt% of water was added, the clear solution became turbid. The addition of water was continued until 25 wt% of water had been added. Then the sample was put into a dialysis bag (molecular weight cut: 10000) and dialyzed against distilled water for 4 days to remove the organic solvents. To observe the morphologies of these aggregates under TEM, one drop of the diluted suspension was put onto a carbon-coated copper grid, and was negatively stained with uranyl acetate. The observation was conducted with a JEOL 100 CXII transmission electron microscope operated at 100 kV.

Multiple morphologies of aggregates from these PS-*b*-PGEA block copolymer are obtained by using different solvents or changing the initial copolymer concentration. When DMF was used as solvent, small spheres were observed for a large range of initial copolymer concentration for these three PS-*b*-PGEA diblock copolymers as listed in Table 1. One of the typical pictures is shown in Fig. 1(*a*). It can be seen that the spheres are of low polydispersity and their average diameters are *ca.* 25 nm. The small spheres belong to the normal 'crew cut' micelles.[7] The largest initial copolymer concentrations of PS_{88}-*b*-$PGEA_4$, PS_{101}-*b*-PGEA7 and PS_{55}-*b*-$PGEA_9$ in DMF that form spheres in water are 2.5, 3.2 and 4.0 wt% respectively. Above these concentrations, large compound micelles coexisted with the crew cut micelles that were normally observed.

Vesicles were obtained for these three PS-*b*-PGEA block copolymers in other solvents. Fig. 1(*b*) shows a typical example of the vesicular structure obtained from PS_{88}-*b*-$PGEA_4$ in dioxane. The vesicular nature is evidenced by a higher transmission in the center of the aggregates than around their periphery in the TEM pictures. When the initial concentration of PS_{88}-*b*-$PGEA_4$ is within the range of 2.0–4.0 wt%, predominant

Table 1 A summary of the molecular weight, polydispersities and copolymer compositions of PS-*b*-PGEA

Copolymers[a]	GEA content/ mol%	M_n[b]/ g mol^{-1}	M_w/M_n[b]
PS_{88}-*b*-$PGEA_4$	4.3	9 700	1.18
PS_{101}-*b*-$PGEA_7$	6.5	13 000	1.28
PS_{55}-*b*-$PGEA_9$	14.1	8 300	1.24

[a] Degree of polymerization of polystyrene block was determined by GPC; PGEA chain length was determined by measuring the ^{1}H NMR spectra of the copolymer precursor in $CDCl_3$. [b] As determined by GPC in DMF (RI detector, calibrated with polystyrene standards).

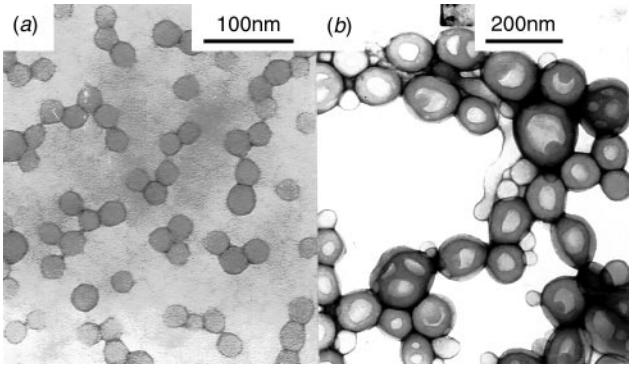


Fig. 1 TEM pictures of (*a*) PS$_{101}$-*b*-PGEA$_7$ aggregates in DMF (the initial copolymer concentration was 2.0 wt%) and (*b*) PS$_{88}$-*b*-PGEA$_4$ aggregates in dioxane (the initial copolymer concentration was 3.0 wt%).

