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

Supervisory team:
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Host institution: University of Exeter (Streatham)
CASE partner: National Physical Laboratory (NPL)

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 primary 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 2023 study – involving our partner, NPL – 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 optical spectroscopy and millisecond time-resolved hydrogen/deuterium-exchange mass spectrometry. You will test the hypothesis that the CRYCT alone is sufficient to generate a magnetic field effect, as suggested and further supported by our preliminary data, and identify the minimal construct needed to achieve this. Additionally, the project will investigate ways to optimize the peptide (mutants or truncations) to create a bare-bones magnetic-field sensor for synthetic biology applications, exploring its potential for magneto-opto-genetics.

This project will suite you if you seek an interdisciplinary project involving a broad range of approaches ranging from modelling, over advanced spectroscopy to protein engineering. Prior knowledge in all areas is not required. The project offers training and the flexibility to tailor the focus to the candidate's interests. The student will work within the Kattnig and Phillips groups at Exeter's Living Systems Institute, collaborating with the Mulholland group (Bristol), the Dodson group (Bath), and the CRYCT discovery team (NPL, Leicester, Manchester, who will undertake in vivo studies). For more information, contact Daniel Kattnig (d.r.kattnig@exeter.ac.uk).

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.