PhD studentship at Queen Mary, University of London - starting 1st September 2010
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The studentship pays a stipend for 4 years, in return for some undergraduate teaching duties.

Cellular communication channels in cyanobacteria

Filamentous cyanobacteria are true multicellular prokaryotes. Different cells in the filament communicate and co-operate for the benefit of the filament as a whole. One form of this co-operation occurs in heterocyst-forming cyanobacteria such as *Anabaena*. These organisms carry out nitrogen fixation in specialised cells called heterocysts. The remaining vegetative cells perform oxygenic photosynthesis. It has been understood for many years that the two cell types must exchange metabolites (sugars and amino acids). The mechanism of this molecular exchange remained unclear until very recently, when the supervisor (in collaboration with groups in Seville and Leeds) showed that tiny protein channels allow the rapid, non-selective diffusion of small molecules from cytoplasm to cytoplasm. A protein called FraG is essential for this molecular exchange and is almost certainly the main structural component of the channels: it is an integral membrane protein with a permease-like domain located at the cell-cell interface. Key to the work was a technique devised by the supervisor for observing and quantifying the diffusion of a fluorescent tracer molecule from cell to cell using confocal microscopy and Fluorescence Recovery after Photobleaching (Fig.1). See [1] for an account of this work, and [2] for further discussion, including an account of the remaining controversies in the field.

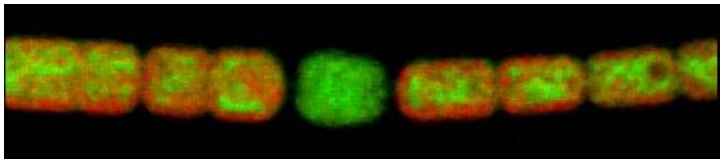

Fig. 1. Confocal fluorescence micrograph showing a filament of *Anabaena cylindrica* loaded with the fluorescent tracer calcein in the cytoplasm. Calcein fluorescence in green, chlorophyll fluorescence in red. The enlarged green cell in the middle is a heterocyst.

The project

The student will use a range of approaches to reveal more about intercellular communication in *Anabaena*, taking advantage of a superb range of multidisciplinary expertise available in QMUL and through established outside collaborations. We expect the work to deepen our understanding of this prokaryote as a multicellular organism, shedding light on cellular co-operativity, developmental pattern formation, and perhaps other communication mechanisms similar to nerve impulses.

1. What is the structure of the channels? The student will isolate channels from *Anabaena* using affinity tagging of FraG, followed by membrane solubilisation and affinity chromatography (collaboration with Prof Peter Nixon, Imperial College). The structure of the channels will then be investigated by single-particle electron microscopy.
2. How is channel activity regulated? We have good evidence that the channels are activated post-translationally when filaments are deprived of nitrate [1]. The student will use a combination of molecular biology, biochemistry and functional assays (as in [1]) to test hypotheses for the mechanism of channel activation.
3. Are there other mechanisms for exchange of molecules and/or signals? Possibilities include exchange of molecules via the periplasm [2] and membrane depolarisation as a rapid signalling mechanism involved in motility. Approaches based on quantitative confocal microscopy with fluorescent probes will be used. Motility work will be in collaboration with Dr David Adams (Leeds).

Training provided by the project

The project will provide multidisciplinary training in microbiology, molecular biology, cell biology, confocal microscopy and quantitative image analysis, biochemistry and electron microscopy.

References

1. Mullineaux, C.W., Mariscal, V., Nenninger, A., Khanum, H., Herrero, A., Flores, E. and Adams, D.G. (2008) Mechanism of intercellular molecular exchange in heterocyst-forming cyanobacteria. *EMBO J* 27, 1299-1308
2. Haselkorn, R. (2008) Cell-cell communication in filamentous cyanobacteria (MicroCommentary). *Mol. Microbiol.* 70, 783-785