Self-Organization in Solutions of Stiff-Chain Amphiphilic Macromolecules

V. V. Vasilevskaya,*,† V. A. Markov,‡,§ G. ten Brinke,§ and A. R. Khokhlov†,‡

A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Vavilova Ul.28, Moscow 119991, Russia, Physics Department, M. V. Lomonosov Moscow State University, Leninskie Gory, Moscow 119992, Russia, and Department of Polymer Chemistry, Zernike Institute for Advanced Materials, University of Groningen, Nijenborgh 4, 9747 AG Groningen, The Netherlands

Received March 3, 2008; Revised Manuscript Received July 28, 2008

ABSTRACT: Conformational properties of amphiphilic stiff-chain macromolecules in concentrated solutions in poor solvent have been studied via computer modeling. We have found that the conformational state of macromolecules in such systems depends on the macromolecular stiffness and on the way the solution has been prepared. Thus, if the concentration of globules increased from a very diluted solution, the globules remain stable, independent of the macromolecular stiffness, and do not aggregate even in concentrated solutions. On the other hand, if the solvent quality is gradually decreased in a solution with a concentration much larger than that of a semidilute solution, then relatively flexible chains form separate globules, whereas semirigid macromolecules tend to aggregate and form braid-like conformations. The results obtained agree with the published experimental data and can be used for directed synthesis of macromolecules modeling the behavior of biopolymers.

1. Introduction

As a rule, water-soluble macromolecules contain both hydrophilic and hydrophobic groups in each monomeric unit and are amphiphilic in this sense. Many synthetic polymers (poly-(1-vinylamidazole), poly-(*N*-isopropylacrylamide), poly-(2-ethylacrylic acid), and so on) are thus amphiphilic at the single monomeric unit level and so are protein molecules and single chains of DNA macromolecules.

Being located in a continuous emulsion phase, monomeric units of amphiphilic macromolecules often tend to arrange themselves at the interfaces and not in the emulsion bulk, so that the corresponding parts of the units are exposed to the phases with preferred interaction type.[1] This approach to describing monomeric units allowed introducing a new two-dimensional classification of synthetic polymers and aminoacids[2,3] and lead to the introduction of a new model for a monomeric unit, which accounts for the dualistic nature of monomeric units of amphiphilic macromolecules.[4] In this model, a monomeric unit *A* is represented as a dumbbell of a hydrophobic *H* and a hydrophilic *P* bead connected by a fixed-length link.

We have used the molecular dynamics technique to study the collapse of macromolecules built of amphiphilic monomeric units *A*, as well as of copolymers containing also hydrophilic *P* and hydrophobic *H* units in a poor (for *H*-beads) solvent.[4−8] We have found that, as a rule, the globule shape of macromolecules consisting of amphiphilic units is not spherical and depends on the value of the interaction parameters, the macromolecular length, as well as on the distribution statistics of the units in the copolymers. Thus, homopolymers of *A* units and regular copolymers of amphiphilic *A* and hydrophobic *H* units form spherical, disk-like, or cylindrical globules, and copolymers with a protein-like distribution statistics of *H* and *A* units form only spherical globules.[5] Some of the segments in cylindrical globules of hydrophilic *P* and amphiphilic *A* units are helically arranged, and elements of secondary structures are also observed.[6]

The formation of globules with an unusual morphology is due to intramolecular phase separation of hydrophilic and hydrophobic parts of the units: hydrophobic groups are located in the interior part of the globule and form its nucleus, whereas hydrophilic ones are arranged on the surface of the nucleus and form the globule's shell. Due to the specific structure of the monomeric units in amphiphilic macromolecules, such globules have, as a rule, a dense hydrophobic nucleus and a dense hydrophilic shell, independent of the globule's shape.

This hydrophilic shell protects the hydrophobic groups in the macromolecule from interacting with such groups of other macromolecules and thus prevents aggregation and precipitation of such macromolecules. A study[5] of semidilute solutions of *HA* copolymers has shown that spherical globules of protein-like copolymers, in fact, do not change shape and do not aggregate even in very poor solvents. Cylindrical globules of regular copolymers also retain their shape in such solutions but they can form filament-like aggregates. Such filaments are formed by several cylindrical globules connected via their ends, where the hydrophilic shell is not dense enough for a complete screening of the intermolecular interaction.

The conformational properties of macromolecules[7−20] and properties of their concentrated solutions[21,22] depend essentially on the polymeric chain stiffness. The collapse of stiff macromolecules is accompanied not only by a great reduction of the entropy of the monomeric units, but also by essential energy losses due to the bends in the polymeric chain. To decrease these losses, homopolymer stiff-chain macromolecules form not spherical globules but globules of complex toroidal or rod-like form.[8−17] The amphiphilic stiff-chain macromolecules while collapsing are obliged form structures which have both minimal bend energy and "core-shell" organization. Our calculations show that depending on stiffness parameters amphiphilic macromolecules form cylindrical globules with a blob-like chain organization, collagen-like, and toroidal structures.[18−20] Hydrophobic groups in such structures occupy the inner parts, and hydrophilic ones are arranged at the surface. The total bending stress of the chain in this case is rather high because of the high stiffness of the macromolecule. Therefore, stiff-chain

* To whom correspondence should be addressed. E-mail: vvvas@ineos.ac.ru.
† Russian Academy of Sciences.
‡ M. V. Lomonosov Moscow State University.
§ University of Groningen.

10.1021/ma800465j CCC: $40.75
Published on Web 09/24/2008

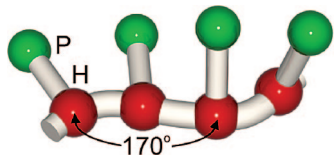

Figure 1. Schematic representation of the model of a stiff amphiphilic homopolymer.

macromolecules can be expected, in spite of the hydrophilic shell, to prefer forming aggregates of several chains in order to reduce this stress, which is especially high in collagen-like and toroidal structures.

The aim of the present paper is to study self-organization processes of amphiphilic macromolecules with various stiffness and in solvents of different qualities.

2. Macromolecular Model and Experimental Technique

A schematic representation of the model of the macromolecule used is shown in Figure 1. Each amphiphilic monomeric unit is a dumb-bell of a *H* and a *P* bead connected by a rigid bond of fixed length. The dumb-bells are connected into a amphiphilic polymeric chain of length *N* with a backbone of hydrophobic *H* beads and pendant hydrophilic beads *P*. The backbone of *H* beads is semiflexible, with a preferred angle θ_0 between the neighboring bond vectors in the chain.

