25th Meeting of the Club of Invertebrate Neurobiology

Saint-Germain-au-Mont-d'Or

Program

Monday , May 12th, 2025

Session 1 : 14:00-17:35 (chair : Alain Garcès)

14:00-15:00	Invited conference 1: **Giovanna Ponte**, *Stazione Zoologica Anton Dohrn* Exploring the Complex Neural Networks of Octopus
15:00-15:25	**Jean-Maurice Dura**, *IGH/Neurogenetic and memory* Orion and the neuron-glia cross talk during neuronal remodelling
15:25-15:50	**Raouf Issa**, *Brain Plasticity unit CNRS-ESPCI* A subset of dopamine neurons persist across distinct life stages to modulate locomotion
15:50-16:20	Coffee break
16:20-16:45	**Qian Cao**, *iEES-Paris, CREA* A calcium-activated chloride channel is involved in olfactory transduction in *Drosophila Melanogaster*
16:45-17:10	**Léo Sillon**, *TPI team, CSGA* Taste regulation of immunity
17:10-17:35	**Claude Collet**, *INRAE UR406* Diamide insecticides as pharmacological tools to study the function and roles of insect calcium channels in neurons, skeletal muscle cells and cardiomyocytes.
17:35-18:30	Club general assembly meeting and group photo
18:30-20:00	Apéro-posters
20:00-21:30	Dinner
21:30-22:00	Surprise animation

Tuesday , May 13th, 2025

7:30-9:00 Breakfast

Session 2 : 9:00-12:15 (chair : Lydie Stoclet)

9:00-9:25 **Alice Pavlowsky**, *UMR8249 CNRS ESPCI-PSL, Equipe : Energie et Mémoire*
Neuronal fatty acid oxidation fuels memory after intensive learning

9:25-9:50 **Victor Girard**, *The Francis Crick Institute, Alex Gould Laboratory*
A genetically-encoded method for *in vivo* tagging and tracing of lipids from cell-to-cell

9:50-10:15 **Pierre Dourlen**, *UMR1167*
Expression of the Alzheimer susceptibility gene BIN1 in the presynaptic compartment leads to isoform-specific synaptotoxicity

10:15-10:40 Coffee Break

10:40-11:00 **Enisa Aruçi**, *TPI team, CSGA*
Caloric frustration memory leads to feeding disorder in *Drosophila Melanogaster*

11:00-11:25 **XiaoJing Yue**, *LBMC, ENS de Lyon, Bertrand Mollereau team*
Understanding the Role of Lipid Droplets and α-Synuclein in Parkinson`s Disease

11:25-11:50 **Marion Celle**, *LBMC, ENS de Lyon, Bertrand Mollereau team*
Establishing a *Drosophila* model for BPAN Disease

11:50-12:15 **Laurent Seugnet,** *CNRL-UCBL1-INSERM U1028, WAKING team*
Amino acids and the Regulation of the Sleep-wake cycle in *Drosophila*

12:15-13:30 Lunch

Session 3 : 13:30-17:00 (chair : Laurent Seugnet)

13:45-14:45 Invited conference 2: **Stephen Montgomery**, *University of Bristol, School of biological sciences*
Evolution of expanded learning and memory centres in *Heliconius* butterflies

14:45-15:10 **Hugo Vey-Payre**, *Centre de Recherche sur la Cognition Animale / IVEP team*
Behavioral flexibility comparison in social and solitary bees

15:10-15:35 **Julie Vittet,** *Team Persing, CSGA, Université de Bourgogne*
Behavioral Effects of Volatile Compounds on *Drosophila* Species: Towards Ecological Solutions for Managing Invasive Pests in Fruit Crops

15:35-16:00 Coffee Break

16:00-16:25 **Iago Bueno da Silva**, *IDEEV/EGCE, EvolBee Team - Université Paris-Saclay*
Relationship between ontogeny and experience shaping brain plasticity and defensive behavior in termite soldiers

16:25-16:50 **Justin Flaven-Pouchon**, *Team Persing, CSGA, Université de Bourgogne*
Behavioral regulation by LAT1-like amino acid transporter minidiscs and glutamate signaling in the *Drosophila* mushroom bodies

16:50-17:00 Farewell Word –

We kindly ask that you return your badge holder at the end of the conference.

