**BBSRC MIBTP Studentship Project**

**September 2023**

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| **Project Title** | The circadian clock of Drosophila melanogaster: molecular and cellular contributions to rhythmicity. |
| **Project Summary**  |
| The circadian clock is an endogenous mechanism that synchronizes almost all behaviour and physiology with the Earth’s 24 hour environmental cycles. Predictably, the circadian clock has a huge impact on health and quality of life. Dysfunction of the clock not only generates temporal disorientation and sleep problems, but also is involved in pathologies such as obesity, mental illness, cardiovascular disease and cancer. Clearly, it is extremely important to achieve a comprehensive understanding of how the circadian clock works [reviewed in 1]. The fruitfly *Drosophila melanogaster* is an ideal organism for the study of circadian rhythms, its clock shares design and molecular components with that of mammals but it is much easier to manipulate. We discovered that different clock neurons in the fly tend to cycle with different speeds and that only their mutual synchronization keeps the fly running with a common 24 h cycle [2]. Consequently, in addition to studying the regulation of genes and molecules in single neurons we must investigate the organization of the clock network as a whole.  This proposal aims to study the circadian clock in terms of molecules, cells and networks. We will use a combination of classic and original approaches. We will analyse the cycling of clock proteins in different neurons, but we will also develop novel markers of neuronal activity that are better suited than available tools to circadian experiments (see 3 as an example). We will study classic mutants and widely used mosaics (GAL4/UAS lines) but we will also develop our own mutants and mosaics, for instance using CRISPR/CAS9 a state-of-the-art genome-editing tool. Finally, we will use new genomics techniques, such as single cell RNAseq. We envisage that our work will provide a new framework for a fuller comprehension of the biology of the circadian clock of *Drosophila*, but will also generate novel tools that will be useful for studying circadian clocks in general. Techniques that will be undertaken during the project:*Drosophila* genetics and behaviour, imaging techniques, molecular biology, biosensors, advanced statistics and bioinformatics. Imaging techniques and advanced statistics and bioinformatics are recognised by the BBSRC as new ways of working BBSRC Strategic Research Priority: Understanding the Rules of Life - Neuroscience and behaviour, Systems Biology |
| **References** |
| 1. Ozkaya & Rosato (2012) The circadian clock of the fly: a neurogenetics journey through time. Advances in Genetics, 77: 79-123. 2. Dissel S, Hansen CN, Ozkaya O, Hemsley M, Kyriacou CP, Rosato E. (2014) The logic of circadian organization in Drosophila,  Curr Biol, 24: 2257-2266  |