Correlative Light and Electron Microscopy of whole-central nervous system in *Drosophila* adults

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Abstract

Correlative microscopy is a powerful tool that combines different imaging techniques to provide a more complete picture of biological specimens across different scales. In this project, we aim to use correlative microscopy to study the cell biology of a subset of identified neurons within the Drosophila brain, a well-established model system for neuroscience research.

Our approach involves integrating light sheet, super-resolution light- and electron- microscopy to investigate the ultrastructure of specific neurons of the Drosophila brain at high resolution. Light sheet microscopy allows us to visualize quickly large volumes of tissue with minimal photodamage, super-resolution is able to focus on groups of neurons with greater detail, while electron microscopy provides the resolution necessary to examine the fine details of cellular and subcellular structures.

To achieve this, we will first acquire light sheet microscopy images of freshly dissected Drosophila brains. We will use these images to identify areas of interest. Super-resolution and quantitative analysis of mitochondrial distribution in defined groups of axons will be able to shed some light on the ageing process of the brain. Next, we will prepare the brain tissue for volume electron microscopy (vEM). The stained and resin embedded brain will be checked for homogenous staining using x-ray-computed tomography before sectioning and imaging using the Zeiss Array Tomography system providing detailed information on the cellular and subcellular structures within the identified regions of interest.

To facilitate the integration of the light sheet and electron microscopy data, we will use a combination of external sample morphology and fluorescence-based labelling. This will allow us to accurately align images across scales, enabling us to identify specific morphology patterns within the tissue.

Overall, this project aims to provide a comprehensive view of the Drosophila brain and the insights gained from this work will advance our understanding of the cellular and physiological processes underlying age-related neuronal decay, potentially leading to new therapeutic strategies for neurological disorders.