Can dendrimers be viewed as compact colloids? A simulation study of the fluctuations in a dendrimer of fourth generation

H. M. Harreis and C. N. Likos
Institut für Theoretische Physik II, Heinrich-Heine-Universität Düsseldorf, Universitätsstraße 1, D-40225 Düsseldorf, Germany
M. Ballauff
Polymer-Institut, Universität Karlsruhe, Kaiserstraße 12, D-76128 Karlsruhe, Germany

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By employing monomer-resolved Monte Carlo simulations, we analyze the conformations, density distributions, correlation functions, and the form factor of model dendrimers of fourth generation. We find that these objects are hybrids between polymer chains and compact colloidal particles, with the fluctuations of the monomers being correlated at length scales of the order of the bond length but practically uncorrelated for lengths exceeding this scale. We discuss the implications of this finding on the possibility of regarding dendrimers as “soft colloids,” on the detection of these fluctuations in scattering experiments and on the inversion of intensity profiles obtained in small-angle neutron scattering measurements. © 2003 American Institute of Physics.

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I. INTRODUCTION

Dendrimers are synthetic macromolecules with a treelike architecture.1–5 The recent advances in developing well-controlled chemical techniques allow for the synthesis of well-characterized branched macromolecules with a prescribed number of branching bonds b at every connection point and generation number g. In Fig. 1 we show a scheme of a dendrimer with b = 3 and g = 4, which is conventionally termed fourth generation (G4)-dendrimer. Dendrimers have attracted a lot of attention in the last few years, for a variety of reasons. First, their peculiar architecture establishes them as hybrid model systems between polymer chains and hard colloids, in terms of both the sphericity and compactness of their conformations and of the softness of their effective interactions.6–8 This property, together with the possibility of tuning their conformations by changing b and g render them into macromolecules of fundamental interest for the soft matter scientists. Second, on the practical level, the possibility to influence the equilibrium monomer density distributions of dendrimers by controlling the pH or salinity of the aqueous solvent and to “switch” thereby from “dense-shell” to “dense-core” configurations9,10 has established them as candidate carrier molecules for drug delivery.11 The complexation of dendrimers with DNA macromolecules and the possibility of using them in order to engineer gene transfer is another exciting aspect that has attracted quite some attention recently.12,13 Associated with the theoretical and simulational studies of dendrimers are small-angle experiments (employing either x rays or neutrons) that provide information on the shape of isolated dendrimers in dilute solutions and the correlations between the same in concentrated ones.

In this work, we focus our attention on G4-dendrimers without charged groups, corresponding either to nonpolar solvents or to aqueous ones in high pH-conditions. Despite original claims that these macromolecules assume typical configurations with a density profile that grows from the origin to their periphery13 (the so-called “dense-shell model’’), a number of experimental14,15 simulational,16–24 and theoretical studies25 have demonstrated that the opposite is true: due to thermal fluctuations of the monomer groups, which are quite familiar from polymer science, a considerable degree of backfolding results and the density of the macromolecule is higher in the center than at the end (the “dense-core model’’). Hence, the apparent dense-shell picture seen in Fig. 1 is misleading if one interprets it literally: the chemical unities are not located at the positions shown in that drawing but they fluctuate and are allowed to explore the inner parts of the molecule as well.

Strong experimental evidence for this fact rests on small-angle neutron scattering (SANS) data that show a density profile that has a Gaussian shape in q-space.8,26 Treating then the dendrimers as compact objects, in which the monomer degrees of freedom are only very weakly fluctuating around their equilibrium positions in an uncorrelated manner, one obtains the density distribution as the inverse Fourier transform of the square root of the scattering intensity I(q) (form factor), as we explain in detail below. The latter being given by a Gaussian function, it follows that the density distribution also has a Gaussian form. Though intuitively appealing, this procedure suffers from an inconsistency, in that the fluctuations of the monomers, which are responsible for the backfolding of the arms in the first place, are left out of the picture in the inversion of the SANS-data.

In this paper, we report on monomer-resolved Monte Carlo (MC) simulations of a G4-dendrimer. Our work serves a double purpose: on the one hand, we propose a specific microscopic model of a dendrimer and we demonstrate by direct comparison with experimental data that, with the suitable choice of a single length scale, the measured scattering factor of the molecules can be very accurately reproduced.
Thus, it represents a step in the microscopic modeling of these highly interesting macromolecules. On the other hand, based on the fact of this accurate description, we then put into test the validity of the inversion procedure mentioned in the preceding paragraph by examining in detail the correlations of the fluctuations of the monomers of a G4-dendrimer. A wealth of relevant quantities pertinent to the molecules have been calculated and compared to experimental data. The main finding of our analysis is that the monomer fluctuations are correlated at length scales that are typically not reachable by SANS-techniques, i.e., of the order of the Kuhn length scales. When applied to an isotropic fluid, for example, the second term in the rhs above turns into $\rho_0$, and the one-particle density operator $\hat{\rho}(\mathbf{x})$ of the system is defined as usual through the relation,

