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Improved simulation method for the calculation of the intrinsic viscosity of some dendrimer molecules

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Abstract

A method previously proposed for calculating the radius of gyration and the intrinsic viscosity of dendrimers is modified to give a more accurate description of existing experimental data. The new method includes some features that were not previously considered, namely: (a) a correction term to take into account the contribution of individual friction beads, whose volumes are not negligible in comparison with the molecule size, (b) a realistic distribution of internal angles between successive beads that define branching points in the molecule, (c) a distribution of distances between branching points computed from molecular dynamics simulations of a small dendrimer with explicit solvent. Modification (a) alone is able to give a good description of the experimental results obtained for polypropylene-imide with a diaminobutane core in water, while the simultaneous use of the three modifications is needed to adequately describe the experimental data of monodendrons and tridendrons of polybenzylether in THF.

Keywords: Dendrimers; Monte Carlo simulation; Intrinsic viscosity

1. Introduction

The peculiar physical properties of dendrimers constitute one of the reasons explaining the current interest for this type of molecules [1,2]. Different theoretical models and simulation methods have been devoted to understand these properties. Thus, Monte Carlo (MC) [3,4], Brownian dynamics [5] and molecular dynamics (MD) methods [6–8] have been applied to different ideal and atomistic representations of the dendrimer molecules. From the experimental point of view, a particularly dramatic effect is observed in the experimental data of the intrinsic viscosity, $[\eta]$. This property is usually employed as a standard characterization technique in conventional polymers due to its simplicity from the experimental point of view and its direct relation with the molecule size. In the case of dendrimers, however, the variation of $[\eta]$ with molecular weight, or with the generation number, g, often exhibits a maximum, whose location depends on the dendrimer chemical structure.

In previous work [9], we proposed a computational method to describe this maximum. As explained in detail in Ref. [9] a first description of the maximum correlates this feature with a minimum in density. When the number of generations is low, dendrimer growth leads to a significant congestion of units for increasing g. It is customary to describe the variation of the mean radius of gyration, R_g, as a function of the molecular weight, M, as $R_g \approx M^{\nu}$, where ν is an effective exponent. It turns out that larger dendrimers in most solvents show an effective exponent ν close to 0.30 [1] which is about half of what is expected for a flexible polymer in good or theta solvents. This exponent is usually smaller than the 1/3 prediction

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for a collapsed polymer, modelled as a compact sphere. Assuming constant permeability, the intrinsic viscosity is inversely proportional to density, i.e., $[\eta] \approx R_g^3/M$. Therefore, this assumption gives $[\eta] \approx M^{3\nu-1}$, implying that any value of ν smaller than 1/3 yields a decrease of intrinsic viscosity at higher generations. However, a precise location and quantitative prediction of the viscosity maximum also have to be taken into account the more subtle variation of the solvent permeability in these relatively small molecules. Therefore, a simple lattice or bead chain model, similar to those used to describe universal properties in polymer systems, is not able to give an acceptable quantitative description of the experimental viscosities for the available range of values of g unless some information about structural details of the real molecules is incorporated.

Our method is based on a model for Monte Carlo (MC) simulations that considers a bead for each branching point and an additional bead in the middle point between them. Since the main aim of the present publication is to incorporate some improvements to this method, we describe it briefly now. The beads' positions are changed by a ‘‘single-bead jump’’ algorithm in which the distances between neighbouring units and neighbouring branching units follow a broad distribution in a range of realistic values. The limits of this range are set according to the results obtained by relatively short molecular dynamics (MD) simulations previously performed for an atomistic model. (It is shown that these MD simulations would require much more computational time to directly provide accurate viscosity results.) The MD simulations were performed in the absence of solvent molecules. However, the van der Waals' cutoff of the force field was modified from its default value to give an approximate description of the solvent effects. With this aim, the cutoff value was reduced and fitted to give the best reproduction of the experimental radii of gyration corresponding to different generations of dendrimer molecules in the considered solvent. The MC model also introduces a rigid-spheres' potential to avoid overlapping of non-neighbouring beads in terms of a distance, σ, which is set to yield the closest reproduction with the MC samples of the existing data for the mean radius of gyration, for a given set of dendrimer molecules and different generation numbers [1,10,11]. Accordingly, our method can somehow be considered multi-step, since some parameters derived from a MD simulation with an atomistic model are employed in a coarse-grained model devised to perform MC calculations.

The intrinsic viscosity calculations are performed using the ‘‘lower bound’’ computational scheme devised by Fixman [12]. In these calculations, we assume that the molecules are constituted by friction beads centered in the branching point units. A value for the friction radius of the bead, r_f, is needed to evaluate the viscous drag forces experienced by the beads to describe hydrodynamic interactions. This parameter is set to give the closest quantitative reproduction of the experimental viscosity data (though this fit alone is unable to warrant a good reproduction on the maximum location for this property and sometimes the quantitative agreement can be only limited to a narrow range of generation numbers). In the lower-bound calculations, the results are obtained by averaging some intermediate terms over a statistical sample. These terms are products of different matrices. We have to evaluate the averages $\langle \mathbf{R}_i^c \cdot \mathbf{R}_j^c \rangle$, obtained from the vectors defining the position of the beads from the center of masses. Also, we need the pre-averaged hydrodynamic interaction matrix of the standard Rouse–Zimm theory, whose non-diagonal elements depend on reciprocal averages of distances between different beads, $\langle R_{ij}^{-1} \rangle$. A more elaborate term includes the explicit calculation of the elements of the Rotne–Prager–Yamakawa tensor, depending on distances between beads, R_{ij}, and direct products of vectors between beads, $\mathbf{R}_{ij}\mathbf{R}_{ij}$. These elements should be obtained for each conformation. A detailed description of the numerical procedure to obtain a lower bound for the intrinsic viscosity can be found in Ref. [13]. In our case, the sample is constituted by randomly selected conformations resulting from the MC simulations described above.

