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Application of High Performance Computing for Comparison of Two Highly Branched Lysine Molecules of Different Topology

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High performance computations were performed for comparison of size and other properties of big heavily charged biocompatible molecules of complex topology in water. Lysine dendrimer and short dendritic brush of the same molecular weight were studied by molecular dynamics simulation method and GROMACS software package. The size and structural properties of these two systems were compared. It was shown that dendritic brush has smaller size and more dense core than the dendrimer. Radial density profile for both molecules is not monotonous and has minimum near core of molecules. This minimum is wider and deeper for dendrimer than for dendritic brush. Thus dendrimer has larger region of low density than dendritic brush and is more suitable for use for encapsulation and delivery of hydrophobic drugs.

Keywords: high performance computing, dendrimer, dendritic brush, Poly-L-lysine.

Introduction

High performance computing are widely used for molecular simulation of complex biological and biocompatible molecules. Lysine dendrimers were studied in several papers both by computer simulation using molecular dynamics method [6, 7, 10, 13, 15] and theoretically using numerical SCF approach [14]. At the same time there is almost no papers on theory and simulation of lysine dendritic brushes and comparison of properties of these molecules with properties of lysine dendrimers. The goal of the present paper is to compare the size and internal structure of these two types of molecules.

1. Model and Method

We studied dendrimer and dendritic brush of the same molecular weight but with different core structure. The dendrimer of the fifth generation has point-like core (one lysine residue) and the short dendritic brush has a linear core consisting of 8 lysine residues in main chain and 8 lysine dendrons of 2nd generation [6, 15]. The molecular weight M=16496 and 16553, total number of atoms N_a=2810 and 2819 and number of charged terminal NH3+ groups N_t=128 and 128 were for dendrimer and brush, correspondingly.

The computer simulation was performed by using the molecular dynamics method on the base of the Gromacs-4.5.6 package and the full atomic AMBER99SB-ildn force field. The simulation box contained one dendrimer or dendritic brush, water molecules and chlorine counterions. We also used several computer programs from our previous simulation of linear polymers [1, 11], dendrimers [8, 9, 17, 18], polymer brushes [12] and polyelectrolytes [2–5]. More simulation details could be found in [6].

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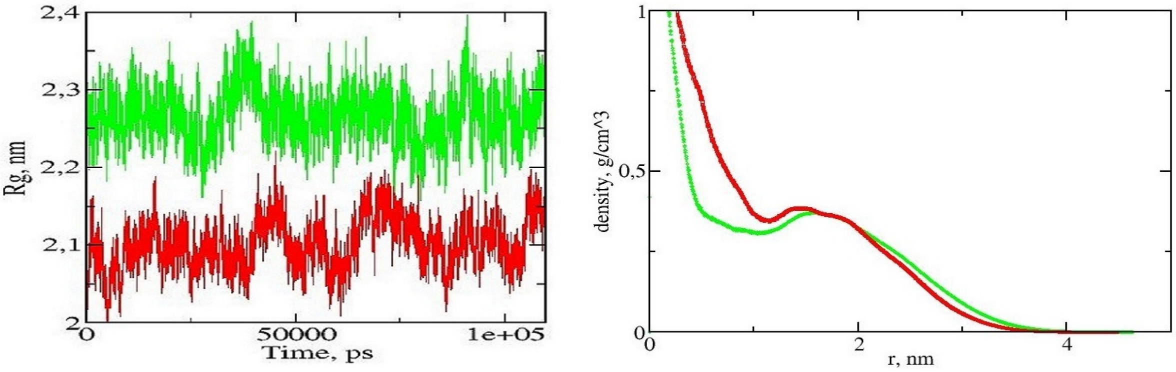
2. Results

2.1. Large-Scale Properties



(a) (b)

Figure 1. (a) the gyration radius R_g as function of time and (b) the density profiles of simulated molecules – dendrimer (green color) and dendritic brush (red color)

The dependence of instant size (gyration radius R_g) on time t during production run 120 ns was calculated (see Fig. 1a). The values of R_g for both systems fluctuate but their average values practically does not change with time and R_g for dendrimer (green line in Fig. 1a) is always greater than R_g for dendritic brush (red line in Fig. 1a). The average values of R_g are equal 22.6 and 20.8 for dendrimer and dendritic brush correspondingly. The asphericity parameter of both molecules is smaller than 0.04. It means that the shape of both molecules is very close to spherical.

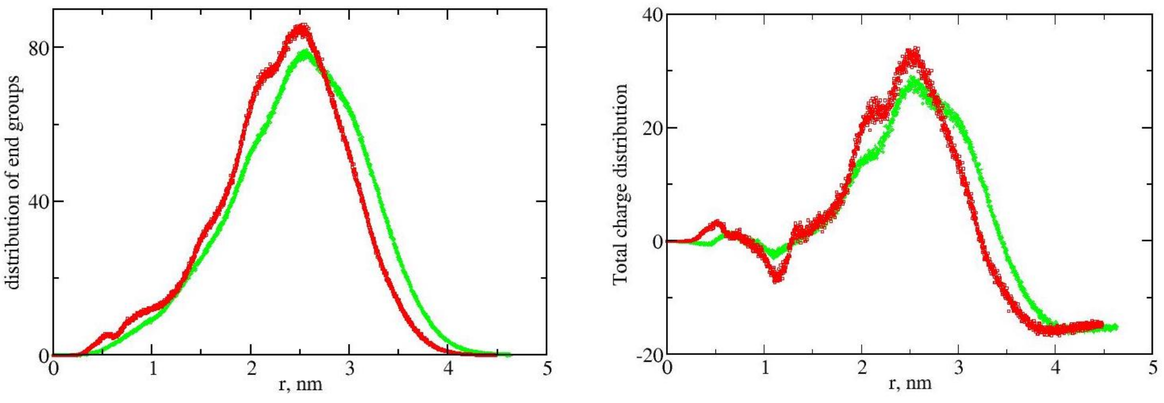
2.2. Internal Structure

Internal structure of both molecules could be characterized by the radial density profile $\varphi(r)$ around center of mass. The density profiles for both molecules (see Fig. 1b) decrease from the core to the periphery for both molecules. For the dendrimer a wide minimum of density near core of molecule is observed. For dendritic brush there is similar minimum but it is not so wide and less deep.

Figure 2a demonstrates that terminal monomers distributed almost over all possible distances r from their center of mass. This phenomenon ("backfolding") is well known for dendrimers. However such behavior was not known earlier for short dendritic brushes (Fig. 2a). The total charge distribution function shows that the charge of positive NH3+ are almost neutralized by the negative chlorine counterions at small r (i.e. it is suitable for encapsulation of hydrophobic drugs). Non-compensated NH3+ groups are concentrated near the outer layer (see positive maximum on Fig. 2b) with chlorine counterions forming spherical layer.

Conclusions

It was shown that both molecules have spherical shape but the dendrimer has greater gyration radius R_g and more deep density minimum (void) near core than dendritic brush. Therefore,



(a) (b)

Figure 2. The radial distributions of number of terminal NH3+ groups (a) and of the total charge (b) for dendrimer (green color) and brush (red color).

dendrimer is more suitable for use for encapsulation and delivery of drugs than dendritic brush with the same molecular weight.

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