

Hierarchical Spatial-Temporal Modelling of Microglia Patterns: Towards Non-Invasive Diagnostics for Neonatal Hypoxia and Neurodegenerative Disorders

Supervisors: Dr Hannah Mitchell, UCL and STFC

Microglia, a type of immune cell in the central nervous system (CNS), play a key role in removing pathogens, dead cells, and protein aggregates. They are also crucial for neuroprotection, reducing excitotoxic injury and regulating synaptic plasticity. In healthy conditions, microglia in the brain and eye exhibit a regular distribution. However, upon activation, they change behaviour, migrating and forming clusters around sites of inflammation or injury.

Differences in the spatial distribution and morphology of microglia have been observed during development, potentially explaining gender-based susceptibility to neonatal hypoxia, which affects around 0.3% of births in the UK. Gaining a statistically robust understanding of microglial behaviour at the population level could deepen our knowledge of their natural roles in tissues and support the development of non-invasive diagnostic tools. Such tools could rapidly identify CNS disorders like neonatal hypoxia, addressing an unmet clinical need.

Recent progress in non-invasive diagnostic technology, such as the DARC (Detection of Apoptotic Retinal Cells) system developed by Professor Corderio, shows the potential of retinal analysis for diagnosing CNS disorders. Understanding microglial distribution in the retina, and how it relates to cellular pathology, would enhance both the feasibility and diagnostic power of such technologies.

This study, a collaboration between STFC, UCL, and QUB, aims to model 3D cellular point patterns from Light Sheet micrographs of brain and eye tissue using established datasets derived from well-established murine models of neonatal hypoxia.

Experiments that were conducted at UCL and imaged at STFC's Central Laser Facility (OCTOPUS group), provide point pattern samples comprising 200–1000 microglia per tissue sample. Morphological data, in the form of binary masks, allow for additional fractal and morphological analysis. The hierarchical complexity of the dataset spans control vs. hypoxia conditions across groups, multiple timepoints post-model induction, repeat samplings, brain region comparisons, and eye-brain tissue relationships.

This study will improve hierarchical spatial statistical models (point processes) for cell populations, enhancing the statistical methods available to the Light Sheet Microscopy user community at STFC by enabling complex data to be analysed. Ultimately, these models may contribute to the development of novel diagnostic tools, using the eye as a non-invasive window to detect neurological conditions.