Wellcome Trust ICD Vacation Bursary Scheme Summer 2025

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Using novel EEG methods to examine category representations in the brain.

Name of Supervisor: Alissa Ferry/Szilvia Linnert

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Humans naturally group the world around them into categories, usually based on visual or functional similarity. Language can also shape categories, with consistent labels allowing us to group even visually disparate objects into the same category. Much of this research has used behavioural methods, examining how people put objects into groups and how different factors like labels or diversity of images shape those categories. Our project aims to **develop novel electroencephalogram (EEG) methods to examine how to brain encodes visually-based categories.** The student will use a novel EEG technique, called **steady-state visual evoked potentials (SSVEPs)** that allow us to see how the brain groups objects into categories based on oscillation patterns to rapidly presented visual stimuli, along with more commonly used **event-related potentials (ERPs)** to examine how the brain groups objects into categories. We will use a series of novel creatures that are created by incrementally morphing one novel animal into another. When shown all examples, participants tend to treat them as one broad category, but when shown examples only from the extremes, participants tend to encode them as two distinct categories. By manipulating what they are shown we would expect to see particular patterns of categorisation. The student will collect data from adults, and 9-month-old infants with the aim of identifying **1) if a particular EEG method is more effective at identifying category representations, and 2) how category representations develop in human infants.** This work will show not only how novel visual categories are encoded in the brain, but it is also foundational for understanding how the ability to form category representations develop in children. By showing that it is possible to measure rapid category formation, we can investigate how individuals might differ in forming category representations, with implications for understanding how these processed might lead to cognitive processing difference in neurodiverse populations.

https://lucid.ac.uk/

https://sites.manchester.ac.uk/child-study-centre/

Role of protein tyrosine phosphatases during appendage regeneration

Name of Supervisor: Enrique Amaya

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A primary goal in regenerative medicine is to identify and implement novel treatments aimed at improving our ability to regenerate injured, diseased or aged tissues and organs, including the heart. My research group has been investigating the molecular and cellular mechanisms involved in tissue formation, repair and regeneration in Xenopus and zebrafish, two vertebrate model organisms with high regenerative capacity. Recent work in my laboratory has revealed the importance of sustained reactive oxygen species (ROS) during appendage regeneration and embryonic development.[1-2] This project will extend these findings by identifying the critical downstream targets of ROS during adult caudal fin regeneration in zebrafish, with a particular emphasis on the family of protein tyrosine phosphatases.[3]

1. Love, N. R. *et al.* Amputation-induced reactive oxygen species are required for successful Xenopus tadpole tail regeneration. *Nat. Cell Biol.* **15,** 222–228 (2013).
2. Chopra, K., Folkmanaitė, M., Stockdale, L., Shathish, V., Ishibashi, S., Bergin, R., Amich, J., **Amaya, E.**, 2023. Duox is the primary NADPH oxidase responsible for ROS production during adult caudal fin regeneration in zebrafish. *iScience* 26, 106147. https://doi.org/10.1016/j.isci.2023.106147
3. Helston, O. and **Amaya, E.**, 2021. Reactive oxygen species during heart regeneration in zebrafish: Lessons for future clinical therapies. *Wound Repair Regen*. 29(2):211-224. PMID: 33471940 https://doi.org/10.1111/wrr.12892.

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Investigating factors influencing undergraduate optometrists' intentions to participate in low vision service provision.

Name of Supervisor: Gemma Gould

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The prevalence of blindness and sight loss in the UK is projected to dramatically increase within the next 30 years. Low vision rehabilitation services can help people to overcome difficulties caused by blindness and sight loss and improve their quality of life. UK low vision services are unevenly distributed with insufficient capacity to help everyone who may benefit and optometrists working in primary care currently represent a significantly underutilised resource in service provision. Increasing participation of primary care optometrists in low vision services will improve service accessibility and availability and help to reduce health disparities linked to blindness and sight loss. A 2023 survey of 451 UK qualified optometrists identified that optometrists who do not work in a low vision service have relatively low confidence in low vision, which could contribute to low motivation to participate in low vision service provision (Gould et al., 2024).

The proposed project aims to investigate factors influencing UK undergraduate optometrists' intentions to participate in low vision service provision by using a survey based on the COM-B (capability, opportunity, motivation and behaviour) model. The survey will be circulated at the end of the 2024/25 academic year. Findings will add to the important evidence base around understanding the determinants of optometrists' participation in low vision services, which is key to developing effective behaviour change intervention(s) to increase participation.

The student will conduct a literature search to develop an understanding of behaviour change theory and its increasing application in healthcare. They will analyse data collected from the undergraduate optometry student survey, and they may compare this data to similar data collected in the previous survey of UK qualified optometrists. The student will have the opportunity to engage in discussion about how their analyses can inform later stages of the project.