The temporal evolution of the system was found by solving a system of Newton equations via the molecular dynamics technique.[23] Unity bond length $b = 1.0$ in the macromolecule was chosen and ensured with the RATTLE algorithm.[24]

The excluded volume interaction between the nonconnected beads was given by the repulsion potential of the Lennard−Jones type

$$u_{ev} = \begin{cases} 4\varepsilon\left[\left(\frac{\sigma}{tij}\right)^{12} - \left(\frac{\sigma}{tij}\right)^{6} + \frac{1}{4}\right], & r_{ij} \le r_0 \\ 0, & r_{ij} > r_0 \end{cases} \quad (1)$$

where r_{ij} is the distance between the interacting centers *i* and *j*, and $r_0 = 2^{1/6}$ is the cutoff radius of the potential. Parameter ε in eq 1 determines the interaction strength and controls the energy scale, whereas parameter σ characterizes the spatial scale. We have set $\sigma = \epsilon = 1$ for all the pairwise interactions, and all the results discussed below are, therefore, reported in terms of these natural units.

The solvent molecules were not considered explicitly in the calculations, but represented as a continuous medium. Terms describing friction and terms R_i for Langevin's uncorrelated noise were introduced into the equations of motion to account for the solvent being in contact with an external reservoir with temperature *T*. The solvent-induced intrachain hydrophobic−hydrophilic interactions were described with a Yukawa-type potential

$$u_s(r_{ij}) = \frac{\varepsilon_{ab}\sigma}{r_{ij}} f(r_{ip}r_c)h(r_c r_{ij}) \quad (2)$$

where $f(r_{ij},r_c) = \left[1 - \left(r_{ij}/r_c\right)^2\right]^2$ is the screening function; $r_c = 4\sigma$ is the screening radius of such interactions; $h(r)$ is the Heavyside function; and parameters ε_{ab} (= ε_{HH}, ε_{PP}, ε_{HP}) describe the amplitudes of the interactions between the corresponding bead types.

Potential (2) describes the solvent-mediated short-range hydrophobic-hydrophilic interactions. In the case of $\varepsilon_{\alpha\beta} = 0$, there are no additional interactions (either attraction or repulsion) between the units except the excluded volume interactions given by the potential (1). We have set the following values for the parameters in the computer experiments performed: $\varepsilon_{PP} = 0$, $\varepsilon_{HP} = 3$, and $\varepsilon_{HH} < 0$. The nonzero (positive) value of ε_{HP} stands for the repulsion between the *H* and *P* groups; the negative parameter ε_{HH} describes the attraction between the hydrophobic groups. We have performed calculations for two values of ε_{HH} chosen so that a single macromolecule is either in the coil state ($\varepsilon_{HH} = -2.0$) or in the globular state ($\varepsilon_{HH} = -5.0$).[18]

The stiffness of the polymeric chains was introduced by an additional interaction potential between the neighboring units along the chain

$$U(\vartheta) = \varepsilon_{st}(\theta - \theta_0)^2 \quad (3)$$

where ε_{st} is the stiffness parameter; θ is the angle between the neighboring bond vectors in the chain; θ_0 is the preferred angle, which was set to 170° in this study.

The stiffness of the chain is characterized by the Kuhn segment length L_b, which was determined by calculating the radius of gyration for equivalent chains without the excluded volume interactions for various values of the stiffness parameter ε_{st} (the calculation procedure is described in detail in paper [4]). The calculations were performed for flexible ($L_k = 2.9$), semiflexible ($L_k = 19.6$), and semirigid ($L_k = 29.2$) macromolecules (corresponding to stiffness parameter values $\varepsilon_{st} = 0$; 6; 10 ε/rad^2).

To study the properties of stiff-chain amphiphilic molecules, *n* polymeric chains were placed into an $m \times m \times m$ cell employing periodic boundary conditions.

The sequence for preparing the initial system configuration of several macromolecules was as follows. One chain in a coil state ($\varepsilon_{HH} = 0$) was initially placed into a relatively large cell (cell size $m = 1000$) and equilibrated, then the energy ε_{HH} was slowly (with steps $\Delta\varepsilon_\varepsilon = 5 \times 10^{-6}$) reduced to $\varepsilon_{HH} = -5.0$, so that the macromolecule went through the coil−globule transition. Globules equilibrated at $\varepsilon_{HH} = -5.0$ were then cloned and *n* such globules were uniformly distributed within a cell of smaller size *m*, and then the study of the system evolution began. Two different techniques were used in this study. In the first procedure the stable state of the system was determined at the energy value $\varepsilon_{HH} = -5.0$, at which the initial state of the concentrated system of several macromolecules was actually formed. For this purpose long enough simulations were performed for this value of ε_{HH}. In the second approach, the effective solvent quality (ε_{HH}) was first increased to −2.0, so that the globule−coil transition occurred, and then the system was returned to the state with $\varepsilon_{HH} = -5.0$ and the properties of the resulting solution were studied.

The number of chains, *n*, the degree of polymerization, *N*, of the macromolecules and the cell size, *m*, were the same in all the experiments ($n = 9$, $N = 96$, $m = 26$). The concentration of units in the cell, $C = 2Nn/m^3$, was 0.1. The cell size m_{semi}, for which the globules overlap, can be estimated as $m_{semi} = (4\pi/3R^3_{g,0.5}n)^{1/3}$, where $R_{g,0.5}$ is the radius of gyration of a single macromolecule at $\varepsilon_{HH} = -5.0$. The radius of gyration $R_{g,0.5}$, and therefore, the cell size, m_{semi}, depends on the macromolecular stiffness. It was shown experimentally that the mean square radius of gyration $R^2_{g,0.5} = 14.2$ at $L_k = 2.9$, $R^2_{g,0.5} = 18.4$ at $L_k = 19.6$, and $R^2_{g,0.5} = 20.1$ at $L_k = 29.2$. Therefore, the cell size m_{semi} that will cause $n = 9$ globules to overlap is $m_{semi} = 13$; 14 and 15 for chains with $L_k = 2.9$; 19.6, and 29.2, respectively. Thus, the calculations were performed in a cell large enough to allow all the macromolecules in the globular state to "float" freely in the solution, in spite of the rather high concentration of monomeric units significantly exceeding the overlap concentration for chains in the coil state.

