Project outline

Information transmission in the nervous system relies on synaptic connections between neurons. Each of these connections is made up of several release sites. At each site, neurotransmitter-filled synaptic vesicles are stored, ready to be released upon arrival of an action potential. Release sites can be distributed along the axon of the presynaptic cell or clustered together to form giant synapses (e.g. Calyx of Held). The structure of individual release sites is remarkably similar across different types of synaptic connections. One of the common characteristics of synaptic release sites across the brain, is the high degree of variability of vesicular release in response to individual action potentials. In spite of this variability, information transmission in the brain is reliable and the strength of individual connections can be modulated.

Recent evidence shows that morphology and ultrastructural organization of synapses plays an important role in neurotransmitter release. This project will use a combination of techniques to investigate the rules governing neurotransmitter release at synapses in the central nervous system. The function of individual synapses will be studied using electrophysiology and live imaging in mouse brain slices, while synaptic ultrastructure will be investigated by combining optogenetics with recently developed methods to visualise activated synaptic vesicles at the nanoscale level.

Connections in the auditory pathway will be used to investigate the impact of morphology on the functional properties of synapses. In particular, small synapses that convey information from the thalamus to the cortex will be compared with the Calyx of Held, a giant synapse in the brain stem (in collaboration with Prof Forsythe).

This project has the potential to uncover unique mechanisms used by individual neurons to ensure reliable transmission and to investigate how global properties contribute to normal network function, learning and memory in the brain and to understand the changes that occur during ageing and degeneration.

References:


BBSRC Strategic Research Priority: World Class Underpinning Biosciences.

**Techniques that will be undertaken during the project**

- Live confocal imaging of synaptic vesicles and calcium signals
- Optogenetics
- Whole-cell patch clamp
- Extracellular recordings
- Brain slice preparation
- Correlative Light and Electron Microscopy (CLEM)
- Interfacing experimental data with computational modelling

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