CBMNet
CROSSING BIOLOGICAL MEMBRANES NETWORK, A BBSRC NIBB

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Interactions between mimetic bacterial membranes

The Challenge

The World Health Organization and the Centre for Disease Prevention and Control have made drug-resistant bacteria a priority research area. One of the main challenges facing development of new antimicrobial agents (AMAs) is the lack of accurate mimetic bacteria membrane models, posing a barrier to progression due to the lack of understanding of the mode of action of AMA compounds. This affects our ability to design effective AMAs. Physical disruptions of the bacterial membranes are a direct and effective bactericidal route, and thus one of the important prerequisites for the development of next generation AMAs is to understand how the pathogen coats will interact with the AMAs.

Thus, there is an urgent need for development of mimetic membranes that capture the structural and compositional sophistication of bacterial outer membranes.

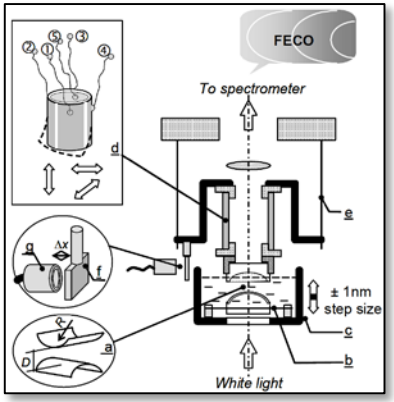
The Research

Dr Wuge Briscoe is a Reader in Physical Chemistry at the University of Bristol. The research in his laboratory focuses on the surface forces mediated by surfactants, polymers and nanofluids, and on fundamental aspects of biolubrication and nanotoxicity.

Proctor and Gamble (P&G) make quality personal care products that improve people's lives.

Building on previous collaborations supported by CBMNet-funding, Dr Briscoe applied for a CBMNet Proof-of-Concept award with Dr Eric Robles at P&G Newcastle Innovation Centre, an R&D facility of the world's largest consumer products manufacturer.

The central aims of this project were to: (1) design, fabricate and characterise the inner leaflet of bacterial membranes using solid-supported asymmetric lipid membranes; (2) study the fusion of these mimetic membranes using the Surface Force Apparatus (SFA).



CBMNet Proof of Concept Funding

The Result

In order to optimise the design of asymmetric lipid membranes, Π-A isotherms were obtained of varying membrane systems. These were then characterised using BAM imaging and by X-ray reflectivity (XRR). The results showed that incorporation of cardiolipin in the lipid mixtures had effects on lipid tail orientation and created much smaller and more stable liposomes.

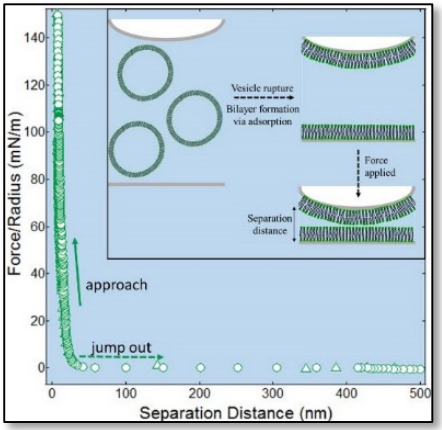
Initial SFA measurements were undertaken, starting out with DOPE monolayers, and LPS-Ra monolayer adsorbed onto DOPE. The initial SFA results showed that DOPE dry monolayers are a separation distance of about 3-4 nm. Once LPS-Ra had been deposited, using the Langmuir-Schaefer approach, the thickness of the supported lipid bilayers is around 4.5 nm (in water).

The Future

In the future, membranes will be further characterised using XRR to understand how lipid bilayers differ depending on the lipid composition.

The initial SFA studies will be built upon by varying the composition of the initial monolayer. Currently in progress is a detailed AFM study varying the temperature, $CaCl_2$ concentration, and incubation time of LPS-Ra on different membrane systems in order to study the stability and adsorption of LPS-Ra in more detail. Studies are also underway that will compare the deposition of LPS-Ra on different membrane monolayers using XRR.

The project has opened up opportunities for further investigations relevant to fundamental research as well as product formulations.



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