

3D structure of dendritic and hyper-branched macromolecules by X-ray diffraction

Valeri Petkov^{a,*}, Vencislav Parvanov^a, Donald Tomalia^b, Douglas Swanson^b,
Debora Bergstrom^b, Tom Vogt^{c,d}

^aDepartment of Physics, Central Michigan University, Mt Pleasant, MI 48858, USA

^bDendritic NanoTechnologies, Mt Pleasant, MI 48858, USA

^cPhysics Department, Brookhaven National Laboratory, Upton, NY 11973, USA

^dCenter for Functional Nanomaterials, Brookhaven National Laboratory, Upton, NY 11973, USA

Received 11 October 2004; received in revised form 19 February 2005; accepted 6 March 2005 by J.A. Brum

Available online 23 March 2005

Abstract

The atomic ordering in dendritic and hyper-branched macromolecules has been determined by X-ray diffraction. The approach of the atomic pair distribution function technique has been used due to the lack of 3D periodicity in these polymeric materials. Dendrimers are found to possess a semi-regular structure riddled with nanosize cavities. The cavities are joined into channels connecting dendrimer's surface and core. In contrast, hyper-branched polymers are rather irregular at the atomic scale and with less accessible interior.

© 2005 Elsevier Ltd. All rights reserved.

PACS: 61.10.Nz; 61.41.+e; 61.43.Bn

Keywords: A. Nanostructured materials; C. X-ray diffraction

Dendrimers are a novel class of structurally controlled macromolecules derived through a so-called 'branches-upon-branches' growing process. Branches radiate from a central core and are synthesized through a repetitive reaction sequence that guarantees a complete shell for each generation, leading to polymeric macromolecules that are globular in shape and are monodisperse [1]. Dendrimers can be designed with a variety of organic and inorganic cores and branches, with tunable branch length, multiplicity, and surface functionality. The ability to control the structure at this level has created substantial interest in the use of dendrimers as polymers mimic globular proteins [2,3] and

building blocks of multifunctional nanocomposites [4]. Hyper-branched polymers are made through similar but less directed procedures and do not truly achieve regular dendritic growth. As a result they show many but not all of the useful properties of dendrimers.

The concept of an empty interior is central to the understanding of important properties of dendrimers and hyper-branched polymers, in particular the ability to accommodate guest molecules and nanoparticles. Early theoretical studies of de Gennes and Hervet [5] concluded that dendrimers evolve in concentric shells enclosing a plenty of open space. Major assumptions of the model are that the branches are dominated by a single conformation and always stretch out as the generation number increases. Later theoretical studies [6] questioned those assumptions and arrived at the conclusion that dendrimers are indeed with filled interior. Experimental evidence is also

* Corresponding author. Tel.: +1 989 774 3395; fax: +1 989 774 2697.

E-mail address: petkov@phy.cmich.edu (V. Petkov).

controversial. While SAXS data [7] have been interpreted in terms of globular macromolecules with dense interior, NMR experiments [8] have found considerable free volume inside dendrimers. Not much is known for the atomic ordering in hyper-branched polymers either. Good knowledge of the geometrical characteristics of dendrimers and hyper-branched polymers is an important prerequisite to understanding and utilizing the great potential of this novel class of materials.

Here we use X-ray diffraction and the atomic pair distribution function (PDF) technique to determine the atomic arrangement in dendritic and hyper-branched poly (amidoamine) (PAMAM) macromolecules. This approach has been widely used to study bulk polymers [9] and only recently has been successfully applied to study the structure of inorganic nanocrystals [10]. Here we demonstrate that it also can be used to determine the 3D structure and geometrical characteristics of polymeric macromolecules a few nanometers in size.

We find that monomer branches in dendrimers are arranged in a semi-regular network supporting cavities with diameter ranging from 5 to 15 Å. The cavities are uniformly distributed throughout the interior of the macromolecules and are organized into channels connecting its surface and core. The picture is distinctly different from that observed with hyper-branched polymers that appear to be rather irregularly structured and with much less accessible interior.

