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Self-diffusion of low-generation PAMAM dendrimers with hydroxyl surface groups in solutions: a general regularity

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Abstract

An experimental study of the self-diffusion and nuclear magnetic relaxation of poly(amidoamine) dendrimers with hydroxyl surface groups (PAMAM-OH) dissolved in methanol over a wide range of concentration (φ) is reported. It is shown that experimental concentration dependences of PAMAM-OH self-diffusion coefficients (D) can be reduced to the so-called generalized φ dependence. Over macromolecular concentration range studied, the generalized concentration dependence of PAMAM-OH D coincides with analogous curve obtained for poly(allylcarbosilane) dendrimers of high generations. This result confirms the existence of common regularities of the dendritic macromolecule self-diffusion, and their independence of the individual physicochemical and structural properties of dendrimer, solvent, and features of their interactions in the given systems. The concentration dependence of the PAMAM-OH diffusion also exhibits a clear signature of an inflexible molecule.

Keywords: Dendrimer; Self-diffusion; Scaling

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1. Introduction

In the past decades, a number of interesting results have been obtained in the field of synthesis of dendrimers characterized by various chemical nature and physicochemical properties [1–6]. Nowadays the emphasis of the dendrimer science shifts from the synthesis problems to detailed investigation of the dendrimer properties and to the determination of common laws characterizing this macromolecular type. That permits the determination of the specific fields of the dendrimer applications in practice. Unfortunately, against the background of very active study of physicochemical properties of dendritic macromolecules, their diffusion behavior, especially in the semidilute and concentrated solution regimes, has not yet been studied thoroughly. Nevertheless it is sufficiently clear that the general and particular regularities of the dendrimer self-diffusion would have high practical and fundamental profiles. For instance, such results could stimulate the development of the dendrimer dynamic theory, which would permit to predict the macromolecular behavior in real physical systems. The dendrimer dynamics has a strong impact for possible practical applications such as catalysts, gene or drug delivery agents or modifiers for bulk polymers.

An empirically obtained generalized concentration dependence of self-diffusion coefficients of high-generation ($G = 5–7$) poly(allylcarbosilane) dendrimers (PACS) was described in Ref. [7]. This dependence allows to open a discussion concerning the common regularities of PACS diffusion behavior in solution. From that the following questions arise: Is the obtained result valid to be applied to another dendrimer series? How strong do the chemical and physical features of dendrimers and their solutions influence the form of the mentioned dependence? For this matter, the aim is to obtain (or not to obtain) an analogous dependence for dendrimers of another chemical structure and generations. This would allow the discussion of the universal regularities of the dendrimer diffusivity, independent on macromolecular structure and on the properties of a dendrimer/solvent system. In the present work, we performed such study for two low generations (the third and fourth) of poly(amidoamine) dendrimers with hydroxyl

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surface groups (PAMAM-OH) dissolved in methanol over a wide enough range of macromolecular concentration.

2. Background

The procedure to generalize concentration dependences of macromolecular diffusion coefficient has been developed on the basis of the voluminous experimental data [8–12] and their analysis using the fundamental positions of the phenomenological models for polymer dynamics [13,14]. In order to obtain the generalized (universal) concentration dependence of the macromolecular diffusion coefficient, D, it is necessary to re-plot the experimental dependences $D(\varphi)$ in dimensionless coordinates $\log(D'(\varphi)/D_0)$ vs. $\log(\varphi/\hat{\varphi})$ [8], where $D(\varphi)$ and $D_0 = \lim_{\varphi\to 0} D(\varphi)$ are, respectively, the polymer diffusion in solution with macromolecular concentration φ and in an infinitely dilute solution; $L(\varphi)$ is a normalizing function taking the information about local mobility of macromolecular segments into account; $D'(\varphi)$ is so-called a normalized self-diffusion coefficient which is defined through relation