Alternatively, it is possible to use the Kirkwood–Riseman–Zimm method to calculate the intrinsic viscosity for instantaneously rigid conformations. The results from this method would provide an upper bound of this property when averaged on a similar conformational sample. Differences between the upper- and lower-bound results are usually small, but the lower-bound method is significantly more efficient from the computational point of view for the treatment of many-bead flexible molecules, since the upper-bound algorithm requires the numerical inversion of a matrix for each conformation [2].

Our procedure was able to give a fair quantitative description of the intrinsic viscosity data of some dendrimer molecules. Thus, for polyamidoamine dendrimers with a ethylenediamine core (PAMAM–EDA), the simulation results were compatible with the somehow scattered experimental data of these dendrimers in water [1] (the relatively large non-systematic changes in the variation of the $[\eta]$ vs g data reported in the bibliography do not allow us to expect that a better agreement can be reached with any improved model. Consequently, these dendrimers are not considered in the present work). For the case of polypropylene-imide with a diaminobutane core (PPI–DAB) in water we considered a set of data [10] that include four generation numbers, not far from the results obtained independently for the same dendrimers in methanol [14]. Also, two additional bibliographic data corresponding to successive generations have been reported [15]. The latter data are, however, in disagreement with the larger set and show a difference between the values higher than in any other available set of $[\eta]$ data for dendrimer systems. The simulation results showed a qualitative description of the more consistent experimental set of data, but with significantly smaller quantitative values. Consequently, we were not able to offer an adequate agreement with the experimental data for the PPI–DAB case.

The best performance of our previous method was achieved for the case of monodendrons and tridendrons of polybenzylether (PBzE). We performed a comparison with an experimental set of $[\eta]$ vs g data obtained time ago for tetrahydrofuran (THF) solutions [16] and a reasonable agreement was obtained for both types of molecules. In spite of this general agreement, some consistent differences between the experimental and simulation data still remained. Thus, the simulation results clearly overestimated the experimental data for the smallest values of g. Moreover, the same overestimation is also shown for the highest g in the case of the tridendrons, where the viscosity peak is more prominent. These differences indicate the convenience of devising an improved method, where more details of the molecular structure are incorporated.

In this work, we describe some refinements with which we have been able to achieve a significantly better agreement between experimental and simulation data for PPI–DAB in water and for the monodendrons and tridendrons of PBzE in THF. In the first stage, we have introduced a simple correction to the simulation data, based on adding a term representing the contribution of an individual friction bead which is absent in the Kirkwood–Riseman–Zimm or Fixman treatments of long linear polymers for Monte Carlo samples, but may be important if the number of beads is small. In these treatments, the expressions employed to compute the intrinsic viscosity give a zero value when they are particularized for a single bead. The reason is that, in the theories, the frictional drag forces are assumed to act on the centers of the spherical beads, when they are actually distributed over its surface. The intrinsic viscosity is calculated from a surface integration of terms of the generic form $\mathbf{r} \times \mathbf{F}$, where $\mathbf{F}$ is the force on a surface element, and $\mathbf{r}$ is its position vector; in the standard treatment the continuous integration is replaced by a discrete sum over the bead centers. With this correction, the intrinsic viscosity of a single bead is not zero but has the correct value corresponding to a rigid sphere with the chosen friction radius. Details on the justification of this correction as the 0th-order term to the conventional Kirkwood–Riseman calculation of the intrinsic viscosity, which accounts for hydrodynamic interactions with terms of order -1 in interbead distances, can be found elsewhere [17]. Some kind of correction of this type should actually be introduced in all systems but the correction is commonly ignored in the case of long polymer chains, where the hydrodynamic volume is much higher than the beads' individual contribution. The correction should obviously be also pertinent for our results which provide a lower-bound estimation for the considerable smaller dendrimer molecules but it was ignored in our previous treatment. We anticipate that this modification alone is adequate to correctly describe the experimental intrinsic viscosities of PPI–DAB.

In our previous simulations we obtained a fair agreement between experimental data and our previous MC results for the PBzE dendrimers. However, we will see that the introduction of the single-bead correction actually worsens this agreement, especially in the case of tridendrons. Therefore, assuming that a bead correction is pertinent for all types of small dendrimer structures, it is apparent that a good description of the PBzE structures should incorporate further details to the molecular model. These molecules have particularly rigid connections between their branching points. Consequently, as a first refinement in the MC model should include a realistic distribution of the internal angle Θ, formed by the connections between successive branching points. This improvement will be proved to be sufficient to provide again a fair agreement between MC and experimental results.