The atomic PDF is a function that gives the number of atoms in a spherical shell of unit thickness at a distance r from a reference atom. It peaks at characteristic distances separating pairs of atoms and thus reflects the structure of materials. The PDF, $G(r) = 4\pi r[\rho(r) - \rho_0]$, is the sine Fourier transform of the so-called total scattering structure function, $S(Q)$,

$$G(r) = (2\pi) \int_{Q=0}^{Q_{\max}} Q[S(Q) - 1] \sin(Qr) dQ \quad (1)$$

where ρ_0 is the average atomic number density, $\rho(r)$ the atomic pair density, Q the magnitude of the wave vector and $S(Q)$ is the corrected and properly normalized powder diffraction pattern of the material [11]. As Eq. (1) implies, the PDF is obtained with no assumption of periodicity. Thus materials exhibiting any degree of structural coherence, ranging from crystals to glasses and liquids, can be studied using the same approach. In addition, the PDF is a sensitive, structure-dependent quantity that provides directly the relative positions of atoms in materials. This enables the convenient testing and refinement of structural models.

Three samples were measured. One was crystalline buckminsterfullerene (C_{60}) obtained from MTR Ltd. The second was dendritic PAMAM polymer. It was made by alkylating dodecanediamine with excess methyl acrylate followed by amidation with excess ethylenediamine (EDA) at low temperatures. The product from each step was purified. This reiteration of methyl acrylate and EDA was

repeated to produce dendrimer macromolecules of 7th generation. The third sample was hyper-branched PAMAM polymer. The sample was made by adding methyl acrylate to tris(2-aminoethyl) amine. The material was heated until the ester carbonyl, as identified by infrared spectroscopy, had completely disappeared, and the size of the resulted hyper-branched macromolecules approached that of 7th generation PAMAM dendrimers. It is well known that dendrimers swell or shrink when in solution, i.e. that solvents modify their geometrical characteristics [12]. To avoid any such effect we carefully dried the polymeric samples before subjecting them to X-ray diffraction experiments. The samples were sealed between Kapton foils and their diffraction patterns measured using X-rays of energy 29.09 keV ($\lambda = 0.425$). The experiments were carried out at the beam line X7A of the National Synchrotron Light Source (NSLS), Brookhaven National Laboratory. Scattered radiation was collected with an intrinsic germanium detector connected to a multi-channel analyzer. The raw diffraction data were corrected for flux, background, Compton scattering, and sample absorption. The intensities were normalized in absolute electron units, reduced to structure functions $S(Q)$ and Fourier transformed to the corresponding PDFs, $G(r)$. All data processing was done using the program RAD [13]. Experimental atomic distribution functions are shown in Fig. 1. They all show a strong first peak centered at approximately 1.54 Å which is the first neighbor distance within the carbon backbone of the materials studied. In addition, the first peak in the PDFs for dendritic and hyper-branched macromolecules has a low- r shoulder at 1.1 Å. This is the hydrogen-carbon pair distance in these polymeric materials.

Buckminsterfullerene is a molecular crystal made of

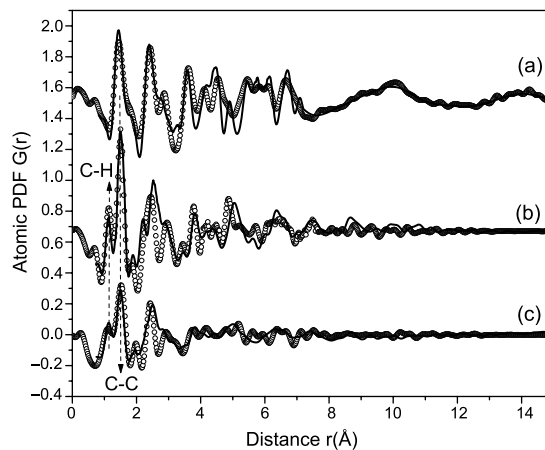


Fig. 1. Experimental (symbols) and model (solid line) atomic PDFs for (a) crystalline C_{60} , (b) dendritic and (c) hyper-branched PAMAM macromolecules. First PDF peaks are labeled with the corresponding atomic pairs. The model atomic PDFs shown in (a), (b) and (c) are calculated from the atomic configurations presented in Fig. 2(a)–(c), respectively.

