Creating a functional map for brain-gut signalling in a simple worm model

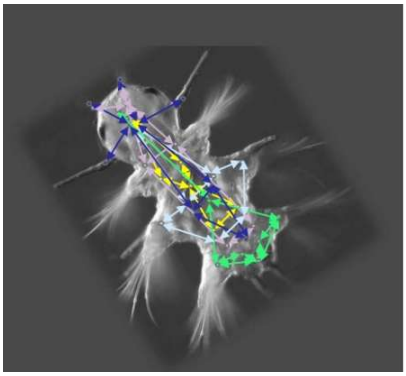
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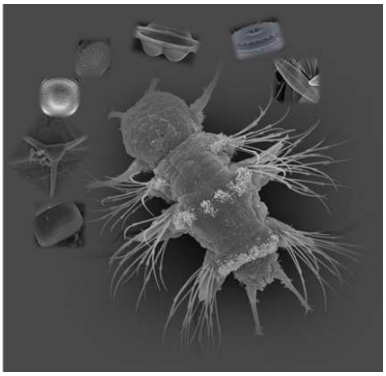
Supervisory team

Main supervisor: Dr Elizabeth Williams (University of Exeter)
Second supervisor: Dr Alex Corbett (University of Exeter)
Non-academic (CASE) supervisor: Dr Sam Swift (Cairn Research Ltd)

Host institution: University of Exeter (Streatham)

CASE partner: Cairn Research Ltd





Project description: The ability to actively locate and consume food is essential for life in many animals. Successful feeding requires sensory-neuroendocrine systems to interpret multiple cues and output coordinated behavioural sequences. The feeding process is challenging to study in its entirety because most animal digestive systems lie deep within the body, and their nervous and digestive systems are large and complex. We do not yet know the full extent of the signalling that guides feeding, from initial food detection to muscular gut contraction. This project aims to pick apart the feeding process one molecule and cell at a time using the transparent microscopic juvenile stage of the marine worm, Platynereis dumerilii. Platynereis is ideal for this goal as it maintains complex active feeding behaviours and neuroendocrine signalling within the framework of ~12,000 cells. The Platynereis life cycle includes a non-feeding planktonic larva that starts feeding only after it settles down on the sea floor and transitions to juvenile life. We will study the very first feeding in the 'naive' guts of juvenile Platynereis, giving a unique perspective on how different food cues shape feeding networks with precise control. To identify the signalling networks regulating feeding, the project incorporates recent advances in imaging technologies and automated analyses to allow high-throughput functional and behavioural screens. Brain-gut signalling will be resolved through a three-pronged approach: (1) High-throughput behavioural screening experiments will investigate the role of different neuropeptides in feeding behaviour. This analysis will be enabled by use of a new state-of-the-art random access parallel microscopy concept, the 'MultiScope', provided by our CASE project partner Cairn Research Ltd. (2) Mapping of neuropeptidergic signalling networks in the juvenile Platynereis through single-cell transcriptome analyses to generate testable hypotheses for mechanisms controlling gut-brain signalling. (3) Identification of enteric neuron identity, position and morphology through wholemount immunohistochemistry labelling with antibodies targeting specific neuropeptides and neurotransmitters, imaged by fluorescence microscopy. This project will elevate our understanding of the environmental and neuroendocrine interplay required for the activation and coordination of feeding in a whole-body context, potential for the translation of the results delivered by this project to more complex animal models and by extension into clinical medicine. Through this project, you will develop skills in advanced microscopy and molecular biology and undertake on-site training at Cairn Research Ltd, where you will gain further experience in microscopy, imaging and electronics and equipment development from an industry perspective. Continued on next page……..

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.