$$\hat{\rho}(\mathbf{x}) = \sum_{i=1}^{N} \delta(\mathbf{x} - \mathbf{r}_i(t)),$$

and the one-particle density $\rho(\mathbf{x})$ as the ensemble average of $\hat{\rho}(\mathbf{x})$ in equilibrium,

$$\rho(\mathbf{x}) = \langle \hat{\rho}(\mathbf{x}) \rangle.$$  

A further useful quantity is the partially integrated density–density autocorrelation function $G(\mathbf{r})$ of the assembly, defined as

$$G(\mathbf{r}) = \frac{1}{N} \int \mathrm{d}^3 r' \langle \hat{\rho}(\mathbf{r} + \mathbf{r}') \hat{\rho}(\mathbf{r}') \rangle = \frac{1}{N} \left( \sum_{i=1}^{N} \sum_{j=1}^{N} \int \mathrm{d}^3 r' \delta(\mathbf{r} + \mathbf{r}' - \mathbf{r}_i) \delta(\mathbf{r}' - \mathbf{r}_j) \right) = \frac{1}{N} \sum_{i=1}^{N} \sum_{j=1}^{N} \delta(\mathbf{r} - \mathbf{r}_i) \delta(\mathbf{r} - \mathbf{r}_j),$$

where $\mathbf{r}_i = \mathbf{r}_j - \mathbf{r}_i$ and we have used Eq. (1). Thus, $G(\mathbf{r})$ is proportional to the probability of finding a pair of particles with their coordinates separated by the vector $\mathbf{r}$. Note that $\mathbf{r}$ is a free vector, i.e., it is not associated with any particular coordinate system. It is also usual to separate the contributions in the double sum of Eq. (3) above from the terms with $i = j$ and to write

$$G(\mathbf{r}) = \delta(\mathbf{r}) + \frac{1}{N} \sum_{i=1}^{N} \sum_{j \neq i}^{N} \delta(\mathbf{r} - \mathbf{r}_j).$$

When applied to an isotropic fluid, for example, the second term in the rhs above turns into $\rho g(\mathbf{r})$, with the average density $\rho$ of the fluid and the well-known radial distribution function $g(\mathbf{r})$. The whole function depends then only on the magnitude $r = |\mathbf{r}|$ of the separation vector.

Let us now introduce the Fourier transform (FT) of the one-particle density operator of Eq. (1), $\hat{\rho}_\mathbf{q}$, given by

$$\hat{\rho}_\mathbf{q} = \frac{1}{(2\pi)^3} \int \mathrm{d}^3 \mathbf{r} \hat{\rho}(\mathbf{r}) e^{-i \mathbf{q} \cdot \mathbf{r}}.$$
Calculating convenient since it allows immediately also to measure the instantaneous center-of-mass of the dendrimer. This is scattering delta spikes at the vectors of the reciprocal lattice. In the latter case, the result follows that \( S(q) \) is a sum of delta spikes at the vectors of the reciprocal lattice associated with a single macromolecular object \( q \) and is related to the well-known structure factor \( S(q) \) of the fluid through

\[
S(q) = (2\pi)^3 \rho \delta(q) + S(q).
\]

In the latter case, the result follows that \( S(q) \) is a sum of delta spikes at the vectors of the reciprocal lattice (Bragg scattering).

We now turn our attention to solutions of complex molecules, i.e., macromolecular aggregates of mesoscopic dimensions, such as colloids or polymers. When scattering from a dilute solution of the same, the contribution to the scattering factor arising from interactions between the whole macromolecules can be ignored. Thus, the scattering experiment provides information about the spatial correlations between the constituent atoms (scattering centers) of the macromolecule, i.e., about the internal correlations in the colloidal aggregate. It is common to call the scattering factor \( S(q) \) associated with a single macromolecular object form factor and in what follows we denote it as \( F(q) \).

We consider, then, a single mesoscopic particle consisting of \( N \) atoms that scatter as point particles. Since only the differences \( \mathbf{r}_{ij} \) of the position vectors appear in Eqs. (3) and (7), it is immaterial where the origin of the coordinates is positioned. Therefore, as we let the molecule diffuse into the solution (as it happens in real experiments) we can measure for every position and conformation the distances \( \mathbf{r}_{ij} \) from the instantaneous center-of-mass of the dendrimer. This is convenient since it allows us immediately also to measure the density distribution around the center of mass, so this is the technique adopted in our simulations. Moreover, since in calculating \( G(\mathbf{r}) \) or \( F(q) \) thermodynamic averages over all conformations are involved (including averaging over all rotations), these two functions become dependent solely on \( r \) and \( q \), respectively; even if the instantaneous conformations of the macromolecule strongly depart from sphericity, the process of averaging restores spherical symmetry. This holds also in particular for the density distribution around the center of mass of the particle, Eq. (2), when all distances are measured with respect to this point.

As is clear from Eq. (7), the form factor \( F(q) \) delivers information about pair correlations between the atoms. In some special cases, though, this information can be directly linked to the density distributions \( \rho(\mathbf{r}) \) around some “pinning center” (emerging through a pinning potential that depends only on the distance of the particles to this central point) or the density around the center of mass, as we demonstrate below.

