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LATERAL AND NORMAL DIFFUSION IN POPC/SOPC/SAPE/POPE MIXED BILAYER: A MOLECULAR DYNAMICS STUDY

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Abstract

We have performed a 40-ns molecular dynamics simulation of POPC/SOPC/SAPE/POPE mixed Bilayer. The diffusion properties of lipid molecules have been studied. The corresponding diffusion coefficients of lipids have been estimated, and the findings are in good agreements with experimental data.

Keywords and phrases

Mixed bilayers, lipids, molecular dynamics, diffusion coefficients, cholines, thanomalines, phospholipids, NAMD, GROMACS.

ԼԱԹԵՐԱԼ ԵՎ ՆՈՐՄԱԼ ԴԻՖՈՒԶԻԱՆ POPC/SOPC/SAPE/POPE ԽԱՌՔ ԵՐԿՇԵՐՏՈՒՄ. ՄՈԼԵԿՈՒԼԱՅԻՆ ԴԻՆԱՄԻԿ ՀԵՏԱԶՈՏՈՒԹՅՈՒՆ

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Համառոտագիր

Մենք իրականացրել ենք POPC / SOPC / SAPE / POPE խառը լիպիդային համակարգի մոդելավորում մոլեկուլային դինամիկայի մեթոդով (40 նվ): Ուսումնասիրվել են լիպիդային մոլեկուլների դիֆուզիոն հատկությունները: Գնահատվել են համապատասխան դիֆուզիոն գործակիցները, և ստացվել է բավականին լավ համընկում փորձարարական տվյալների հետ:

Բանալի բառեր և բառակապակցություններ

Լիպիդներ, մոլեկուլային դինամիկա, դիֆուզիոն գործակիցներ, խոլիններ, ֆոսֆոլիպիդներ:

ЛАТЕРАЛЬНАЯ И НОРМАЛЬНАЯ ДУФФИЗИЯ В POPC/SOPC/SAPE/POPE СМЕШАННОМ БИСЛОЕ: МОЛЕКУЛЯРНО-ДИНАМИЧЕСКОЕ ИССЛЕДОВАНИЕ

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Аннотация

Мы провели 40-нс моделирование молекулярной динамики смешанного бислоя POPC/SOPC/SAPE/POPE. Изучены диффузионные свойства липидных молекул. Соответствующие коэффициенты диффузии липидов были оценены, и результаты находятся в хорошем согласии с экспериментальными данными.

Ключевые слова и фразы

Смешанные бислои, липиды, молекулярная динамика, коэффициенты диффузии, холины, фосфолипиды.

Introduction

The MD simulations of heterogeneous membrane systems are currently in great interest [1-3], and lots of MD simulations of mixed lipid bilayer have been reported [4-6]. The structural parameters (area per lipid on the surface of the bilayer, the

thickness of bilayer, order parameters and electron density) were calculated to verify with experimental findings.

The goal of this paper is the detailed analysis of normal and lateral diffusion of lipid molecules in a mixed system. The lateral diffusion, i.e. the thermal motion of lipid in two directions, in the heterogeneous system was intensively reported since 1984 both experimentally [7,8] and theoretically[9]. The lateral diffusion, as known, is defined from average mean displacement (MSD) of the molecule, and the latter formulated as:

$$MSD = \sum_{all} <| \vec{r}(t) - \vec{r}(0) |^2 > \qquad (1)$$

where the r designation is the position and the sum is over all molecules of a given kind. The resulting lateral diffusion coefficient is estimated to be $D_{lat} = MSD/4 \cdot t$, where the t is the simulation time. The lateral diffusion assumed to be in $x - y$ the plane of the bilayer. The phospholipid bilayer of erythrocyte membrane was investigated.

Simulation details

The initial random distributed 128 POPE/SOPC/SAPE/POPC bilayer with ~32 water hydration has been simulated using NAMD package [10] with CHARMM all27 force field [11]. The molecule's number ration was 36:34:32:26/POPC:SOPC:SAPE: POPE, as in erythrocyte membrane. Periodic boundary conditions were applied, the pressure and temperature were set to $320K$ and $1atm$, correspondingly, maintaining both using Langevin and Nose-Hoover Langevin piston methods [12]. The Particle Mesh Ewald (PME) method for electrostatic and cutoff (12A°) for van der Waals interactions were used. The initial configuration of the system was stabilized by energy minimization. Then, the system was gradually heated from $0K$ to $300K$ and kept at $300K$ until the volume of the system became equilibrated at the NPT ensemble. The integration time step was 2 *fs*, and the total MD simulation was 40ns. The computation was carried out with a Linux cluster (Intel Xeon 3.2 GHz, 48 CPU, Myrinet net) using 24 nodes. Total computation time consumed by the simulations was about 15 days.

Details and Discussion

Lateral and Transversal Diffusion

The MSD plots of center of mass (COM) position of POPC/SOPC/POPE/SAPE molecules in the bilayer $x - y$ plane are shown in Figure 1.