Poster list:

Lennart Baumeister, *Experimental Morphology and Neuroanatomy, AG Ito*
Neuronal correlates underlying sepsis induced anorexic behaviour and hyperlocomotion in *Drosophila Melanogaster*

Khalid Boussaine, *P2E laboratory / NNIC*
Nicotinic Acetylcholine Receptors in Ticks: Recent Advances and Future Directions

Claire Brossier, *UMR8249 CNRS ESPCI-PSL, Equipe : Energie et Mémoire*
Mitochondrial Ca2+ efflux controls neuronal metabolism and long-term memory across species

Manon Carrière, *Laboratoire Jean Perrin*
Maturation of the head direction system of a vertebrate

Céline Costa, *CNRS UMR 8251, Université Paris Cité /DNSA team (S. Birman - V. Monnier)*
Role of glial reactivity in behavioral and neurodegenerative symptoms in a *Drosophila* model of Parkinson's disease.

Camille Dumas, *CNRS UMR 8251, Université Paris Cité /DNSA team (S. Birman - V. Monnier)*
Role of the vacuolar ATPases of dopaminergic neurons in the pathogenesis of Parkinson's disease studied in *Drosophila*

Benjamin Jauffret, Laboratoire d'Ethologie Expérimentale et Comparée (LEEC)
Does environmental enrichment impact ants' learning abilities?

Zihao Jia, *CNRS UMR 8251, Université Paris Cité /DNSA team (S. Birman - V. Monnier)*
Investigating the role of LRRK2 and its phosphorylation in the gut-brain axis in Parkinson's disease using *Drosophila*

Mariana Da Silva Malheiro, *CRCA / ExPlain*
Does the social environment influence behaviour in a *Drosophila* model of Alzheimer's disease?

Marco Paoli, *Team Persing, CSGA, Université de Bourgogne*
Statistical olfactory learning in honey bees

Maureen Pred'homme, *MERSEA laboratory, Université de Caen Normandie*
Post-reproductive Neurodegeneration in Cuttlefish: Unveiling an Alzheimer's-like Tauopathy?

Héloise Prévot, *Decision and Bayesian ComputaVon Lab , InsVtut Pasteur*
Understanding Circuit Function Through Dynamics-Based Comparison of Neural Motifs in the *Drosophila* Larva Connectome

Lydie Stoclet, *Centre de Recherche en Neurosciences de Lyon, WAKING team*
Sleep and neuroglial interactions in a critical period of the *Drosophila* olfactory system

Oriane Turrel, *AG Sigrist - Genetics*
Diversity of the roles of Mushroom Body's Active Zone proteins in memory formation

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Abstracts :

Aruçi Enisa
TPI team, CSGA
Caloric frustration memory leads to feeding disorder in *Drosophila Melanogaster*.

Sweeteners serve as sugar substitutes providing sweetness without or very low caloric content in modern food products. Research has suggested that the dissociation between sweet taste perception and caloric intake significantly influences feeding behavior across species from insects to humans. However, mechanisms underlying how this sweet taste-to-calory uncoupling affects organism from behavioral responses to central nervous system processing remain poorly understood. In this study, we use *Drosophila Melanogaster* as a model organism to investigate the effects of sweeteners on three key aspects: feeding behavior, metabolic responses, and the underlying neuronal circuitry. We present findings from two experimental approaches: the Proboscis Extension Response (PER) assay and fly Proboscis and Activity Detector (flyPAD) methodology, which enabled detailed examination of how sweeteners influence feeding behaviors in *Drosophila*. Our behavior data shows that sweeteners consumption induced the formation of caloric memory frustration leading to feeding disorder.