The first example is the case in which all particles are connected to a common center but they are otherwise independent from each other, i.e., there is no coupling between \( \mathbf{r}_i \) and \( \mathbf{r}_j \) for \( i \neq j \) in the Hamiltonian of the system. Then, the expectation value in Eq. (9) factorizes into [setting now \( S(q) \rightarrow F(q) \)]

\[
F(q) = 1 + \frac{1}{N} \left( \sum_{i=1}^{N} \exp(-i q \cdot \mathbf{r}_i) \right) \left( \sum_{j \neq i} \exp(i q \cdot \mathbf{r}_j) \right)
\]

\[
\approx 1 + \frac{1}{N} \tilde{\rho}(q) \tilde{\rho}(-q) = 1 + \frac{1}{N} \tilde{\rho}(q),
\]

where, in the second line, we assumed that \( N \ll 1 \) so that the exclusion \( j \neq i \) has minimal effects on calculating the function \( \tilde{\rho}(q) \) and in the third line we used the spherical symmetry of \( \rho(\mathbf{r}) \) around the pinning center in order to obtain \( \tilde{\rho}(q) = \tilde{\rho}(q) \).

The second example pertains to “rigid mesoscopic particles.” With this term, we mean that the position vectors \( \{ \mathbf{r}_1(t), \mathbf{r}_2(t), \ldots, \mathbf{r}_N(t) \} \) of the individual atoms fluctuate very weakly around their average positions and the latter can be taken as frozen degrees of freedom in an excellent approximation. In this case, performing the averages \( \langle \cdots \rangle \) in the various equations above is practically equivalent to calculating the sums or the integrals for this one, frozen configuration. Typical such particles are colloidal silica or PMMA hard spheres, or core-shell particles that can be treated as compact, rigid objects. To simplify things, we assume that the atoms are positioned in a configuration that possesses inversion symmetry around the particle’s center of mass. By taking into consideration the weak fluctuations and/or by performing a coarse-graining procedure on length scales of a few angstroms, we can thereby describe the object by a spherically symmetric one-particle density \( \rho(\mathbf{r}) \) around its center of mass. The suitable starting point is relation (8) together with Eq. (5). The coordinates of the scattering centers, \( \mathbf{r}_i \), can now be considered as discrete sampling points that have been selected in order to approximate an integral by the sum given on the right-hand side of Eq. (5). Calling this integral \( J(q) \), we have thus

\[
J(q) = \sum_{i=1}^{N} \exp(-i q \cdot \mathbf{r}_i).
\]

Approximating the integral by the sum above is justified as long as the integrand varies slowly on the scale of \( \Delta \mathbf{r} \), where
\( \Delta \mathbf{r} \) is the typical spacing between two neighboring points on the discrete grid \( \{ \mathbf{r}_k \}, k=1,2,\ldots,N \). In this dense-point limit, the centrosymmetric distribution of the set \( \{ \mathbf{r}_k \} \) implies that the sum will approximately depend only on the magnitude \( q \) of the wave vector. Dropping then the ensemble averages, as discussed above, and using Eq. (8), we obtain for the form factor the expression

\[
F(q) = \frac{1}{N} \tilde{J}^2(q),
\]

under the condition \( q \cdot \Delta \mathbf{r} \leq 1 \).

We examine now the connection of \( J(q) \) with \( \rho(r) \). If the coarse-grained density \( \rho(r) \) is uniform within a sphere of radius \( R \), then the points \( \{ \mathbf{r}_k \}, k=1,2,\ldots,N \) are uniformly distributed within this domain and the integral that the sum approximates is simply

\[
J(q) = \frac{3N}{4\pi R^3} \int d^3r \Theta(R-r) \exp(-iq \cdot \mathbf{r})
\]

\[
= \tilde{\rho}(q),
\]

with the Heaviside step function \( \Theta(x) \). Equations (13) and (14) give then rise to the well-known form factor of hard spheres in the Rayleigh–Gans–Debye limit.31 If now the density \( \rho(r) \) has a smooth \( r \)-dependence, then the set of coordinates \( \{ \mathbf{r}_k \}, k=1,2,\ldots,N \) will be nonuniformly distributed and they can be thought of as random variables drawn from a probability density \( p(r) \). Then, it is straightforward to show, by performing a change of variables and their distributions, that \( \tilde{\rho}(q) \)

\[
J(q) = \frac{4 \pi}{q} \int_0^\infty dq' \int d^3r r \rho(r) \sin(q'r) \tilde{\rho}(q).
\]

Thus, for arbitrary density distributions \( \rho(r) \) of spherically symmetric rigid objects, the result is obtained

\[
F(q) = \frac{1}{N} \tilde{\rho}^2(q),
\]

allowing us to relate the form factor to the square of the Fourier transform of the density distribution around the center of mass of the colloid. Associated with this equation is a relation between \( G(r) \) and \( \rho(r) \) that reads as

\[
G(r) = \frac{1}{N} [\rho \otimes \rho](r),
\]

with \( [\rho \otimes \rho](r) \) denoting the autoconvolution of the density \( \rho(r) \). We emphasize, however, that relation (16) holds as long as \( q \cdot \Delta \mathbf{r} \leq 1 \) is satisfied, so that approximating a sum by an integral is justified. For high enough values of \( q \), the form factor must tend to unity, as is clear from Eq. (9), whereas \( F(q) \) given by Eq. (16) above tends to zero as \( q \to \infty \).

