

Size Invariance of Polyelectrolyte Dendrimers

Giovanni Nisato,[†] Robert Ivkov, and Eric J. Amis*

Polymers Division, National Institute of Standards and Technology, 100 Bureau Dr. Stop 8540, Gaithersburg, Maryland 20899-8540

Received August 30, 1999; Revised Manuscript Received March 28, 2000

ABSTRACT: To quantify the swelling response of polyelectrolyte dendrimers in aqueous solutions as affected by changes in solution conditions, we have studied eighth generation, G8, poly(amidoamine) (PAMAM) dendrimers in D₂O using small-angle neutron scattering. The charge density is manipulated by varying the pH of the solution in order to protonate and deprotonate the primary and tertiary amines. The coherent scattered intensity at high q values yields size information from the form factor of individual dendrimers. The distance distribution functions of the dendrimers in a variety of experimental situations were determined by indirect Fourier transform. For all the conditions studied, we find that the size of G8 dendrimers is essentially insensitive to variations of the pH ($4.7 < \text{pH} < 10.1$) and of ionic strength (up to 3 M of NaCl). In all cases, the scattering curves yield density profiles that correspond well to a uniform sphere with a radius of gyration $R_G = 4.0 \pm 0.15$ nm. We conclude that the dendrimer size is essentially independent of the charge density or ionic strength of the solvent, contrary to the predictions of current models and simulations.

Introduction

Dendrimers are macromolecules consisting of a multifunctional core to which repeat units are sequentially added to create hyperbranched and topologically regular molecules. The most widespread water-soluble dendrimers contain amine-terminated end groups and tertiary amines in their repeat units.¹ These molecules can therefore be charged by varying the pH of the solution and can be viewed as polyelectrolyte networks of nanoscopic dimensions.

A number of potential applications for dendrimers, for instance in the biomedical domain, require a firm understanding of their behavior in aqueous solution. Aside from specific interactions arising in a biological environment, the physical–chemical parameters most likely to influence the intermolecular interactions and the dendrimer conformation are the pH and the ionic strength of the solution. Among the possible applications of molecules having a dendritic architecture, perhaps one of the most interesting is their use as molecular cages in host–guest complexes. It is therefore interesting to consider possible volume changes of dendrimers in response to variations in solution pH or ionic strength that might provide controlled release of drug molecules or dyes through volume and conformation changes.

Significant effort has been devoted to both modeling^{2–5} and experimental^{6–9} characterization of the conformations and density profiles of dendrimers in solution as a function of the generation number and solvent quality. Recently, Welch and Muthukumar predicted that polyelectrolyte dendrimers should undergo significant variations of size (up to a factor 1.8) and density profile upon changes in the solution pH or salt concentration.¹⁰ These predictions, which were based on Monte Carlo simulations of G5 dendrimers and scaling laws, are unverified experimentally.

PAMAM dendrimers contain both primary and tertiary amines, and their charge density can be tuned by

varying the pH of the solution. Previous investigations have shown that increasing the ionization of the amine groups gives rise to liquidlike ordering.^{11,12} These charged dendrimer solutions show a characteristic interaction peak in the small-angle scattering curves, signaling the presence of a very strong contribution of the intermolecular structure factor to the overall scattering intensity.

For the present investigation it is important to be able to attribute unambiguously variations of some features of the scattering profiles to the form factor of the individual dendrimers. Prosa et al. have investigated thoroughly the evolution of the scattering profile that is associated with the form factors of PAMAM dendrimers as a function of generation number. Lower generation dendrimers appear to be slightly more compact than traditional starlike molecules. On the other hand, higher generation dendrimers, such as G8 PAMAM, display characteristic high-order features due to their spherelike form factor which are particularly helpful to monitor variations of their size.⁶ To quantify the swelling response of dendrimers in aqueous solutions as it is affected by changes in solution conditions, we measured SANS from G8 PAMAM dendrimers in D₂O in various pH and salt concentration conditions.