vesicular structures were detected, however, there were also a few small spheres and occasionally short cylinders. Most of the vesicles are single-room and coexist with some two- or multiple-room ones. The sizes of the vesicles are very polydisperse with the outer diameters ranging from 100 to 200 nm. The vesicles formed from PS$_{55}$-*b*-PGEA$_9$ in dioxane (3.5 wt%) were irregular in shape and coexisted with tubular aggregates as shown in Fig. 2(*a*). The overall sizes of vesicle vary very much. The outer diameter ranges from 100 to 300 nm. PS$_{101}$-*b*-PGEA$_7$ did not yield vesicles in dioxane, however, it formed primarily single-room vesicles in dioxane–DMF (1 : 1, v/v, 2.5–4.0 wt%). The outer diameter of the vesicles ranges from 250 to 500 nm. The present results indicated that the sizes of the vesicles were sensitive to the solvent and the initial copolymer concentration, however, the wall thickness of the vesicle was very uniform and independent of the size of vesicles.

More interestingly, PS$_{55}$-*b*-PGEA$_9$ also formed tubular structures in dioxane as shown in Fig. 2(*c*). The wall thickness of the tubules is equal to the wall thickness of the vesicles [Fig. 2(*a*)]. The tubular aggregates have not been found for the other two PS-*b*-PGEA copolymers. When the initial copolymer concentration in dioxane is 2.5–3.0 wt%, vesicles are predominate, and when the concentration is 3.0–4.0 wt%, tubules coexisted with vesicles. The morphologies shown in Fig. 2(*b*) are the intermediate shape of vesicles and tubules, which can usually be obtained from a 3.5 wt% dioxane solution. This suggests the transition of morphologies from vesicles to tubules upon increasing the initial copolymer concentration.

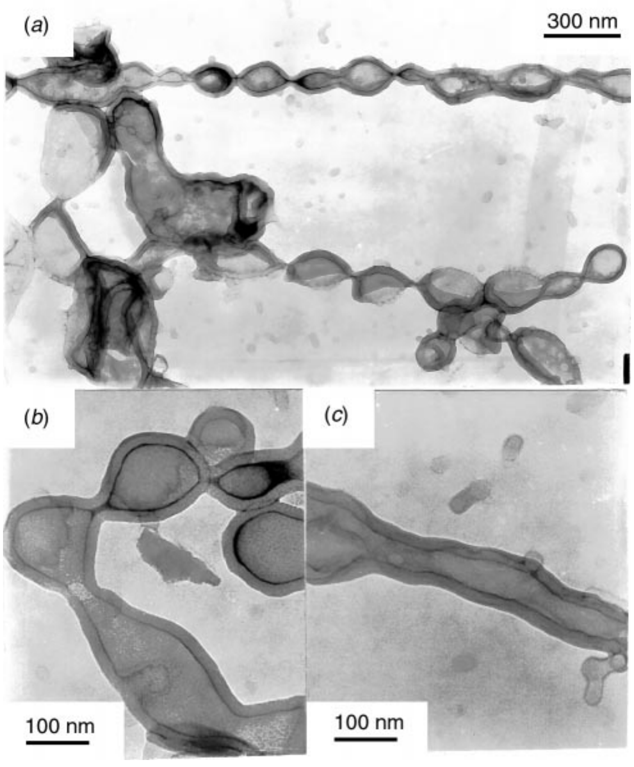


Fig. 2 TEM pictures of PS$_{55}$-*b*-PGEA$_9$ aggregates in dioxane. The initial copolymer concentrations were (*a*) 2.5, (*b*) 3.5 and (*c*) 4.0 wt%.

Besides the above-mentioned morphologies, other aggregates of PS-*b*-PGEA, such as large compound micelles (LCMs) and large compound vesicles (LCVs) were also observed. Their diameters range from 100 nm to 2 μm. It is also worth noting that the spheres and vesicles formed from the present block copolymers tend to connect with each other. This might be caused by hydrogen bond interactions between the PGEA blocks that constitute the outer surface of the aggregates.

