Project title: **Dissecting the emergence of complexity in living bacteria, one molecule at a time**

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Studying the emergence of complexity in living cells is challenging. Bacterial sporulation however, presents a fantastic model system for doing so. Using exciting state-of-the-art microscopy and genetics techniques we can now follow the emergence of cellular complexity one molecule at a time as it actually happens in living cells. To survive starvation and/or stress, bacteria such as Bacillus and Clostridia abandon growth and follow a pathway of cell differentiation to form a metabolically dormant spore. These spores are resistant to heat, chemical stresses and antibiotic treatment and, as a result, spores of pathogens such as B. cereus and C. difficile are associated with food poisoning and hospital acquired infection respectively. Sporulation begins when the rod-shaped bacterial cell divides asymmetrically giving rise to genetically identical daughter cells with different fates. Different sets of genes are expressed in the larger mother cell and the smaller forespore.

The mother cell then engulfs the forespore, and in the nurturing environment of the mother cell cytoplasm, protein layers are deposited around the forespore as it matures into a resistant spore. Finally, in an act of sacrifice, the mother cell lyses releasing the mature spore which can survive indefinitely and germinate when favourable conditions for growth are restored.

Spore formation presents a treasure trove in molecular cell biology featuring starvation sensing and signal integration, polar cell division, differential gene expression, phagocytosis and programmed cell death. For many years, AJW has been investigating structure-function relationships in these proteins using techniques of protein biochemistry and crystallography and the student will gain exposure to, and training in, these techniques. The central and distinct focus, here, will be the determination of structures of complexes in live sporulating cells. Using advanced microscopes designed and built in the laboratory of MCL, the student will observe individual complexes in living bacterial cells and determine their composition and stoichiometry as well as the dynamics of their assembly and disassembly. In order to carry out these studies, the student will use genetic engineering methods to generate strains expressing target proteins fused to fluorescent reporter proteins. Specifically, we are interested in (i) a protein phosphatase that activates compartment specific gene expression in the forepore (ii) complexes of membrane proteins that facilitate the movement of the mother cell membrane around the forespore membrane during cell engulfment and (iii) a protein that mediates the fusion of the engulfing membranes at the completion of engulfment.

*The studentships are available to UK and EU students who meet the UK residency requirements. Students from EU countries who do not meet the residency requirements may still be eligible for a fees-only award. Further information about eligibility for Research Council UK funding can be found at the following website: [http://www.bbsrc.ac.uk/documents/studentship-eligibility-pdf/](http://www.bbsrc.ac.uk/documents/studentship-eligibility-pdf/) Students with, or expecting to gain, at least an upper second class honours degree, or equivalent are invited to apply. The interdisciplinary nature of this programme means that we welcome applications from students with backgrounds in any biological, chemical, and/or physical science, or students with mathematical backgrounds who are interested in using their skills in addressing biological questions.

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Application closing date: Sunday 8 January 2017

Interview date: To be confirmed

Funding source: BBSRC

Funding scheme (if any): White Rose DTP

Funding Types: Competition

Eligibility: UK *