London Worm Meeting

Date: 27th April 2026
Time: 2-5 pm

Location: Francis Crick Institute

Agenda

2.00-2.25 **Shruti Apurva (Barrios Lab)**, University College London
How do Memories become Behaviour?

2.25-2.50 **William Schafer**, MRC Laboratory of Molecular Biology, Cambridge, UK; KU Leuven

2.50-3.25 **Lightning talks**

3.25-4.00 **Coffee break**

4.00-4.25 **Erik Griffin**, University of Warwick
Patterning translation dynamics in the early C. elegans embryo

4.25-4.50 **Saman Rashid (Dimitriadi Lab)**, University of Hertfordshire
Dopaminergic regulation of autophagy reveals a therapeutic axis in spinal muscular atrophy

4.50-6.00 **Drinks & snacks**

Abstracts

How do Memories become Behaviour?

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Experiences shape memory, which, in turn, shapes behaviour. Animals often form multiple memories, stored as engrams (biophysical imprints), about the same stimulus. However, only some of these memories are expressed as behaviour, while others remain latent. In disorders like PTSD, the retrieval of a latent memory can lead to maladaptive actions. Therefore, understanding what determines expression of memories is a fundamental problem in neuroscience.

C. elegans can learn to associate a single odour with both a punishing and a rewarding experience. When stored together, one of these memories guides the worm's behaviour and the other remains latent. This offers an opportunity to dissect how memories compete for behavioural expression within a compact and fully mapped nervous system.

We aim to explore how classical conditioning to an odour influences *C. elegans* navigational strategies within an odour gradient. To analyse navigation, we measure and quantify specific navigation strategies such as weathervaning, turns and reversals, each of which are regulated by specific neurons. By identifying which parameters characterise the navigational strategy linked to learned odour avoidance or learned odour attraction, we can infer the neurons underlying each engram.

This study will enhance our understanding of memory storage versus memory expression and the neural circuits underlying learned behaviour.

Title TBC

William Schafer

MRC Laboratory of Molecular Biology, Cambridge, UK; KU Leuven

Abstract TBC

Patterning translation dynamics in the early *C. elegans* embryo

Stephanie Miller, Bernardo Chapa y Lazo, **Erik Griffin**

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Translational regulation is critical for the patterning of early, transcriptionally-quiescent embryos. In the *C. elegans* embryo, polarity regulators drive the asymmetric inheritance of translational regulators among the early blastomeres where they establish distinct translational programs. To quantify real-time translational dynamics in the living worm embryo, we adapted the HA Frankenbody system (Zhao N, Nature Communications 2019) to *C. elegans*. In this system, the GFP::HA Frankenbody is rapidly recruited to translation sites by the high concentration of HA epitopes in the nascent peptides of N-terminally tagged proteins of interest. We have quantified the translation dynamics of 5 maternal mRNAs (ZIF-1, PAL-1, APX-1, MOM-2, SAS-6), each of which displays a unique translation pattern. Strikingly, we find that RNA-binding proteins that control cell identity in the early embryo act as both translational activators and as repressors, depending on which transcript they target. We will present both our ongoing efforts and future plans to understand how translation is temporally and spatially regulated in the early worm embryo.

Dopaminergic regulation of autophagy reveals a therapeutic axis in spinal muscular atrophy

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Spinal muscular atrophy (SMA) is a severe neuromuscular disorder caused by mutations or deletions in the *SMN1* gene, leading to reduced levels of survival motor neuron (SMN) protein. While SMN is best known for its role in small nuclear ribonucleoprotein biogenesis and pre-mRNA splicing, it also contributes to multiple cellular processes, including mRNA trafficking, cytoskeletal dynamics and protein homeostasis. Although current therapies improve survival and motor function, they do not fully restore all SMN-dependent pathways, highlighting the need for combinatorial approaches.