In conclusion, PS-*b*-PGEA belongs to a novel class of amphiphilic AB block copolymers, exhibiting interesting aggregation behavior in aqueous medium. Several morphologies of aggregates, such as micelle-like spheres, vesicles and tubules have been observed from PS-*b*-PGEA block copolymers with different compositions. The morphologies are also found to be dependent on the solvent, and the initial copolymer concentration. These aggregates will be used as models to study cell–lectin recognition.

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Notes and references

† PS-*b*-PGEA was synthesized as follows: First, styrene was polymerized with 1-phenylethyl bromide, CuBr and 2,2′-bipyridine in chlorobenzene at 110 °C for 20 h (conversion was about 90%) and the bromo-terminated polystyrene (Br-PS) was isolated by precipitation from MeOH. The dried sample was then used as a macroinitiator for the polymerization of the second monomer. In the second step, the OH protected monomer [2-(2′,3′,4′,6′-tetra-*O*-acetyl-β-D-glucopyranosyloxy)ethyl acrylate (AcGEA)] was polymerized with a pre-determined amount of CuBr, 2,2′-bipyridine and the macroinitiator to obtain the block copolymers, PS-*b*-PAcGEA. The precursor block copolymer was deprotected to the target amphiphilic block copolymer by treatment with a dilute solution of freshly prepared MeONa in a mixed solvent of anhydrous MeOH and CHCl$_3$ at room temperature. The final product was further purified by extraction with cyclohexane and water repeatedly to remove the homopolymers. IR and NMR analysis confirmed the quantitative deprotection without any degradation of the polymer main chain.

1 Z. Tuzar and P. Krattochvil, in *Surface and Colloidal Science*, ed. E. Matijevic, Plenum, New York, 1993, vol. 15, pp. 1–83.
2 V. Moffit, K. Khougaz and A. Eisenberg, *Acc. Chem. Res.*, 1996, **29**, 95.
3 F. L. Baines, S. P. Armes, N. C. Billingham and Z. Tuzar, *Macromolecues*, 1996, **29**, 8151.
4 I. Stupp, V. LeBonheur, K. Walker, S. Li, K. E. Huggins, M. Keser and A. Amstutz, *Science*, 1997, **276**, 384.
5 S. A. Jenekhe and X. L. Chen, *Science*, 1998, **279**, 1903.
6 V. Burun, N. C. Billingham and S. P. Armes, *J. Am. Chem. Soc.*, 1998, **120**, 11 818, 12 135; 1999, **121**, 4288.
7 L. Zhang and A. Eisenberg, *Science*, 1995, **268**, 1728; K. Yu and A. Eisenberg, *Macromolecules*, 1996, **29**, 6359; L. Zhang and A. Eisenberg, *Polym. Adv. Technol.*, 1998, **9**, 677.
8 G. Wulff, J. Schmid and T. Venhoff, *Macromol. Chem. Phys.*, 1996, **197**, 259.
9 K. Kobayashi, A. Tsuchida, T. Usui and T. Akaike, *Macromolecules*, 1997, **30**, 2016.
10 Y. Qiu, T. Zhang, M. Ruegsegger and R. E. Merchang, *Macromolecules*, 1998, **31**, 165.
11 K. Yamada, K. Yamaoka, M. Minoda and T. Miyamoto, *J. Polym. Sci., Polym. Chem. Ed.*, 1997, **35**, 255.
12 K. Ohno, Y. Tsujii and T. Fukuda, *J. Polym. Sci., Polym. Chem. Ed.*, 1998, **36**, 2473.
13 M.-P. Labeau, H. Cramail and A. Deffieux, *Macromol. Chem. Phys.*, 1998, **199**, 335.
14 J.-S. Wang and K. Matyjaszewski, *J. Am. Chem. Soc.*, 1995, **117**, 5614; A. Muhlebach, S. G. Gaynor and K. Matyjaszewski, *Macromolecules*, 1998, **31**, 6046.
15 Y. Z. Liang, Z. C. Li and F. M. Li, manuscript in preparation.

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