Furthermore, it should be considered that the large interactions between the phenyl groups are conditioning the conformational characteristics of the whole molecule, particularly the distribution of distances between branching points, separated by a few flexible bonds. The presence of real solvent molecules, especially if they are anisotropic rings, may partially shield these interactions giving more flexibility to the bonds and, therefore, smoothing the distribution of distances. We have verified this point, obtaining a new distribution of distances between neighbouring branching units (or branching units and ends) from MD simulations that explicitly include solvent THF and incorporating these data to the MC simulations. (Previously, we obtained the distance distribution from MD simulations performed for single molecules without solvent.)

With all these new features incorporated to the model, we have finally been able to obtain a good description of the experimental data corresponding to radius of gyration and intrinsic viscosity for several generations of PBzE dendrimers.

2. Computational methods

Our original method was previously detailed [9] and was summarized above. It incorporates data to describe the range of realistic distances between neighbouring units and also between neighbouring branching units. These data were obtained from MD simulations for single dendrimer molecules. A description of the particular chemical structures of the considered molecules, and details on the choice of units and the (non-standard) definition of the generation numbers that are also employed in the present work can also be found in Ref. [9].

For models with identical beads as in our case, the simplest correction for the contribution of individual beads to the intrinsic viscosity [17] consists in adding the viscosity of a single rigid sphere obtained from the Einstein formula to the "raw" simulation viscosity, $[\eta]_{\mathrm{sim}}$, which we computed with the lower-bound method. This way

$$[\eta]_{\mathrm{corr}} = [\eta]_{\mathrm{sim}} + (10/3)\pi r_{\mathrm{f}}^3/m_{\mathrm{u}} \tag{1}$$

where m_{u} is the mass of the unit, obtained from the molecular weight of the chemical groups engulfed by each friction bead. m_{u} can be directly computed from total number of friction units $(N - N_{\mathrm{i}})$ and the molecular weight of the dendrimers reported in Table 1 of Ref. [9]. Therefore, the procedure to calculate the $[\eta]_{\mathrm{corr}}$ values is: (1) to select a value of the friction radius, (2) to compute $[\eta]_{\mathrm{sim}}$ with the lower-bound approximation, i.e., performing the adequate averages from a statistical sample extracted from the Monte Carlo simulation, and (3) to add the individual bead correction, contained in Eq. (1), which is slightly changing with the generation number for a given type of dendrimer. This process has to be repeated with several r_{f} values until the best description of the experimental data (at least in a particular range of values of g) is achieved. Therefore, the MC configurational samples obtained in our previous work can be employed again to obtain $[\eta]_{\mathrm{sim}}$ and $[\eta]_{\mathrm{corr}}$ and new simulations are not required if this correction alone is able to reproduce the experimental data. In theory, a similar correction term for the individual bead should be added to the simulation data to calculate the corrected squared radius of gyration [18]. However, we have verified that this correction is significantly smaller than that in the intrinsic viscosity case and, actually, it is practically irrelevant in the fit of distance σ to reproduce the existing experimental data of R_g.

In our previous calculations [9], the MD simulations covered several generation numbers and were performed for single molecules. Since flexible molecules in the vacuum tend to collapse, we had to impose a reduction of the potential cutoff to avoid this trend [19]. In order to incorporate solvent effects to our model, we have performed new MD simulations for the system constituted by the small monodendron of PBzE with $g = 2$ immersed in a bath of THF molecules. With this aim, we use the "Amorphous Cell" module of the "Materials Studio 4.0" software package [20]. With this software, we prepare a simulation box with the selected $g = 2$ dendrimer and 50 solvent molecules. The box size is fixed to yield a system density of 0.9 g/cc similar to that of THF at room temperature. The resulting system is conveniently thermalized with a series of short MD runs at different temperatures. Finally we perform a MD run over 4×10^6 steps, equivalent to 4 ns, which gives us a trajectory useful to analyse the properties. The MD runs are performed with module "Discover". For the MD simulations we have used the same procedures and parameters described in our previous work [9], except in the case of the potential cutoff value. Now, we employ the relatively high fixed cutoff default value of 9.5 Å, instead of the lower fitted values previously used for the single molecules. We have computed the distance distribution over 400 frames (each one collected after 10^4 MD steps). This function has been obtained for the $g = 2$ monodendrons by averaging over the 4 distances joining the non-central branching units and the end units.

In addition to considering a distribution of distances, the modified model for the PBzE molecules proposed in this work also uses distribution of angles between neighbouring branching units, Θ. (In these molecules, the angle formed by two branching units and the middle point between them is rigid.) The distribution is estimated from the analysis of MD simulations performed with an atomistic model for the $g = 2$–4 dendrimers and it has been computed by taking into account the different angles formed by the connected branching points or end units. The estimated results are introduced as input data in a new MC code that takes care of the distribution of angles between neighbouring branching points. Specifically, we have 9 new probability checks per branching bead move in the most general case of an inner branching unit not located in the dendrimer core. These new probabilities correspond to the angles altered due to length and orientation changes in the connecting segments between the bead and neighbouring branching points. We consider the three angles that are centered by the given bead. Also, we have two new angles formed by the bead, the preceding branch unit and two other branch points connected with this unit. We have four more new angles corresponding to the bead, the two successive branch units and the other two branch points connected with them.