$$D'(\varphi) = D(\varphi)/L(\varphi). \tag{1}$$

$\hat{\varphi}$ is the critical macromolecular concentration, at which the macromolecules start to overlap with the neighboring polymer coils, and, as a result, the interactions between polymers strongly influences their self-diffusion. The values of critical concentration is experimentally defined through the crossover of two characteristic asymptotes which are analytically described by the relation

$$D(\varphi) \propto \varphi^{-\alpha} \tag{2}$$

with the exponent $\alpha = 0$ for the asymptote at the dilute solution limit ($\varphi \to 0$), where the diffusion coefficient is independent of the dendrimer concentration, and $\alpha = 3$ for that in the range of concentrated solutions ($\varphi \to 1$). The existence of these limits was predicted by the theory of dynamic scaling [14].

The normalization using L function (Eq. (1)) is applied to take into account the changes of the local mobility of monomeric units as the macromolecular concentration increases and thus to exclude the effects of individual features of intramolecular and intermolecular interactions in the polymer/solvent system from the data analysis [8,9].

In terms of the polymeric chain correlation times, τ_c, characterizing the local mobility of monomers, L function can be defined as $L(\varphi) = \bar{\tau}_c(0)/\bar{\tau}_c(\varphi)$, where $\bar{\tau}_c(0) = \lim_{\varphi\to 0} \bar{\tau}_c(\varphi)$ and $\bar{\tau}_c(\varphi)$ are the mean correlation times of polymer in an extremely dilute solution and in solution with the polymer content φ, respectively [8–10]. In practice, this function can be derived from the independent measurements of the nuclear magnetic relaxation times, T_2 (transversal relaxation time), of polymers. If the relaxation measurements are made in the so-called high-temperature regime, and if the condition $\bar{\tau}_c \ll T_2$ is held then, in this simple case, the relation $T_2 \propto \bar{\tau}_c^{-1}$ is valid for polymers. Finally, the L function can be experimentally executed from the concentration dependence of relaxation times, $T_2(\varphi)$, through following

$$L(\varphi) = \frac{\bar{\tau}_c(0)}{\bar{\tau}_c(\varphi)} = \frac{T_2(\varphi)}{T_2(0)}, \tag{3}$$

where $T_2(0) = \lim_{\varphi\to 0} T_2(\varphi)$ and $T_2(\varphi)$ are the transverse relaxation times of polymer in an extremely dilute solution and in solution with polymer content φ, respectively. The approach developed in Ref. [8] was successfully applied to suspensions of the globular protein [15].

3. Experimental

3.1. Materials

The solutions of PAMAM-OH dendrimers with methanol were obtained from *Sigma-Aldrich Corporation*. The synthesis and structure of PAMAM and the similar dendrimers were described in detail by Tomalia [1]. Fig. 1 illustrates the structure of the first generation of PAMAM-OH.

The general characteristics of PAMAM-OH and their solutions are given in Table 1. The dendrimers have been used without further purification.

3.2. NMR measurements

The relaxation and diffusion measurements were performed on the NMR spectrometers Bruker AVANCE 300 and AVANCE 500 operating at proton resonance frequencies of 300 and 500 MHz, respectively. The Carr–Purcell–Meiboom–Gill pulse sequence was used to obtain the T_2 values at ^{1}H frequency of 300 MHz. Diffusion measurements

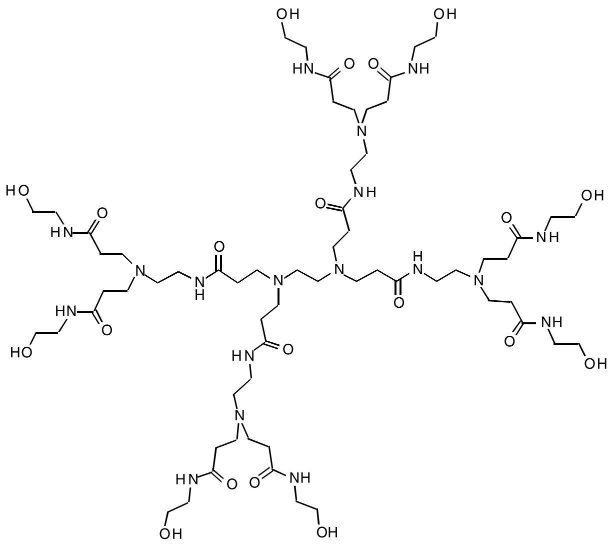

Fig. 1. The first generation of PAMAM-OH dendrimer.