The pair correlation function $g(r)$, the statistical structure factor $S(q)$, and the average aggregation number $<M>$ have been calculated for hydrophobic units. They were determined for each L_k value and two different ε_{HH} values ($\varepsilon_{HH} = -2.0$ and -5.0). A visual analysis has also been performed.

The pair correlation function $g(r)$ was determined via the standard expression

$$g(r) = \frac{V}{4\pi r^2 (Nn)^2}\left\langle \sum_i^N \sum_{j \ne i}^N \delta(r - r_{ij}) \right\rangle$$

where *Nn* is the number of hydrophobic units in the system, r_{ij} is the coordinate of the chosen particle, and *V* is the system's volume.

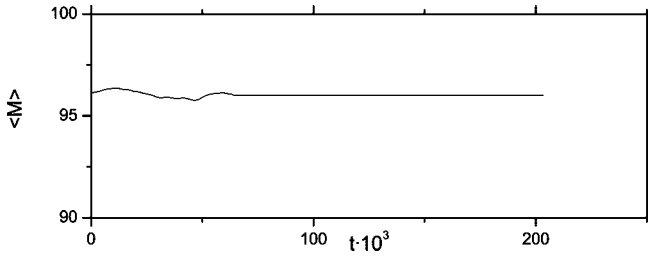

Figure 2. Time t dependence of the average aggregation number $<M>$; $\varepsilon_{HH} = -5$, $L_k = 19.2$.

The statistical structure factor $S(q)$ was calculated as follows

$$S(q) = \frac{1}{Nn}\sum_{\alpha=1}^{N}\sum_{\beta=1}^{N}\langle \exp(i\vec{q}\vec{r}_{\alpha\beta})\rangle$$

where q is the wave vector and Nn is the number of the hydrophobic units in the system. The normalization for S is $S(0) = k_B T \rho \chi_T$, where $\rho = Nn/V$ is density and X_T is the compressibility. Peaks in $S(q)$ indicate an inhomogeneous monomer units distribution. The characteristic scale r^* of this inhomogeneity is related to the wave vector value q^* of the peak by the familiar relation $r^* = 2\pi/q^*$.

The aggregation number M was determined as the number of hydrophobic units in a single cluster. The cluster was determined as the group of monomers for which the smallest pairwise distance is less than the critical value: $r_{ij} < 1.4$. To evaluate the average aggregation number $<M>$, the M values have been averaged over all the clusters.

The transitions from energy $\varepsilon_{HH} = -5$ to $\varepsilon_{HH} = -2$ and backward from $\varepsilon_{HH} = -5$ to $\varepsilon_{HH} = -2$ were carried out by annealing procedure with 10^3 time steps. Regardless of macromolecules stiffness, all types of initial systems, that is, systems obtained by cloning of macromolecules and solution arising after both annealing procedures, were equilibrated during 2×10^6 time steps, and then the production runs were performed. Equilibration was checked via the observation that the same results can be obtained by starting from different initial configurations and by running the simulations for more time steps. Each production run was equal to 3×10^6 time steps independent of the chain stiffness and effective solvent quality ε_{HH}. For each set of parameters the calculations were performed for three independent instances.

3. Results and Analysis

Figure 2 shows the dependence of the aggregation number $<M>$ on time t for a solution of semistiff macromolecules (polymerization degree $N = 96$, Kuhn segment length $L_k = 19.6$), calculated using the first procedure, that is, via studying the equilibrated solution of cloned globules at constant energy $\varepsilon_{HH} = -5.0$. The average aggregation number $<M>$ normalized to the total number of hydrophobic units in the chain is practically unity: $<M>/N = 1$. This value is keeping as constant over the whole time of the experiment (e.g., 3×10^6 time steps) in the course of which the macromolecules colloid with each other many times. Figure 3 presents the dependence of mean-square displacement of center of mass of macromolecules $<\Delta R^2>$ on time t, and the dashed line shows the square of average distance between the macromolecules. One can see that the mean-square displacement distance $<\Delta R^2>$ becomes equal to the average distance between the macromolecule shells after approximately 2×10^5 times step, and thus, one can conclude that the simulation was run long enough to ensure many globule−globule collisions.

The fact that the aggregation number $<M>/N$ is equal to unity means that separate globules do not aggregate in such solutions. It is clear that the structure of the globules is responsible for their stability (nonaggregation): hydrophobic groups are located in the inner part of the globule and are thus protected from

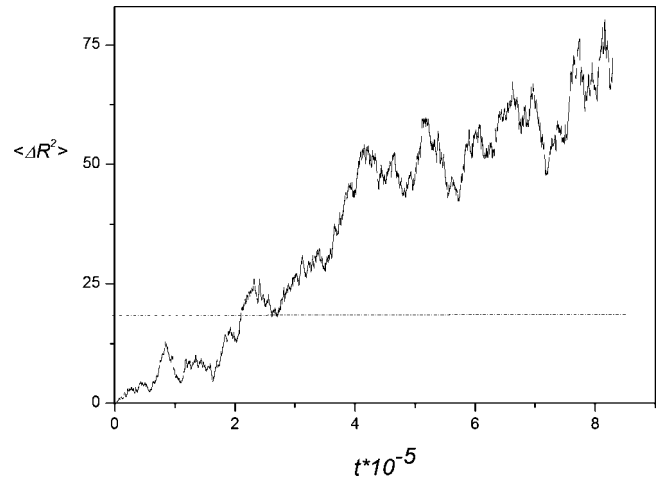

Figure 3. Time t dependence of the mean-square displacement $<\Delta R^2>$ of macromolecule center of mass; $\varepsilon_{HH} = -5$, $L_k = 19.2$. Dashed line shows the average distance between globule surfaces.

interacting with hydrophobic groups of other chain by a shell of hydrophilic groups. Similar results have also been obtained for relatively flexible ($L_k = 2.9$) and stiff ($L_k = 29.2$) macromolecules. Thus, in contrast to the cylindrical globules of hydrophobic−amphiphilic *HA* copolymers studied in paper,[5] globules (also cylindrical in shape) of homopolymeric macromolecules, both stiff-chain and flexible-chain ones, do not form band-like clusters of several macromolecules.

Snapshots of these solutions are shown in Figures 4a,b. Separate globules can be discerned in all these snapshots. Note the visible difference in the globule shape of macromolecules with different stiffness. Thus, in case of stiffer macromolecules ($L_k = 19.6$ and 29.2), the chain in the globule forms strands of intertwined chain segments. No such strands can be seen in globules of more flexible macromolecules ($L_k = 2.9$); the globule has a cylindrical shape with blob-like chain arrangement within this cylinder.