3. Results and discussion

The results for the radial distribution of distances between the branching points, b_c (placed in the center of the phenyl rings), $p = 4\pi b_c^2 F(b_c)$, for the $g = 2$ monodendron PBzE dendrimer molecule are given in Fig. 1. $F(b_c)$ is the punctual distribution and the functions are normalized so that integration over the spatial coordinates gives 1. Consistently with the results previously obtained for larger dendrimers [9], the distance distribution obtained with the single molecule shows a peak close to the upper limit of the distance range, consistent with a "*trans*" conformation of the three flexible bonds linking two successive phenyl groups. However, the distribution obtained for the system with explicit solvent is more symmetric and flatter than that obtained in the absence of solvent, which implies a certain increase of "non-*trans*" conformations. A significant increase (about 10%) in the statistical weight of the "non-*trans*" conformations due to the presence of solvent molecules has been verified in the simpler case of *n*-butane solutions [21]. In the present case, the solvent is constituted by anisotropic ring molecules. These molecules may partially screen out the strong interactions between phenyl groups which strongly condition the distribution of distances between branching points. Consequently, it is reasonable to assume that the solvent effect can be magnified.

In Fig. 2 we present the distribution of −cos(Θ) in six equally spaced intervals (equivalent to the mean probability in these intervals). The angle distribution shows a clear peak

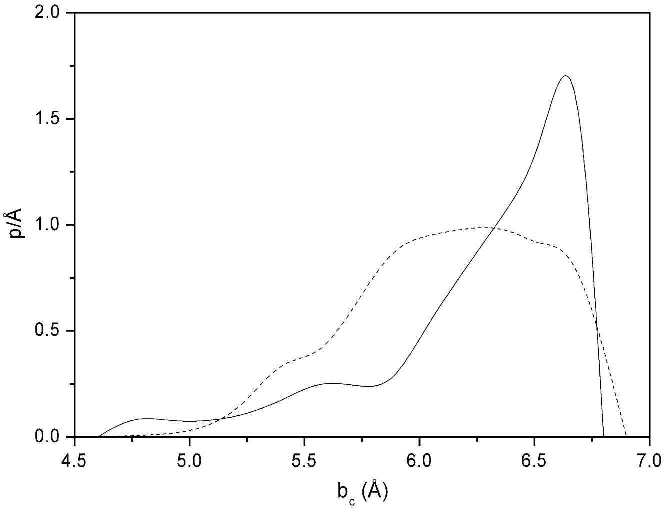

Fig. 1. Distribution of distances between the non-central branching points and ends corresponding to a $g = 2$ PBzE dendrimer, expressed as probability per Å, $p(b_c)$. These results have been obtained from MD simulations for the following systems: (a) single dendrimer, solid lines; (b) dendrimer in THF, dashed line.

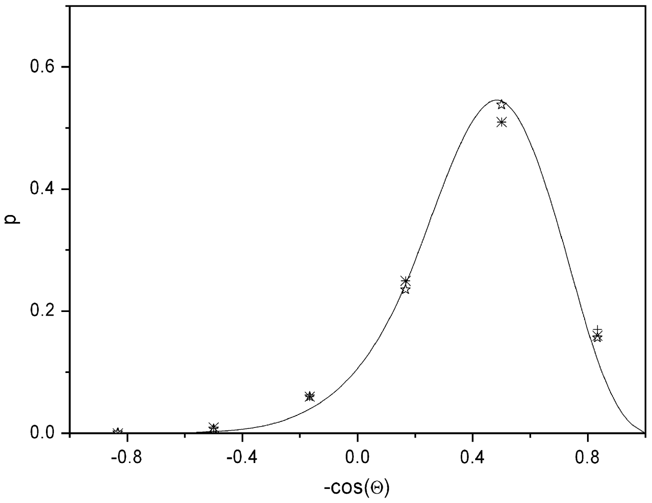

Fig. 2. Distribution of branching point angles between six interval of cos(Θ) used as input for the MC simulations, expressed as the normalized probability in each one of these intervals, p (smooth line). The distribution has been estimated from MD results for the dendrimer with $g = 2$, stars; $g = 3$, ×; $g = 4$, +.

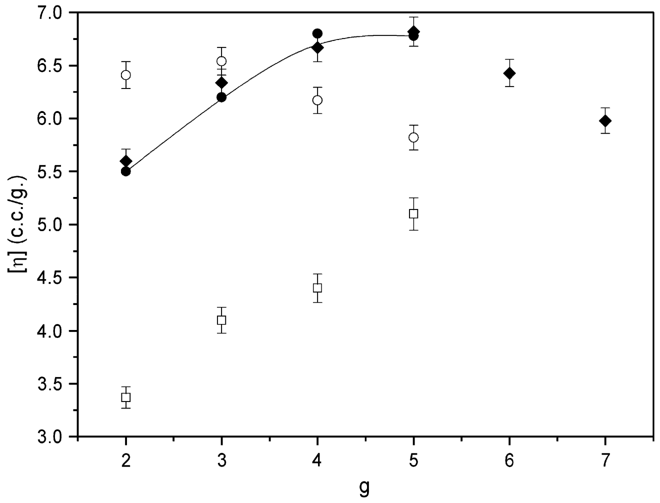

Fig. 3. Simulation and experimental (filled circles) intrinsic viscosity results for the PPI–DAB dendrimers. The simulation data correspond to the MC conformational sample reported in Ref. [9], $\sigma = 4.0$ Å. Open circles: results from Ref. [9], $r_f = 4.60$ Å; open squares, results from Ref. [9], $r_f = 2.55$ Å; filled diamonds: results with the single-bead correction, $r_f = 2.65$ Å. The line is a spline showing the general trend of the experimental data. Experimental data are taken from Ref. [10].

