

Molecular structures and interactions of bacterial outer membranes: Rational antimicrobial agent design in personal care product formulation

The Challenge

Antimicrobial agents (AMAs) are essential drugs for human health and animal health and welfare. Resistance to antimicrobials is a global public health concern that is impacted by both human and non human usage.

One of current challenges facing development of new AMAs, whether it is new drugs, peptides, or cationic polymers, is the lack of accurate mimetic gram-negative bacteria membrane models. A realistic mimetic membrane system will enable bona fide laboratory evaluations of the impact of different product ingredients on the integrity of bacterial cell membranes, guiding fast rational design of new generations of fast acting AMAs.

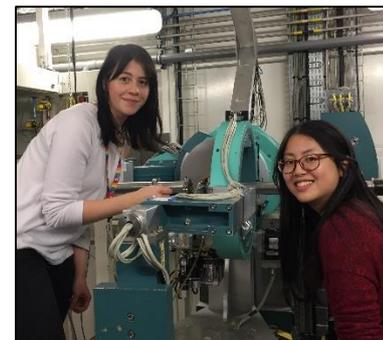
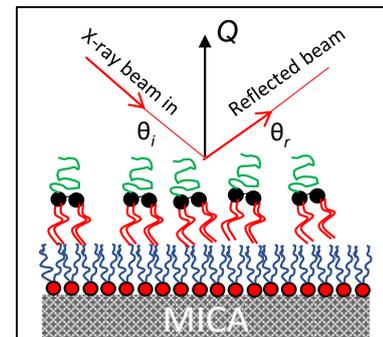
Hitherto, most of the existing mimetic bacteria models for testing AMAs (including those used by Procter and Gamble), however, comprise symmetric phospholipid bilayers, which are oversimplistic and thus compromise the validity and efficacy of AMA testing and development.

The Research

Dr Wuge Briscoe is a Reader at the University of Bristol. The research in his laboratory focusses on the characterisation of soft matter structures at interfaces and the interactions they mediate, using a range of physicochemical techniques, including synchrotron X-ray and neutron scattering, and the surface force apparatus.

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

Dr Briscoe applied for a CBMNet Business Interaction Voucher with Dr Eric Robles at P&G Newcastle Innovation Centre, an R&D facility of the world's largest consumer products manufacturer. The central aim of this project is to prepare, characterise and understand the structure of supported lipid bilayers at different substrates (silica, mica and graphene) that mimic the structural and compositional sophistication of gram(-) bacteria membranes.



CBMNet Business Interaction
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The Result

Model membranes have been successfully assembled at the solid-liquid interface to resemble the structure of gram-negative bacteria membranes, meaning that they have an asymmetric structure with an inner leaflet composed of DOPE phospholipids deposited using the Langmuir-Blodgett method, and an outer leaflet composed of bacterial liposaccharides (LPS) deposited in the presence of Ca^{2+} at two different temperatures (45 and 60 °C) through a simple adsorption process. The structure of these mimetic membranes has been characterised using synchrotron X-ray reflectivity (XRR) at the European Synchrotron Radiation Facility (ESRF) at Grenoble, France.

The project has also provided invaluable learning and training opportunities for a number of postgraduate students (e.g. Laura Fox and Liangzhi Zhou, shown to inspecting the XRR liquid cell in the previous photo) and postdoc fellow (Dr Luisa Islas, supported by CONYCAT).

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The Future

This fruitful project has further stimulated interactions between P&G and the University of Bristol. They have since been jointly awarded a CBMNet Proof of Concept grant to further pursue preparation and characterisation of the mimetic membranes developed, as well as further enhance the sophistication of the model with inclusion of cardiolipin and cholesterol. To lay the foundation for these further activities, they will submit a proposal to Diamond Light Source (I07) for XRR of the membrane structure and its disruptions by AMAs at the air/water interface. They also have the ambition to expand this work to gram-positive bacteria membranes, via proposals to attract high quality CDT students from the Bristol Centre for Functional Nanomaterials (BCFN).

The experience and outcome from this project has helped Dr Luisa Islas to secure a 1-year renewal to her CONACYT fellowship, to continue the work on the mimetic membranes.

“The CBMNet Business Interaction Voucher has allowed us to work closely with P&G to develop the bacteria mimicking membranes. We feel that we are contributing to a fundamentally important area, and our academic pursuits are helping P&G and other industries to design more effective antimicrobial agents.”

Dr Wuge Briscoe
University of Bristol



“The CBMNet Business interaction Voucher has allowed us to widen the scope of our collaboration with Dr Wuge Briscoe’s research team at Bristol, provide access to reflectometry techniques in the company and most importantly, identify potential new approaches to understand how antimicrobial agents interact with cellular membrane.”

Eric Robles, Research Fellow
Procter & Gamble