The structure of the globules of stiff-chain amphiphilic macromolecules is discussed in more detail in our previous papers on this topic.[15−17] Note that the procedure for preparing the solution of globules via placing macromolecules previously compacted in an excess of solvent into smaller cells corresponds to the experimental technique of preparing a concentrated solution of globules via evaporating a part of the solvent from a dilute solution.

Then, in accordance with the main aim of this paper stated above, we enhanced the solvent quality, increasing the interaction parameter of hydrophobic units from $\varepsilon_{HH} = -5$ up to $\varepsilon_{HH} = -2$. As a result, the macromolecules went through a globule−coil transition, and then the simulation was carried on at $\varepsilon_{HH} = -2$ for a long time until full equilibration and further measurements.

Figure 5 shows $S(q)$ obtained according to the procedure described above for macromolecules with different chain stiffness. The statistical structure factor S decreases monotonously for solutions of rigid chains ($L_k = 29.2$), which indicates, in the case of finite systems (or systems with periodic boundary conditions), the formation of a homogeneous solutions.[22] The q-dependence of $S(q)$ for the more flexible chain ($L_k = 19.6$) has two small peaks at $q/2\pi = 0.16$ and $q/2\pi = 0.18$. A peak at somewhat larger wave vector value $q/2\pi = 0.19$ occurs for the low-stiffness chains ($L_k = 2.9$); this means that regions with higher concentration of hydrophobic groups can be formed in such solutions (at distances $r \sim 5\sigma/6\sigma$). This local microstructuring phenomenon is apparently due to the combination of two factors: first, the attraction between the hydrophobic groups and

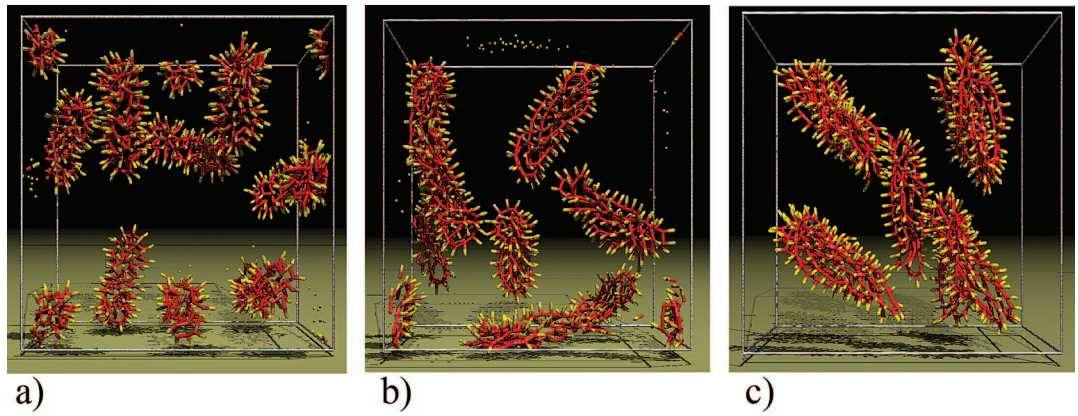

Figure 4. Snapshots of the system at $\varepsilon_{HH} = -5$ and $L_k = 2.9$ (a), $L_k = 19.2$ (b), $L_k = 29.2$ (c).

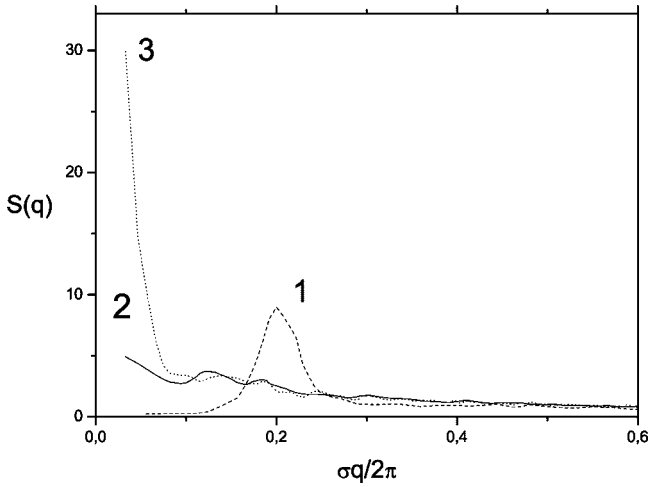

Figure 5. Dependences of the statistical structural factor S on wave vector q at $\varepsilon_{HH} = -2$ and $L_k = 2.9$ (curve 1), 19.6 (curve 2), and 29.2 (curve 3).

second, the tendency of hydrophilic groups to avoid contact with each other and with other hydrophobic groups. This microstructuring phenomenon is not observed in the case of stiff macromolecules, because the higher the chain stiffness, the greater the conformational losses connected with a redistribution of hydrophobic units. The energy advantage due to microstructuring is apparently higher than the loss in conformational free energy for the system parameters described above. No definite conclusion concerning the presence or absence of microstructuring in the system can be made from the solution snapshots at $\varepsilon_{HH} = -2$ shown in Figure 6. The visual impression is that the macromolecules fill the total volume of the cell; the chains are intertwined and the solution appears to be homogeneous.

Figure 7 shows the statistical structure factor $S(q)$ for the solution at $\varepsilon_{HH} = -5$, obtained via a slow reverse change of the interaction parameter value from $\varepsilon_{HH} = -2$ down to $\varepsilon_{HH} = -5$.

Two peaks (at $q/2\pi \sim 0.11$ and 0.13) can be seen (Figure 6, curve 1) for relatively flexible chains ($L_k = 2.9$). This means that separate objects are present in the system with a distance of $r \sim 7\sigma$ and 10σ between them, respectively. These data are confirmed by the study of the correlation function of the centers of mass of the macromolecules, $g_{cc}(r)$, shown in Figure 8. The maxima in $g_{cc}(r)$ clearly occur at exactly the distances $r = 7\sigma$ and 10σ. This means that the ordering in such system exists in terms of the relative position of separate macromolecules. Bimodality of $g_{cc}(r)$, that is, the presence of two characteristic distances between the globules' centers of mass, indicates that ordering of the relative positions of the globules exists in more than one direction. No orientation ordering in the relative positioning of cylindrical globules has been found.

The existence of separate nonaggregating globules in this case has also been confirmed by the study of the hydrophobic group cluster distribution over the aggregation number M (Figure 9). The maximum value of M can be seen to be always below the degree of polymerization $N = 96$. This means that separate globules completely isolated from each other are in fact formed upon solvent quality decrease in concentrated solutions of amphiphilic macromolecules with relatively low Kuhn segment lengths.