References

GOULD, G., HARPER, R., BOWEN, M. & DICKINSON, C. 2024. Confidence in low vision rehabilitation and attitudes towards further learning: A survey of UK optometrists. Ophthalmic and Physiological Optics, 44, 829-839.

The effect of the size of the TIGIT ECD on sub-synaptic distribution and function in T cells

Name of Supervisor: Jonathan Worboys

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This project aims to establish how the size of the extracellular domain (ECD) of the immune receptor TIGIT impacts its localisation at immune synapses (specialised contact sites between immune cells), and its subsequent ability to inhibit T cell activation. TIGIT is an inhibitory receptor targeted in cancer that upon ligation with CD155 (found on interacting cells), clusters and colocalises with the T cell receptor (TCR; Worboys *et al*, 2023). We hypothesise that TIGIT-TCR co-proximity is important for both TIGIT activation and ability to inhibit T cells (Worboys & Davis, 2024). TIGIT has a short ECD, and this project aims to vary the bulk of the ECD to drive physical exclusion away from the TCR, which is known to localise to close membrane contact sites. This knowledge will aid design of novel therapeutics targeting TIGIT beyond ligand blockade.

The student will produce lentivirus from pre-designed plasmids in the lab containing different TIGIT constructs with varying ECDs using our HEK293 cell transfection protocol. Jurkat T cells expressing a specific TCR (ILA1) will be transduced and TIGIT-expressing cells will be sorted by Fluorescence-activated cell sorting (FACS; TIGIT construct contains cytoplasmic GFP; Timeframe = 2 weeks). The cells will then be subjected to two functional assays:

I. Functional assessment of TIGIT inhibition through incubation with either CD111- or CD155-expressing Raji HLA A*02:01 cells pulsed with the ILA1 peptide (ILAKFLHWL). T cell activity will be measured through flow cytometric analysis of the cell surface marker (CD69) and quantification of IL-2 cytokine release using an ELISA (2 weeks).
II. Spatial analysis of the localisation of TIGIT with the TCR, upon ligation with CD155 and TCR in planar lipid bilayers. The student will use our lab's own TIRF microscope to image and analyse the colocalisation of GFP and TCR stained through our standard immunofluorescence protocols (2 weeks).

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Exploring Health-Climate Interaction for better health prediction

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Aim is to understand and capture climate-health interaction using, empirical (statistical) methods. Emphasis will be given to understanding how climate impacts health outcomes. In the first stage the candidate will learn by reviewing the WHO model on malaria & climate. In the second stage the candidate will study how such models can be extended to other diseases, e.g. dengue. In the learning phase the candidate will identify key similarities and dis-similarities between such disease-climate interplay for these different diseases (e.g. malaria & dengue). In the application phase objective would be to first use existing methods and assess their performance. Expected shortcomings of such models are in their limitations in adopting to various spatio-temporal levels at which these are used to predict outcome. For example whether we are interested in "nowcast" or forecast, or we are limited to a small geographic, say a municipality or we are predicting at a much larger spatial region (like a county or a country). Next, we expand these basic models to accommodate some of these more complex but realistic interactions scenarios and assess how the extended models perform.

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The Pocket Therapist: real-time responsive mode emotion detection and intervention using mobile platforms and smart sensors

Name of Supervisor: Mike O'Toole

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We propose a new device to support therapeutic interventions for mental health and neurodevelopmental disorders with a special focus on autism. The aim of the device is to support emotional regulation by delivering therapy to a mobile platform at a time of most need responsive to the emotional state of the user.

The concept is to use discrete and unobtrusive wearable sensors to measure the user's physical and autonomic responses, such as heart-rate, perspiration, etc. The measurements are then used to profile their emotional state – whether they are angry (red), anxious or worried (yellow), low or depressed (blue) or optimum, relaxed or regulated (green) – and send a prompt to a mobile device initiating some action developed by the user to support them.

The student's project will be to investigate one of several different elements currently in progress to realise the project and support our current research in emotion detection [1]. Depending on the applicant's skills, this could include:

- Review and testing of smart wearables, and early exploration of software development to assess suitability.
- Support app development, in particular, the development of a real-time app-based survey tool link to a smart-wearable for state-of-the-art data collection.
- Exploration of the interface and systems to enable users to input and control their own emotional regulation strategies, linked to the emotion detection function.

The research would suite well a candidate with excellent interpersonal and presentation skills with interests in programming and software development, or sensors and instrumentation, working at the interface between technology and mental health.

[1] Whyte et al. IEEE Sensors Applications Symposium, 2024.

