Neuronal control of mitochondrial trafficking down long-range axons

Supervisory team:
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Project description:

To support the energy demands of synaptic transmission, neurons have many thousands of mitochondria located along their highly branched and very long axons. Throughout a neuron's entire lifetime, it must solve the unique cell biological problem of delivering these mitochondria to the correct axonal locations. Mitochondria are known to move around within axons and mitochondrial distribution is affected in many neurological diseases, which tells us that that this is a highly regulated and important process. However, we do not how neurons control mitochondrial movement in axons within the brain, or how this influences their overall distribution. In this project, we will combine in vivo 2-photon imaging of neuronal mitochondria with computational modelling to solve how neuronal activity controls the delivery and distribution of mitochondria in axons that is fundamental to every neuron in the brain.

In the Ashby lab, we have developed in vivo 2-photon microscopy techniques to track individual mitochondria in neurons of the living mouse brain over the course of minutes through to days. Using these approaches in this project will allow us to define how mitochondria move around functioning axons and how that movement is controlled by neuronal activity. We will then test whether these local trafficking rules can explain how mitochondria end up distributed across the axon. To do this, extending previous approaches by the O'Donnell lab, we will build sophisticated computational models of anatomically real neurons that simulate the trafficking of mitochondria across the entire axonal tree. By pulling together the power of the in vivo measurements and the large scale of the computational models, we will define how neurons overcome the challenge of ensuring they have the right numbers of mitochondria in the right place to maintain their function.

This is an interdisciplinary project that is built on the close collaboration between the Ashby and O'Donnell labs. The nature of the project means that the student will receive training in a wide-range of technical skills ranging from cutting edge imaging to in vivo experimental skills and coding for computational neuroscience.