### III. MONTE CARLO SIMULATIONS OF AN ISOLATED DENDRIMER

From Eqs. (11) and (16), it is clear that the form factor can be utilized to obtain directly information about the density distributions only at two specific limiting cases; either when the correlations between the fluctuations of the particles vanish [Eq. (11)] or when the fluctuations themselves are very weak in the first place [Eq. (16)]. Though the second case is quite common when dealing with compact, “hard” particles, things change in the case of “polymeric colloids” that consist of polymer chains synthesized carefully in order to produce various architectures.

Polymer chains are a relevant example: the form factor of ideal (Gaussian) polymers is known to be given by the form

\[
F(q) = N_f \frac{f_D(q^2R_g^2)}{2(z-1+e^{-z})/z^2},
\]

In this case of strongly fluctuating monomers, relation (17) does not hold and hence a back transformation of \( F(q) \) in real space only yields \( G(r) \); it does not deliver information about \( \rho(r) \). Increasing the “stiffness” of the polymeric colloid can be achieved by constructing a star polymer through anchoring of \( f \) chains on a common center. Star polymers are indeed hybrids between polymers and colloids. There, one distinguishes two mesoscopic length scales, the diameter of the outermost blob \( \xi_{max} \) and the radius of gyration \( R_g \). For separations \( \xi_{max} \leq r \leq R_g \), a star polymer with large functionality \( f \) appears compact and a relation of the form (17) approximately holds.27 However, for \( r < \xi_{max} \), one encounters the typical pair correlations akin to those of isolated polymer chains, leading to the linear chainlike scaling \( G(r) \sim r^{1/n-3} \), with the Flory exponent \( n \approx 0.6 \) that characterizes self-avoiding random walks. Similar considerations have been put forward for the case of block copolymer micelles.34 Therefore, the deviation of the pair correlation function from the “rigid particle form,” Eq. (17) can be used as a diagnostic tool for measuring the strength of the correlated fluctuations. Alternatively, the deviations of \( F(q) \) from the form (16) provide an indication for the length scales at which these fluctuations are correlated.

Dendrimers represent a novel type of hybrid particles between soft polymers and hard colloids. Their effective interaction can be tuned by controlling the generation number and the length of the spacers within the dendrons. It is at the same time directly influenced by the monomer density distribution around the dendrimer’s center. Therefore, it is important on the one hand to develop reliable microscopic models describing the isolated dendrimer’s conformations and on the other hand to establish quantitative measures for the degree in which these conformations differ from those of rigid objects. This point is of central importance for a clear understanding of the information to be gained from scattering experiments.14 We investigated these questions by means of Monte Carlo simulations and we present our model below.

### A. The model and simulation details

To mimic the dendrimer whose chemical structure is schematically depicted in Fig. 1, our model-molecule has the same topology as the one shown there, whereby, however, the atomic groups are replaced by spherical beads that build...
up the dendrimers’ dendrons. The beads represent thereby “effective monomers” consisting of all units within one Kuhn segment grouped together. As we do not introduce any intrinsic stiffness in the model in the form of orientational bias of the interaction, the identification of the bead with the Kuhn segment is justified. To model the steric, excluded-volume interactions between Kuhn segments in good solvent conditions, we introduce a purely repulsive Lennard-Jones-type potential, \(V_0(r)\), acting between all beads, where \(r\) denotes the separation between the bead centers. The interaction \(V_0(r)\) is obtained by truncating the Lennard-Jones potential \(V_{LJ}(r)\) at the minimum position \(r_{\text{min}}=2^{1/6}\sigma_{LJ}\) and shifting it by the constant \(V_{0}(r_{\text{min}})\) to get \(V_0(r_{\text{min}}) = 0\).

\[
V_0(r) = \begin{cases} 
4\epsilon \left( \frac{\sigma_{LJ}}{r} \right)^{12} - \left( \frac{\sigma_{LJ}}{r} \right)^{6} + 0.25 & ; \quad r \leq 2^{1/6}\sigma_{LJ} \\
0 & ; \quad r > 2^{1/6}\sigma_{LJ}.
\end{cases}
\]  

(18)

The energy scale is set by \(\epsilon\), the length scale by the Lennard-Jones diameter \(\sigma_{LJ}\) of the beads. In addition to the repulsion present for all monomers, neighboring (connected) monomers along one dendron interact via the attractive finite-nonlinear-extensible-elastic (FENE) potential, \(V_{ch}(r)\), which reads as

\[
V_{ch}(r) = \begin{cases} 
-15\epsilon \frac{R_0^{2}}{\sigma_{LJ}} \ln \left[ 1 - \left( \frac{r}{R_0} \right)^2 \right] & ; \quad r \leq R_0 \\
\infty & ; \quad r > R_0.
\end{cases}
\]  