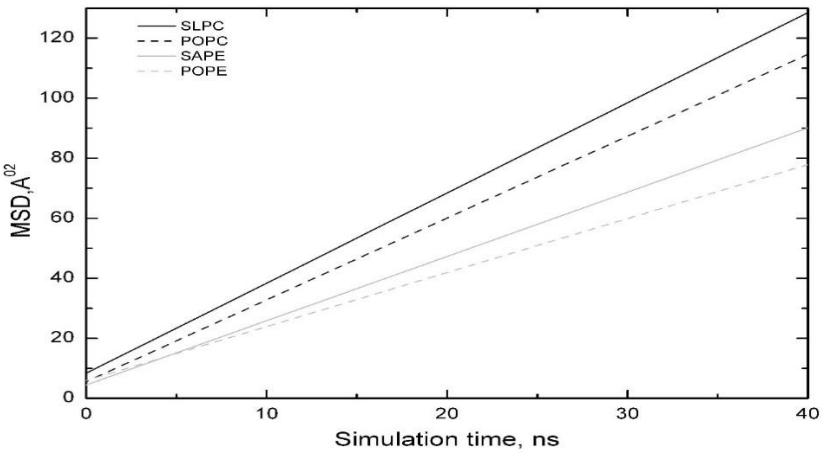

Figure 1. *The MSD plots of COM position of POPC/SOPC/POPE/SAPE molecules in* $x - y$ *plane of bilayer. The linear fitting is applied.*

We have plotted the location of COM position of lipid from the initial configuration (in $x - y$ the plane) in Figure 2. As already mentioned the initial setup was created randomly, and some small sub-domains (clusters) of separate types of phospholipids in bilayer and forms randomly distributed small clusters. The linear fitting of the MSD plot of SOPC molecule shows higher value over the simulation time. Having two 18:0/18:1 tails, the SOPC molecule, as seen in Figure 2, initially creates only two sub-domains – pairs and triplets of SOPC molecules (dotted circles in Figure 2). Overall, the profiles show that the diffusion of PC is higher than the PE. The estimated average lateral diffusion length of the PC is about $14A^o$ and for PE - $10A^o$.

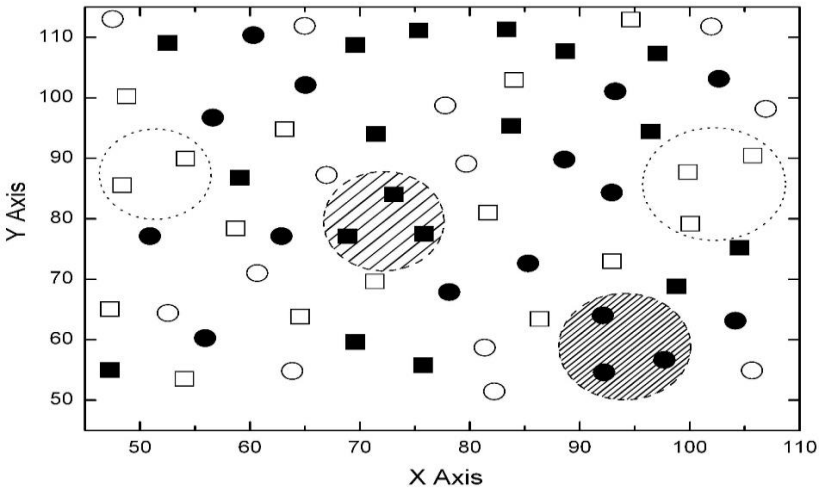

Figure 2. *The COM position of the initial structure of the mixed system, where the full square is POPC, the empty square – SOPC, the full circle is SAPE and the empty circle – POPE.*

The calculated diffusion coefficients are shown in Table 1. The experimental findings on the diffusion coefficient of the mixed lipid bilayer are in the range of $\approx (4-30)\times 10^{-8}\ cm^2/s$ [13,14]. Therefore the estimated results from MD simulation may be considered as a good agreement with experimental data.

The diffusion coefficients for various phospholipids in the bilayer. Table 1.

Phospholipids in a mixed system	SOPC	POPC	SAPE	POPE
Diffusion coefficient (cm^2/s)	4.2 x 10^{-8}	3.7 x 10^{-8}	2.9 x 10^{-8}	2.6 x 10^{-8}

The transversal (i.e. normal) diffusion length is $8-10\,A^o$. In Figure 3, the Z-axis movement of COM of individual SOPC molecule is shown.

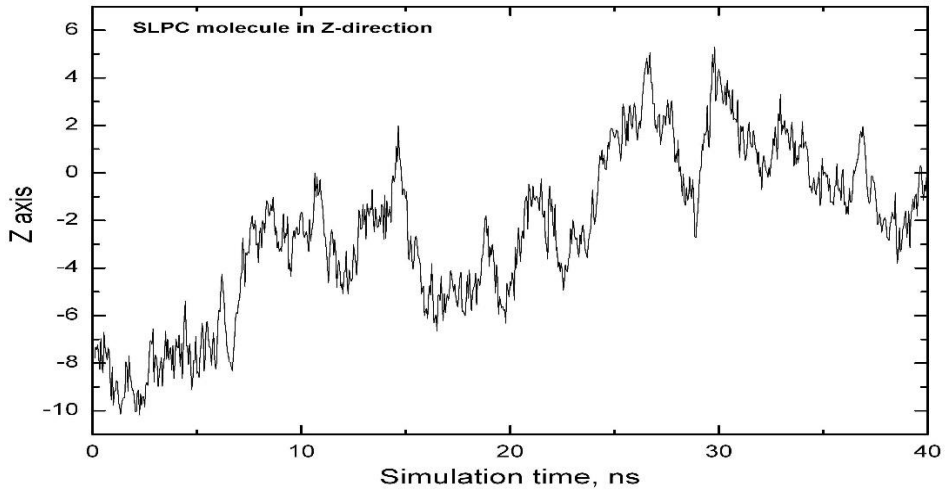

Figure 3. *A 40-ns trajectory of center of mass of a SOPC molecule in Z -direction of bilayer (vertical movement of individual SOPC molecule)*

As it is evident from Figure 3, the protrusions in the z-direction occur, which is due to the thermal movements of phospholipids molecules.

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