Experimental Section

Materials. Generation 8 (G8) poly(amidoamine) (PAMAM) dendrimers were obtained from Dendritech, Inc., Midland, MI.^{1,13} The theoretical molar mass of a G8 PAMAM dendrimer is 230 000 g/mol. The G8 dendrimer solutions we measured were prepared from a 0.22 mass fraction aqueous stock solution as follows. Aliquots of the stock solution were diluted with ultrapure H₂O (18 M Ω /cm, Barnstead) and dialyzed to remove low molar mass impurities. Dialysis was performed using a Spectrum microdialyzer with a 10 mL half-cell volume and a 12 000–14 000 g/mol molecular mass cutoff (MWCO) cellulose membrane (Spectra/Por, Spectrum). H₂O solvent was exchanged by dialysis against 99.9% (low paramagnetic) D₂O (Cambridge Isotopes, Inc.).¹³ The final D₂O volume fraction of the solvent was >97.5%, as measured from the incoherent scattering intensity of the solution. Some samples where obtained by freeze-drying water solutions of the dendrimers

[†] Current address: Philips Research, Prof. Holstlaan 4, NL-5656 AA Eindhoven, Netherlands.

Table 1^a

sample	preparation	C_D	C_S (M)	pH	R_G (nm) ITP	$q_{\min}$ (nm ⁻¹)	R_G (nm) min
D3-500-0	dialyzed	0.03	0.5	9.1	4.00	0.92	3.91
D3-500-5	dialyzed	0.03	0.5	8.3	3.90	0.91	3.96
D3-500-1	dialyzed	0.03	0.5	7.7	4.05	0.89	4.07
D3-500-2	dialyzed	0.03	0.5	7.6	4.05	0.89	4.07
FD1-B01	freeze-dried	0.01	0	9.5	3.95	0.93	3.87
FD1-B1	freeze-dried	0.01	0	10.1	3.95	0.93	3.87
FD3-0-0	freeze-dried	0.03	0	9.15	3.95	0.93	3.87
FD3-3k-5	freeze-dried	0.03	3	8.25	3.95	0.95	3.81
FD3AC	freeze-dried	0.05	0	4.7	4.03	0.89	4.07

^a Note: R_G values determined from the $q_{\min}$ values using $q_{\min} = 3.62/R_G$ are reported in the last column. Another size estimate, the maximum dimension, of a G8 dendrimer can be estimated to be $R_{ETE} = 7.5$ nm for the end-to-end radius with fully stretched bonds.

and subsequent dissolution in D₂O; these solutions were filtered (Gelman Acrodisk, 0.2 μ m) prior to the measurement. The mass fraction of the dendrimers and the concentration of added NaCl are noted C_D and C_S , respectively.¹⁴ The main characteristics of the samples studied are listed in Table 1.¹⁵

Full generation PAMAM dendrimers are weak polybases and can be ionized in aqueous solvents by adjusting the pH. The pH of the dendrimer solutions was varied by adding small amounts of concentrated HCl or NaOH solutions. To measure the scattering from solutions of neutral dendrimers, we neutralized with NaOH the residual charged groups from autoionization. The pK_a values for the primary and tertiary amine groups in G8 PAMAM were determined by Valachovic¹⁶ and are $pK_a^1 = 8.6$ and $pK_a^3 = 5.5$, respectively. These values are in agreement with data obtained from G5 PAMAM dendrimers reported by Ottaviani et al.,¹⁷ who reported a pK_a^1 of 8 for the primary amine groups in G5 PAMAM. Our pH values are the result of three independent measurements performed with a standard pH-meter equipped with a microelectrode (M1-410, Microelectrodes).

SANS. The small-angle neutron scattering (SANS) experiments were performed on a 30 m instrument (NG7) located at the Center for Neutron Research at the National Institute of Standards and Technology in Gaithersburg, MD.¹⁸ The SANS experiments were conducted using two sample-to-detector configurations (1.5 and 8 m). The neutron wavelength was 0.6 nm, having a distribution with a full width at half-maximum $\Delta\lambda/\lambda = 0.11$. These conditions correspond to q values ranging from 0.04 to 4.6 nm⁻¹, where q is the magnitude of the momentum transfer vector.¹⁹ All the samples were contained in quartz cells having circular windows and path lengths of 1 mm. The raw (2-D) data were reduced using the standard data reduction software available at the Cold Neutron Research Facility.²⁰ The corrected intensities were converted to an absolute scale using secondary standards, and data sets from different instrument configurations overlap without scale adjustments. The incoherent contribution to the scattered intensity from these dendrimer solutions can be fairly important, due to their high content of hydrogen, to isotopic substitution effects, and to residual H₂O present in the samples. The incoherent scattering intensity for each data set (1.5 m configuration) was estimated by using the Porod approximation in the high q range^{21,22} and subtracted from the scattering data to yield the I vs q plots for each sample, where I is the coherent scattering intensity.