close to $-\cos(\Theta) = 0.5$ (i.e., $\Theta = 2\pi/3$). It is observed that the results obtained for the angle distribution in single dendrimers with different generation numbers are very close. Actually, we have verified that introducing moderate changes to the angle distributions does not significantly affect the final results. (Only the distributions with a flat shape yield substantially different Monte Carlo averages.) Therefore, we assume that the variation of the distribution with the generation number, topology, the position of the branching unit inside the molecules or specific details in the MD procedure cannot change much the final results. Consequently, a single angle distribution function is used in all our MC calculations for the PBzE dendrimers. It should be considered that the consideration of different types of angle distributions would add a non-desirable complexity to the model.

As we have explained above, the method that we have previously proposed was able to give a qualitative variation of the intrinsic viscosity vs g similar to that exhibited by the most consistent experimental set of data for PPI–DAB [10]. However, the friction radius employed to obtain this qualitative agreement rendered quantitative simulation values that were consistently and significantly smaller than the experimental values of $[\eta]$ (see open squares in Fig. 3). On the other hand, higher values of the friction radius give results quantitatively closer to the experimental data but showing a substantially different trend (open circles in Fig. 3). (This case clearly shows that a simple fit of r_f cannot describe the experimental data unless a correct theoretical procedure is employed.) Accordingly to these conclusions, it seems that the introduction of the correction for individual beads according to Eq. (1) may be particularly useful in this case. In Fig. 3 we also show the $[\eta]$ results obtained from the same MC samples obtained in Ref. [9] for these molecules with $\sigma = 4.0$ Å, and application of Eq. (1) with the value $r_f = 2.65$ Å (filled diamonds). A good accordance is observed between the simulation results and this experimental set, in spite that we do not consider angle restrictions and we are not introducing a solvent-dependent distance distribution. Therefore, we conclude that the model employed in our previous work can accurately reproduce the $[\eta]$ vs g behaviour. This agreement for PPI–DAB might be extended for any other dendrimer with a not very rigid chain and not too long segment between the branching points, once the individual bead correction term is introduced.

A comparison between the experimental data in THF [16] and different MC results is shown in Fig. 4 for the intrinsic viscosity of the PBzE monodendrons. A similar comparison is included in Fig. 5 for the PBzE tridendrons. The simulation results previously obtained with the original method, which did not include individual bead corrections (open circles in Figs. 5 and 6), showed a fair agreement with the experimental data using a single value of r_f for monodendrons and tridendrons, $r_f = 4.65$ Å. (However, this value is unrealistically high when compared with the range of distances between branching points and some discrepancies with the experiments are observed both for the lowest and highest generation numbers.) In Figs. 4 and 5 we also show the results obtained now with the MC samples that we have previously generated ($\sigma = 3.5$ Å) and the correction term corresponding to the common friction radius $r_f = 2.65$ Å, for monodendrons and tridendrons (open squares). Although the simulation results for monodendrons in Fig. 4 are still in reasonable accordance with the experimental data, it is observed in Fig. 5 that there is a strong disagreement between the general trend of the simulation data and the experiments for tridendrons of high generation number. (This illustrates again that the fit of r_f may not lead to a reasonable agreement between MC results and experimental data unless the correct features are introduced in the numerical method.) Therefore, if we want to consistently

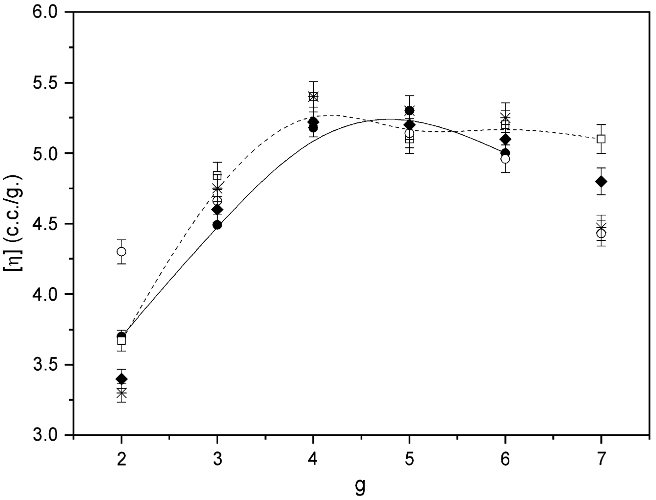

Fig. 4. Simulation and experimental (filled circles) intrinsic viscosity results for the PBzE monodendrons. The simulation data correspond to different types of calculations. Open circles: results from Ref. [9], $\sigma = 4.0$ Å, $r_f = 4.65$ Å; open squares: results from the conformational sample of Ref. [9], but with the single-bead correction, $r_f = 2.65$ Å; stars: results with the single-bead correction and the distribution of angles between branching points, $\sigma = 1.2$ Å, $r_f = 2.37$ Å; filled diamonds: results with the single-bead correction, the distribution of angles between branching points and a distribution of distances calculated from explicit solvent MD, $\sigma = 0.5$ Å, $r_f = 2.60$ Å. The solid and dashed lines are splines corresponding to the experimental data and the MC with only the single-bead correction, respectively, and show the general trend of these data. Experimental data are taken from Ref. [16].

introduce the individual bead corrections which have been revealed successful for the PPI–DAB case, the molecular model for the PBzE molecules clearly needs further improvements.

