Location of Terminal Groups of Dendrimers: Brownian Dynamics Simulation

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There has been an increasing interest in efforts to understand the solution and bulk behavior of perfectly branched macromolecules (i.e., dendrimers) over the past two decades.[1−3] Theory, simulations, and experimental results give a picture of high generation dendrimers as spherical molecules with a rather monodisperse distribution and uniform segment density in the interior. The spatial distribution and location of the terminal groups, however, remain a challenging problem.

Recently, Topp et al.[4] published the results of small-angle neutron scattering experiments on poly(amido amine) (PAMAM) dendrimers using deuterium labeling and scattering contrast variation. For generation 7 PAMAM the obtained radius of gyration of deuterated terminal units, $R_{g,t} = 39.3 \pm 1.0$ Å, is significantly larger than that for the whole dendrimer, $R_{g,w} = 34.4 \pm 0.2$ Å. These data were used to conclude that the terminal groups within generation 7 PAMAM are concentrated near the periphery. This result is inconsistent with previous computer simulations.[5,6]

In this paper we report Brownian dynamics simulation results of a dendrimer with branching at every bead (model A) or at every other bead (model B). Beads possess a friction coefficient ζ and are connected by rigid rods of length l. The total number of generations for a given dendrimer is denoted by g where a $g = 0$ dendrimer contains a central core with three (model A) or six (model B) rigid bonds. Up to the $g = 6$ generations are simulated. Torsional and valence angle potentials are not employed, and the Ermak−McCammon[7] equation of motion in the presence of hydrodynamic and excluded-volume interactions is used. A procedure proposed by Murat and Grest[6] is implemented to generate the initial configurations. The dendrimer is allowed to equilibrate for 500 000 time steps. Following equilibration, production runs are performed consisting of 400 000−3 000 000 time steps, depending on the size of the dendrimer. Further simulation details are found within a previous publication.[8]

For the largest $g = 5$ model B dendrimer of the present study, the normalized radius of gyration comprised only of terminal units, $R^*_{g,t} = R_{g,t}/l$, is 5.4 ± 0.1. This is larger than the normalized radius of gyration of the whole dendrimer, $R^*_{g,w} = R_{g,w}/l$, which is 4.9 ± 0.1 using all the beads within the dendrimer. The relative difference,

$$\Delta = \frac{R^*_{g,t} - R^*_{g,w}}{R^*_{g,w}} \quad (1)$$

is equal to $\Delta = 0.10 \pm 0.03$ for the simulated data and $\Delta = 0.14 \pm 0.03$ for the neutron scattering data of Topp et al.[4] for a generation 7 PAMAM dendrimer. Figure 1 gives the radial distribution function of the terminal groups for the $g = 5$ model B dendrimer and a $g = 6$ model A dendrimer and the radial distribution function for all segments for the corresponding dendrimers. The area beneath each of the curves denoted by open symbols is equal to the number of terminal groups within the given dendrimer. Similarly, the area beneath each of the curves denoted by closed symbols is equal to the number of beads within the given dendrimer. It is seen that segments belonging to the last generation are dispersed throughout the *whole* molecule for both models except in the region nearby the core. The curves actually plateau at their maximum values around x values of approximately 2−4. This latter result is in agreement with previous simulations[5,6] and contradicts the conclusions of Topp et al.[4] about location of these groups near the surface. It is important to emphasize that this observation is true for the $g = 5$ model B dendrimer where it is known that $R^*_{g,t} > R^*_{g,w}$. The remaining portion of this paper addresses the extent to which the location of terminal groups within a dendrimer can be determined through the comparison of radii of gyration.

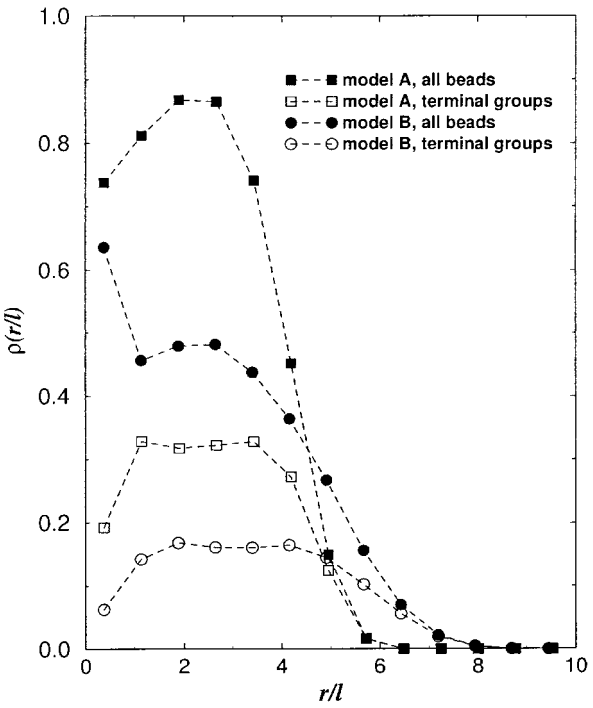

Figure 1. Dependence of the radial distribution function of beads on the distance from the center of mass for a model A and a model B dendrimer. The distribution functions of the terminal groups only are shown also.