Analysis of Scattering Data. For a homogeneous and monodispersed solution of randomly oriented particles, the total (coherent) scattering intensity can be written as

$$I(q) = KP(q) S(q) \quad (1)$$

where K is the contrast factor (proportional to the particle concentration), $P(q)$ is the form factor of the particles, arising from intraparticle scattering contributions, and $S(q)$ is the structure factor, arising from interparticle scattering contributions.^{19,21}

The scattering data were analyzed by the indirect Fourier transformation method in order to extract as much information as possible about the dendrimer size and shape.^{23–26} The

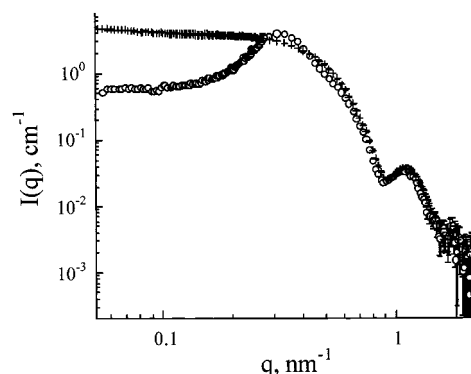


Figure 1. Comparison between the scattering profiles of PAMAM G8 dendrimers in charged (O) and screened conditions (+). In both cases $C_D = 0.03$ (dendrimer mass fraction). Symbols: (O) pH = 7.2, $C_S = 0$; (+) pH = 9.1, $C_S = 0.5$ M.

indirect Fourier transformation determines the end-to-end distribution function,

$$p(r) = \frac{1}{2\pi^2} \int_0^\infty I(q)(qr) \sin(qr) dq \quad (2)$$

without any a priori assumptions about the symmetry of the particles. Alternatively, it can be seen that $p(r) = g(r)r^2$, where $g(r)$ is the intraparticle density correlation function. The maximum dimension of the particle, $D_{\max}$, is given by $p(D_{\max}) = 0$, and the radius of gyration can be calculated for a given $p(r)$ using $R_G^2 = \int_0^\infty P(r)r^2 dr / \int_0^\infty P(r) dr$. The density profile of the scattering particles can also be obtained from the $p(r)$ functions by a deconvolution technique. Alternatively, the $p(r)$ functions can be fitted with analytical expressions available for known shapes and density profiles (e.g., uniform spheres, hollow spheres, shells).²¹ To exclude the effects of interparticle interactions on the determination of $p(r)$, the lower q range of the data was excluded from the fit.²⁷ These effects can be neglected for the higher values of q , as $S(q)$ tends toward a constant for $qD_{\max} \gg 1$. The smearing introduced by the wavelength distribution ($\Delta\lambda/\lambda = 0.11$) and the instrumental resolution were taken into account. Given the monodisperse character of PAMAM dendrimers, it was not necessary to include the effect of size polydispersity in the fitting procedure.

Results and Discussion

The typical scattering profiles of charged and uncharged dendrimer solutions are shown in Figure 1 in which we compare two systems: one highly charged without added salt and the second partially neutralized with excess salt added to screen the electrostatic interactions. The scattering intensity of the unscreened solutions is lower in the $q < 0.3$ nm⁻¹ region, presumably because of decreased osmotic compressibility. We also observe a strong interaction peak (centered at 0.3 nm⁻¹) signaling the presence of dendrimer–dendrimer interparticle repulsions as discussed in previous stud-

