Research paper

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Free energy of adsorption of supported lipid bilayers from Molecular Dynamics simulation

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A novel method is presented for the calculation of adhesion energies of lipid bilayers on solid surfaces from molecular dynamics simulation. We illustrate the method with a fully atomistic model comprising a gold surface and an adsorbed lipid bilayer. We use our technique to scale the lipid-surface interactions to reproduce the experimental value for adsorption of DMPC bilayers on gold surfaces. Finally we estimate the entropic contribution to the free energy change on adsorption of the bilayer.

INTRODUCTION

The free energy of adsorption of lipid bilayers on solid surfaces is a key parameter that determines the passive cellular response to the presence of solid materials. It is of particular interest in developing models of nanoparticle uptake by human cells for the purpose of understanding potential cytotoxicity. Although it is common for cells to transport particles across the membrane via activated cellular processes it is also possible for particles to become engulfed by cells passively when the adhesion energy is sufficient to overcome the bending energy associated with membrane deformation during particle wrapping [1]. Knowledge of the adsorption energy of lipid bilayers, taken as a first approximation to real cell walls, is therefore of some importance in the design of safe nanoparticles for industrial and medical applications [2]. Molecular dynamics simulations of particle-bilayer interactions are an attractive source of data to inform safe nanoparticle design as they provide molecular detail inaccessible to experiment [3,4,5,6]. However, the quantitative predictions of such simulations are only as accurate as the interaction potentials employed. A great deal of effort has been expended to optimise lipid-lipid and lipid-water interaction potentials by calibration against empirically determined macroscale properties [15,16,17]. Similarly, interaction potentials between water with inorganic surfaces are typically calibrated to reproduce interfacial properties determined by experiment. Lipid-substrate interactions, on the other hand, are usually generated by cross averaging using geometric or arithmetic averages. In order to conduct realistic and predictive simulations lipid-substrate interactions should also be calibrated using experimental data. The obvious choice for such data is the free energy of adsorption and a prerequisite for using this data is a simulation method that can accurately predict the adsorption energy for a given set of potentials

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Simulations of *free* bilayers are typically conducted in the canonical ensemble with a periodic membrane spanning the simulation cell under tension that is controlled by an anisotropic barostat. When a periodic solid surface is introduced to the simulation cell in this geometry

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