Table 1
PAMAM-OH dendrimers and their solutions with methanol alcohol

Notation of dendrimers	Generation no.	Molar mass, M_w (g mol^{-1})	Range of the dendrimer volume fraction in solutions
PAMAM-OH G3	3	6941	0.001–0.48
PAMAM-OH G4	4	14279	0.001–0.45

were performed using stimulated echo with the pulsed magnetic field gradient [16] (PFG NMR) with both spectrometers. The 300 MHz spectrometer was equipped by microimaging accessory (Bruker Micro 2.5) operating at maximum gradient amplitude up to 1 T m^{-1}; the 500 MHz spectrometer employed a diffusion probe Diff30 generating magnetic field gradients up to 12 T m^{-1}. All experiments have been conducted at temperature of 20 °C. The experimental data were processed by the MatNMR program (written by van Beek) working with software of MATLAB.

4. Results and discussion

4.1. Diffusion of PAMAM-OH

The PAMAM-OH diffusion rates, D, were extracted from slope of the diffusion decays of spin-echo signal. As the experiments show, the diffusion decays obtained for the ^{1}H NMR spectrum lines, corresponding to different protons of the dendrimer, are characterized by single value of self-diffusion coefficient depending on macromolecular concentration only. The set of the diffusion decay curves, which have been obtained for PAMAM-OH of the fourth generation in solutions with different dendrimer content, is depicted in Fig. 2. As seen in Fig. 2 in a linearized Stejskal–Tanner plot, all decays have the simple monoexponential form, showing that diffusion of monodisperse particles is monitored which excludes any aggregation. They can be satisfactorily described by Stejskal–Tanner expression [16]

$$A(g^2)/A(0) = \exp(-\gamma^2 g^2 \delta^2 (\Delta - \delta/3) D) \qquad (4)$$

where γ is the gyromagnetic ratio of proton, g, δ are the amplitude and duration of the magnetic field pulse, respectively, Δ is the delay between two gradient pulses in the sequence, $A(0)$ is the stimulated spin-echo amplitude at $g = 0$, D is the self-diffusion coefficient of PAMAM-OH.

The influence of macromolecular concentration on the dendrimer mobility in the given solutions is illustrated in Fig. 3; the concentration dependences of D for PAMAM-OH of the third and fourth generations are shown here. As seen in the figure, it is easy to distinguish two characteristic domains on the obtained curves, these concentration dependences of the dendrimer D can be described by Eq. (2) with $\alpha = 0$ at the limit of dilute solutions and with an exponent α about 5 in the concentrated solutions range.

In order to realize the normalization procedure (Eq. (1)) of the obtained φ dependences of PAMAM-OH D, it is necessary to define the normalizing L functions for each generation of macromolecules in additional experiments.

4.2. The transverse NM relaxation of the dendrimers, and the obtaining L functions

The T_2-relaxation times of the dendrimers were measured to obtain L functions for all systems studied. In Fig. 4(a), the concentration dependences of the relaxation times, which have been obtained for protons in the methylene and the secondary amino groups of the fourth generation PAMAM-OH dendrimer, are shown. In Fig. 4(b), the data from Fig. 4(a), are depicted normalized to the