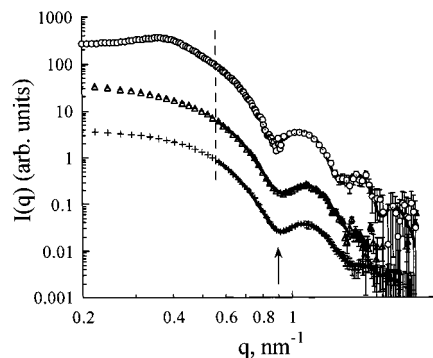


Figure 2. Comparison of the scattering profiles of PAMAM G8 dendrimers in different aqueous environments. Symbols: (○) pH = 4.7, $C_s = 0$; (△) pH = 10.1, $C_s = 0$; (+) pH = 7.7, $C_s = 0.5$ M. For clarity, the data sets have been vertically offset by an arbitrary amount. Solid lines are fits to the data in the high q range using the ITP procedure.^{23–26} The arrow indicates the position of the first local minimum, $q_{\min}$, of the scattering curves.

ies.^{11,12} This feature of the scattering curve can be attributed to the contribution of the structure factor to the total scattering intensity. The presence of the maximum in the scattering intensity demonstrates that dendrimers are electrostatically charged and repel one another.

In the high q range the scattering intensity is dominated by the form factor of the dendrimer. The first local minimum of the scattering curve located around 0.9 nm^{-1} and the following peak are characteristic features of higher generation dendrimers.⁶ Most information on dendrimer size and conformation is extracted from this q range.

In Figure 2 we show a representative sample of the coherent scattering intensities of dendrimers in three aqueous solutions. These three curves correspond to extreme variations of the total electrostatic charge density of the dendrimers (from neutral to completely charged dendrimers) and of the ionic strength of the solution. The data were offset vertically and limited to three curves. In the first data set (circles) the pH of the solution is 4.7 so that, according to Ottaviani et al.,¹⁷ all of the primary amine groups are charged and most of the tertiary amines are charged as well. Since no salt was added to the solution, the ionic strength is estimated to be less than 1 mM, which corresponds to a Debye screening length $\kappa^{-1} \geq 9.6 \text{ nm}$. The second curve (triangles) corresponds to a pH of 10.1, which was achieved by adding a strong base (NaOH) to the stock dendrimer solution. No salt was added, and at this pH the few amine groups of the dendrimer are protonated so these molecules can be regarded as neutral. The third curve (plusses) shows data for a sample that is both charged (pH = 7.7) and highly screened by the addition of 0.5 M salt, giving $\kappa^{-1} = 0.43 \text{ nm}$.

The position of the first minimum, $q_{\min}$, in the high q range of the scattering curves yields the overall size of the dendrimer, as reported by Prosa et al.⁶ In the case of a uniform sphere, $q_{\min} = 3.62/R_G$, where R_G is the radius of gyration of the sphere. It is clear from Figure 2 that the position of the first minimum is independent of the dendrimer charge and the solution ionic strength. A more quantitative analysis of the data was performed using the indirect Fourier transformation procedure (ITP program) of Glatter, described in refs 24–27.

In Figure 3 we show a comparison of the end-to-end distribution functions, $p(r)$, for PAMAM G8 dendrimers

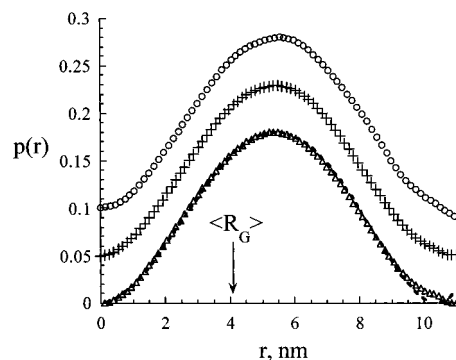


Figure 3. Distance distribution functions of PAMAM G8 dendrimers in various solvent conditions (see Figure 2). Symbols: (○) pH = 4.7, $C_s = 0$; (△) pH = 10.1, $C_s = 0$; (+) pH = 7.7, $C_s = 0.5$ M. The dotted line represents a nonlinear least-squares fit to the data with the distance distribution function of a uniform sphere: $p(r) = 12(r/D)^2[2 - 3(r/D) + (r/D)^3]$, where D is the diameter of the sphere.²¹ The arrow indicates the average value of the radius of gyration. The data have been offset vertically for the sake of clarity. Uncertainty bars are on the order or smaller than the symbol size.

