EFFECTS OF LIPID COMPOSITION ON DEFECT FORMATION IN BILAYERS

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Abstract— **Biological membranes are composed of a great variety of lipid species such as the lamellar dioleoyl-phosphatidylcholine (DOPC) and the non-lamellar dioleoyl-phosphatidylethanolamine (DOPE) lipids. The lamellar/non-lamellar lipid ratio in a membrane affects its structural characteristics. In this work, we study the effect of this ratio on the formation of hydrophilic transmembrane pores. We employ molecular dynamics simulations to study pore formation in five different DOPC/DOPE lipid bilayers, immersed in water, using semi-anisotropic stretching to generate the desired pores. Our preliminary results show that for unitary membranes the formation of the transmembrane pore occurs with similar levels of stretching. Whereas for binary membranes a greater proportion of lamellar lipids requires a greater stretching to achieve the same defect than if the non-lamellar lipid is dominant. Thus, changes in the lamellar/non-lamellar ratio changes the mechanical properties of biological membranes.**

I. INTRODUCCIÓN

Biological cells are protected by membranes which separate the cell contents from the environment.[1] Defects in cell membranes, such as pores and domain borders, play an important role in many cellular processes, such as drug delivery and ion transport.[2] For certain physiological functions, such as transfer of drugs into cells, these defects are needed. Characterising pores experimentally is a complex task due to their transient nature. Computer simulation, on the other hand, allows us to accurately quantify the size and shape of a given pore. The ratio of lamellar lipids such as dioleoyl-phosphatidylcholine (DOPC) to non-lamellar dioleoyl-phosphatidylethanolamine (DOPE) lipids is believed to affect membrane functionality.[3] Herein, molecular dynamics simulations are used to generate transmembrane pores for varying lipid composition to test this theory.

II. MATERIALES Y MÉTODOS

The system is formed by 288 lipids and 9520 polarizable water molecules. We simulate a DOPC:DOPE lipid bilayer in polarizable water, with different mixing ratios; 1:0, 1:3, 1:1, 3:1 and 0:1. All systems are modelled using the coarse-grained force field, MARTINI. Molecular dynamics (MD) simulations are performed using the LAMMPS code. The generation of transmembrane pores is achieved by semi-isotropic stretching of the system in the bilayer plane during a period of 100ns. Then, systems are then equilibrated for 500ns at 300K and atmospheric to allow pore to form.

The technique used to open transmembrane pores was first described by Tolkepina et al., in 2004, where pores form by stretching the lipid bilayer beyond its equilibrium surface area. In our investigation we stretched each system by 10-50 % in the x and y directions. After equilibration any observed pores were characterised using a Monte Carlos based sampling algorithm.

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III. RESULTADOS

Our preliminary results show that for unitary membranes, i.e. consisting solely of DOPC or DOPE, the formation of the transmembrane pore occurs with similar levels of stretching. In binary systems, however, the elasticity is improved with greater proportions of the lamellar DOPC lipid. Note that the DOPC 3:1 DOPE system is the most elastic system studied, requiring a 11 % greater stretch than the second most elastic system in the study (DOPC1:1 DOPE). Using the Monte Carlo based sampling algorithm the overall pore volume was determined for each system. As pores are approximately cylindrical in nature, the pore radius was obtained from the equation of a perfect cylinder, where the membrane width was used as the height of the cylinder. In Fig. 1 it is clear that the radius of a given pore depends upon the level of stretching applied to the given system

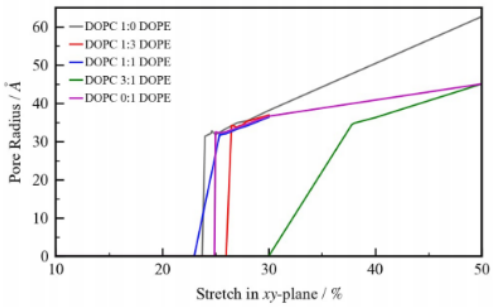

Figure 1. Plot showing the dependence of pore radius on the % stretch of five membrane systems of varying DOPC:DOPE ratios.

IV. DISCUSIÓN & CONCLUSIONES

Membranes of unitary composition are more plastic than those of binary compositions. The radius of a given pore increases in response to increased levels of stretching. Examining the local lipid compositions close to the pore would provide this study with further data from which the effects of increasing the lamellar/non-lamellar ratio may affect pore formation.

REFERENCIAS

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