



Structures of single, double and triple layers of lipids adsorbed on graphene: Insights from all-atom molecular dynamics simulations



Timothée Rivel^a, Semen O. Yesylevskyy^b, Christophe Ramseyer^{a,*}

^a Laboratoire Chrono Environnement UMR CNRS 6249, Université de Bourgogne Franche-Comté, 16 route de Gray, 25030, Besançon Cedex, France

^b Department of Physics of Biological Systems, Institute of Physics of the National Academy of Sciences of Ukraine, Prospect Nauky 46, Kiev-28, 03680, Ukraine

ARTICLE INFO

Article history:

Received 8 November 2016

Received in revised form

21 March 2017

Accepted 22 March 2017

Available online 23 March 2017

ABSTRACT

Non-covalent functionalization of graphene with phospholipids is a promising technique for biosensing applications and intracellular delivery of analytical probes and drugs. However, molecular details of the self-assembly of lipids on graphene surface is still poorly understood and hard to control. There is a clear lack of understanding of why various kinds of lipid aggregates can form on graphene. In the current work, we address this question by investigating equilibrium and dynamical properties of lipid layers adsorbed on graphene in water environment and in vacuum using all-atom Molecular Dynamics simulations. It is shown that a variety of lipid aggregates can form on top of graphene depending on initial orientation, number of adsorbed lipid layers and the presence of water. The lipid layers self-organize and reorient in order to minimize hydrophobic mismatch on graphene-lipid, lipid-lipid and water-lipid interfaces. Obtained structures range from homogeneous layers to the networks of inverted micelle-like structures and weakly bound cylindrical micelles on top of monolayers. Our results are in excellent agreement with recent experimental findings. Another pronounced effect of graphene is the strong ordering of the lipid atoms which are in direct contact with it. In all studied systems at least two well-structured atomic shells are formed above the graphene surface at the distances of 0.35 and 0.85 nm.

© 2017 Elsevier Ltd. All rights reserved.

1. Introduction

Graphene, in its pristine state, is a one-atom thick two-dimensional structured layer of carbon that exhibits remarkable mechanical, thermal, electrical and optical properties [1–3]. Since its discovery it has been considered as a unique platform for many applications [4–7] including molecular sensing [8–14] and drug delivery [15,16]. This promising material can be easily covalently or non-covalently functionalized either for solubility reasons or for desired chemical reactivity. Strongly hydrophobic nature of graphene makes lipids attractive candidates for its non-covalent functionalization. Several nanocomposites functionalized by lipids have already demonstrated great potential for biosensing applications or intracellular delivery of analytical probes and drugs [17–21]. Particularly, phospholipids, which are the structural components of cell membranes and which play an important role in the intracellular signaling, have been shown to interact strongly

with graphene. For instance, it was shown, both experimentally [22,23] and theoretically [24,25], that pristine graphene (PG) and graphene oxide (GO) nanosheets can induce cell membrane damages to the Gram-negative *Escherichia Coli* bacteria by extracting large amounts of phospholipids from both inner and outer cell membranes. This demonstrates the potential application of graphene as a novel antibacterial compound but also raises questions on its potential cytotoxicity. The strong interaction between graphene and the lipids was also utilized to exfoliate graphite and to produce graphene nanosheets [26] or to assist in the detachment of lipid bilayers from mica substrate [27]. The lipid-graphene interaction is strong enough to destroy self-assembled lipid structures like micelles, liposomes, or vesicles allowing them to cover the graphene's surface and to self-assemble again on it in different arrangements [28]. For now, the fusion of lipid vesicles or liposomes is often considered as a routine technique of depositing lipid layers on graphene [29,30] and its derivatives [30–34]. Supported lipid bilayers (SBL) are usually obtained on hydrophilic substrate like GO while, on hydrophobic supports like PG, supported monolayers (SML) and triple layers of lipids are also observed [26]. The lipids can also be deposited and manipulated directly on a substrate

* Corresponding author.

E-mail address: christophe.ramseyer@univ-fcomte.fr (C. Ramseyer).

by a high-precision tool, e.g. an ink-jet nozzle, a microstamp or a microfluidic device [35,36]. The scanning probe-based fabrication is assumed to be a better way to control solid-supported lipid aggregates [37–39]. Although the nature of lipid deposition looks simple at first glance, the structure of the lipid layers on graphene is quite complex and mobile. It strongly depends on various internal and external parameters. For instance, the layer-by-layer assembly of lipids by vesicle fusion was shown to depend on the sizes of graphene support and the vesicles themselves [32]. Quartz Cristal Microbalance and Atomic Force Microscopy experiments revealed that spontaneous liposome rupture onto GO occurs only for large lateral dimensions of the GO sheets. The charges of the lipids also play a crucial role in deposition. For instance, it was shown that only anionic liposomes could spontaneously self-organize into lipid monolayers that partially cover graphene surface [29]. The support on which graphene is grown (usually silicon dioxide) and the media where the measurements are performed (either air or buffer solution) can also affect the nature of the lipid layers. An interesting study has been conducted recently by Hirtz et al. [37,38] who showed that the membrane organization on graphene can be understood in terms of hydrophobicity differences between graphene and its surrounding medium. AFM and Raman spectroscopy observations suggested that bilayers with hydrocarbon chains directed away from graphene are formed in the air while single layers with hydrocarbon chains facing the graphene sheet prevail in the systems immersed in buffer solution. In contrast, thin monolayer of lipids with an additional bilayer on top of it is observed in air on pure silicon dioxide.