(19)

The location of divergence in the FENE potential, \(R_0\), determines the maximum bond length between two monomers and was fixed to the standard literature value of \(R_0 = 1.5\sigma_{LJ}\). The total potential, \(V(r) = V_0(r) + V_{ch}(r)\) then has a minimum at \(r_g = 0.97\sigma_{LJ}\), see Fig. 2. This way, it is guaranteed that occurrence of “ghost chains” in the Monte Carlo moves is avoided. Finally, the temperature of the system is fixed at \(T = 1.2\epsilon/k_B\). The microscopic identification of \(\sigma_{LJ}\) will then follow from comparison with experimental data.

Canonical Monte Carlo (MC) simulation techniques, making use of the Metropolis algorithm were employed in the present work. Typically, \(N_{MC} = 1 \times 10^7\) MC cycles were simulated, with one MC cycle being comprised of one trial move for each of the \(N = 62\) monomers. Of the \(N_{MC}\) steps, 20% were used for equilibration. In the remaining MC cycles, \(4 \times 10^5\) configurations were used to calculate statistical averages of the radial density distribution \(\rho(r)\) of the dendrimer around its center-of-mass, the pair distribution function \(G(r)\), the form factor \(F(q)\), as well as its radius of gyration \(R_g\).

B. Results

In order to assess the isolated dendrimer’s equilibrium properties, we first record the radial density distribution function of the dendrimer’s monomers with respect to the dendrimer’s center-of-mass, \(\mathbf{r}_{\text{CM}}\), being defined as

\[
\rho(r) = \left\langle \sum_{i=1}^{N} \delta(\mathbf{r} - \mathbf{r}_i) \right\rangle,
\]  

(20)

with \(N\) being the number of monomers. Here, \(\mathbf{r}\) and \(\mathbf{r}_i\) are measured with respect to the dendrimer center of mass, \((\mathbf{r},\mathbf{r}_i) = (\mathbf{r} - \mathbf{r}_{\text{CM}},\mathbf{r}' - \mathbf{r}_{\text{CM}})\), where \((\mathbf{r}',\mathbf{r}'')\) are the position vectors with respect to a fixed coordinate system and \(\mathbf{r}_{\text{CM}} = (1/N)\sum_{i=1}^{N} \mathbf{r}_i\). As we expect the dendrimer to be spherically symmetric on average, it is justified to work with the spherosymmetric density distribution as introduced above. Moreover, in order to make a further connection with recently obtained, accurate SANS-results on end-monomer distributions, we also measured the quantities \(\rho_{ch}(r)\), \(G_{ch}(r)\) and \(F_{ch}(q)\) pertaining to particles of the last generation only, employing obvious notation. This result can therefore be directly compared to recent experimental data pertaining to the distribution of endgroups in a dendrimer.

In Fig. 3 we show a snapshot of a fourth generation dendrimer from the MC simulation. It can be seen that there the deviations from sphericity are small and, in any case, much less pronounced than those seen in linear polymer
chains with the same degree of polymerization $N$. Due to the choice of the interparticle potentials causing a stiff minimum at separations $r_g = 0.97 \sigma_{LJ}$ between adjacent beads, the latter attain configurations that are practically indistinguishable from those of tangent hard spheres of diameter $\sigma = r_g$. It can be seen that the connectivity of the monomers produces a compact object with a dense core; there is no sign of a dense shell configuration of the dendrimer in any of the typical snapshots we looked at.

The simulation results for the density $\rho(r)$ are shown in Fig. 4 and corroborate the dense core picture: the general trend is that the profile is decreasing as one moves away from the center. There is a pronounced peak at about $r/\sigma_{LJ} = 0.4$, originating from the two beads comprising the zeroth generation of the dendrimer. Since the beads are practically indistinguishable in their behavior from tangent hard spheres of diameter $r_g \equiv \sigma_{LJ}$, the ideal position of the center-of-mass would be in the midpoint between the zeroth-generation bond and this would produce a peak in $\rho(r)$ at $r/\sigma_{LJ} = 0.5$. The fact that this peak is located at the smaller value 0.4 is a clear indication that the center of mass of the dendrimer wanders around significantly, and that it often comes closer to the center of one the two beads of the zeroth generation. There is an alternative explanation regarding the position of this peak, namely, the zeroth generation bond length is shrunk due to the osmotic pressure exercised by the higher-generation monomers surrounding the zeroth-generation. However, this was ruled out by performing Monte Carlo simulations employing a different microscopic model: the beads were modeled as true hard spheres of diameter $\sigma$, connected by threads of maximum extension $e \sigma$, with $e = 0.05, 0.1$. Very similar results were obtained for the density profile and thus the shrinking scenario can be ruled out since hard spheres cannot be found in separations smaller than their diameter. On the other hand, the strong similarity of the results obtained using the two different microscopic models leads to the conclusion that the details of the short-range steric repulsions do not matter, as in the case of linear polymer chains, the excluded volume effect dictates the main physics of the conformations of the macromolecules. A detailed account of the results from the bead-thread model for various generation numbers will be presented elsewhere.

