The role of GABA signalling in the electrical timekeeping of the master circadian clock to drive circadian rhythms

Supervisory team:
Main supervisor: Dr Mino Belle (University of Exeter)
Second supervisor: Prof Krasimira Tsaneva-Atanasova (University of Exeter)
Dr James Hodge (University of Bristol)

Collaborators: Dr Casey Diekman (New Jersey Institute of Technology, USA), Dr Michael Weedon (University of Exeter), Prof Robert Lucas (University of Manchester), Prof Steve Brown (University of Zurich)

Host institution: University of Exeter (Streatham)

Project description:

Our daily or circadian body clock is one of the most important timing systems in our body, ensuring that our brain activity is appropriately aligned with our homeostatic, physiological, and behavioural needs across the day. This includes the timing in our sleep-wake cycle, peak cognition ability, and metabolic activity. Disruption of this daily rhythm can lead to severe health consequences, including premature ageing and mental health disorders.

In mammals, the master circadian clock is located in the hypothalamic suprachiasmatic nucleus (SCN). In the SCN, the activity of clock genes produces daily excitability rhythms in SCN neurons, causing them to spike at higher rates during the day with high intracellular calcium and less active at night with low intracellular calcium. This daily rhythm in gene expression and electrical activity is vital for clock function, promoting well-being and good health.

GABA is the main neurotransmitter in the SCN and is critical for the generation of circadian rhythms. Remarkably, although GABAergic signalling in the SCN is critical for our sense of daily rhythm, how GABA signals regulate SCN electrical and intracellular calcium activity remain poorly understood. Here, we will investigate when and how synaptic GABA signalling regulates SCN neurophysiology, clock gene rhythms, and behaviour. To achieve this, we are combining some state-of-the-art and powerful research technologies, including whole-cell, extracellular and dynamic clamp electrophysiology, real-time clock gene expression and calcium imaging, optogenetics, and using appropriate transgenic models. We will also employ sophisticated behavioural measurements and mathematical modelling. This is an exciting and interdisciplinary project, supported by strong collaborations between the Belle's, Tsaneva-Atanasova's and Hodge's labs. This work will also be supported by strong international collaborations. The student will therefore receive training in a wide-range of technical skills, coupled with the opportunity to conduct multi-disciplinary research at a national and international level in well-funded labs.