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Letter

Mechanical responses of the bio-nano interface: A molecular dynamics study of graphene-coated lipid membrane

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ABSTRACT

Bio-nano interfaces between biological materials and functional nanodevices are of vital importance in relevant energy and information exchange processes, which thus demand an in-depth understanding. One of the critical issues from the application viewpoint is the stability of the bio-nano hybrid under mechanical perturbations. In this work we explore mechanical responses of the interface between lipid bilayer and graphene under hydrostatic pressure or indentation loads. We find that graphene coating provides remarkable resistance to the loads, and the intercalated water layer offers additional protection. These findings are discussed based on molecular dynamics simulation results that elucidate the molecular level mechanisms, which provide a basis for the rational design of bionanotechnology-enabled applications such as biomedical devices and nanotherapeutics.

Recently there have been significant interests rising in developing bionanotechnologies such as bioelectronics platforms that interface biological materials such as cells or tissues with functional nanostructures [1–6]. Biosensory functions can be enabled by detecting the biophysiochemical signals transduced across at this interface, which allows extracting valuable information from biologically important reactions, as well as controlling cellular activities through nanoscale contacts with integrated devices. Bio-nano hybrids with high complexity in integration require massively interconnected arrays of processing devices, completed with integrated power supply and heat removal networks [7]. As a result, the bio-nano interface that conveys energy and information exchange between biological materials and nanostructures are pivotal in designing relevant technological applications. The structural and physiological stabilities of such an interface under external mechanical perturbation are important issues to be addressed practically in order to design reliable bionanotechnologies, which are crucial not only for preserving functions of bioelectronics, but also to conduct subcellular engineering of the biological processes [8].

Graphene and its derivatives such as graphene oxide are flexible single-atom-thick layers that are able to form compatible interface with lipid bilayers that constitute the cell membrane, which have been studied recently as functional nanostructures interfacing with biological materials. Nanocomposite structures have been constructed by depositing lipids onto graphitic layers or intercalating them into an assembly in a layer-by-layer fashion [2–4,9–11]. Researchers have found that graphene layers could confine the cell as an easy-to-apply impermeable and electron-transparent encasement that retains the cellular water content [4]. More interestingly, the graphene sheet deposited on the cell wall permits a free functioning of the plasma membrane it encapsulates [3]. The interface between graphitic layers and the cell membrane is the essential pathway that conveys information and energy exchange, where evidences have been reported for the existence of a layer of trapped water within this interface. The thickness of this intercalated water layer (IWL) is only a few nanometers, although its dependence on the physiological condition is still not clear. However, it effectively weakens the dielectric coupling across the interface and thus the disruptive effects to the cellular membrane [2,9]. In additional to these biochemical effects, the nanostructural coating using graphene could also protect the cell under physical or chemical attacks. The stability of both the living system and the bio-nano interface could also be broken down under external mechanical perturbations. This fact, however, has only very limited understandings in the community.

In this work, we explore mechanical responses of the lipid bilayer–graphene interface as a model system for general bio-nano interfaces. Empirical forcefield based molecular dynamics (MD) simulations are performed to probe the nanoscale structures and dynamics of the hybrid. We find that under external loads, the graphene coating provides an outstanding protection function for

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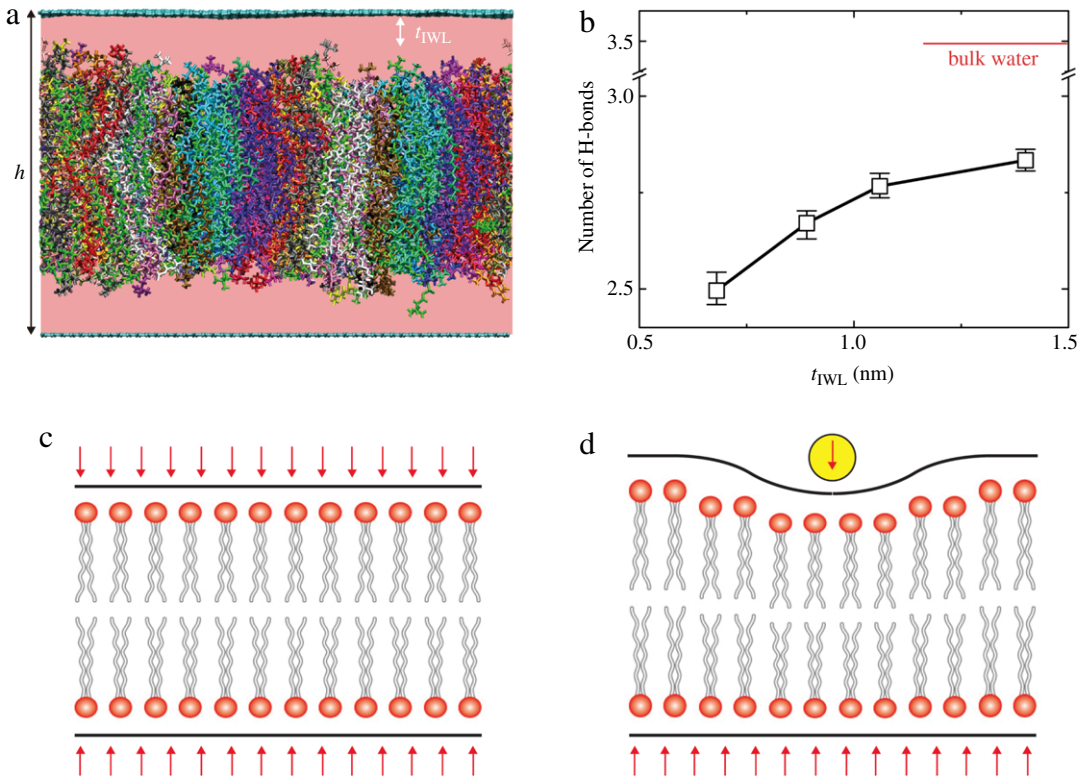