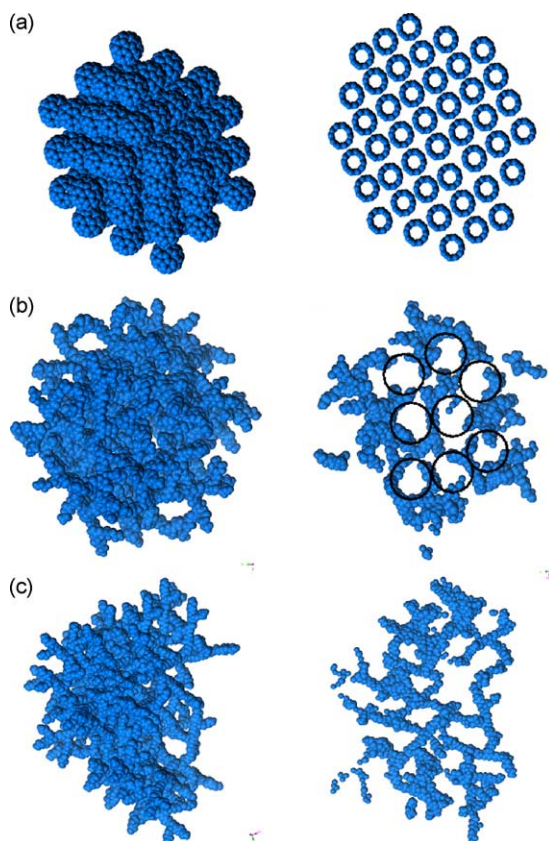


Fig. 2. 3D models (on the left) for (a) fullerene C_{60} , (b) dendritic and (c) a hyper-branched PAMAM macromolecules. Slices cut through the central part of the models are shown on the right. PAMAM dendrimers with the structure shown in (b) exhibit relatively open interior with cavities (big open circles) ranging from 5 to 15 Å in diameter.

rigid units ordered in a face centered cubic arrangement as shown in Fig. 2(a). Each fullerene molecule consists of 60 carbon atoms bonded in a nearly spherical configuration enclosing a cavity with diameter of 7.1 Å. Since the molecule is rigid, all interatomic distances within it are well defined and the corresponding peaks in the atomic PDF are well resolved (Fig. 1(a)). At room temperature C_{60} molecules spin almost freely in their crystal positions, so they look like soccer balls. The correlation between the carbon atoms from neighbouring molecules are lost and, starting at 7.1 Å, the atomic PDF turns into a low-frequency oscillation reflecting the ‘ball–ball’ correlations. A model PDF calculated from crystal structure data for fullerene [14] is shown in Fig. 1(a). The agreement between calculated and experimental PDF data is very good. The results for the buckminsterfullerene demonstrate the fact that the atomic PDF is sensitive to both intra and intermolecular ordering of nanosized objects and may serve as a reliable basis for studying their geometrical characteristics. If the molecular branches in dendrimers are arranged in a regular pattern and

enclose nanosized cavities, just like C_{60} molecules in buckminsterfullerene do, then the atomic PDF for dendrimers should bear similarities to that of buckminsterfullerene. A careful inspection of the experimental data presented in Fig. 1(b) suggests that this indeed may be the case since the PDF for PAMAM dendrimers too shows a series of well-defined peaks extending to approx. 8 Å followed by an almost featureless tail. With crystalline fullerene the change in the shape of PDF at 7.1 Å is very sharp since the intra and intermolecular correlations do not overlap. This behavior reflects the presence of a 3D ordered array of identical cavities inside the molecular solid (Fig. 2(a), on the right). In PAMAM dendrimers the change in the shape of PDF is not so abrupt indicating that the intra and intermolecular correlations overlap to a certain extent, i.e. that the branches may approach each other at various distances. This behavior implies a smaller degree of atomic ordering and the presence of cavities of somewhat different dimensions. The PDF for hyper-branched PAMAM polymers also shows peaks extending to approx. 8 Å but these peaks are rather poorly defined (Fig. 1(c)). Obviously the spatial arrangement of molecular units/branches in this material is less regular and the distribution of cavities is much broader than those in dendritic macromolecules.

