

College/University PhD Studentship in Neuroscience & Behaviour

Studentship Number: MBSP-12/06
Supervisor: Professor Nick Hartell
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Host Department: Department of Cell Physiology and Pharmacology
Project Title: Visualisation of synaptic transmission.
Duration: 3.5 years

Project Description

Changes in the strength of synaptic transmission represent a molecular mechanism for learning and memory storage in the central nervous system. Synapses are early targets of neurodegenerative conditions such as Alzheimer's disease and so understanding how synapses transmit and store information is an essential prerequisite to examining their dysfunction in disease.

We have developed a series of fluorescent protein based bio-sensors that allow the visualisation and quantification of synaptic transmission using state of the art imaging techniques. In neuronal culture models, we have shown that second messengers such as cAMP enhance transmitter release and this effect is accompanied by a prolongation of the underlying calcium signal within presynaptic terminals. We have now incorporated one of our ratiometric calcium sensors into a transgenic mouse so that it is expressed exclusively in presynaptic terminals in the CNS. We now wish to use this mouse strain to evaluate the role of presynaptic calcium on short and long-term plasticity at model synapses and the roles of diffusible anterograde and retrograde messengers on release properties.

The successful applicant will learn a range of techniques including high speed multiphoton and confocal microscopy, electrophysiology and molecular biology. He or she should be highly motivated and enthusiastic.

- Birnstiel S, Slater NT, McCrimmon DR, Mugnaini E, Hartell NA (2009) Voltage-dependent calcium signaling in rat cerebellar unipolar brush cells. *Neuroscience* 162:702-712.
- Endo S, Shutoh F, Dinh TL, Okamoto T, Ikeda T, Suzuki M, Kawahara S, Yanagihara D, Sato Y, Yamada K, Sakamoto T, Kirino Y, Hartell NA, Yamaguchi K, Itohara S, Nairn AC, Greengard P, Nagao S, Ito M (2009) Dual involvement of G-substrate in motor learning revealed by gene deletion. *ProcNatlAcadSciUSA*.
- Jacoby S, Sims RE, Hartell NA (2001) Nitric Oxide is required for the induction and heterosynaptic spread of cerebellar LTP. *Journal Of Physiology-London* 535:825-839.
- Sims RE, Hartell NA (2005) Differences in Transmission Properties and Susceptibility to Long-Term Depression Reveal Functional Specialization of Ascending Axon and Parallel Fiber Synapses to Purkinje Cells. *Journal Of Neuroscience* 25:3246-3257.
- Sims RE, Hartell NA (2006) Differential susceptibility to synaptic plasticity reveals a functional specialization of ascending axon and parallel fiber synapses to cerebellar Purkinje cells. *J Neurosci* 26:5153-5159.