Autophagy, a highly conserved lysosomal degradation pathway essential for neuronal health, has emerged as a potential therapeutic target in SMA. However, its role remains unclear due to conflicting reports regarding autophagic flux. Here, we investigated autophagy using transcriptomic, imaging, pharmacological and genetic approaches in the *Caenorhabditis elegans smn-1(ok355)* severe SMA model.

Autophagy-related genes were upregulated in *smn-1(ok355)* mutants, indicating increased pathway initiation. However, this was not matched by enhanced lysosomal function; instead, lysosomal capacity appeared compromised, consistent with reduced expression of vacuolar ATPases. Reporter analyses confirmed increased autophagosome formation and largely intact autophagosome-lysosome fusion, but elevated p62/SQSTM1 levels indicated impaired degradation at the final stage of autophagy.

Pharmacological activation, but not inhibition, of autophagy improved neuromuscular function and lifespan in *smn-1*mutants. Fluphenazine, a dopamine D2 receptor antagonist, produced the strongest phenotypic rescue, enhancing both autophagy induction and degradative capacity. Loss of the D2-like receptor *dop-3* phenocopied these effects, while inhibition of autophagy abolished the rescue, demonstrating that *dop-3*-mediated protection is autophagy-dependent. Importantly, D2-like receptors were differentially expressed in a disease-specific manner in severe SMA mice.

Together, these findings identify defective autophagic degradation as a key feature of SMA and reveal a dopamine-autophagy signalling axis that represents a promising target for combinatorial therapeutic strategies.

Lightning talks

Computational modelling of neuronal control of behaviour in *C. elegans*

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Although *C. elegans* has a fully mapped 302-neuron connectome, how its nervous system structure generates behaviour is still poorly understood. Existing computational models either focus narrowly on specific circuits or use large-scale optimized “black box” networks whose biological relevance is often unclear.

We present a tool, Worm2D, that lets researchers build intermediate-size, hypothesis-driven neural network models for specific behaviours of interest. Users can incrementally add neuron types and connections, place the network within a 2D worm body locomotion model, and couple it to configurable sensory environments such as concentration gradients. By default, the model uses empirically derived connectivity, synaptic weights, and neurotransmitter properties, but parameters such as connection strengths, sensory gains, and cell time constants can also be fine-tuned using optimization methods like evolutionary algorithms.

Worm2D is configured and run through Python scripting and modifying JSON files, and optimized models can be exported to NeuroML format for visualization, connectome comparison, or for use in more complex 3D body simulations such as Sibernetic. We illustrate the Worm2D framework on locomotion switching and klinotaxis, demonstrating that it provides experimentalists with a practical way to test circuit hypotheses linking neural structure to behaviour.

Investigating the role of the operon CEOP5212 in the response to oomycete infection and abiotic stress in *C. elegans*

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Oomycetes are fungal like eukaryotes found in aquatic and terrestrial environments that naturally infect both plants and animals. Although the mechanisms of oomycete infection have been extensively studied in plant hosts, the immune responses of animal hosts remain largely unknown. Natural infection of *C. elegans* by Myzocytiopsis humicola provides a valuable opportunity for investigating animal host responses to an oomycete infection. The chil genes have been previously identified as the hallmark of immune response induction that is specific to oomycete infection and requires the epidermal receptor tyrosine kinase OLD-1. Here, the operon CEOP5212, comprising B0507.8, ddn-1 and B0507.7, was found to be upregulated in both the Oomycete Recognition Response (ORR) and the Intracellular Pathogen Response (IPR). Using CRISPR-genome editing, we deleted this operon and found that animals exhibited significantly reduced induction of chil genes upon old-1 overexpression and increased susceptibility to oomycete infection. To further investigate this operon, a transcriptional reporter and a translational reporter of B0507.8 were generated and their inducibility was characterised in response to infection and stress, such as heat stress, protein stress, starvation and heavy metal treatment. The B0507.8 translational reporter exhibited localization to spherical aggregates within the hypodermis in response to oomycete infection, within the intestine under heat stress and heavy metal stress, and in both tissues under protein stress and starvation. Forward and reverse genetic screens revealed that the size of these spherical aggregates in the hypodermis was influenced by ZC196.4, a gene that is also included among ORR and chaperone genes such as hsp-110. Interestingly, hypodermal overexpression of B0507.8 and ddn-1 induces aggregate formation in the absence of external stimuli. We propose that the CEOP5212 operon may play a broader role coordinating multiple stress responses across tissues in *C. elegans*.

