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Transport Properties of RNA Nanotubes Using Molecular Dynamics Simulation

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Abstract. We present novel molecular dynamics studies of transport properties of RNA nanotubes. Specifically, we determine the velocity trajectories for the phosphorous atom at the phosphate backbone of the RNA nanotube, the oxygen atom at sugar ring, and the $^{23}Na^{+}$and $^{35}Cl^{-}$ions in physiological solutions. At the constant temperature simulation it has been found that the fluctuation of the velocities is small and consistent with simulation time. We have also presented the velocity autocorrelation function for the phosphorous atom in RNA nanotubes that provides better insight into the diffusion direction of the system in physiological solution. We compare our results calculated computationally with the available experimental results.

1 Introduction

The RNA nanoclusters have a wide range of current and potential applications in a variety of fields, and in particular in nanomedicine. As a result, it is becoming increasingly important to study the properties of these systems in solutions. Particularly, in studies of transport phenomena, properties, and characteristics, including diffusion coefficients and velocity autocorrelation functions for these systems, are the subject of interest. Several experimental studies have been performed to analyze the diffusion coefficients of the biomolecular systems [1,2,11,12]. Furthermore, substantial efforts were devoted to computational studies where molecular dynamics simulations and other methodologies were applied to DNA polymers (e.g. [8,14]). In some such cases the average diffusion coefficient for the solvent as a function of the distance from the solute was reported. By using the molecular dynamics simulation the diffusion coefficient for the single strand RNA can also be calculated [15].

The self-diffusivity of the system of molecules under such studies in molecular dynamics simulations is defined by the random motion of the molecules in the media in which the change of the mass flux is zero. The self-diffusion coefficient can be calculated in two different ways. One is from the root mean square deviation and the other one is from the velocity autocorrelation function. More specifically, once the mean square deviation of the system is defined as

$$MSD(t_1,t_2) = \frac{1}{N}\sum_{i=1}^{N} \|x_i(t_2) - x_i(t_1)\|^2, \tag{1}$$

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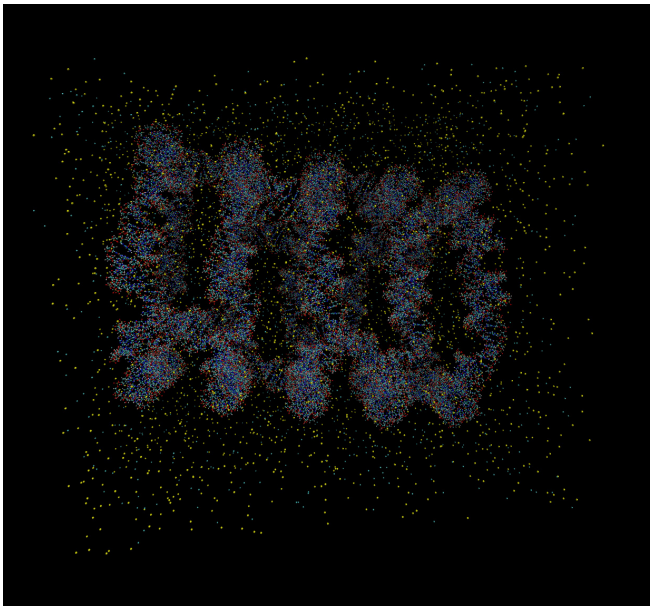

Fig. 1. (Color online.)The VMD generated structure of the RNA nanotube with 5 rings in a physiological solution (water molecules are not shown)

then the self-diffusion coefficient can be expressed as

$$D_s = \lim_{t\to 0} \frac{1}{6Nt} \sum_{i=1}^{N} \|x_i(t_2) - x_i(t_1)\|^2. \tag{2}$$

The autocorrelation function of the system can be expressed as

$$VACF(t) = \frac{< v(t)v(0) >}{(v(0))^2}. \tag{3}$$

In the study of the dynamic properties of the system consisting of RNA nanoclusters we use the structures modeled in the earlier studies [4,9,16]. However, unlike these earlier papers our focus here is on the transport properties such as velocity trajectories, autocorrelation functions and the diffusion coefficient of the nanocluster in physiological solutions The building blocks for these RNA nanoclusters are based on the RNAIi/RNAIIi complexes which are taken from the protein data bank with the pdb code (2bj2.pdb) [6]. A typical example of the RNA nanocluster in the physiological solution is presented in Figure 1.