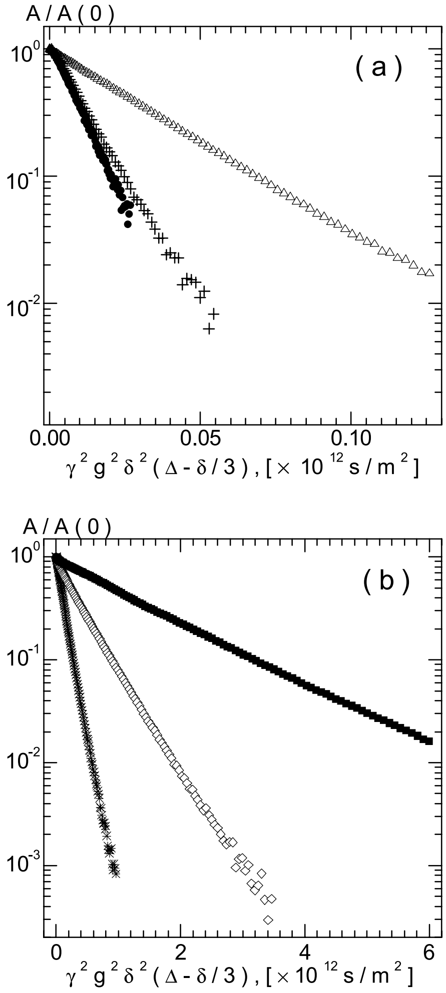

Fig. 2. Diffusion decays obtained for solutions of the fourth-generation PAMAM-OH with the macromolecular volume fraction: (a) 0.04 (●), 0.08 (+), 0.15 (△); (b) 0.26 (✱), 0.34 (◇), 0.45 (■).

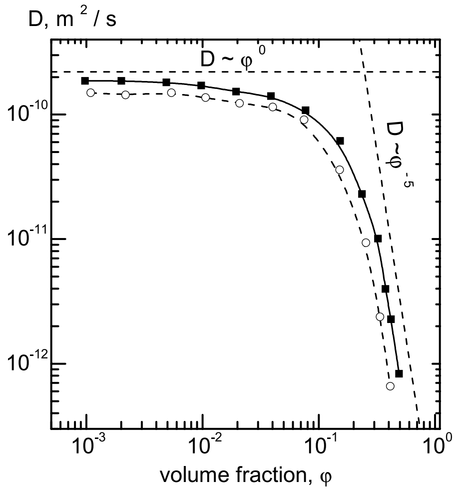

Fig. 3. Concentration dependences of the PAMAM-OH diffusion for macromolecules of the third (■) and fourth (○) generations.

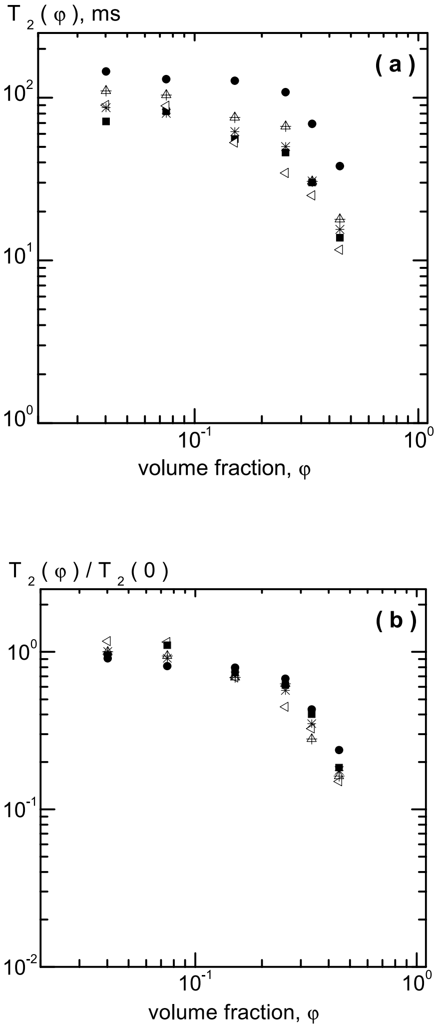

Fig. 4. (a) Concentration dependences the PAMAM-OH G4 transverse relaxation times for: protons of methylene chemical groups of the dendrimer (■, ◁, ⊕), protons of the amine groups (●, ✳), (b) concentration dependences of the relative transverse relaxation times extracted from dependences, depicted in Fig. 3(a).