Recent study of the self-limited spreading of phospholipids on graphene confirmed these findings. It was shown that DOPC lipids form an inverted “tails out” bilayer on graphene surface in air, while a stable monolayer with the head groups oriented away from graphene is formed in water [40].

Another example concerns the formation of lipid membranes on graphene films supported by sapphire substrate displaying different degrees of hydrophilicity [30]. When the substrates, which support graphene, display low hydrophilicity no formation of lipid layers is observed. In contrast, lipid monolayers are formed easily if substrates, which support graphene, are highly hydrophilic.

Thus it is possible to conclude that deposition of lipid layers on hydrophobic surfaces, including graphene, depends on many factors which found their origin at the molecular level. There is no clear picture how lipid self-organization occurs on graphene. In addition almost no attention is paid to the structure and dynamics of the lipid layers formed on graphene and its derivatives. Currently, there is only a very limited knowledge about the thickness of lipid layers on graphene and almost nothing is known about their lateral organization and dynamical behavior. In contrast to limited possibilities of experimental techniques, atomistic Molecular Dynamics (MD) simulations provide a unique opportunity to study interactions of lipids with graphene in atomic details and to reveal molecular organization of the lipid layers. Surprisingly, there are no dedicated MD simulations aimed at revealing properties of lipid layers adsorbed on graphene. Existing MD studies of lipid-graphene interactions are mostly focused on extraction of the lipids and cholesterol by graphene from the cell membranes [23,41] and on disruption of bacterial membranes by graphene [22].

The goal of the present study is to fill this gap. We study molecular structure and stability of different arrangements of 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC) lipids on top of pristine graphene. Single, double and triple layers of lipids adsorbed on graphene in different orientations are examined in a systematic manner. We use atomistic molecular dynamics to investigate time-dependent and equilibrium properties of the lipid layers. The simulations are conducted either in vacuum or in water

in order to study the effect of surrounding media on the layers' stability. Section 2 deals with the numerical backgrounds while the results of MD simulations are presented in Section 3. In Section 4, we compare our numerical findings with few experimental results available so far. In this last section, we also discuss the validity and limitations of our findings.

2. Methods

In this work, we have investigated in a systematic manner the structure and dynamics of mono-, bi- and trilayers of neutral DOPC lipids deposited on a graphene sheet using all-atom molecular dynamics simulations. The DOPC molecule is shown in Fig. 1. It exhibits hydrophobic tails and a polar head group linked by a carbonyl-glycerol group. These three groups will be used to identify the molecule throughout this work.

At the first stage, fully hydrated DOPC bilayer containing 100 lipids in each leaflet is simulated at 320 K and 1 atm for 100 ns in NPT conditions until it reaches a constant area per lipid. Comparison with experimental data [42] shows that density profiles of the different lipid chemical groups are close to the experimental ones. Slipids force field for DOPC from Jämbeck et al. [42,43] is used in the present study since it has been used extensively and is assumed to be one of the most accurate force field for phospholipids [45–48]. The system is simulated in a triclinic box in order to keep the same hexagonal symmetry as the graphene sheet (see Supplementary material Fig. S.1.). The area per lipid obtained in the reference simulation of DOPC bilayer is equal to 75.4 Å², which is in excellent agreement with previous computational [43] and experimental [48] studies. The monolayers of this equilibrated bilayer were then used as initial configurations for the subsequent simulations of lipid deposition. They were extracted from the last simulation frame and transferred as a whole onto the graphene.

A 10.2 × 9.8 nm graphene sheet is used in this work. Its area corresponds to the mean area of pre-equilibrated DOPC bilayer from the reference simulation. The force field parameters for graphene were chosen accordingly with previous studies [49–51]. Graphene carbon atoms are modeled as uncharged particles interacting with the rest of the systems by means of the van-der-Waals interactions only. The bonded interactions between carbon atoms are represented by bond stretching and angle bending harmonic potentials and improper dihedral potential centered at each carbon atom, which ensures planarity of the graphene sheet. The values of all parameters are chosen to be a reasonable compromise between two widely used parameters for graphene introduced by Gao et al. [49] and Patra et al. [52,53] (Table S.1).

Up to 3 lipid layers with different initial orientations with respect to the graphene sheet are tested. Individual lipid monolayers, which were previously equilibrated in the reference system, were oriented appropriately and positioned above the graphene at minimal possible distance from each other and from graphene surface which ensures the absence of steric clashes.

The following naming convention is used in this work. Lipid layers are numbered as 1, 2 or 3 starting from the closest to graphene's surface. Orientation of each layer is encoded as “t” (tails pointing toward graphene) or “h” (heads pointing toward graphene). Thus, system 1t represents a monolayer initially oriented “tails down”; 1t2h is a bilayer which has two layers, the first one being oriented “tails down” and the second one being oriented “heads down”, and so on. Accordingly, 14 combinations can occur. In order to focus on the most practically interesting systems and to keep the number of simulations tractable we excluded some double and triple layer systems, which have multiple thermodynamically unfavorable interfaces with hydrophobic mismatches (1h2h, 1h2t3t, 1h2t3h, 1h2h3t, 1h2h3h, 1t2h3h, represented as

Download English Version:

<https://daneshyari.com/en/article/5432031>

Download Persian Version:

<https://daneshyari.com/article/5432031>

[Daneshyari.com](https://daneshyari.com)