Baumeister Lennart
Experimental Morphology and Neuroanatomy, AG Ito
Neuronal correlates underlying sepsis induced anorexic behaviour and hyperlocomotion in *Drosophila Melanogaster*

Microbial hazards and pathogen contamination are ubiquitous in the environment, prompting the evolution of complex defence mechanisms. These include physical barriers, rapid nonspecific responses, and specific immune strategies. In addition to these classical immune defences, higher organisms have developed behavioural immunity or sickness behaviours to adapt to microbial threats. These behaviours include infection-induced anorexia, reduced reproductive activity, and increased sleep. For accurate behavioural responses during infection, the nervous system must integrate immune system signals with internal and external stimuli. Although much is known about environmental stimulus perception, the neural mechanisms behind immune system evaluation and behaviour modulation during bacterial infections are poorly understood. In our study, we observed female flies' responses to acute sepsis-like bacterial infection (Erwinia carotovora carotovora), showing anorexia and hyperlocomotion. To identify the neural basis of these behaviours, we used the mLexA-VP16-NFAT reporter to monitor neuronal activity. We found that leucokinin/dopamine co-expressing neurons in the abdominal ganglion play a key role in modulating feeding and locomotion during a bacterial infection. These findings provide insights into the neural circuits that drive sickness behaviours in response to microbial threats.

Boussaine Khalid
Physiology, Ecology and Environment (P2E) laboratory
Nicotinic Acetylcholine Receptors in Ticks: Recent Advances and Future Directions.

-Authors : **Khalid Boussaine**, Philippine Chartier, Alison Cartereau, Daniel Auguin, Emiliane Taillebois and Steeve H. Thany
Ticks are obligate hematophagous ectoparasites of significant medical and veterinary interest. They are major vectors for numerous infectious agents such as bacteria, viruses, and protozoa. The European castor bean tick, Ixodes ricinus, is the most prevalent tick species in France and a major vector of several pathogens including: Borrelia burgdorferi sensu lato causing Lyme disease. These pathogens are transmitted by ticks

through the saliva. Acetylcholine (ACh) is known to be the major excitatory neurotransmitter in the central nervous system of several arthropod species. Recent publications demonstrated that cholinergic pathways could be involved in the control of the tick salivary glands, and nicotinic acetylcholine receptors, which are the target of compounds used as acaricides, are expressed in the synganglion. We demonstrated that 6 α and 2 β genes coding for nicotinic acetylcholine receptor (nAChR) subunits are expressed in the tick synganglion. This number is relatively low compared to 12 potential genes suggested for the I. scapularis. Comparative analyses indicate they share similar characteristics with insect subunits and the electrophysiological recordings of native neurons are key to understand their pharmacological properties.

Brossier Claire
Laboratoire de Plasticité du Cerveau UMR8249 CNRS ESPCI-PSL
Mitochondrial Ca2+ efflux controls neuronal metabolism and long-term memory across species.

-Authors: Anjali Amrapali Vishwanath, Typhaine Comyn, **Claire Brossier**, Chaitanya Chintaluri, Carla Ramon-Duaso, Ruolin Fan, Riya Sivakumar, Mario Lopez-Manzaneda, Thomas Preat, Tim P. Vogels, Vidhya Rangaraju, Arnau Busquets-Garcia, Pierre-Yves Placais, Alice Pavlowsky and Jaime de Juan-Sanz*****
While impairing neuronal metabolism limits brain performance, it remains poorly understood whether enhancing metabolism in neurons, in contrast, could boost certain brain functions. We find that reducing the expression of the mitochondrial H+/Ca2+ exchanger Letm1 causes increased Ca2+ retention in the mitochondrial matrix of firing rodent neurons. Knocking down Letm1 overactivates neuronal metabolism in neurons of central memory circuits of both flies and mice, which enables long-term memory storage in training paradigms in which wild-type counterparts of both species fail to remember. Our findings unveil an evolutionarily conserved mechanism that controls mitochondrial metabolism in active neurons and suggest its involvement in shaping higher brain functions, such as long-term memory.

Bueno da Silva Iago
IDEEV/EGCE (Evolution, Génomes, Comportement, Ecologie)
Relationship between ontogeny and experience shaping brain plasticity and defensive behavior in termite soldiers.

