Biophysical theory and simulation of stratum corneum lipid bilayers

Chinmay Das, Simon Connell and Peter Olmsted

Introduction

Lipid bilayer membranes are an essential component of all biological systems, forming a functional barrier for cells and organelles from the surrounding environment. The advent of new experimental techniques has led to an explosion in understanding the basic physical mechanisms behind membranes.

Stratum Corneum Bilayers

Stratum corneum (SC), the outermost layer of skin, consists of keratin-filled rigid non-viable corneocyte cells surrounded by multilayers of lipids; it is responsible for the barrier properties of skin. The composition (ceramide NS-24:0, free fatty acid 24:0 and cholesterol) plays a key role in determining the SC membrane structural properties, such as high density, low permeability, and the nature of the gel phase of these bilayers. One important result is that the bilayer phase is probably most likely to form (rather than a disordered inverse micellar phase) in the presence of external fields or templating effects, such as the keratin protein that takes up a large fraction of the SC. Our simulations suggest that the composition ratio in native SC lipid layers is responsible for both the good barrier properties and the stability of the lipid structure against mechanical stresses.

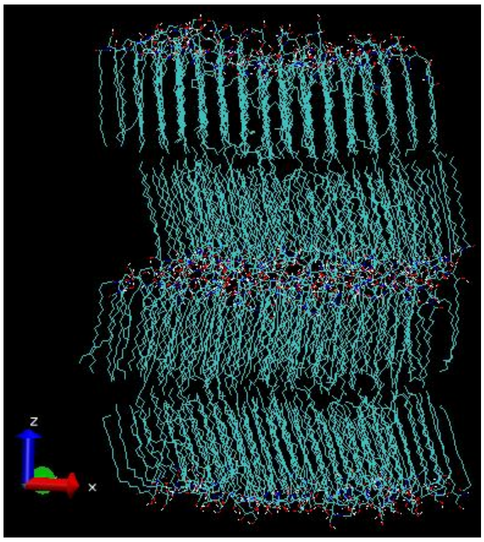

Figure 1: simulation of a ceramide bilayer showing tight hydrogen bonding between opposing leaflets.

We have developed a method to use AFM to extract the local stretching modulus of lipid bilayers. This is the first technique that can measure the mechanical properties of different regions of the same membrane, and we have demonstrated the technique on a three component mixture (DOPC, cholesterol, sphingomyelin) that exhibits liquid-liquid phase separation analogous to lipid rafts. We have shown that mechanical force can induce a transition from the liquid-ordered to liquid-disordered phases, and we have interpreted this in terms of the breaking of hydrogen bonds that stabilize the cholesterol-rich liquid-ordered phase.

We are in the second round of funding, in collaboration with Unilever, and the Universities of Bradford and Hull. This has provided a number of further insights and new findings about the design principles behind skin lipid membranes. The lipid compositions are highly hydrophobic, with the opposing leaflet head groups often strongly hydrogen-bonded. This helps with impermeability, and a layered structure can be maintained by the templating effect of the keratin bodies. The membranes are typically in the gel phase, but the asymmetric ceramide tails lead to an unusual soft amorphous layer between the stiffer leaflets. This seems to play an important role in flexibility and mobility, despite being in the gel phase, and allows facile membrane reorganization during swelling of keratin by water, or when under “normal” mechanical stresses.

Funding
This work was funded by the EPSRC, Yorkshire Forward, the EU (FP7 Network of Excellence SOFTCOMP), and Unilever.

Collaborators
This work was carried out in close collaboration with Massimo Noro and colleagues at Unilever Research Port Sunlight, as well as with groups at the Universities of Hull and Bradford.