At larger distances, the second and third shell of the dendrimer are resolved as well, their peaks being, however, much less pronounced and indicating that the fluctuations of higher generations become broader. As a matter of fact, one can roughly discern a “plateau” at the density profile, located between $\sigma_{LJ}$ and $2\sigma_{LJ}$. The extent of this “flat” region grows as one increases the maximum generation number. Dendrimers represent a model polymeric system that features constant density profiles, $\rho(r) \sim r^0$, within a certain region, and this characteristic can be compared to the $\sim r^{-43}$ behavior of the density that one obtains for star polymers, for example. It can be nicely seen how the architecture of the macromolecule that combines starlike elements but supplemented by a high degree of branching, affects the monomer distribution around the center. Finally, we note that the shape of our measured density profile is in agreement with the results of previous simulational studies employing a variety of microscopic models. The strength of the ordering oscillations close to the molecule’s center depends, however, on the specific model used and in particular on the length of the spacer connecting adjacent monomers in relation to the diameter of the latter.

At distances $r/\sigma_{LJ} \approx 2$, the structure is lost and a smooth decay of $\rho(r)$ to zero is observed. The whole behavior of $\rho(r)$ is indicative of increasing fluctuations for monomers with higher generation number, which is further sustained by the broad density distribution of the outermost generation, shown in Fig. 4 as the dotted line. The $\rho_g(r)$-profile is in agreement with recent SANS-results on the endpoint distribution of fourth-generation dendrimers, obtained by using suitably labeled macromolecules.

We now have a tool at hand to bridge the gap to experimental length scales and to give a microscopic meaning to the model parameter $\sigma_{LJ}$. This is provided via the dendrimer’s radius of gyration, that can be measured both in the simulation and in SANS. Its definition reads as

$$R_g = \sqrt{\frac{1}{N} \sum_{i=1}^{N} (\mathbf{r}_i - \mathbf{r}_{CM})^2}.$$ (21)

In the simulation, we obtain the value $R_g = \bar{R}_g \sigma_{LJ}$, with $\bar{R}_g = 2.518$. Experimentally, this corresponds to the so-called “radius of gyration at infinite contrast,” $R_{g,\infty}$, which has been obtained for the molecules at hand by performing a series of careful experiments at different contrasts, the so-determined gyration radius is $R_{g,\infty} = 1.489$ nm. The simulation model reproduces, then, the real molecule’s radius of gyration with the choice $\sigma_{LJ} = R_{g,\infty} / \bar{R}_g = 0.591$ nm. This result compares favorably to the bond length calculated based on the chemical structure of the molecule under experimental observation. For a typical bond length $a = 1.5$ Å and a Kuhn length $l_K$ of three to four monomer lengths, $l_K \equiv 6$ Å is obtained that agrees very well with the above-determined value of $\sigma_{LJ}$ and thus further supports the interpretation of the latter as the length of a Kuhn segment of the polymer.

Additional information about the internal structure of the dendrimer can be obtained from the pair distribution function

![Graph showing the radial density distribution with respect to the center-of-mass, $\rho(r)$, as a function of $r/\sigma_{LJ}$, and the density profile $\rho_g(r)$ for dendrimers.](image-url)
Can dendrimers be viewed as compact colloids?

G(r), defined in Eq. (4) and depending only on r due to the restoring of spherical symmetry after averaging over all conformers. To this end, we measured the average number of pairs being separated by r and normalized the histograms appropriately in order to obtain G(r). We omit in what follows the trivial δ-function contribution and display in Fig. 5 only the second term in the rhs of Eq. (4). The results further illustrate the statements made above based on the knowledge of the radial density distribution. The highly pronounced peak at r ≈ 0.97σLJ, the equilibrium distance of the Lennard-Jones-FENE potential, arises mainly from the strong correlations between directly connected beads. A considerably less pronounced structure is also seen at r ≈ 2σLJ, stemming from the second neighbors, which are however much more weakly correlated than the first ones. For higher r-values, these correlations are washed out and result in a smoothly decaying curve. As can be expected, the pair distribution function which is restricted to the monomers being members of the outermost (fourth) generation, is also peaked at the typical nearest neighbor distance. The relative height of the peak is much smaller, pointing at the fact that on average the monomers far out fluctuate the strongest, resulting from the facts that (i) their movement is less restricted due to a reduced number of neighbors and (ii) beads of the last generation lack any direct connections among them.

We further measured the form factor F(q) of the molecule by performing the averages given in its definition, Eq. (9), “on the fly” during the simulation. A comparison with the Fourier transformed G(r) yielded identical results, thus providing an independent check of the validity of the procedure. The simulation yields F(q) as a function of the dimensionless variable qσLJ and the identification σLJ = 0.591 nm obtained above through the radius of gyration, allows us to express F(q) in physical units and permits a comparison with experimental data. In the experiment, the total scattering intensity I(q) is obtained, which is normalized at q = 0 as I(q = 0) = Vr, with Vr = 9.818 nm³ being the volume of the dendrimer molecule. Thus, we furthermore rescale the ordinate to satisfy this condition for the simulation data as well. The result is shown in Fig. 6. Clearly, there is excellent agreement between the MC-simulation results and the SANS-data. Only in the range 1.5 nm⁻¹ ≤ q ≤ 2 nm⁻¹ do small deviations exist, but they are within the error bars. We can thus be confident that the model at hand does indeed capture the characteristics of the real dendrimers.