-Authors : **Iago Bueno da Silva**[1], Lohan Valadares[1], David Sillam-Dussès[2], Jean-Christophe Sandoz[1]
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[2] Laboratoire d'Ethologie Expérimentale et Comparée (LEEC), Université Sorbonne Paris Nord, 99 avenue Jean-Baptiste Clément, 93430 Villetaneuse, France.
Termites are "eusocial cockroaches" that live in populations of soft-bodied individuals, and may represent a relatively low-cost food source for predators. Predation is pointed out as one of the selective pressures for the emergence of the soldier caste in termites, which constitutes the colony's defensive frontline. Termite soldiers differentiate from workers via hemimetabolous molting, which includes an intermediate stage termed presoldier. Worker-to-soldier molting represents a complete body and behavioral reprogramming, including the development of mechanical and chemical weapons and strong neural rearrangements. Our recent findings have shown that soldiers face a reduction of the mushroom bodies, centers related to sensory integration, learning, and memory, possibly due to the behavioral shifts to display defensive tasks. Moreover, there is an enlargement of the subesophageal zone (SEZ), mandibular motoneurons, and nerves. Physiologically, soldiers present increased brain and SEZ levels of the biogenic amines related to aggressiveness, such as serotonin. However, it is hitherto unknown if the soldier defensive performance and related neuroplasticity rely solely on ontogeny or if defense experience plays a role. We thus aim to evaluate if naïve presoldiers and soldiers differentiated under laboratory conditions, after being submitted to

aggressive encounters, become better defenders than inexperienced counterparts. Moreover, we also ask if the defensive-related brain plasticity of soldiers, comprising the enlargement of the SEZ and increased serotonergic levels, relies on ontogeny (experience-expectant), on their cumulative experience as defenders (experience-dependent), or both. We expect to contribute to a better understanding of the overlooked termite neuroplasticity and behavior.

Cao Qian
iEES-Paris, CREA (Chimioreception and Adaptation)
A calcium-activated chloride channel is involved in olfactory transduction in *Drosophila Melanogaster*.

Insects rely on their highly sensitive olfactory system to detect chemical cues in the environment, enabling essential life activities. In turbulent environments, odorants are heterogeneously distributed, requiring insects with powerful dynamic encoding abilities to rapidly and accurately with different concentrations and compositions. The olfactory signals transduction involves the concerted activity of diverse receptors and ion channels. It has been confirmed that the activation and opening of olfactory receptors (ORs) expressed on the dendritic membranes of olfactory receptor neurons (ORNs) initiate olfactory signal transduction. However, the subsequent cascade of electrical conductance triggered by the influx of sodium, potassium, calcium, and other cations following OR activation remains poorly characterized. In previous research, we identified a calcium-gated chloride channel gene specifically expressed in the antennae of *Drosophila Melanogaster* through bioinformatic and functional analyses, which we named DmelAno5. To determine whether DmelAno5 participates in olfactory signal transduction, we employed electrophysiological techniques to record the response patterns of different ORNs to different odor stimuli at similar time sequences. Initially, we observed that DmelAno5 mutant flies exhibited different response patterns in both receptor potentials and action potentials upon odor stimulation. Combined with electroantennogram (EAG) and single sensillum recording (SSR) results, we propose that DmelAno5 plays a critical role in olfactory signal detection and transduction. We are comparing the effects of DmelAno5 mutation across different types of sensilla or ORNs. Moreover, the potential repercussions of DmelAno5 deficiency on olfactory behaviors is currently investigated. The employment of fluorescently labelled DmelAno5-producing cells and ANO5-tagged proteins will facilitate the analysis of its function in ORN physiology.

Carrière Manon
Laboratoire Jean Perrin
Maturation of the head direction system of a vertebrate.

This PhD project aims at exploring the fundamental principles underlying the organization, function and maturation of the head-direction system in the vertebrate brain. For this study, we use a recently introduced model vertebrate system, Danionella cerebrum (DC). The brain of this freshwater fish remains small and quasi transparent throughout its life. This unique trait enables us to monitor the whole-brain activity with cellular resolution across development using calcium imaging. During this project, we use a virtual reality setup to identify and characterize the dynamics and sensory response of HD circuits in DC at various developmental stages (1 to 6 weeks old). New transgenic lines will be designed, which will be used to dissect the HD circuit organization. In particular, optogenetic lines will allow an all-optical interrogation of the circuit by combining 2P optogenetic activation and light-sheet calcium imaging. These various data will be used to infer a minimal set of developmental rules that could emulate the emergence of a HD circuit during development.