This contribution is organized as follows. In section 2, we describe computational details used in our analysis of RNA nanoscale systems and highlight the main features of this analysis. The results are presented and discussed in Section 3, while concluding remarks are found in Section 4.

2 Computational Details

In order to perform all atom molecular dynamics simulations on the RNA nanoclusters we used CHARMM27 force field [10] implemented by NAMD package [7] The potential of the system used during the molecular dynamics simulation using CHARMM force filed can be expressed as follows:

$$V_{total} = \sum_{bond} K_b(r-r_0)^2 + \sum_{angle} K_\theta(\theta-\theta_0)^2 + \sum_{dihedral} K_\phi(1+cos(n\phi-\gamma)) + \sum_{Hbond}(\frac{C_{ij}}{r_{ij}^{12}} - \frac{D_{ij}}{r_{ij}^{10}}) + \sum_{Vanderwaals}(\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{10}}) + \sum \frac{q_{ij}}{\varepsilon r_{ij}}, \quad (4)$$

where the first term corresponds to bonds, second corresponding to angle parameters, the third term corresponds to the potential energy and interactions arised from the dihedral angles in the molecular system, the fourth term defines the interaction coming from the hydrogen bonds which includes the base pairing as well as the hydrogen bonding between the RNA and the water molecules. Finally the last term in the potential expression represents the long distance interactions known as the (van der Waals' interactions). As it was done for the nanoclusters in [4,9] the modeling of RNA nanotube including pre and post processing of the input-output files have been performed by using the visualization software software VMD and gnuplot. The main features of our analysis here are to calculate the velocity trajectory along the path of molecular dynamics simulation and then to calculate the autocorrelation function which can later be used for calculation of the diffusion properties of the RNA nanocluster in physiological solutions. We note that the RNA-nanotube was solvated by the water in a water box. The size of the box is taken in such a way that the distance wall of the water box is at a distance larger than the cut off radius used in the MD simulation. In order to make the system neutral we have added 594, 924, 1254 and 1584 $^{23}Na^+$ for two ring, three ring, four ring and five ring nanotubes, respectively. Furthermore, in order to make the solution equivalent to the physiological solution we have added extra $^{23}Na^+$ and $^{35}Cl^-$ ions. This system was simulated at constant temperature and pressure using NAMD software. The temperature in the system is controlled by the Langevin method [5] with damping $\eta = 5$ ps^{-1}.

3 Results and Discussion

Recently, we succeeded in describing RNA nanoclusters of variable sizes by using the molecular dynamics techniques [3,4]. Specifically, we used the RNA building blocks and self assembled them to construct the RNA nanotube using the VMD and the protocols available in the software NAMD. Now, for these nanoclusters we have calculated the trajectories for the velocities, focusing on atoms that may influence substantially dynamical properties of these RNA nanoclusters. Hence, this contribution represents a new steps in the study of transport properties including diffusion phenomena in the RNA nanocluster that can be analyzed via molecular dynamics simulations. In particular the trajectories for the phosphorous atom in the phosphate backbone, the sodium ion in physiological solution, the chloride ion and the oxygen atom at sugar ring of the