Early-life exposure to Cannabidiol: Safety assessment of a chronic exposure in *Caenorhabditis elegans*

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Cannabidiol (CBD) is known for antioxidant, anti-inflammatory, and neuroprotective properties, but its early-life effects remain poorly understood. *C. elegans* is a useful model for long-term toxicological studies due to its simplicity and translational relevance. In this study, synchronized L1 larvae from multiple transgenic strains were exposed to CBD (10, 150, or 600 µM) or 2% DMSO for 60 minutes, followed by recovery on NGM plates with E. coli OP50 for 48–72 h. Endpoints included survival, development, locomotion, reproduction, neuronal integrity, and oxidative stress. CBD at 10 and 150 µM showed low toxicity. A slight reduction in body length was observed at 150 µM, without affecting survival or development. Locomotion, neuronal integrity, and oxidative stress markers remained unchanged. Although egg production decreased at 150 and 600 µM, brood size was maintained, suggesting compensatory mechanisms. In contrast, 600 µM CBD induced significant toxicity, including reduced survival, smaller body size, increased ROS levels, and lack of antioxidant response, indicating oxidative stress and cellular damage. Overall, early-life exposure to CBD is well tolerated up to 150 µM, while higher concentrations lead to harmful effects, highlighting the importance of dose in safety assessments.

Sexually dimorphic regulation of lipid metabolism by SKN-1B in *C. elegans*

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How nutrient sensing in the nervous system coordinates systemic metabolism remains a key question (1). In C. elegans, the transcription factor SKN-1B functions in ASI chemosensory neurons to couple food perception with satiety and exploration.

Across multiple physiological measures, skn-1b mutants display sexually dimorphic phenotypes. Consistent with previous reports, hermaphrodite skn-1b mutants show reduced exploratory behaviour (2), whereas males exhibit distinct behavioural responses linked to altered feeding and food-seeking strategies. This is accompanied by differences in physiological traits including body size and pharyngeal pumping, suggesting altered regulation of energy balance.

skn-1b mutants display altered lipid accumulation compared with wild-type animals, with sex-specific differences in fat storage and distribution. While wild-type animals adjust to supplementation with oleic acid, skn-1b mutants show altered responses, indicating impaired regulation of lipid homeostasis. Preliminary RNA-seq analysis reveals transcriptional changes in metabolic and stress-responsive pathways, supporting a role for SKN-1B in coordinating systemic metabolic regulation.

Together, these findings support a model in which neuronal SKN-1B coordinates behavioural and metabolic responses to diet and reveal sex-specific regulation of lipid metabolism.

(1) Blackwell et al., 2015

(2) Tataradis et al., 2021

The Open-source Nematode DrugBase

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The Open-source Nematode DrugBase (ONDB; https://ondb.org.uk) is an open-access project addressing neglected diseases caused by parasitic nematodes, which infect around one billion people worldwide and contribute to malnutrition, anaemia, and disability. Despite their impact, these diseases remain underfunded due to limited commercial incentives. ONDB aims to bridge the gap between nematode gene/protein databases and drug-like chemical repositories by creating a platform for identifying novel therapeutic targets. Developed by University of Westminster students within an open-source framework, the project promotes global collaboration and interdisciplinary research. The project integrates bioinformatics and artificial intelligence tools, including protein structure prediction and virtual screening, to identify and evaluate potential drug candidates, followed by database expansion and experimental validation. Beyond accelerating early-stage drug discovery, the initiative enhances student employability and supports global health equity by contributing to research, education, and sustainable development goals.