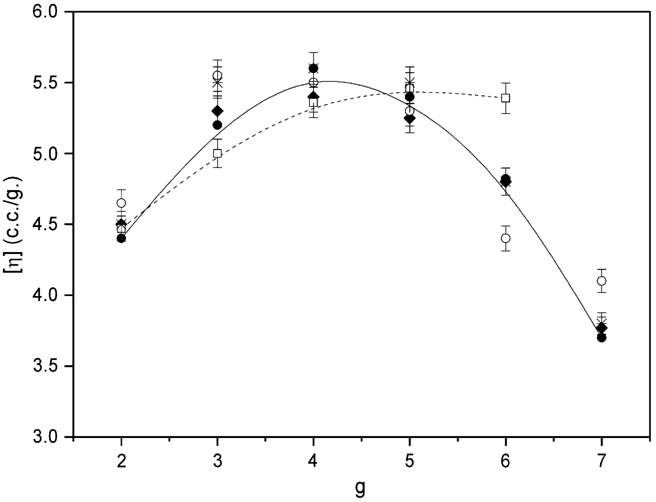

Fig. 5. Simulation and experimental (filled circles) intrinsic viscosity results for the PBzE tridendrons. The simulation data correspond to different types of calculations. Open circles: results from Ref. [9], $\sigma = 4.0$ Å, $r_f = 4.65$ Å; open squares: results with only the single-bead correction, $r_f = 2.65$ Å; stars: results with the single-bead correction and the distribution of angles between branching points, $\sigma = 1.2$ Å, $r_f = 2.60$ Å; filled diamonds: results with the single-bead correction, the distribution of angles between branching points and a distribution of distances calculated from explicit solvent MD, $\sigma = 0.5$ Å, $r_f = 2.60$ Å. The solid and dashed lines are splines corresponding to the experimental data and the MC with only the single-bead correction, respectively, and show the general trend of these data. Experimental data are taken from Ref. [16].

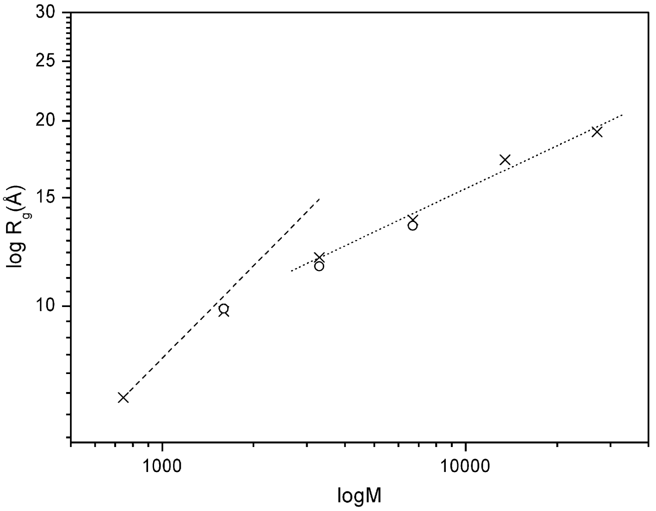

Fig. 6. Log–log representation of the mean radius of gyration vs molecular weight for the PBzE monodendrons. Crosses: MC results. Dashed line: $\nu = 0.5$ prediction for a flexible polymer. Dotted line: linear fit of the last 4 points, $\nu = 0.23$. Circles: experimental data (Ref. [11]).

The most significant feature of the angle distributions for the PBzE monodendrons as shown in Fig. 2 is the sharp peak close to 4π/3. Considering the three angles corresponding to a single intermediate branching unit (i.e., a unit not placed in the molecule core or in end groups) the distribution implies that this unit, the preceding unit and the two successive branching points are near to be coplanar. This special disposition is explained by the geometry of the bulky and anisotropic phenyl rings associated to the branching units and the short link between them (in this link, only a O–CH_2 bond is not rigidly connected to the ring structures). Therefore, the main contribution to the molecule flexibility is provided by the fluctuations in the orientation of every ring with respect to the bond joining it to the methylene unit of their preceding branch. This orientation automatically defines the orientation of the bonds joining the ring to the oxygen atom in the two successive branches.