IV. DISCUSSION

We now wish to put into test the degree in which the form factor of the fourth-generation dendrimer can be approximated by Eqs. (11) or (16). Apart from the constant term of unity that corresponds to incoherent scattering, these are both expressions pertaining to molecules with uncorrelated fluctuations between the monomers or to very weak fluctuations in the first place. Adopting these expressions also for molecules in which correlations are present amounts to a mean-field approximation (MFA) of their conformations; here one replaces G(r) by the autoconvolution of p(r).

In Fig. 7, we show the comparison of the form factor...
that the MFA should be valid in this void of any structure. There is, however, no reason to expect defined any more. Moreover, the typical wavelength of the oscillations stemming from the short-range correlations becomes visible at scattering wave vectors above, roughly, \(2.5-3.0\) nm. Nonetheless on this level we can, from this data, conclude that the inherent approximation as discussed above, is very good and thus surmise that the dendrimer does not exhibit exceedingly large correlated fluctuations. On the other hand, it is clear that the question at hand should be further pursued, in particular with respect to first where the fluctuations are the most pronounced in the molecule and second what their absolute value, irrespective of the degree of correlation.

In Fig. 8 we show the form factor in comparison to the MFA in more detail for high values of the scattering wave vector. To make the comparison easier, we have now subtracted the value 1 from the simulation data and we show thus only the coherent part, \(F_{\text{coh}}(q) = F(q) - 1\). Here, significant deviations can be seen, in the sense that \(F(q)\) displays oscillations stemming from the short-range correlations between the particles, whereas the quantity \((1/N)\tilde{\rho}^2(q)\) is devoid of any structure. There is, however, no reason to expect that the MFA should be valid in this \(q\)-domain since here \(q\sigma_{1,1}\) exceeds unity and the condition \(q \cdot \Delta r \ll 1\) is not satisfied any more. Moreover, the typical wavelength of the oscillations of \(F(q)\) seen in Fig. 8 demonstrates that the fluctuations are correlated on the scale of the Kuhn length. We are thus dealing with oscillatory structure in \(q\)-space that becomes visible at scattering wave vectors above, roughly, \(q = 2.5-3.0\) nm\(^{-1}\), and which cannot be easily resolved in the small-angle scattering experiments.

As an additional diagnostic tool for the deviations of the dendrimer from a rigid configuration, we measured the variance of the Fourier-transform of the density operator, \(\Delta \tilde{\rho}(q)\), defined as

\[
\Delta \tilde{\rho}(q) = \sqrt{\langle \tilde{\rho}_q^2 \rangle - \langle \tilde{\rho}_q \rangle^2} = \sqrt{\tilde{\rho}_2(q) - \tilde{\rho}^2(q)}, \tag{22}
\]

where

\[
\tilde{\rho}_2(q) = \langle \tilde{\rho}_q^2 \rangle = \left\{ \sum_{i=1}^{N} \sum_{j=1}^{N} \exp[-i \mathbf{q} \cdot (\mathbf{r}_i + \mathbf{r}_j)] \right\}. \tag{23}
\]

If marked, correlated fluctuations occur in the molecule, we expect significant differences in these two observables to show up. The result is shown in Fig. 9. As can be seen, \(\tilde{\rho}_2(q)\) and \(\tilde{\rho}^2(q)\) are practically indistinguishable. We may thus put forward the notion that the dendrimer does not, in its behavior regarding fluctuations, differ significantly from that of a spherically symmetric object whose constituents show uncorrelated fluctuations. Although this might sound counterintuitive at first sight, there is good grounds for such a notion, since the density profile indicates that the dendrimer is very dense in its inner part. Here, only small fluctuations, showing up for very high \(q\) should occur. As we could already further surmise from the density profile, the fluctuations are the strongest in the outer shell. Here, however, they are the least correlated, since the monomers in the outermost generation are the least connected, with only one bond per particle, inducing only weak correlations.