under solvent conditions corresponding to the data sets shown in Figure 2. To avoid artifacts introduced by the structure factor of the dendrimer solution, which are particularly noticeable for “salt-free” charged dendrimer solutions, we restrained the fits to the upper q range of the data sets as marked by the vertical dashed line in Figure 2.²⁷ The three curves corresponding to extremely different solvent conditions are indistinguishable within the experimental uncertainty. The distance distribution function of a uniform sphere $p(r) = 12(r/D)^2[2 - 3(r/D) + (r/D)^3]$, where D is the diameter of the sphere²¹ is also shown for comparison in Figure 3. The agreement with this model is good, except for minor discrepancies at large values of r . This result indicates that the density profiles of these dendrimers do not depend on solvent quality or their degree of ionization. We do not observe a transition from a uniform sphere to a hollow shell profile. The density of the dendrimer can be estimated to be $0.73 \pm 0.05 \text{ g/cm}^3$, suggesting a very compact structure. The deviation from the uniform sphere model for high values of r can be attributed to either a density gradient at the interface or a slight ellipticity. These dendrimers can be viewed as uniform spheres with “fuzzy” interfaces or slightly oblong particles, and it is not possible to discriminate between these possibilities from neutron scattering data alone. The value of the maximum dimension of the dendrimers is more tainted with uncertainties than R_G , which can be obtained by other analyses. In Table 1 we report the radii of gyration estimated from the position of the first local minimum in the scattering function in the high q range and by using the ITP procedure. The agreement is good, once again indicating that G8 dendrimers can be treated as uniform spheres. The slight systematic discrepancies between the R_G found with the two methods can be attributed to wavelength smearing effects.

The invariance of the dendrimer size under diverse conditions in aqueous solution is remarkable. In Figure 4 we plot the values of the radii of gyration for dendrimers in different salt solutions as a function of pH, which reflects the ionization state of the dendrimers. In a previous study we reported similar results showing no significant size variation for generation PAMAM G5 dendrimers.¹¹ However, this earlier study was limited to high salt concentration so that estimates

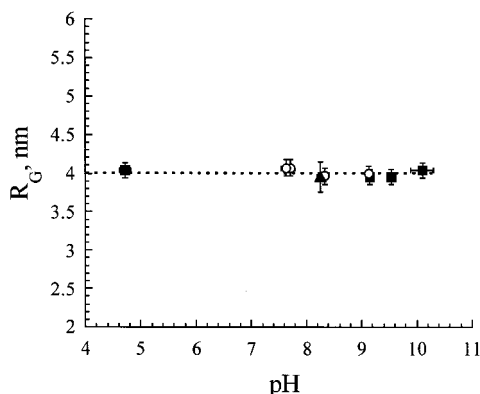


Figure 4. Radius of gyration of PAMAM G8 dendrimers as a function of pH in various solvent conditions measured using the ITP procedure. Symbols: (■) $C_s = 0$, (○) $C_s = 0.5$ M, and (▲) $C_s = 3$ M.

of R_G values were restricted to fits in the Guinier regime. The results of the present paper are particularly interesting in comparison with recent theoretical modeling of the conformation of dendritic molecules.

Charged dendrimers are polyelectrolyte networks of nanoscopic dimensions. Their highly regular structure and the absence of topological constraints and defects (such as dangling ends) makes them particularly good candidates for simulations and theoretical modeling. In a recent study, Welch and Muthukumar used a combination of scaling arguments and Monte Carlo simulations to study the effect of electrostatic charge and salt concentration on the size and the density profile of dendrimers. By treating dendrimers as polyelectrolyte nanonetworks composed of ideally flexible chain elements, the authors predict that these molecules should swell substantially under the influence of the excluded-volume and intramolecular Coulombic repulsions between the charged subunits. The effect of electrostatic interactions was described in terms of an excluded-volume-like interaction of electrostatic origin. The elasticity of the network, which is assumed to consist of Gaussian subchains, mostly opposes volume changes. Their scaling analysis yields²⁸