To reveal the atomic ordering in the studied polymeric materials in more detail we constructed 3D atomic models as follows: amidoamine ($CH_2-CH_2-CO-NH-CH_2-CH_2-NH_2$) monomer units were attached to a diaminododecane core ($C_{12}H_{28}N_2$) and then to each other in a repetitive manner mimicking the chemical route employed in the preparation of dendrimers. Care was taken that each monomer unit/branch has the same end multiplicity of two and the units do not overlap each other. It turned out that different amidoamine conformations, derived by preliminary *ab initio* calculations [15], had to be taken into account to make the building process successful. Realistic bond angles and lengths around the branch points (nitrogen atoms) were strictly enforced. Modeling was done with the help of Materials Studio software. The use of plausible chemical constraints and rigid building units (amidoamine monomers) resulted in a polymeric macromolecule with a very little degree of backfolding of the constituent branches. This is in contrast to many previous modeling studies [16] using flexible spacers as building blocks of dendrimers. Thus constructed model of a 7th generation PAMAM dendrimer involving 9186 atoms is shown in Fig. 3(a) (on the left). As can be seen the model atomic configuration is fairly well ordered and with a very open interior (Fig. 3(a) on the right). An atomic PDF calculated from the model reflects the very high degree of atomic ordering and shows well defined peaks out to large interatomic distances (Fig. 4(a)). This is not exactly the picture seen with real dendrimers as a comparison between the experimental and model PDF data show (Fig. 4(a)). To obtain a more realistic model we relaxed the initial one using COMPASS-type [17] atomic-level force fields designed explicitly for polymer and

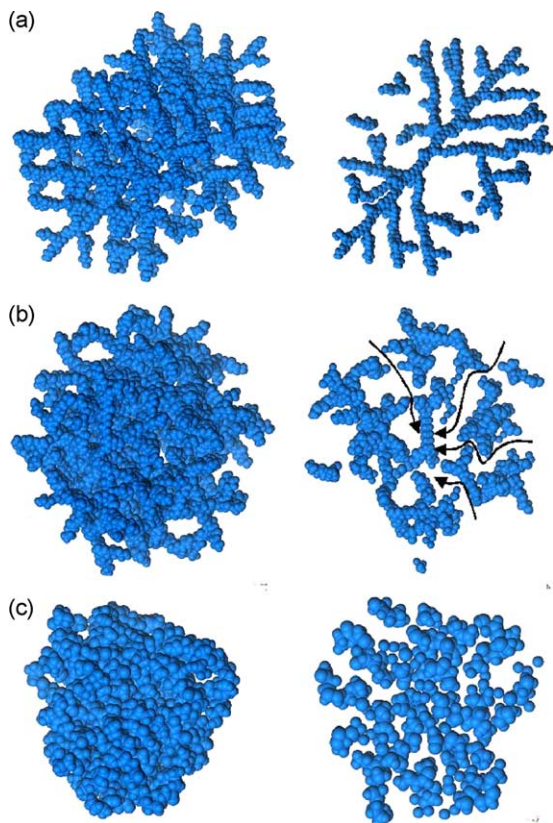


Fig. 3. 3D models (on the left) of PAMAM dendrimers with (a) unrealistically highly ordered, (b) semi-regular and (c) collapsed structure as explained in the text. Slices cut through the central part of the models are shown on the right. Dendritic PAMAM macromolecules with the structure shown in (b) are penetrated by channels (marked with arrows) connecting molecule's core and surface.

