Self-assembly and interactions of bacterial membrane lipids

About the project or challenge area: Antibiotic resistance has become an important issue due to excessive use of antibiotics in agriculture and health industry. To develop effective and alternative antibacterial agents, it is crucial to understand the structure of, and fundamental interactions at, the bacterial cell wall. Lipopolysaccharide (LPS) is a key structural component of the outer membrane of gram-negative bacteria and fulfil two major functions: 1) as an effective permeability barrier against xenobiotic agents, antibiotics and the host cell defence system; and 2) as a highly potent mammalian toxin when released from cells into a host's bloodstream (*i.e.* the endotoxic effect). The amphiphilic nature of LPS causes the molecules to form aggregates above certain concentrations in solution. Cations can complex with LPS and lead to LPS aggregates structure transformation, which affects bacterial membrane integrity and LPS virulence (Fig.1). The accumulation of various cations, *e.g.* Na^+, Ca^{2+}, and Mg^{2+} around the bacterial cell membrane is regulated by highly negatively charged phosphate groups present in LPS. Many naturally occurring antimicrobial peptides (AMPs) are also multiply charged cations. Understanding interactions between different cations and cationic species with LPS is thus critically important to antibiotic and antiendotoxic mechanisms and antimicrobial agent design. This project will utilize quantitative state-of-the-art physicochemical methods, including neutron and X-ray scattering (at central facilities in the UK, France, and Germany), AFM and cryo-TEM imaging, to interrogate the structure of a plethora of self-assembled structures in solution and at interfaces.

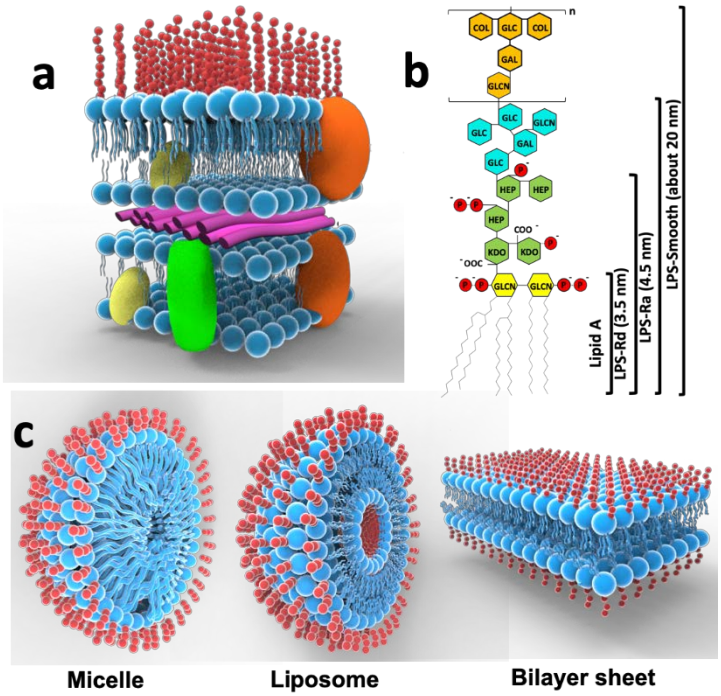

Fig. 1 (a) Gram-negative bacterial envelope. (b) LPS molecular structure. (c) Possible LPS aggregate structures in solution with ions.

Why choose this opportunity? Antimicrobial resistance is a major challenge we face in the 21st century. The work in this area can make a real impact on the global challenge and will also advance our fundamental knowledge in self-assembly. You will develop knowledge in fundamentals of lipids, surfactants, polymers, colloid and interface science underpinning many current health and environment global challenges. You will also develop expertise in quantitative physicochemical techniques. Our group is highly international and dynamic, with extensive industrial and academic links in the UK and worldwide. You will have the opportunity to interact and collaborate with the members across the group, developing transferrable skills. Your professional and personal development, as well as enriching cultural experience, is central to the training programme. You will be supported throughout the project through individual and group meetings, graduate courses, and technical training, tailored to your specific needs. You are encouraged and supported to present your work at international conferences publish your work at international journals.

About you: Skills and knowledge in physics, materials, chemistry, analytical methods, and colloid science is desirable but not essential. Training will be provided.

Bench fees: A bench fee of £4000 is required. A small number of School of Chemistry Bench fee bursaries are available to part-cover bench fees

How to apply: Applications are accepted throughout the year and you should complete the online application form for Chemistry (MSc by Research).

Supervisor: Dr Wuge Briscoe, Reader in Physical Chemistry in the School of Chemistry. You can contact him at +44 (0) 117 3318256 or email wuge.briscoe@bristol.ac.uk

Find out more about your prospective research program: *Natural and bioinspired nanostructured bactericidal surfaces* https://doi.org/10.1016/j.cis.2017.07.030; *Interactions between Mutant Bacterial Lipopolysaccharide (LPS-Ra) Surface Layers: Surface Vesicles, Membrane Fusion, and Effect of* Ca^{2+} *and Temperature* https://doi.org/10.1021/acs.langmuir.9b02609