Let us now discuss Figure 7 once again. Two peaks can be seen in $S(q)$ for macromolecules with higher stiffness as well ($L_k = 19.6$ and 29.2, Figure 7, curves 2 and 3, respectively). The positions of the maxima are at $q/2\pi \sim 1.3-1.4$ for intermediate L_k and $q/2\pi \sim 0.05$ for large L_k. This means that ordering in such systems is observed at two scales: first, at distance $r \sim 7\sigma$, second, at $r \sim 20\sigma$, which is close to the size of the cell studied.

Visual analysis (Figure 10) has helped us understand the type of microscopic ordering occurring in the system. We see that a system of separate, nonaggregating cylindrical globules has been formed in the solution of macromolecules with relatively low stiffness ($L_k = 2.9$). Thus in this case the process of increasing the interaction parameter ε_{HH} and subsequent returning to the initial state leads to a complete recovery of the state of the system.

No such recovery was observed in case of more rigid chains (Figures 10c−f). The macromolecules form braids of several intertwined chains upon reduction of the solvent quality (increase of the attraction energy between the hydrophobic groups), and not separate globules of intertwined segments, as observed in the initial conformation. It was found that losses in chain conformation energy is lower for such structures than for globules because of the absence of sharp bends in the macromolecules observed in the latter case. In fact, the total energy E per chain with Kuhn segment $L_k = 29.2$ in the case of a solution of separate globules is $E = 54.7\varepsilon$, while in the case of braid-like conformations it is more than twice as low, that is, $E = 21.1\varepsilon$. Braids formed by several chains have a high bending stiffness, and they bend at the cell size scale. This is apparently the reason for the large-scale correlations in such systems.

Figure 11 shows the ε_{HH} dependence of the average aggregation number $<M>$ for a stiff chain with $L_k = 29.2$, acquired in the process of slow increase of the ε_{HH} parameter. The aggregation number $<M>$ grows monotonously and rather quickly ($<M> \sim (-\varepsilon_{HH})^{3.9}$) and reaches $<M> \sim 288$ at $\varepsilon_{HH} = 5.0$. This seems to indicate the formation of three braids with three chains each. However, visual analysis has shown that the

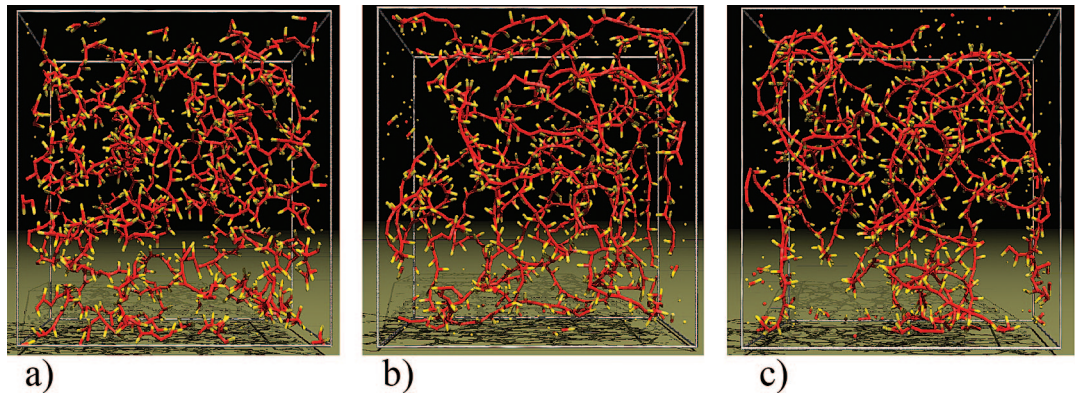

Figure 6. Snapshots of the cell at $\varepsilon_{HH} = -2$ and $L_k = 2.9$ (a), $L_k = 19.2$ (b), and $L_k = 29.2$ (c).

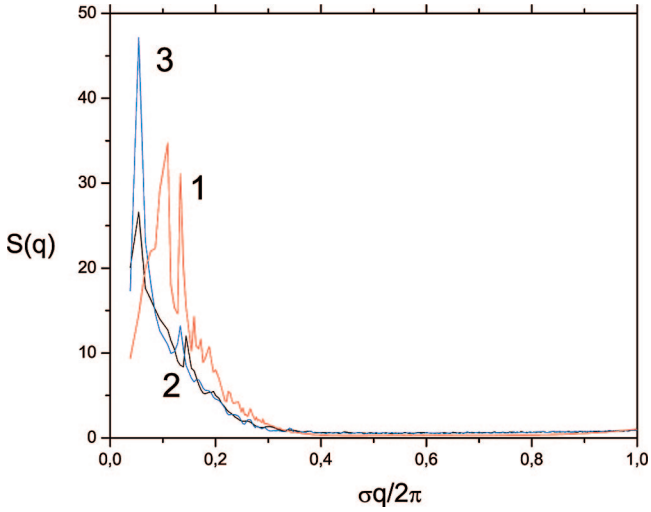

Figure 7. Dependences of the statistical structure factor S on wave vector q at $\varepsilon_{HH} = -5$, $L_k = 2.9$ (curve 1), $L_k = 19.6$ (curve 2), and $L_k = 29.2$ (curve 3).

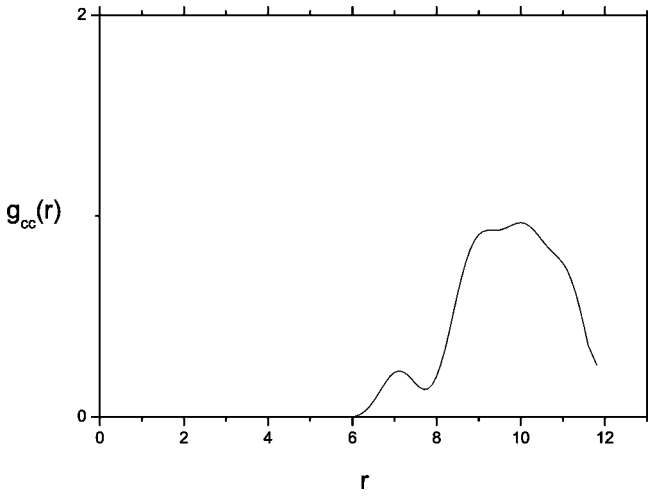

Figure 8. Dependence of the pair correlation function g of centers of mass of macromolecules on distance r at $L_k = 2.9$ and $\varepsilon_{HH} = -5$.

chains can also form braids with different number of chains, from two to four. Separate parts of the braids can be connected via a bridge consisting of a single chain. Because such bridges are strongly stretched, the distance r_{ij} between their hydrophobic units is larger than 1.4 and, therefore, according to the definition of a cluster introduced above, such units do not form a cluster.