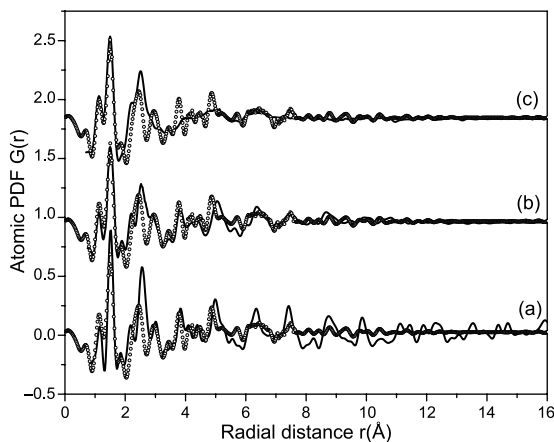


Fig. 4. Experimental PDF for PAMAM dendrimers (symbols) and model PDFs (solid line) calculated: (a) from the 3D atomic configurations shown in the Fig. 3(a), (b) from that in Fig. 3(b) and (c) from that in Fig. 3(c).

organic applications. Several relaxation runs were carried out, each ending with a model relaxed to a different degree, the resulted atomic configurations were saved, the corresponding atomic PDFs calculated and compared to the experimental PDF. The approach of using a structure-sensitive experimental quantity to discriminate between competing models is widely applied in traditional crystallography. Here we apply it in search of a model that is not only chemically correct and relaxed using realistic interatomic potentials but consistent with the experimental PDF data as well.

A model that is relaxed and shows a PDF (Figs. 1(b) and 4(b)) in good agreement with the experimental data is presented in Figs. 2(b) and 3(b). A model that is relaxed but shows a PDF (Fig. 4(c)) that does not agree with the experimental data is presented in Fig. 3(c). The latter model features a very disordered arrangement of monomer units/branches that approach each other closely and leave little open space inside the macromolecule. Such a type of atomic arrangement and a PDF lacking any sharp features already at 3–4 Å is the usual picture seen with glass-like polymers [9].

A similar approach was adopted to build a model for the hyper-branched PAMAM polymer. The only difference was that the degree of branching of amidoamine units was kept lower than that with the dendritic PAMAM macromolecule. A model atomic configuration that is relaxed and shows a PDF (Fig. 1(c)) in good agreement with the experimental data is presented in Fig. 2(c). It is worth noting that both macromolecules shown in Fig. 2(b) and (c) have the same building molecular units and total number of atoms. What is different is the way the individual branches are arranged in space.

Analysis of the model atomic configurations shown in Fig. 2 allows one to draw important conclusions about the atomic ordering in dendritic (Fig. 2(b)) and hyper-branched (Fig. 2(c)) macromolecules. PAMAM dendrimers of higher generation, when not affected by any solvent, turn out to be globular in shape and with a relatively open structure. The diameter of the 7th generation PAMAM macromolecule shown in Figs. 2(b) and 3(b) is approx. 85 Å which is in line with the findings of SAXS and size exclusion chromatography experiments [1,7]. For comparison, the diameter of the macromolecule with collapsed structure shown in Fig. 3(c) is only 65 Å. Branches inside dendrimers are not arranged in exactly concentric shells, as the model of de Gennes suggests, but in a semi-regular pattern forming a network-like structure. This branched network supports cavities with a narrowly distributed diameters ranging from 5 to 15 Å (Fig. 2(b)). The cavities occur throughout the interior of the macromolecule and some are joined into channels connecting its surface and core (Fig. 3(b)). As can be seen in Fig. 2(c) hyper-branched PAMAM macromolecules appear with rather irregular atomic arrangement and are not globular in shape. These findings are well in line with the predictions of other independent studies [18]. In particular, the macromolecule shown in Fig. 2(c) (left) has a

long and short dimension of 110 and 70 Å, respectively. Branches inside the hyper-branched PAMAM macromolecules form an irregular but still relatively open network supporting cavities with a broad distribution of sizes. Many of the cavities, however, are enclosed within ring-like structural fragments and are almost isolated from each other (Fig. 2(c)). The interior of hyper-branched macromolecules thus appears to be less accessible than that of dendritic ones.