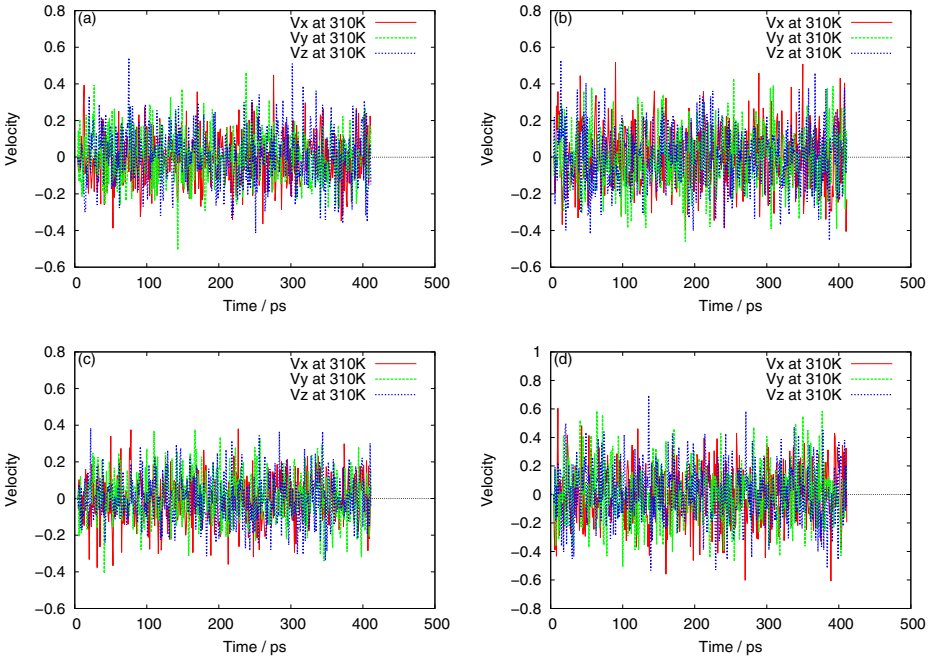

Fig. 2. (color online)The trajectories of the velocity for (a) Phosphorus at the phosphate backbone (b) Sodium ion in a physiological solution (c) Chloride ion in a physiological solution and (d) The oxygen atom at a sugar ring

five ring RNA nanotube are presented in Figure 2. For each of the atoms the velocities have been tracked consistently along all directions i.e x, y, and z. From the plots it is clear that the variation in the velocities during the molecular dynamics simulations is small and consistent in all directions, given constant temperature. This consistency of the velocity components during the MD simulation is due to the consistency of the temperature, along with some variations due to damping. The nature of the fluctuation of the velocities during molecular dynamics simulations is similar to the fluctuations observed for the temperature reported in earlier studies [3,4]. This feature has been observed because the classical velocities are proportional to the temperature of the system. In Figure 3, we have also presented the results for the velocity autocorrelation function in three different directions for the phosphorus atom in the RNA nanotube using molecular dynamics velocity trajectories in physiological solutions. From the plots in Figure 3, we conclude that the variations of the velocity autocorrelation function(VACF) in x direction is significantly different than those in the y and z directions. These velocity autocorrelation functions are primary characteristics for the estimates of diffusion coefficients of the molecular systems under considerations.

Up till now, very limited experimental studies have been done for the diffusion properties of the RNA nanoclusters. However, it is worthwhile noting that some experimental studies on the conformational diffusion coefficient for a typical biopolymer has recently been performed by using the experimental technique force spectroscopy [13]. This shed further light on the inter chain motion in complex biological polymers.

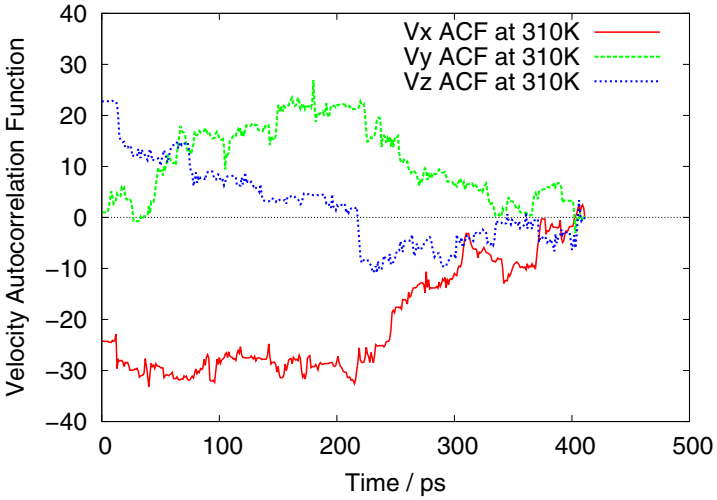

Fig. 3. (color online) Velocity autocorrelation function for the phosphorous atom in the RNA nanotube using molecular dynamics simulation

4 Conclusions and Outlook

In this contribution, we presented new results on dynamic properties of RNA nanotubes, in particular the velocity trajectories and velocity autocorrelation functions for P, O, $^{23}Na^{+}$, and $^{35}Cl^{-}$atoms during molecular dynamics simulations of RNA nanotubes in physiological solutions. Such systems are of particular interest in nanomedical applications [4,9]. In typical NVT runs of constant temperature molecular dynamics simulations for these RNA nanotubes, we found that the velocity is fluctuating in all directions rather uniformly. We have presented the VACFs, focusing on the phosphorous atom at the phosphate backbone of the RNA nanotubes. At the same time, it would be very interesting to calculate the VACFs for other atoms in order to better understand the trend of their velocity variations in different directions. Using these autocorrelation functions deduced from velocity trajectories, a detailed study of diffusion characteristics of such systems represents an important avenue of future work that should provide additional insight into transport phenomena in RNA nanotubes and their applications in biomedicine as well as other fields. Finally, we note that, despite efficient coarse-graining procedures, our current studies have been limited by severe computational challenges and were naturally limited in time scales smaller than realistically required for many biological processes. Longer simulations would provide a better understanding about the transport properties of the RNA nanoclusters. Undoubtedly, these studies should encourage experimentalists to do such kind of measurements that would provide the diffusion parameters on the RNA nanoclusters.