However, it is clear that the macromolecule forming bridge between different braids is part of the supramolecular aggregates.

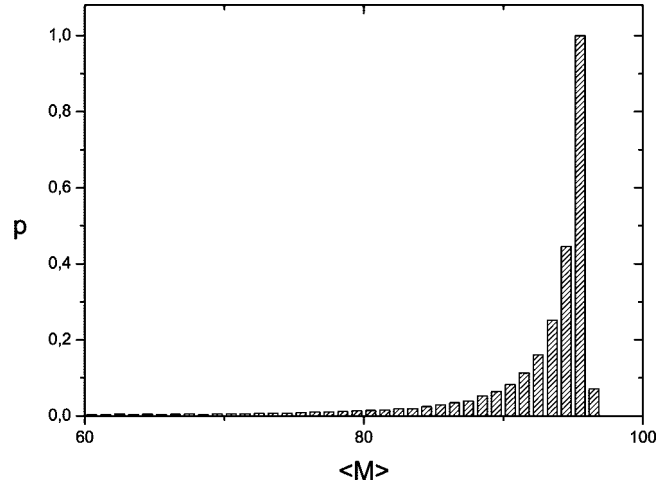

Figure 9. Histogram of the average aggregation number $<M>$; $\varepsilon_{HH} = -5$, $L_k = 2.9$.

One can propose that two chains are part of supramolecular aggregate if there exists a contact between any pair of hydrophobic units H in which one member belongs to one chain and the other member to the other. To address the number of macromolecules entering to the supramolecular aggregates we calculate the aggregation number $<M_{ch}>$ proposing that the macromolecules enter to one aggregates if the distance between any two hydrophobic units belonging to different macromolecules is less that 1.4σ. Our calculation shows that in poor solvent (at $\varepsilon_{HH} = -5.0$) for stiff macromolecules with $L_k = 29.2$ the supramolecular aggregation number $<M_{ch}> = 9$, that is, all macromolecules form the only aggregate. In case of flexible macromolecules with $L_k = 2.9$ in correspondence with above conclusion the aggregation number $<M_{ch}> = 0$ and separate globules do not aggregate.

4. Discussion and Conclusions

Concentrated solutions of amphiphilic stiff-chain homopolymers have been considered in this paper.

Solutions of macromolecules in a poor solvent prepared via two different techniques were studied. The first preparation technique consisted in cloning globules previously compacted in an excess of solvent into cells of smaller size. The second one involved decreasing the solvent quality in a concentrated solution of amphiphilic macromolecules.

Amphiphilic macromolecules in a dilute solution form rod-like globules upon compaction, and the details of the globular structure depend on chain stiffness. Macromolecules with low stiffness form rod-like globules with blob-like chain arrangement, whereas stiffer ones form collagen-like structure of chain

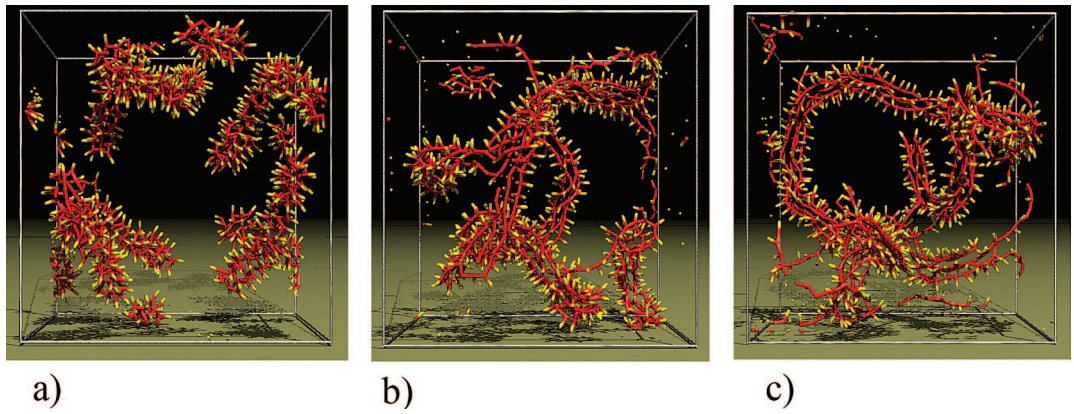

Figure 10. Snapshots of the system at $\varepsilon_{HH} = -5$ and $L_k = 2.9$ (a), $L_k = 19.2$ (b), and $L_k = 29.2$ (c).

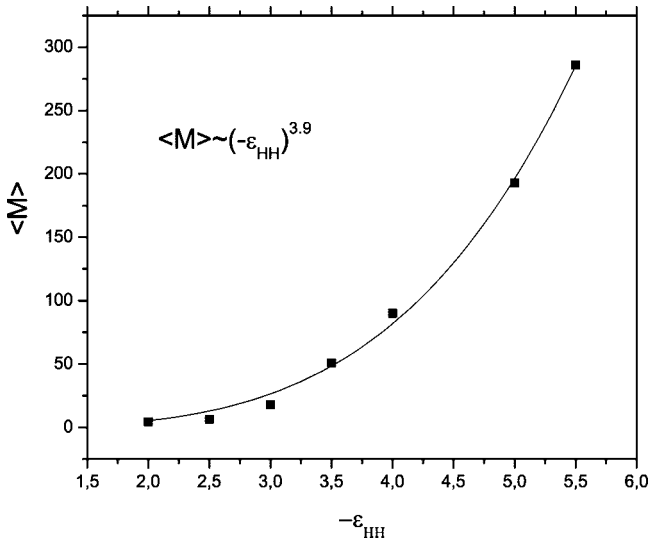

Figure 11. Dependence of the average aggregation number $<M>$ on ε_{HH} at $L_k = 29.2$.

strand folded upon themselves and intertwined. Macromolecules with intermediate stiffness also form globules with blob-like substructure, but there is collagen-like ordering within each blob. Such globules are characterized by a dense shell of hydrophilic groups, which prevents aggregation of the globules. Therefore, globules in solutions formed via concentrating dilute solutions are very stable.

