

CRYCT - A peptide magnetosensor to engineer magnetic field sensitivity in biological systems

Project ID: 280

Supervisory team

Main supervisor: Prof Daniel Kattnig (University of Exeter)

Second supervisor: Dr Jonathan Phillips (University of Exeter)

Non-academic (CASE) supervisor: Dr Alex Jones (National Physical Laboratory)

Other supervisors: Prof Frank Vollmer (University of Exeter), Prof Richard Baines (University of Manchester), Prof Charalambos Kyriacou (University of Leicester), Prof Ezio Rosato (University of Leicester)

Collaborators: Dr Jess Ramsay (University of Leicester)

Host institution: University of Exeter (Streatham)

CASE partner: National Physics Laboratory

Project description: Magnetoreception, the ability to sense weak geomagnetic fields, is a fascinating yet poorly understood trait essential for navigation in many animals and present in some non-migratory organisms. Despite extensive research, the mechanisms behind magnetic field sensing and transduction remain elusive. We aim to uncover these molecular mechanisms and provide a framework to engineer magnetosensitivity in biological systems that lack it. In the past two decades, the blue-light-sensitive flavoprotein cryptochrome (CRY) has emerged as the leading candidate for explaining magnetoreception. CRY is thought to transduce magnetic information via a quantum effect on a radical pair formed during light-induced electron transfer between a CRY-bound flavin adenine dinucleotide (FAD) and a conserved tryptophan residue. However, recent findings suggest that this may not fully explain biological magnetosensitivity. A groundbreaking study demonstrated that only 10% of the CRY protein is required to potentiate the magnetoresponse of free FAD in fruit fly neurons [Nature 2023, 615(7950):111-116]. This discovery presents a significant shift in understanding, as it reveals an unexpected pathway to magnetosensitivity involving just a 52-amino-acid peptide from the C-terminal tail of CRY protein, which lacks the canonical FAD binding pocket. The precise details of how this unexpected magnetosensitivity is realized are still unknown. This project aims to investigate the cryptic magnetosensitivity of CRY and its C-terminal tail using a combination of molecular dynamics and spin dynamics simulations, along with experimental methods including single-molecule sensing based on whispering gallery modes and hydrogen-deuterium exchange mass spectrometry. You will test the hypothesis that the CRYCT alone is sufficient to generate a magnetic field effect and identify the minimal construct needed to achieve this. Additionally, the project will investigate ways to optimize the peptide to create a bare-bones magnetic-field sensor for synthetic biology applications, exploring its potential for magneto-opto-genetics. This project will be suitable for everybody eager to engage in an interdisciplinary project involving a broad range of approaches ranging from modelling, over advanced spectroscopy to protein engineering. The project provides training and allows flexibility to align the research focus with the candidate's strengths and interests. The student will work with the Kattnig, Phillips, and Vollmer groups at Exeter's Living Systems Institute, as well as with the Biometrology Division at the National Physical Laboratory (NPL) under Dr. Alex Jones. This includes a 9-month placement at NPL and collaboration with the CRYCT discovery team (based at NPL, Leicester, and Manchester), who will carry out complementary in vivo studies.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.