magnitude $T_2(0)$ corresponding to each curve. The $T_2(0)$ values have been obtained by extrapolation of the given dependences $T_2(\varphi)$ to the zero-concentration limit. As seen in Fig. 4(b), all the T_2 values vary equally as the dendrimer concentration increases in solution. Thus, for the definition of the L function, it is possible to use the function $T_2(\varphi)/T_2(0)$ depicted in Fig. 4(b). The study of macromolecular NM relaxation of the third-generation PAMAM-OH led to analogous results.

As a final point, the L functions for the third and fourth-generation PAMAM-OH dendrimers were derived from the experimental concentration dependences of the transverse relaxation times with use of Eq. (3). Fig. 5 shows the normalizing functions obtained this manner.

4.3. Generalized concentration dependence of D for PAMAM-OH dendrimers

According to Eq. (1), the concentration dependences of the PAMAM-OH diffusion coefficient D (Fig. 3) and the semiempirical L functions (Fig. 5) corresponding to each generation of the macromolecules, two similar curves characterized by two asymptotes were obtained in the coordinates $\log(D'(\varphi)/D_0)$ vs. $\log\varphi$. The mathematical form of the asymptotes can be satisfactorily described by Eq. (2) with $\alpha = 0$ in the limit of dilute solutions and with $\alpha \approx 3$ in the concentrated solution range ($\varphi \rightarrow 0.5$). Critical concentrations were determined from the crossover of these asymptotes; the values are 0.149 ± 0.005 and 0.133 ± 0.005 for dendrimers of the third and fourth generations, respectively. It should be noted that the critical concentration values decrease as the dendrimer molecular mass increases. This permits to state that behavior of PAMAM-OH macromolecules cannot be simulated by the simplest model of hard spheres, because molecular mass dependence of critical concentration (concentration of overlapping) would not exist for them.

The replotted (normalized) concentration dependences of the dendrimer diffusion coefficient are shown in Fig. 6 in the coordinates $\log(D'(\varphi)/D_0)$ vs. $\log(\varphi/\hat{\varphi})$. As seen in Fig. 6, two curves are united into the generalized concentration dependence of PAMAM-OH diffusion coefficient in the given coordinate frame. Moreover, the obtained curve coincides with the generalized dependence for PACS dendrimer [7] (Fig. 6). This result shows that some common regularity of the dendrimer diffusivity may be exist not only for series of PAMAM-OH dendrimers but also for dendrimers with another chemical nature. Besides, for the examined samples of the dendrimer solutions (PAMAM-OH with methanol and PACS with deuterated chloroform [7]), the generalized concentration dependence of self-diffusion coefficients of dendrimers does not depend on the

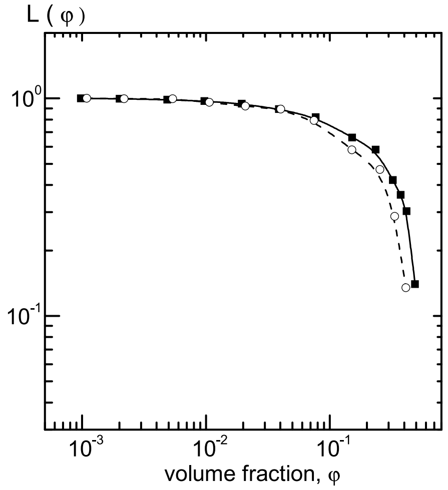

Fig. 5. The L functions obtained for the dendrimers PAMAM-OH G3 (■) and PAMAM-OH G4 (○).

individual properties of the solvents and of the dendrimers. The effect of the dynamics of the individual molecules in solvent has been eliminated by the normalization procedure. A change in the critical concentration or the generalized dependence would indicate a change in the conformation of the dendrimer in the dendrimer/solvent systems studied.