Relatively flexible macromolecules form a solution of separate nonaggregating globules in case of solvent quality decrease in concentrated solutions, as well. The globule structure in this case is almost the same as that of globules formed in dilute solutions, and there is an ordering in the relative position of such globules.

Stiffer amphiphilic macromolecules in similar cases (solvent quality decrease in concentrated solutions) form braids of several intertwined macromolecules; the braids are bent on the scale of the cell size. The number of chains forming the braid depends on chain stiffness and can vary along the braid.

Self-organization of several chains is often met in live organisms. These are, for example, DNA double helix, fibrillar proteins (α-keratine, tropomyosin, etc.) formed by long intertwined spirals, collagen with molecules formed by three intertwined strands, and polysaccharides, such as, for example, κ-carrageenans.[26−28]

Phenylene-based macromolecules are among the synthetic analogues of the natural polymers mentioned above.[29,30]

A series of reports was published on the experimental observation of self-organization effects in the studies of solutions of modified poly(*p*-phenylene)s such as sulfonated poly(*p*-phenylene),[30−32] dodecyl-substituted poly(*p*-phenylene) sulfonate,[33,34] cationic poly(*p*-phenylene) with tetraethylammonium perfluoro-1-octanesulfonate,[35] poly(sodium-*p*-phenylene-sulfonate).[36] The backbone in such macromolecules built of phenylene rings has a rather high stiffness. Either hydrophobic aliphatic groups or sulfonated groups are attached to each ring; the latter acquire charge in water solutions and ensure overall solubility of the macromolecules. Due to such a complex structure, these stiff-chain molecules self-organize themselves in solutions and form cylindrical micelles containing several macromolecules. The hydrophobic units are located in the inner part of such micelles, and charged groups form the outer shell which ensures solubility and stability of cylindrical micelles over a wide concentration range. The aggregation number across the cylindrical micelles can change from two to several tens of macromolecules and vary along the cylinder axis, and the length of such micelles can amount to several lengths of single macromolecules. These values depend on the ionic strength of solution, the nature of the side chains, and the nature and charge of the counterion. Such micelles can form lyotropic liquid-crystal phases under certain conditions.[32,36]

The properties of a more flexible *meta*-poly(phenylene ethynylene) (m-PPE) with and without grafted alkyl side groups have been studied in papers.[37,38] It was shown that m-PPE without such groups in a poor (for phenylene backbone) solvent (90% H_2O/DMSO) form single globules that remain dissolved even in rather concentrated solutions (5000 μg/mL) over several months. Solubility of these globules is due to the NH_3^+ groups grafted to the phenylene units. Globules of m-PPE with additional alkyl side chains in this solvent at 100 times less the concentration (50 μg/mL) aggregate and eventually (after two days) precipitate as the aggregate size increases. It is believed that these macromolecules aggregate through an extended amphiphilic structures organized into layers.[38]

The phenylene-based macromolecules are among most stiff synthetic macromolecules. For polymers with poly(phenylene) backbone and sulfonate ester and dodecyl side chains a persistence length of about 130 Å was determined in ref 39. On the other hand, according to viscometry and translational diffusion dates, the Kuhn segment length of phenylated poly(phenylene) in dioxane solutions is 98 Å.[40] The stiffness of polymers described above varies with regard to charge density and hydrophobicity. Using the Bicerano method,[41] we have found that the Kuhn segment length is equal approximately to 115 Å for sulfonated poly(*p*-phenylene)s, 96 Å for *meta*-poly(phenylene ethynylene) with grafted alkyl group, and 88 Å for *meta*-poly(phenylene ethynylene) without such groups. Generally, the Kuhn segment length of poly(phenylene)s exceeds significantly the value for typical flexible chain polymers (∼20 Å), which

clearly demonstrates the semiflexible character of phenylene-based macromolecules.

Thus, an analogy can be traced between the amphiphilic macromolecules studied in this paper and phenylene-based ones (i.e., *meta*-poly(phenylene ethynylene) without alkyl side chains and modified poly(*p*-phenylene)). The macromolecular backbone is rather stiff and hydrophobic in both cases, and side groups are hydrophilic, that is, they prefer to be exposed to the solvent and tend to avoid contact with each other and with hydrophobic groups. No wonder, therefore, that results obtained in our study qualitatively agree with the experimental ones. These include formation of soluble globules by amphiphilic macromolecules with sufficient fraction of hydrophilic side chains in a poor (for backbone) solvent (e.g., *meta*-poly(phenylene ethynylene) without alkyl groups and less stiff macromolecules), high stability of these globules even in highly concentrated solutions, formation of cylindrical micelles by stiffer amphiphilic chains (i.e., modified poly(*p*-phenylene)s and more stiff macromolecules), so that micelle length exceeds that of a single macromolecule.

The Kuhn segment lengths of m-PPE with and without alkyl side chains are rather closed, so apparently the difference in conformational behavior of these macromolecules is caused by properties of their side-chains. Thus, one can conclude that the structure arising in solution of semiflexible amphiphilic macromolecules depends not only on stiffness of macromolecule backbone but on the affinity of their side-chains with solvent.

Computer experiments with macromolecules modeling poly(phenylene) have been performed in paper.[42] The model molecules had stiff hydrophobic backbone with grafted flexible hydrophobic side-chains containing charged groups. Stability conditions and maximum aggregation numbers for the specially prepared cylindrical micelles have been determined via calculating the stability period for these micelles.

In contrast to paper,[39] we succeeded in obtaining cylindrical aggregates via self-organization of stiff-chain amphiphilic macromolecules from a concentrated solution.

Note, however, that the systems we studied contained only a relatively small number of molecules in each cell. In order to determine the equilibrium number of macromolecules in a braid, calculations for a greater number of chains per cell and chains of smaller length should apparently be performed, and the results should be scaled accordingly. Such calculations will be reported in our future publications.

Acknowledgment. Authors gratefully acknowledge the financial support by the Russian Foundation for Basic Research and The Netherlands foundation for scientific research (Project 047.011.2005.011 and Project 08-03-00281-a). Very useful discussions with Dr. A. V. Berezkin and Dr. Z. B. Shifrina are appreciated.