Celle Marion
Laboratoire de Biologie et Modélisation de la Cellule, ENS de Lyon, Bertrand Mollereau team
Establishing a *Drosophila* model for BPAN Disease.

-Authors : **Marion Celle**, Sahra Aniorte, Ludivine Walter & Bertrand Mollereau
The Beta-Propeller Protein Associated with Neurodegeneration (BPAN) is a rare genetic neurological disease characterized by iron accumulation in the brain of affected individuals. BPAN is caused by mutations in the WDR45 gene, a known regulator of autophagy. Mutations in WDR45 lead to dysregulation of autophagy in several BPAN cellular and animal models. Moreover, iron metabolism is also dysregulated, and the molecular events driving these dysregulations remain largely unknown. To address this question, we used CRISPR-Cas9 to establish a *Drosophila Melanogaster* mutant for CG11975 (hereafter dWDR45), the *Drosophila* homolog of WDR45. We have demonstrated that flies harboring dWDR45 mutation exhibit several hallmarks of BPAN, such as locomotor disorders, decreased mean lifespan, and dysregulations in autophagy and iron homeostasis. Interestingly, we used genetic activation of autophagy in the *Drosophila* BPAN model, which rescued the mean lifespan decrease but not the locomotor disorder. These data suggest that autophagy contributes to some, but not all, phenotypes associated with the dWDR45 mutation. In the long term, our study will contribute to a better understanding of BPAN and provide valuable insights for the development of therapeutic molecules.

Collet Claude
INRAE UR406 Abeilles et Environnement – Neurophysiologie, Comportement et Toxicologie
Diamide insecticides as pharmacological tools to study the function and roles of insect calcium channels in neurons, skeletal muscle cells and cardiomyocytes.

In vitro, anthranilic and phthalic diamides disrupt intracellular calcium homeostasis in peripheral neurons, skeletal muscle cells and cardiomyocytes of the honey bee Apis mellifera. We have also shown that calcium conductances are decreased at the plasma membrane of central neurons and muscle cells. At the tissular level, these insecticides compromise cardiac rhythmicity and contraction kinetics as well as force production from leg muscles. At high doses, compatible with field recommendations, they are lethal to bees and our results demonstrated differential toxicity levels depending on exposed body parts. At lower doses, a single contact exposure modifies behaviour in a quite persistent way, which may create a durable vulnerability in the field. These long-lasting behavioural deficits may be ascribed partially to the multiple toxic effects observed in the heart, muscles and peripheral and central nervous systems, as well as other tissues where calcium is involved in the modulation of vital functions. Synthetic insecticides have been clearly identified as a major driver of a worrying worldwide insect diversity decline, and the global market sales and field usage of this recent neurotoxic insecticide family increased substantially in France and in Europe. This has put the wisdom of their overuse under review. This talk will not only give an overview of the knowledge collected these late years on the global toxicity of diamides to bees but will also emphasize the benefit of using these molecules as pharmacological tools for the study of calcium homeostasis in insects.

Costa Céline
Functional and Adaptative Biology Unit, CNRS UMR 8251, Université Paris Cité
Role of glial reactivity in behavioral and neurodegenerative symptoms in a *Drosophila* model of Parkinson's disease.

-Authors : **Céline Costa**, Amélie Hu, Baya Chérif-zahar and Serge Birman
Parkinson's disease is a neurodegenerative motor disorder characterized by the degeneration of dopaminergic neurons in the substantia nigra, and the presence of neuronal inclusions called Lewy bodies,

whose main component is the protein α-synuclein. This multifactorial syndrome, which is still poorly understood, manifests itself through various cellular disturbances. Neuroinflammatory processes are also involved in the development of the pathology, as evidenced by the increased abundance in the substantia nigra of activated microglial cells, the brain's resident macrophages, and the infiltration of peripheral immune cells. Our aim is to better understand the role of glial cell reactivity in the progression of neurodegeneration in this disease using *Drosophila*. To this end, we are studying the expression levels of different glial genes and their effects on behavioral and neurodegenerative symptoms triggered by the expression of a mutant pathogenic form of human α-synuclein in fly neurons.