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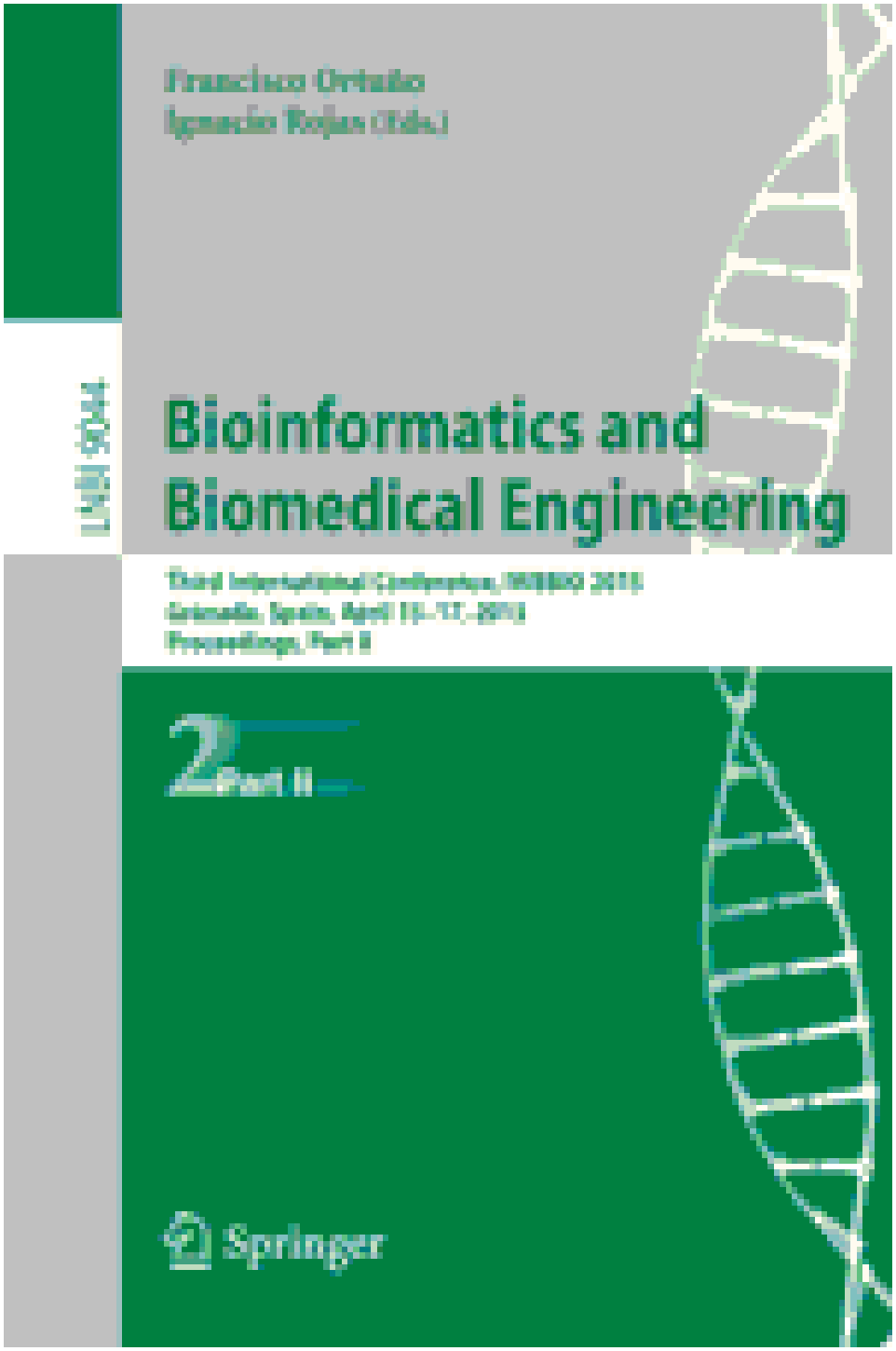
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