References and Notes

(1) Goldar, A.; Sikorav, J.-L. *Eur. Phys. J. E.* **2004**, *14*, 3–211.
(2) Okhapkin, I. M.; Makhaeva, E. E.; Khokhlov, A. R. *Colloid Polym. Sci.* **2005**, *284*, 117.
(3) Okhapkin, I. M.; Askadskii, A. A.; Markov, V. A.; Makhaeva, E. E.; Khokhlov, A. R. *Colloid Polym. Sci.* **2006**, *284*, 575.
(4) Vasilevskaya, V. V.; Khalatur, P. G.; Khokhlov, A. R. *Macromolecules* **2003**, *36*, 10103.
(5) Vasilevskaya, V. V.; Klochkov, A. A.; Lazutin, A. A.; Khalatur, P. G.; Khokhlov, A. R. *Macromolecules* **2004**, *37*, 5444.
(6) Ermilov, V. A.; Vasilevskaya, V. V.; Khokhlov, A. R. *Polym. Sci.* **2007**, *49Å*, 89.
(7) Lifshitz, I. M.; Grosberg, A. Y.; Khokhlov, A. R. *Rev. Mod. Phys.* **1978**, *50*, 683.
(8) Grosberg, A. YU. *Biophysics* **1979**, *24*, 32.
(9) Kroy, K.; Frey, E. *Phys. Rev. Lett.* **1996**, *77*, 306.
(10) Vasilevskaya, V. V.; Khokhlov, A. R.; Kidoaki, S.; Yoshikawa, K. *Biopolymers* **1997**, *41*, 51.
(11) Ivanov, V. A.; Paul, W.; Binder, K. *J. Chem. Phys.* **1998**, *109*, 5659.
(12) Ivanov, V. A.; Stukan, M. R.; Vasilevskaya, V. V.; Paul, W.; Binder, K. *Macromol. Theory Simul.* **2000**, *9*, 488.
(13) Stukan, M. R.; Ivanov, V. A.; Grosberg, A. Y.; Paul, W.; Binder, K. *J. Chem. Phys.* **2003**, *118*, 3392.
(14) Noguchi, H.; Yoshikawa, K. *Chem. Phys. Lett.* **1997**, *278*, 184.
(15) Noguchi, H.; Yoshikawa, K. *J. Chem. Phys.* **1998**, *109*, 5070.
(16) Kuznetsov, Y. A.; Timoshenko, E. G.; Dawson, K. A. *J. Chem. Phys.* **1996**, *105*, 7116.
(17) Li, Y.; Huang, Q.; Shi, T.; An, L. *J. Phys. Chem.* **2006**, *110*, 23502.
(18) Vasilevskaya, V. V.; Markov, V. A.; Khalatur, P. G.; Khokhlov, A. R. *J. Chem. Phys.* **2006**, *124*, 144914.
(19) Markov, V. A.; Vasilevskaya, V. V.; Khalatur, P. G.; ten Brinke, G.; Khokhlov, A. R. *Macromol. Symp.* **2007**, *252*, 24.
(20) Markov, V. A.; Vasilevskaya, V. V.; Khalatur, P. G.; ten Brinke, G.; Khokhlov, A. R. *Polym. Sci.* **2008**, *50A*, 621.
(21) Harnau, L.; Winkler, R.; Reiniker, P. *J. Chem. Phys.* **1997**, *106*, 2469.
(22) Winkler, R. *J. Chem. Phys.* **2003**, *118*, 2919.
(23) Allen, M. P.; Tildesley, D. J. *Computer Simulation of Liquids*; Claredon Press: Oxford, 1990.
(24) Andersen, H. C. *J. Comput. Phys.* **1983**, *52*, 24.
(25) Binder, K. *Monte Carlo and Molecular Dynamics Simulations in Polymer Science*; University Press: Oxford, 1995.
(26) Nelson, D. L.; Cox, M. M. *Lehninger Principles of Biochemistry*; Worth Publishers: New York, 2000.
(27) Finkel'shtein, A. V.; Ptitsyn, O. B. *Fizika Belka. Kurs lektsii (The Physics of Protein: A Course of Lectures)*; Moscow Universitet: Moscow, 2002.
(28) Piculell, L. In *Food Polysaccharides and Their Applications*; Stepen, A. M., Ed.; Marcell Dekker: New York, 1995.
(29) Wegner, G. *Macromol. Chem. Phys.* **2003**, *204*, 347–357.
(30) Rulkens, R.; Wegner, G.; Thurn-Albrecht, T. *Langmuir* **1999**, *15*, 4022.
(31) Bockstaller, M.; Kohler, W.; Wegner, G.; Fytas, G. *Macromolecules* **2001**, *34*, 6353–6358.
(32) Philippova, O. E.; Rulkens, R.; Kovtunenko, B. I.; Abramchuk, S. S.; Khokhlov, A. R.; Wegner, G. *Macromolecules* **1998**, *31*, 1166.
(33) Kroeger, A.; Belack, J.; Larsen, A.; Fytas, G.; Wegner, G. *Macromolecules* **2006**, *39*, 7098.
(34) Kroeger, A.; Deimedo, V.; Belack, J.; Liberwirth, I.; Fytas, G.; Wegner, G. *Macromolecules* **2007**, *40*, 105.
(35) Thunemann, A. F.; Ruppelt, D.; Schnablegger, H.; Blaul, J. *Macromolecules* **2000**, *33*, 2124.
(36) Zaroslov, Y. D.; Gordeliy, V. I.; Kuklin, A. I.; Islamov, A. H.; Philippova, O. E.; Khokhlov, A. R.; Wegner, G. *Macromolecules* **2002**, *35*, 4466.
(37) David, J. H.; Moore, J. S. *Proc. Natl. Acad. Sci. U.S.A.* **2002**, *99*, 5053.
(38) Arnt, L.; Tew, G. N. *Macromolecules* **2004**, *37*, 1283.
(39) Vanhee, S.; Rulkens, R.; Lehmann, U.; Rosenauer, C.; Schulze, M.; Köhler, W.; Wegner, G. *Macromolecules* **1996**, *29*, 5136.
(40) Tsvetkov, N. V.; Bushin, S. V.; Ivanova, V. O.; Bezrukova, M. A.; Astapenko, E. P.; Kuz'mina, O. A.; Shifrina, Z. B.; Rusanov, A. L.; Averina, M. S.; Bulycheva, E. G. *Vysokomolecul. Soed. (Polym. Sci.)* **2004**, *46*, 1695.
(41) Bicerano, J. *Prediction of Polymer Properties*, 3rd edition; Marcel Dekker Inc.: New York, 2002.
(42) Limbach, H. J.; Holm, C.; Kremer, K. *Macromol. Chem. Phys.* **2005**, *206*, 77.

MA800465J