When an angle distribution consistent with this description is included as input in the Monte Carlo calculations, the results differ significantly from those calculated without any restriction for the distribution of the angles between branching points. Specifically, the relatively large radius of gyration obtained experimentally for the $g = 3$ dendrimer [11] is only reproduced when the angle distribution is introduced in our model (see Fig. 6). On the other hand, in the case of the monodendrons with higher generation number, our lower choices of σ ($\sigma = 1.2$ Å or smaller) for the MC simulations with angular distribution always yield values for the radius of gyration that are noticeably above the experimental data (see Table 1). The intrinsic viscosity results are represented by the stars in Figs. 4 and 5. It can be observed that, with this modification, the performance of the [η] simulation data is reasonable. However, we should remark that, in this particular case, the best agreement with the experimental data is obtained with two slightly different values of the bead frictional radius, $r_f = 2.37$ Å for

Table 1
Mean radius of gyration (Å) for PBzE molecules in THF

g	Monodendrons				Tridendrons	
	MC simulation			Experimental	MC simulation	
	a	b	c		a	c
2	5.9	7.1	7.1		7.5	8.0
3	8.5	9.7	9.8	9.9	10.0	10.9
4	11.1	12.3	12.0	11.6	12.7	13.4
5	13.9	14.8	13.8	13.5	15.9	15.9
6	17.1	16.5	17.3		19.1	18.6
7	20.8	20.6	19.2		23.0	21.1

a – from Ref. [9]; b – MC results including distribution of angles, $\sigma = 1.2$ Å; c – MC results including distribution of angles and distribution of distances obtained from MD simulations with explicit THF solvent, $\sigma = 0.5$ Å. Statistical error bars are always smaller than 0.2 Å. Experimental – from Ref. [11].

monodendrons and $r_{\mathrm{f}} = 2.60$ Å for tridendrons. Due to all these remaining deficiencies, we have explored other features that may have a substantial contribution in the MC calculations, yielding a more consistent reproduction of all the different experimental data. Nevertheless, we should also point out that, compared with the MC data for the intrinsic viscosity obtained previously without the single-bead correction (open circles), a moderately better agreement with the experimental data is actually found for the monodendrons at low g and for the tridendrons at high g when both the single-bead correction and the angle distribution are considered.

Investigating the influence of other simple modifications for the PBzE model, we have also verified that the important differences shown in Fig. 1 for the distance distributions obtained for the dendrimer alone and for the system with explicit solvent have a non-negligible influence on the MC final results. In particular, the distance distribution obtained with explicit solvent gives a close description of the experimental data for the radius of gyration and intrinsic viscosity. In Figs. 4 and 5 we include the MC results obtained considering this distribution (filled diamonds). A remarkable agreement is observed between simulation and experimental data of monodendrons and tridendrons, both with a common value of the friction radius $r_{\mathrm{f}} = 2.60$ Å. In most cases the differences between the two sets of data are within the error bars. Only the simulation point for the $g = 3$ monodendron shows a discrepancy with the experimental result, though an improvement with respect to the performance of the original model is also observed for this particular dendrimer. As we have been describing in the preceding paragraphs, the simulation calculations now include the individual bead correction corresponding to this friction radius, the realistic angle distribution and the distance distribution extracted from a dendrimer–solvent system. The hard-spheres' distance parameter σ in the MC simulations was set to the value $\sigma = 0.5$ Å, which reproduces the existing experimental radius of gyration for the different generation numbers for the monodendrons [11] (see Table 1). This value is very small and contrast strongly with the large value fixed in our previous work, $\sigma = 3.5$ Å, that reproduced more closely the radius of gyration when the realistic distribution of angles was not included. We have verified that a moderate increase of the value of σ in our present calculations yields a substantial overestimation of the radius of gyration for the $g = 4-5$ dendrimers, though the reproduction of the viscosity data is similarly satisfactory.

The near to coplanar disposition of every set of four connected branching points, previously discussed, introduces a significant degree of rigidity in the molecules. It seems that, for our present model based on ideal spherical beads, most of the intramolecular repulsions are effectively mimicked by the rigidity effects and, therefore, the parameter representing these repulsions is drastically reduced. A competition between rigidity and long-range repulsions (or "excluded volume") interactions has been commonly observed in the case of partially rigid chains [22]. It could be argued that an attractive–repulsive potential would give a more realistic description of the size of the dendrimer molecules in different solvents. However, we have introduced such a potential in the present model, verifying that attractions are not able to give a significant reduction of the size of the molecules which is mainly determined by the hard-spheres' distance as the single relevant long-range interaction parameter.

It should be pointed out that the final agreement achieved between the MC and experimental values of R_{g} is significantly improved with respect to the results obtained with the simpler original method for the $g = 3$ monodendrons (Table 1). A 15% discrepancy was previously observed for this particular case [9]. As previously stated, this particular experimental data can only be reproduced by using a sharp angle distribution function. This confirms that the introduction of realistic details of the distributions of distances and angles obtained with atomistic representation of the molecules gives a clearly improved description of the experimental data corresponding to the smallest molecules, poorly represented by our original model.

The agreement between experimental data and the simulation results obtained with all the refinements for the monodendrons and tridendrons of PBzE in THF (filled circles and diamonds, respectively) is significantly better than the accordance found with our previous method (open circles) that did not include any of the refinements considered now, as it can be observed in Figs. 4 and 5. In the particular case of the tridendrons, the experimental data [16] show a sharp maximum in the experimental intrinsic viscosity data and the whole curve is now closely reproduced by the simulation results. As in the case of the monodendrons, the results obtained in our previous work without the present refinements showed a fair agreement with the experimental data, but failed mainly in the prediction of the experimental data corresponding to the smallest and highest values of g. It should also be mentioned that the value of the friction radius now obtained for the PBzE molecules, $r_{\mathrm{f}} = 2.6$ Å, is considerably smaller than the unrealistic result $r_{\mathrm{f}} = 4.65$ Å obtained with the previous simpler method. This new value is also very close to the value set to the PPI–DAB dendrimers, as it has been described above, though this type of agreement has to be considered as fortuitous for dendrimers of different chemical structures in different types of solvents.