$$R_G \sim \left(w + \frac{4\pi l_B}{\kappa^2} \right)^{1/5} \quad (3)$$

where w is the classical excluded volume, l_B is the Bjerrum length (≈ 0.7 nm in water), and κ^{-1} is the Debye screening length. The second term in the parentheses is the electrostatic excluded volume due to intraparticle Coulombic repulsion between ionized monomers. In their study Welch and Muthukumar consider variations of the effective combined excluded-volume parameter over several decades, which represents significant variations of the electrostatic screening length, since κ^{-2} is usually the leading term in eq 3. This variation of the effective excluded volume over 3 decades corresponds to a variation of monovalent salt concentration of about 3 decades, since $\kappa^{-2} \sim C_s$. A comparison to experimental results is thus possible, at least from the standpoint of the variation of the electrostatic excluded volume. The Monte Carlo simulations yield apparent exponents that are closer to 1/10 than 1/5. Although these exponents are considerably smaller than the scaling law predictions, the R_G variation should still be detectable.

Clearly, the experimental results conflict with these predictions. The discrepancies could be rationalized by

several factors. First, the repeat units of PAMAM dendrimers, as well as practically all available dendrimers, are constituted of seven aliphatic bonds at most. The Gaussian coil approximation cannot describe properly the entropic elasticity of these short branches that constitute the dendrimers. A more realistic description of the elastic component of the free energy should include the rigidity of these short chain segments. Second, the excluded-volume interaction due to electrostatic interactions in the dendritic structure might be underestimated in this model since physical dendrimers are "stretched" due to the short-range steric interactions between the branches. In this regard, recent work has shown that wide variations of solvent quality, which should affect the classical excluded volume, also have little influence on the R_G of uncharged dendrimers.⁸ The overcrowding can also be related to the topology of the dendritic structure in the same way as for highly cross-linked networks.

Some of these remarks also apply to the Monte Carlo simulations. Perhaps more detailed simulations need to be performed, such as explicitly including the solvent, to capture the behavior of dendritic structures. Finally, and perhaps more fundamentally, one can wonder whether dendrimers are ergodic or whether they should be considered to be glassy networks of nanoscopic dimensions. The assumption of ergodicity is often implicit in the Monte Carlo simulations, but this property is not always present either in simulations or in the real physical systems. Measurements of relaxation processes occurring at varying length scales within the dendrimer dimension, using the neutron spin-echo method, might provide insights into the ergodicity question. Also, dendrimers having longer repeat units would be better candidates with the model simulations of Welch and Muthukumar. It seems likely that the less dense and more regular structures of dendrigrafts or random hyperbranched molecules should have a greater capacity to undergo the significant size variations in response to their environment.

Conclusion

We studied the influence of ionic strength and pH on the size of generation 8 PAMAM dendrimers using small-angle neutron scattering. The form factor of the dendrimers was extracted from the upper q range of the coherent scattering intensity data. For this purpose, the indirect Fourier transform procedure (ITP) was used, which yielded the end-to-end distribution function, $p(r)$, of the dendrimers under the range of experimental conditions. We found that the size of G8 dendrimers is insensitive to variations of the pH and of the ionic strength of the solvent ($4.7 < \text{pH} < 10.1$; $C_s < 3$ M). The $p(r)$ functions were described by the theoretical expression corresponding to a uniform sphere ($R_G = 4.0 \pm 0.15$ nm). The present study shows that polyelectrolyte dendrimers do not respond to ionic strength and pH variations by undergoing the volume changes predicted by scaling law modeling and Monte Carlo simulations.

Arguably, the swelling response of dendrimers might be enhanced by developing more "open" molecular architectures, for example by increasing the number of monomer units between branching points. It would also be interesting to study the swelling response of less topologically regular molecules (e.g., dendrigrafts) to assess the influence of overall crowding and steric

effects. These studies may also contribute to our fundamental understanding of irregular polymer networks.

Although dendrimers do not exhibit a pH-dependent volume transition, which has been proposed as a mechanism for controlled molecular delivery, their remarkable stability at high ionic strength offers the possibility to use electrostatically mediated guest–host interactions that are impossible for traditional polymers. Further investigations of these modes of interactions are the subject of ongoing studies.

Acknowledgment. We are especially grateful to Dr. Donald A. Tomalia for providing the dendrimers used in this study. We thank Professor Otto Glatter for kindly providing the analysis software ITP, Dr. Franziska Gröhn for her help with the data analysis, and Dr. Jack F. Douglas for stimulating discussions. This material is based upon work supported in part by the U.S. Army Research Office under Contract 35109-CH.

