Commun. Comput. Phys.
doi: 10.4208/cicp.230411.230312a

Vol. **13**, No. 4, pp. 1093-1106
April 2013

Measuring the Spontaneous Curvature of Bilayer Membranes by Molecular Dynamics Simulations

Han Wang[1,2,*], Dan Hu[3] and Pingwen Zhang[1]

[1] *LMAM and School of Mathematical Sciences, Peking University, Beijing, P.R. China.*
[2] *Institute for Mathematics, Freie Universität Berlin, Berlin, Germany.*
[3] *Department of Mathematics, MOE-LSC, and Institute of Natural Sciences, Shanghai Jiao Tong University, Shanghai, P.R. China.*

Received 23 April 2011; Accepted (in revised version) 23 March 2012

Communicated by Qiang Du

Available online 21 September 2012

Abstract. We propose a mathematically rigorous method to measure the spontaneous curvature of a bilayer membrane by molecular dynamics (MD) simulation, which provides description of the molecular mechanisms that cause the spontaneous curvature. As a main result, for the membrane setup investigated, the spontaneous curvature is proved to be a constant plus twice the mean curvature of the membrane in its tensionless ground state. The spontaneous curvature due to the built-in transbilayer asymmetry of the membrane in terms of lipid shape is studied by the proposed method. A linear dependence of the spontaneous curvature with respect to the head-bead diameter difference and the lipid mixing ratio is discovered. The consistency with the theoretical results provides evidence supporting the validity of our method.

PACS: 87.16.D-, 82.70.Uv

Key words: Bilayer membrane, Helfrich free energy, spontaneous curvature, molecular dynamics simulation.

1 Introduction

A lipid is an amphiphilic molecule that is made up of one hydrophilic head group followed by one or two hydrophobic tails. When lipids are dissolved into a solvent environment, they will self-assemble into various structures, such as micelles, vesicles and bilayers. The lipid bilayer is the basic component of biomembranes that serve as the

*Corresponding author. *Email addresses:* han.wang@fu-berlin.de (H. Wang), hudan80@sjtu.edu.cn (D. Hu), pzhang@pku.edu.cn (P. Zhang)

boundaries of the cells and the organelles, such as the endoplasmic reticulum (ER), the Golgi apparatus and so forth.

The biological functions of cells are closely related to the membrane's shape and the morphological changes. Therefore, in the past decades, a growing interest has been drawn to the elastic theory that studies the response of a membrane to the shape deformation [1–4]. One of the most important theories was proposed by Helfrich [1]. It was developed by analogizing to the elastic theory of the liquid crystal. At the continuum level, according to the Helfrich's theory, a membrane is regarded as a fluid elastic sheet, and all atomistic details of the membrane are condensed into three effective parameters: the *bending modulus*, the *spontaneous curvature* and the *Gaussian modulus*. The bending modulus has been extensively studied by experiments [5–9] and molecular simulations [10–14].

The experimental studies have discovered and verified various mechanisms of the spontaneous curvature. Nearly all of them can be summarized into two categories: the bilayer asymmetry and the physical constraint (see [15–18] and the references therein). The bilayer asymmetry can be generated by the transbilayer lipid shape asymmetry [16]. With different kinds of head groups and different numbers of tail chains, the shape of a lipid is analogized to a cone, a cylinder or an inverted cone [19], corresponding to negative, zero or positive spontaneous curvature, respectively. The bilayer asymmetry can also be produced by proteins that insert their hydrophobic parts into one leaflet of the bilayer [20, 21]. The physical constraint stems from the attachment of curved macromolecules to the membrane. For example, if a curved protein is sufficiently rigid and exposes its bent interaction surfaces to the lipid bilayer, a spontaneous curvature is enforced [17, 20, 22–24]. This mechanism is also called protein scaffold.

To precisely measure the spontaneous curvature, a few molecular simulation methods have been developed recently. The pressure profile method has been used to measure the spontaneous curvature of the homogeneous monolayer membrane [25] and protein-membrane complex [26]. This method assumes that the spontaneous curvature can be expressed by the first moment of the bilayer pressure profile. It was pointed out that the pressure profile is not uniquely determined because the expression for the local pressure involves an arbitrary choice of an integration contour [27, 28], though it was also shown that the symmetric part of the pressure tensor is unique under certain conditions [29]. The error of the spontaneous curvature reported by this method is roughly 50% [25, 26]. The spontaneous curvature is also measured by fitting the profile of the curved membrane section to a circle [23, 30]. However, the membrane system is hard to reach equilibrium in a few simulation cases [23, 24]. This method is lack of rigorous theoretical support.

The main purpose of the present paper is to develop a mathematically rigorous method measuring the spontaneous curvature by molecular dynamics (MD) simulation. We first prove the main result of this work: for the system setup investigated in the present paper, the spontaneous curvature is equal to a constant plus twice the mean curvature of a membrane in its tensionless ground state. The constant is eliminated by an antisymmetric system setting, so the spontaneous curvature is measured by the mean curvature.