The present results seem to indicate that the introduction of a single-bead correction term is needed to reproduce the experimental intrinsic viscosity data of dendrimers with a coarse-grained model MC method. Including this correction, a simple model with a rough description of the distribution of distances between branching points is probably enough to give a good reproduction of the experimental data in the case of dendrimers with some flexibility in connecting segments (or spacers) of moderate length as in the case of the PPI–DAB dendrimers investigated in this work. As stated in Section 1, the higher dispersion of the experimental intrinsic viscosity data does not allow us to contrast the benefits of this modification for the PAMAM–EDA molecules. These dendrimers with longer spacers have been the object of many experimental and theoretical studies. The most recent MD studies of PAMAM–EDA dendrimers with a detailed coarse-grained model [23] including charges have been mainly focused on the determination of the radius of gyration, density profiles and other conformational and dynamic properties and their interaction with bilayers [24].

However, the consideration of an angle distribution between branching points is needed when the connection between these points has a mainly rigid structure, as in the case of the monodendron and tridendron PBzE molecules. The introduction of distance distributions obtained from MD simulations with explicit solvent leads to closer MC results for these molecules. When all these improvements are taken into account, a good general description of the available radius of gyration and intrinsic viscosity data is achieved both for monodendrons and tridendrons of PBzE. It should be remarked that the reproduction of the intrinsic viscosity dependence with the generation number is consistent with a prominent maximum observed in the experimental data of the tridendron molecules. Our modified method could, in principle, be applied for other dendrimers including planar rings or other anisotropic units. Of course, the general conclusions on the method's usefulness require further verification with other dendrimers of similar characteristics, for which accurate experimental data of the intrinsic viscosity data may be available.

Using the most elaborated MC results obtained in the present work for each type of dendrimer, which cover a relatively broad range of molecular weights, we have investigated if a simple prediction of the intrinsic viscosity can be performed based only on the radius of gyration values. In Figs. 6 and 7 we show the R_g data obtained by simulation for monodendrons and tridendrons of PBzE. (As we have previously discussed, a good agreement is found with the existing experimental data for monodendrons.) It is observed that ν decreases progressively, being always smaller than the unperturbed flexible polymer value, $\nu = 0.5$. Using the results corresponding to the last four generations, we obtain reasonable fits with $\nu = 0.23$ and $\nu = 0.22$ for monodendrons and tridendrons, respectively, in good agreement with previous simulation data for generic models [3,4,10]. We have attempted similar log–log fits for the intrinsic viscosity results corresponding to the highest molecular weights (since curvature is very marked around the maxima, we have used just the last two generations in the range where $[\eta]$ decreases with M). The fitted slopes yield $3\nu - 1$. This way we obtain alternative results, $\nu = 0.30$ for monodendrons and $\nu = 0.22$ for tridendrons. Therefore, the radius of gyration and intrinsic viscosity dependences on the molecular weight are similar for tridendrons, molecules with a high density of atoms that tend to form compact structures, but they significantly differ for monodendrons, less compact structures with a more pronounced variation of permeability with the generation number.

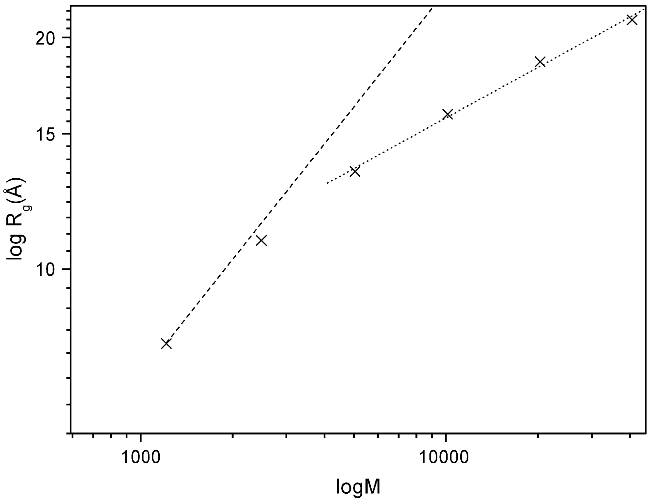

Fig. 7. Log–log representation of the mean radius of gyration vs molecular weight for the PBzE tridendrons. Crosses: MC results. Dashed line: $\nu = 0.5$ prediction for a flexible polymer. Dotted line: linear fit of the last 4 points, $\nu = 0.22$.

In the case of the PPI–DAB dendrimers, the last four generations corresponding to the MC data for the radius of gyration reported in Ref. [9] provide $\nu = 0.29$ (these data were in good agreement with experimental data and have not been reconsidered in the present work), while a fit of the last two generations corresponding to the present set of results for the intrinsic viscosity (with the bead correction) yields $\nu = 0.30$. In all the cases, the fits of the last four generations of intrinsic viscosity data are unsatisfactory and yield considerable higher values of ν, i.e., showing a further disagreement with the estimations obtained from the radius of gyration data. All these results confirm that only a detailed hydrodynamic description of the dendrimer molecules, taking at least a basic description of their main molecular characteristics, is able to give an adequate prediction of their intrinsic viscosity values.

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