In conclusion, using X-ray diffraction and the atomic PDF technique we have provided direct structural evidence that PAMAM dendrimers are well ordered at the atomic scale and with a relatively open interior. Due to their unique structure dendrimers can accommodate small molecules and atomic clusters and provide them with a unique nanoenvironment. This useful property of dendrimers has already found a number of practical applications [19]. Furthermore, as modeling studies [12,20] suggest the size of free volume inside dendrimers may be tuned using appropriate solvents. This opens even more opportunities for future applications. Much easier to synthesize hyper-branched polymers are less ordered at the atomic scale and with a less accessible but still relatively open interior and thus may also be used in controlled delivery applications. The results presented here are another demonstration of the great potential of the PDF technique in determining the atomic ordering in nanostructured materials.

Acknowledgements

Thanks are due to Yongjae Lee for the help with the synchrotron experiments. This work was supported by the Army Research Laboratory under Cooperative Agreement DAAD19-03-2-0012 and in part by NSF through Grant DMR-0304391 (NIRT). Beamline x7a at the NSLS is supported by the US Department of Energy through DE-AC02-98-CH10886.

References

- [1] D.A. Tomalia, A.M. Naylor, W.A. Goggard, *Angew. Chem., Int. Ed. Engl.* 29 (1990) 138.
- [2] D.A. Tomalia, B. Huang, D.R. Swanson, H.M. Brothers, W. Klimash, *Tetrahedron* 59 (2003) 3799.
- [3] H.M. Evans, A. Ahmad, K. Ewert, T. Pfohl, A. Martin-Herranz, R.F. Bruinsma, R. Safinya, *Phys. Rev. Lett.* 91 (2003) 075501.
- [4] B.L. Frankamp, A.K. Boal, V.M. Rotello, *J. Am. Chem. Soc.* 124 (2002) 15146.
- [5] P.-G. de Gennes, H. Hervet, *J. Phys. Paris* 44 (1983) L351.
- [6] T.C. Zook, G.T. Pickett, *Phys. Rev. Lett.* 90 (2003) 015502.
- [7] S. Rathgeber, M. Monkenbush, M. Kreitschmann, V. Urban, A. Brulet, *J. Chem. Phys.* 117 (2002) 4047.
- [8] D.R. Morgan, E.O. Stejskal, A.L. Andradý, *Macromolecules* 32 (1999) 1897.
- [9] M. Vinokur, in: S.J.L. Billinge, M.F. Thorpe (Eds.), *Local Structure from Diffraction*, Plenum Press, New York, 1998, p. 337.
- [10] (a) V. Petkov, P.N. Trikalitis, E. Bozin, S.J.L. Billinge, T. Vogt, M.G. Kanatzidis, *J. Am. Chem. Soc.* 124 (2002) 10157;
(b) V. Petkov, P.Y. Zavalij, S. Lutta, M.S. Whittingham, V. Parvanov, S. Shastri, *Phys. Rev. B* 69 (2004) 085410.
- [11] C.N.J. Wagner, *J. Non-Cryst. Solids* 31 (1978) 1.
- [12] P. Welch, M. Muthukumar, *Macromolecules* 31 (1998) 5892 and references therein.
- [13] V. Petkov, *J. Appl. Crystallogr.* 22 (1989) 387.
- [14] D.L. Dorset, P. McCourt, *Acta Crystallogr. A* 50 (1994) 344.
- [15] M.J. Frisch et al. GAUSSIAN98 package, Pittsburgh, 2003.
- [16] (a) M.L. Mansfield, L.I. Klushin, *Macromolecules* 26 (1993) 4262;
(b) R.L. Lescanec, M. Muthukumar, *Macromolecules* 23 (1990) 2280.
- [17] H. Sun, *J. Phys. Chem. B* 102 (1998) 7338.
- [18] J.M.J. Fréchet, C.J. Hawker, I. Gitsov, J.W. Leon, *J. Macromol. Sci.-Pure Appl. Chem. A* 33 (1996) 1399.
- [19] (a) V.A. Kabanov, et al., *Macromolecules* 32 (1999) 1904;
(b) Kukowska-Latallo, et al., *Proc. Natl Acad. Sci. USA* 93 (1996) 4897;
(c) S.C. Zimmerman, et al., *Nature* 418 (2002) 399.
- [20] P. Welch, M. Muthukumar, *Macromolecules* 33 (2000) 6159.