Keynote Lecture KL 04

Exploring the effect of cholesterol on stratum corneum lipid assemblies

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Key Word (3 words)

Coarse-graining, Skin, Molecular dynamics

Abstract (less than 300 words)

The stratum corneum (SC) is the outermost layer of the skin and functions as the primary barrier between the body and the environment. The SC, composed of dead corneocyte cells surrounded by a matrix of lipid lamellae that provides the only continuous path through which external chemical penetrants and water can cross the SC. The SC lipids are primarily composed of ceramides of 18 subclasses, cholesterol, and free fatty acids. In addition, it has been discovered that deficiencies in certain lipid components and an altered lamellar structure in the SC lipids are associated with skin diseases such as eczema and psoriasis. Thus, exploring the composition-function relationship of the SC lipids, using both real SC samples as well as synthesized membranes, has been the focus of countless publications. Experimental studies, such as neutron scattering and x-ray diffraction have found that two lamellar phases coexist in the SC lipids: the 6 nm short periodicity phase (SPP) and the 13 nm long periodicity phase (LPP), of which the latter only forms in the presence of long esterified (EO) CERs and is unique to the SC [1]. However, experimental techniques are unable to uncover the molecular-scale arrangement or the barrier mechanism of the lipids.

Atomistic molecular dynamics (MD) can be used to model SC lipids since they provide a 3D structure with atomic resolution. However, due to the low mobility of the gel phase SC lipids, atomistic simulations can be heavily biased by their preassembled initial configuration and not reach equilibrium over practical computation times. In addition, due to high computational cost, atomistic MD systems are typically single bilayers, rather than multilayers, which do not provide an accurate representation of the skin lipid lamella. Alternatively, simulations using coarse grained models can feasibly access the long timescales needed to study self-assembly from randomized configurations and achieve the large system sizes required for multilayer systems to provide a more realistic, albeit less detailed, structure. Here the development of a novel computationally efficient coarse-grained model of the CER EOS using multi-state iterative Boltzmann inversion (MSIBI) is presented [2]. Furthermore, the CG model is applied to examine the effect of cholesterol concentration on membrane structure and fluidity for self-assembled SPP and LPP systems.

References

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