References and Notes

- (1) Tomalia, D. A. *Sci. Am.* **1995**, 272, 62.
- (2) de Gennes, P.-G.; Hervet, H. *J. Phys. (Paris)* **1983**, 44, L351.
- (3) Lescanec, R. L.; Muthukumar, M. *Macromolecules* **1991**, 24, 4892.
- (4) Mansfield, M. L.; Klushin, L. I. *Macromolecules* **1993**, 26, 4262.
- (5) Boris, D.; Rubinstein, M. *Macromolecules* **1996**, 29, 7251.
- (6) Prosa, T. J.; Bauer, B. J.; Amis, E. J.; Tomalia, D. A.; Scherrenberg, R. *J. Polym. Sci., Part B: Polym. Phys.* **1997**, 35, 2913.
- (7) Scherrenberg, R.; Coussens, B.; van Vliet, P.; Edouard, G.; Brackman, J.; de Brabander, E.; Mortensen, K. *Macromolecules* **1998**, 31, 456.
- (8) Topp, A.; Bauer, B. J.; Tomalia, D. D.; Amis, E. J. *Macromolecules* **1999**, 32, 7232.
- (9) Topp, A.; Bauer, B. J.; Klimash, J. W.; Spindler, R.; Tomalia, D. A.; Amis, E. J. *Macromolecules* **1999**, 32, 7226.
- (10) Welch, P.; Muthukumar, M. *Macromolecules* **1998**, 31, 5892.
- (11) Nisato, G.; Ivkov, R.; Amis, E. J. *Macromolecules* **1999**, 32, 5895.
- (12) Ramzi, A.; Scherrenberg, R.; Brackman, J.; Joosten, J.; Mortensen, K. *Macromolecules* **1998**, 31, 1621.
- (13) Certain commercial material and equipment are identified in this publication in order to specify adequately the experimental procedure. In no case does such identification imply recommendation by the National Institute of Standards and Technology nor does it imply that the material or equipment identified is necessarily the best available for this purpose.
- (14) The accepted SI unit of concentration, mol/L, has been represented by the symbol M in order to conform to the conventions of this journal.
- (15) The maximum total uncertainties can be estimated to be within 10% of the shown values.
- (16) Valachovic, D. E. Structural Characterization and Polyelectrolyte Behavior of Poly(amido amine) Dendrimers Investigated by Light and Neutron Scattering Methods. Thesis, University of Southern California, 1997.
- (17) Ottaviani, M. F.; Montalti, F.; Romanelli, M.; Turro, N. J.; Tomalia, D. A. *J. Phys. Chem.* **1996**, 100, 11033.
- (18) Prask, H. J.; Rowe, J. M.; Schroeder, I. G. *J. Res. Natl. Inst. Stand. Technol.* **1993**, 8, 1.
- (19) Higgins, J. S.; Benoît, H. C. *Polymers and Neutron Scattering*; Clarendon Press: Oxford, 1994.
- (20) SANS Data Reduction and Imaging Software, NIST-Cold Neutron Research Facility, 1996.
- (21) Glatter, O.; Kratky, O. *Small angle X-ray scattering*; Academic Press: London, 1982.
- (22) Chen, S.-H.; Bendedouch, D. *Methods in Enzymology*; Hirs, C. H. W., Timasheff, S. N., Eds.; Academic Press: New York, 1986; Vol. 130, p 79.
- (23) Glatter, O. *Acta Phys. Austr.* **1977**, 47, 83.
- (24) Glatter, O. *J. Appl. Crystallogr.* **1977**, 10, 415.
- (25) Glatter, O. *J. Appl. Crystallogr.* **1980**, 13, 7.
- (26) Glatter, O. *J. Appl. Crystallogr.* **1980**, 13, 577.
- (27) Recently, Glatter et al. have developed a generalized indirect Fourier transform (GIFT) method that takes into account structure factor contributions to the scattering intensity. Preliminary comparison between the cutoff data analyzed with ITP and the full data sets analyzed with GIFT shows no quantitative difference.
- (28) The original expression also includes the number N of Kuhn segments between branching points, which can be factored out in these expressions as it is a constant for a given dendritic structure.

MA991474P