Fig. 1. (a) The model of graphene-coated lipid bilayer membrane with intercalated water layers. (b) Number of hydrogen bonds (per water molecule) analyzed for different IWL thicknesses, t_{IWL}. (c, d) Illustration of applied hydrostatic pressure and nanoindentation loads.

the lipid membrane. Moreover, the IWL at the lipid–graphene interface is found to play a critical role in modulating the transmission of mechanical signals and the mechanical stability of the hybrid. These conclusions are discussed with respect to their implications in designing related bionanotechnological applications.

We construct a lipid bilayer–graphene hybrid by placing the bilayer at a certain distance from the graphene sheets. Water molecules are added in between, which could enter the spaces in 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) lipid bilayers with a depth of ∼1 nm after thermal equilibration (Fig. 1(a)). The interfaces with top and bottom hydrophilic sides of the lipid bilayer are constructed symmetrically. A two-dimensional supercell is used with periodic boundary conditions (PBCs) along the interface, with lateral dimensions of 10.46 and 10.15 nm, respectively. Free boundary conditions are used in the dimension across the bilayer. Supercells with different lateral sizes are explored to characterize the size effect in the indentation tests, and we find notable size effect in the nanoindentation tests, where mechanical responses are weakened as the lateral membrane span increases under the same indentation force. However, our following discussions are focused on this specific system size for a quanlitative demonstration.

All MD simulations are performed using the large-scale atomic/molecular massively parallel simulator (LAMMPS) package [12]. Interatomic interactions between carbon atoms in graphene are described using the adaptive intermolecular reactive empirical bond order (AIREBO) potential with torsion and van der Waals terms included [13]. The CHARMM36 forcefield is used for the lipid bilayer, and water is simulated using the TIP3P model [14]. The SHAKE algorithm is applied for bond stretching and angle bending terms between oxygen and hydrogen atoms to avoid high-frequency vibrations that require shorter time steps. Interaction between water, graphene and the lipid bilayer includes both van der Waals and electrostatic terms. The former term is described by the 12-6 Lennard–Jones potential $4\varepsilon[(\sigma/r)^{12} - (\sigma/r)^6]$ and the Lorentz–Berthelot mixing rule [14], which is truncated at an interatomic distance $r = 1.0$ nm. Long-range Coulomb interactions are computed by using the particle–particle particle-mesh (PPPM) algorithm [15]. The time step is set to 0.5 fs to assure total energy conservation in absence of thermostat coupling. The whole system is equilibrated at 300 K and 1 a.t.m. (1 a.t.m. = 101325 Pa) (in the lateral dimensions) before the mechanical loadings are applied, using the Berendsen thermostat and barostat [16], respectively.

We carry out MD simulations with both hydrostatic pressure and local indentation loads on the lipid–graphene hybrid. The hydrostatic pressure P_z is simulated by compressing two planar walls towards graphene coatings at both sides of the graphene–lipid–graphene hybrid at a rate of 0.03 nm/ps (Fig. 1(c)). These planar walls interact with the graphene sheet through a harmonic, repulsive-only potential in the form of $U_{rep} = K(r - r_c)^2/2$, where r is the position of wall and the interaction is turned off beyond a cut-off distance $r_c = 0.1$ nm. The spring constant K is set to 200 eV · nm^{-2}. These settings allow us to probe mechanical responses of the hybrid under external pressure P_z, in terms of a compressive strain $\varepsilon_z = -2\Delta h/h$. Here h is equilibrium thickness of the lipid–graphene hybrid, which is defined by the vertical distance between two graphene sheets. Δh is the change. During the loading process we find that the lateral relaxation of simulation box is not significant due to the high in-plane stiffness of graphene.

To probe mechanical responses of the hybrid to local or concentrated loads, we carry out nanoindentation tests where an indenter is pressed towards one side of the lipid–graphene hybrid, while the other side is fixed (Fig. 1(d)). The indentation force f is tracked as a function of indentation depth d. The indenter is a rigid spherical particle with a radius of $R = 1$ nm, interacting with the graphene sheet through a force in the form of $f(r) = -k(r - R)^2$. Here r is the distance measured from the atom to the center of indenter. The specified force constant $k = 10^4$ eV · nm^{-3} is large