The universal concentration dependence of D for macromolecules in linear flexible polymer solutions and melts [8–12] is also depicted in Fig. 6 for comparison. The analysis of the generalized dependence of the dendrimer D on their concentration shows that this curve tends to the analogous dependence for polymers at the limits of extremely dilute and concentrated solutions only. In the intermediate range of $\varphi/\hat{\varphi}$, these curves are considerably different, proving considerable difference of the diffusion behavior of polymeric and dendritic macromolecules in solutions. In the given concentration regime of diffusion, the intermolecular interactions dominantly influence macromolecular mobility. The macromolecular conformation is one of the factors determining the character of macromolecular dynamics [13–15]. Consequently, the significant difference of self-diffusion of dendrimers and linear polymers connects with specific dendrimer conformation [1,3] and Gaussian conformation of the linear flexible-chain polymers.

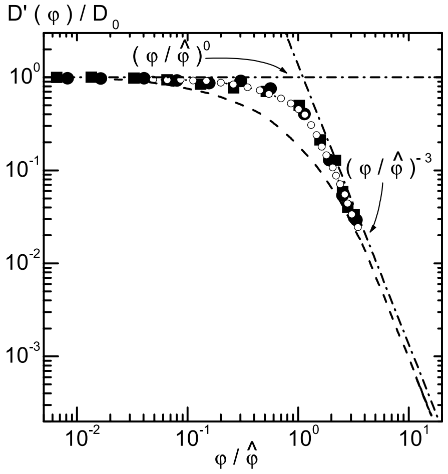

Fig. 6. Normalized concentration dependences of D for PAMAM-OH dendrimers of the third (■) and fourth (●) generations in the methanol alcohol solutions. The generalized concentration dependence of D for PACS dendrimers of high generations [7] (○) and the universal concentration dependence of macromolecular diffusivity for polymeric solutions and melts (- - -) have been also depicted. The characteristic asymptotes, $D'(\varphi)/D_0 \propto (\varphi/\hat{\varphi})^0$ and $D'(\varphi)/D_0 \propto (\varphi/\hat{\varphi})^{-3}$, are denoted by dashed-dotted lines.

It should be also noted that the generalized concentration dependence of D for PAMAM-OH dendrimers coincides with the analogous dependence for globular proteins, which are understood to be inflexible on the time and length scale of the experiment, in aqueous solutions over the whole examined concentration range [15] (the generalized concentration dependence of the globular proteins diffusion, not depicted in Fig. 6, it coincides with the curve found for the dendrimers). The last result allows us to state that the diffusion of globular proteins and dendrimers are generally similar. Consequently, the characteristic feature of the intermolecular interactions between dendrimers, as in the case of globular proteins, is the absence of entanglements and significant penetrations of macromolecules.

5. Conclusions

The results of the self-diffusion study of the third and fourth-generation PAMAM-OH dendrimers permits the discussion on common regularities of the dendrimer diffusion, independent of the individual features of PAMAM-OH and PACS dendrimer structures and their solutions. In particular, the existence of the semiempirical generalized concentration dependence of the dendrimer diffusion coefficients is considered both as the confirmation of these regularities of the dendrimer diffusivity and as a step to the development of a theoretical conception which eventually allows the description and prediction of the dendrimer dynamics in solutions and blends. As the results presented in this paper show, the dendrimers exhibit a scaling behavior at the limits of an extremely dilute and concentrated solution on the dependence $D(\varphi)$ (see Fig. 6). Taking the results of this work into account suggests one of the ways to the development of a theory based on the fundamentals of the ideas of the dynamic scaling [14].

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