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Coarse-Grained Molecular Dynamics Simulation of DPPC Lipid Bilayers: Size Effect on Structural and Dynamic Properties

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Abstract. Coarse-grained molecular dynamics simulations of DPPC lipid bilayers were performed with different system sizes at T = 323 K for a period of 1 μs. The structural properties of the systems were demonstrated by examining the area and volume per lipid, electron density profile, order parameter, and the lipid bilayer thickness. It was shown that the finite system size has a negligible effect on the ensemble averages of the area and volume per lipid, the order parameter, and the bilayer thickness. However, the electron density profiles become smoother and wider at a larger system size due to the increasing surface/interface fluctuation from undulations. On the other hand, the lipid dynamics was quantified by computing the lateral diffusion coefficients of DPPC molecules. It was revealed that, the effective lateral diffusion coefficient of DPPC increases initially by 19% as the bilayer increases from 64 to 256 lipids per leaflet, and then it changes slightly and fluctuates around a steady value as the system further expands.

AMS subject classifications: 65C20, 68U20, 92-08

Key words: Molecular dynamics, coarse-grained model, DPPC lipid bilayer, system size effect.

1 Introduction

Lipid membranes play significant roles in human cells as semi-permeable control gates for maintaining concentrations and separating internal compartments from the outer environment [1]. Their physical and biological functions are crucial for the development of

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bio-applications such as drug delivery, tissue engineering, biofuels, and biosensors [2–5]. One of the major structural lipids in cell membranes is phosphatidylcholine (PC), in which the hydrophilic head group and hydrophobic fatty acids with varying lengths are linked to a diacylglycerol. For example, 1,2-dipalmitoyl-*sn*-glycero-3-hosphocholine (DPPC) is a major constituent of cell membranes, and approximately accounts to 50% of the pulmonary surfactant lipids [6, 7]. The formation of a DPPC-rich monolayer in pulmonary surfactants is responsible for reducing surface tension and facilitating respiration [8]. Recent investigations on structural and dynamic features of DPPC lipid bilayers have shown remarkable influences of lipid bilayers on cellular processes such as ion transport and signaling activities [9–11].

Atomistic-scale computer simulations, particularly molecular dynamics (MD), has been proven to be a powerful tool to investigate nanostructures and behaviors of lipid bilayer membranes [12–17]. Calculated properties derived from MD simulations can depend on system size, and some vary more than others. The effect of the finite system size on equilibrium properties of DPPC lipid bilayers have been reported in literatures [18,19]. Lindahl and Edholm suggested that the area per lipid was in an inversely proportional relation with the system size [18]. de Vries *et al.* pointed out a convergence limit of 36 lipids per leaflet for some structural properties including the electron density profile, order parameter, and the surface tension [19]. Although the converged results were obtained well with small system sizes and short time scales ($3-20$ ns), they suggested that a much longer relaxation time is required to accurately calculate the dynamic properties of the systems. However, the studies of the system size effect on dynamic properties of DPPC bilayers were limited. It is intriguingly noted that a wide range of lateral diffusion coefficients of DPPC have been evaluated by different groups with different system sizes, but varying in cutoff methods and force field comparisons [12, 20, 21].

Furthermore, one drawback of all-atom or united-atom level MD approach is the limitations in time and length scales by computational resources. Coarse-grained MD techniques have been proposed during past decade as simplified but more efficient models for performing molecular simulations [22–28]. In coarse-grained models, the number of translational and rotational degrees of freedom within atomistic models is decreased through the representation of multiple atoms as one coarse-grained bead of a specified mass and charge. For amino acids and lipids, the coarse-grained Martini force field is well-validated and has been extensively used to study the properties and behaviors of proteins and lipids [29–32]. Therefore, in this work, the coarse-grained Martini 2.2 force field with polarizable water model was employed to investigate the structural and dynamic properties of DPPC lipid bilayers as well as the finite system size effect on them.

2 Molecular dynamics simulation and methodology

Fig. 1(a) shows the coarse-grained models of DPPC and water molecules which are standard components in the Martini force field. The coarse-grained DPPC molecule consists