Recently, a mean-field type theory for the effective interactions between G4-dendrimers has been proposed.\(^{7,8}\) It is based on the inversion of SANS-scattering profiles in the spirit of Eq. (16), in which the form factor \(F(q)\) is used to obtain directly the density profile \(\rho(r)\). This is akin to self-consistent field theories of dendrimers in which each monomer finds itself in the mean-field caused by all other monomers.\(^{35}\) Self-consistent field approaches also result into smooth density profiles and into a loss of correlations in the shape of the scattering profiles.\(^{25,38}\) Since the measured form factor of G4-dendrimers is excellently fitted by a Gaussian function in the measured regime, Eq. (16) leads also to a Gaussian density profile. A second ingredient of the theory is the introduction of a Flory-type monomer–monomer interaction \(v_{\text{mm}}(\mathbf{r}_1 - \mathbf{r}_2) = k_B T v_0 \delta(\mathbf{r}_1 - \mathbf{r}_2)\), with the excluded-volume parameter \(v_0\). Under the assumption that the dendrimers maintain their undisturbed shape even in interacting situations, the above procedure leads then to a Gaussian effective interaction between G4-dendrimers that has been shown to provide an excellent theoretical description of the
Can dendrimers be viewed as compact colloids?

scattering profiles from dendrimer solutions below the overlap concentration, with the choice \( v_0 = 0.076 \text{ nm}^{-1} \). In comparing the measured density profile shown in Fig. 4 with the mean-field prediction of a Gaussian shape, it appears that the latter is not particularly accurate; all ordering effects in the inner region of the molecule are lost. Nevertheless, the remarkable success of the Gaussian effective interaction in conjunction with the present accurate data calls for an explanation.

To this end, we have to remember that in the Flory-view of polymers, every monomer is “chopped down” to a continuous distribution of matter that interacts by means of the \( \delta \)-interaction mentioned above, pretty much as discrete charge matter is replaced by a continuous charge distribution in some circumstances. Thus, we proceed by considering every bead in our model as a uniform distribution of monomeric matter and introduce thereby the density of “effective monomers” inside the bead,

\[
\rho_m(r) = \frac{3}{4 \pi R^3} \Theta(R - r),
\]

where \( R = \alpha_d \beta / 2 \) is the radius of the bead and \( r \) is the distance from its center. Accordingly, the distribution of effective monomers around the dendrimer’s center-of-mass, \( \rho_m(r) \) is given by the convolution

\[
\rho_m(r) = [\rho \otimes \rho_b](r).
\]

In Fig. 10, we compare the density \( \rho_m(r) \) with the Gaussian distribution obtained by the inversion of the scattering data in the mean-field approach of Ref. 8; the two are still considerably different from one another. However, the effective interaction \( V_{\text{eff}}(R) \) between the dendrimers is proportional to a second convolution, namely the autoconvolution of the effective monomer density, i.e.,

\[
V_{\text{eff}}(R) = k_B T v_0 [\rho_m \otimes \rho_m](R).
\]

In Fig. 11, we show the final comparison between the effective interaction obtained by the mean-field theory of Ref. 8 and the one obtained by employing the coarse-grained monomer density \( \rho_m(r) \) of Eq. (25) above. It can be seen that the two are very similar to one another and practically identical at separations between 3 and 4 nm. Since the theory of Ref. 8 was put forward for dendrimers below their overlap concentration, such that the macromolecules slightly overlap only on their periphery, it is clear that the two effective interactions will yield identical results for the structure factor there. Thus, the mean-field approach is once more justified, not only for the conformations of dendrimers but for the effective interactions between the same as well.

V. CONCLUSIONS AND OUTLOOK

In conclusion, we have investigated the structural properties of an isolated fourth generation dendrimer. We calculated the density profile, which could confirm that the dendrimer is a dense object in its inner regions. By measuring the form factor \( F(q) \) of the single dendrimer and a comparison to experimental data, an excellent agreement of simulation and experiment was found. By comparing \( F(q) \) to the squared Fourier transform of the density distribution \( \tilde{\rho}^2(q) \), it was shown that the dendrimer is, on average, a spherically symmetric object whose constituents do not show large correlated fluctuations. This was further underlined by comparing \( \langle \tilde{\rho}_q^4 \rangle \) with \( \langle \tilde{\rho}_q^2 \rangle \).

The fluctuations present in a dendritic molecule as investigated in the present study occur for \( q \approx 2.5-3.0 \text{ nm}^{-1} \). With the structural properties of a single dendrimer of the fourth generation having been investigated, we can now turn our attention to two related questions: first, the systematic dependence of the quantities characterizing dendrimer conformations on the maximum generation number \( g \) and the further evolution of the dendrimers towards the compact colloid limit.37 Second, the question of dendrimer–dendrimer interaction: it will be of major interest whether for small overlaps the Gaussian interaction picture will be confirmed and to which extent it will be modified for more significant overlaps between the two dendritic architectures. To answer these questions, we will resort to molecular dynamics.

FIG. 10. The coarse-grained monomer density \( \rho_m(r) \) defined by Eq. (25) (solid line) compared with the mean-field Gaussian density (dotted line). The latter is obtained by the inversion of the Gaussian form factor measured from dilute solutions of G4-dendrimers.

FIG. 11. Comparison of the effective interaction obtained by Eq. (26) of the text by employing the density profile \( \rho_m(r) \) of Eq. (25) (solid line) with the mean-field result based on a Gaussian profile (dotted line). For completeness, we note that the dotted line is obtained from Eq. (18) of Ref. 8, with \( N = 62 \) monomers and \( v_0 = 0.076 \text{ nm}^{-1} \). This value of \( v_0 \) has also been used to produce the solid curve, according to Eq. (26) of the text.
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