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Metabolic Mapping of *Pneumocystis*: A Flux Balance Approach for Improving in vitro experimentation

Name of Supervisor: Norman van Rhijn

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Aim

The project aims to develop a validated Flux Balance Analysis (FBA) model for the opportunistic pathogen *Pneumocystis*, enhancing our understanding of its metabolic dependencies within the host in order to allow *in vitro* culturing of this currently unculturable organism.

Objectives

1. **FBA Model Comparison**
    - **Objective**: Comparison of existing methods for draft network reconstruction, providing a summary of methodologies and suggesting a 'best' method.
    - **Approach:** Utilize pathway databases, such as KEGG and MetaCyc, and relevant literature to reconstruct and refine species-specific pathways, ensuring accurate representation of *Pneumocystis* metabolism.
2. **FBA Model Reconstruction**
    - **Objective**: Provide a preliminary pathway analysis including robustness analysis and in silico growth of *Pneumocystis* to guide *in vitro* culturing methods.
    - **Approach**: Compile and integrate genomic and/or transcriptomic data to create a draft metabolic model for *Pneumocystis*, identifying critical pathways by knocking out each reaction and validate the model through COBRA.

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Pupilometry for real and imagined smell/taste

Name of Supervisor: Sarah Clinch

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Aphantasia is neurological difference in which individuals are unable to mentally recreate sensory experiences. For example, visual aphantasia is commonly referred to as having "no minds eye", that is being unable to bring to mind visual images. Relationships have been established between visual aphantasia and risk taking, episodic memory, reduced PTSD amongst others. There's also strong evidence for comorbitity between visual aphantasia and other aphantasias.

Aphantasias of taste and smell have been relatively underexplored – in this project we aim to measure aphantasia of taste and/or smell using pupillometry, an approach that has been shown to be an effective measure for visual aphantasia. There is evidence that pupil response can be seen for presented tastes and smells and, consistent with approaches for visual aphantasia, this project would set out to explore whether the same effects can be seen for imagined tastes/smells.

Project objectives:

• Identify and familiarise oneself with relevant literature on pupil response to olfactory and/or gustory stimuli, and on aphantasias of these senses. Develop skills in literature search and reading.

• Recruit both visually* aphantasic and non-visually aphantasic participants for an in-person experiment measuring pupillary responses to real and imagined tastes/smells.

• Administer the experiment. Develop skills and understanding in experimental design, development of technical tools, communication with participants.

• Conduct a preliminary analysis to identify if there are differences in pupillary response between real and imagined stimuli. Develop and demonstrate skills in data analysis using Python.

* Comorbitity between visual aphantasia and other aphantasias suggests that recruiting visual aphantasics will ensure some participants with aphantasia of taste/smell. Tests of visual aphantasia exist and are relatively easy to administer, we also have a small pool of participants who have previously engaged in visual aphantasia research who would be more likely to participate in future experiments.

Developing tools for measuring cellular mechanical forces

Name of Supervisor: Sarah Woolner

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Background

Extracellular matrix (ECM) is an often-overlooked component of biological development, tissue architecture, and disease progression. In the context of cancer, altered ECM contributes to tissue stiffness and oncogenic extracellular vesicle (EV) production. In turn this leads to tumour growth, metastasis, and chemotherapy resistance. Yet, the mechanisms that lead to these altered forces in matrix are poorly understood. Molecular tools to study these forces have been developed within our lab and can be utilised for a variety of targets and contexts.

Project Description and aims

This project will investigate how our novel mechanosensors can be used to probe interactions between cancer/EVs and the ECM. We have generated a range of fluorescent mechanosensors that can be used for a variety of ECM targets focusing on advanced microscopy techniques.

The work will involve testing these sensors under different experimental setups. Stretch/force measurements will be conducted using confocal microscopy, in particular fluorescence resonance energy transfer (FRET) imaging, to analyse cell-cell adhesions, ECM-cell binding, and cellular traction forces. This project will provide an interdisciplinary research experience and can be tailored to match the student, focusing on either experimental imaging, cell culture, data analysis, or biochemical sensor optimization.

Objectives:

1. **Utilising advanced microscopy for mechanical force sensing:**
    - Cell culture and sample preparation for imaging applications
    - Gain hands-on experience with the principles of confocal imaging
    - Understand how FRET can be used to measure forces
2. **Investigation of mechanosensor applications:**
    - Develop and adapt protocols to integrate the mechanosensor for specific applications
    - Perform controlled experiments to assess the sensor's performance in these new contexts
3. **Data analysis and presentation:**
    - Analyse experimental data to evaluate the sensitivity and reliability of the mechanosensor for use with these new application(s)
    - Summarize findings in a written brief report