Let us approximate the dendrimer as a rigid sphere with an effective radius R. In light of the data within Figure 1 one can use the following approximation for a

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decreasing density distribution of monomers inside the dendrimer

$$\rho_w = 1 - (r/R)^n, \quad 1 \le n \le \infty \tag{2a}$$

where r is a distance from the center of mass, $0 \le r \le R$. Similarly, for the density distribution of terminal groups

$$\rho_t = C(1 - (r/R)^n), \quad 1 \le n \le \infty, C < 1 \tag{2b}$$

where $R_0 \le r \le R$ and R_0 is some fixed distance from the center of mass. The general form of (2) is a suitable fitting function for the data in Figure 1. When $n = 1$, the density linearly decreases with increasing distance from the center of mass. As $n \to \infty$, both functions tend to a uniform distribution.

For an AB_2 type dendrimer, 50% of the total dendrimer mass is constrained to the last generation. Using the density distributions (2), it is easy to calculate the mass of the dendrimer, M_w, and the mass of the terminal groups, M_t. Constraining M_t to be $0.5M_w$ leads to the following condition on the normalization constant C

$$C = \frac{1/2n}{(1 - x^3)(n + 3) - 3(1 - x^{n+3})} \tag{3}$$

where $x = R_0/R$, $x < 1$.

The radius of gyration for a dendrimer using eq 2a is

$$R_{g,w} = \sqrt{\frac{3(n+3)}{5(n+5)}}R \tag{4}$$

As $n \to \infty$, $R_{g,w}$ tends to the result for a sphere with a uniform density distribution, $R_{g,w} \to (3/5)^{1/2}R$. Assuming the terminal groups are distributed within a sphere of radius R at distances r such that $R_0 \le r \le R$, the radius of gyration of terminal groups with a density defined by eq 2b is

$$R_{g,t} = \left[\frac{3(n+3)\{(1-x^5)(n+5) - 5(1-x^{n+5})\}}{5(n+5)\{(1-x^3)(n+3) - 3(1-x^{n+3})\}}\right]^{1/2} R \tag{5}$$

Equations 1, 4, and 5 afford

$$\Delta = \left[\frac{(1-x^5)(n+5) - 5(1-x^{n+5})}{(1-x)(n+3) - 3(1-x^{n+3})}\right]^{1/2} - 1 \tag{6}$$

When Δ is 0.10 and assuming a distribution of groups given by eq 2, it follows that $x = 0.44$ when $n = 1$ and x approaches a limiting value of 0.64 as $n \to \infty$. Similarly for $\Delta = 0.14$, $x = 0.50$ when $n = 1$ and approaches a limiting value of $x = 0.73$ as $n \to \infty$. These results emphasize an important point when attempting to infer the location of terminal groups based solely on the information that $R^*_{g,t} > R^*_{g,w}$. Under these conditions, the terminal units are still able to be located within the interior of the dendrimer.

Further evidence that radii of gyration are not always a safe measure of the location of terminal groups is through the cumulative distribution functions plotted in Figure 2. The open symbol curves reflect the cumulative sum of terminal beads at given values of r/l from the given dendrimer's center of mass. As indicated previously, this curve is expected to plateau at 0.5 when normalized by the total number of beads within the dendrimer. The filled symbol curves reflect the cumulative sum of dendrimer beads at given values of r/l from the given dendrimer's center of mass. This curve is expected to plateau at 1.0 when normalized by the total number of beads within the dendrimer. It is clearly seen from this figure that about 60% (i.e., 0.30/0.50) of all model B terminal groups are located at values $R_{g,w}/l = 4.9$ from the center of mass or less and about 74% (i.e., 0.37/0.50) are located at values $R_{g,t}/l = 5.4$ from the center of mass or less.

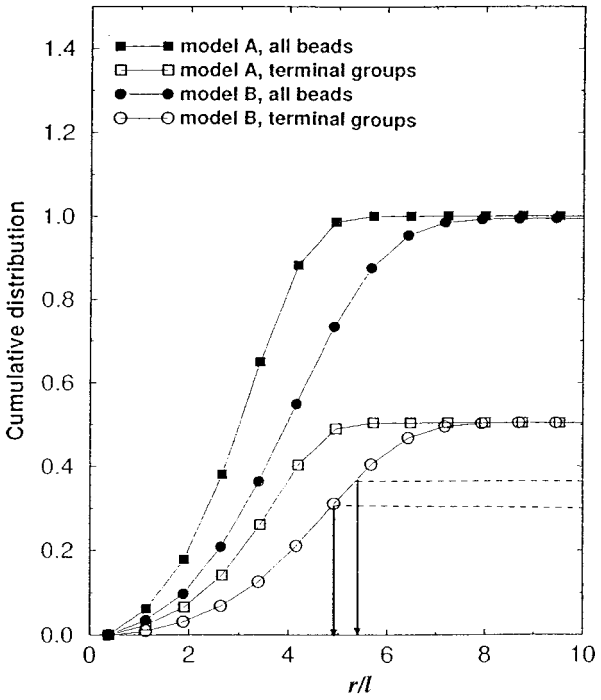

Figure 2. Dependence of the cumulative distribution function of beads on the distance from the center of mass for a model A and a model B dendrimer normalized to the total number of beads. The cumulative distribution functions of the terminal groups only are shown also. Arrows indicate the distance from the center of mass when $r = R_{g,w}$ and $r = R_{g,t}$ for a $g = 5$ model B dendrimer.

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