Dourlen Pierre
UMR1167 Facteurs de risque et déterminants moléculaires des maladies liées au vieillissement
Expression of the Alzheimer susceptibility gene BIN1 in the presynaptic compartment leads to isoform-specific synaptotoxicity.

BIN1 is a major susceptibility gene for AD and BIN1 protein interacts with Tau. However, the contribution of BIN1 and its isoforms to AD pathogenesis remains unclear. We recently showed a functional evolutionary conservation of human BIN1 isoforms in *Drosophila* as expression of human BIN1 isoform8 (BIN1iso8) was able to rescue the locomotor defects of Amph null flies, the *Drosophila* BIN1 ortholog. In addition, we observed that human BIN1iso1 induces an accumulation of early endosome vesicles leading to neurodegeneration in *Drosophila* retina photoreceptor neurons and that the early endosome size regulation was conserved in human induced neurons. This role was specific to BIN1iso1, as compared to BIN1iso8 and BIN1iso9. Because endosomal trafficking is essential for synapse, we further analyzed BIN1 isoforms neurotoxicity at the synaptic level. Using electrophysiology, we observed an early loss of synaptic transmission upon BIN1iso1 expression in *Drosophila* retina photoreceptor neurons. This was characterized by a strong accumulation of abnormally large vesicles in the presynaptic compartment. In addition, expression of BIN1iso1 in motoneurons of the larval neuromuscular junction altered the morphology of synaptic boutons, with an increase in their number and a decrease in their size, and the appearance of satellite boutons. Finally, we tested a functional conservation in rat primary neurons using tricompartment microfluidic devices and assessing a presynaptic vs post-synaptic role. We observed a loss of synaptic connectivity only when expressing BIN1iso1 in the presynaptic compartment. In conclusion, our results suggest that BIN1 has an isoform-specific, deleterious effect on synaptic integrity when expressed in the presynaptic terminal. Therefore, we propose a role for BIN1 in the synaptic loss observed early in AD.

Dura Jean-Maurice
IGH/Neurogenetic and memory, Montpellier
Orion and the neuron-glia cross talk during neuronal remodelling

During animal development, neurons often form exuberant or inappropriate axons and dendrites at early stages, followed by the refinement of neuronal circuits at late stages. This remodelling of neurons is a conserved fundamental mechanism underlying nervous system maturation and function. Neural circuit refinement leads to the production of neuronal debris in the form of neuronal cell corpses, fragmented axons and dendrites, and pruned synapses requiring disposal. Glial cells act as predominant phagocytes during neuronal remodelling and degeneration, and crucial signalling pathways between neurons and glia are necessary for the execution of phagocytosis. Mushroom body neuron-secreted Orion is essential for astrocyte infiltration into the pupal γ axon bundle leading to γ axon pruning during the development of the brain. Orion performs its functions extracellularly and bears some features common to chemokines, a family of chemoattractant cytokines. We also show that Orion is not only required as a signal for glia infiltration but also for axonal debris phagocytosis. Moreover, these two roles of Orion require two forms of secreted Orion.

Orion associated to the axon plasma membrane (PM), likely by glycosaminoglycans, is required for glia infiltration. Orion not associated to the axon PM, likely associated to exosomes, is required for phagocytosis. Importantly, we propose that the way Orion is presented to glial cells determines glia behaviour: either infiltration or phagocytosis.

Dumas Camille
Functional and Adaptative Biology Unit, CNRS UMR 8251, Université Paris Cité
Role of the vacuolar ATPases of dopaminergic neurons in the pathogenesis of Parkinson's disease studied in *Drosophila*.

-Authors : **Camille Dumas**, Zohra Rahmani and Serge Birman
Parkinson's disease (PD) is the second most common neurodegenerative disorder in the world. It is notably due to the loss of dopaminergic neurons in the substantia nigra, and characterized by the presence of neuronal inclusions called Lewy bodies, whose main component is the protein α-synuclein. α-synuclein is present at nerve terminals and interacts with synaptic vesicles, indicating its role in neurotransmission. Toxic oligomers from α-synuclein lead to neurodegeneration, which generally begins at synaptic terminals and propagates towards the cell bodies. Vacuolar ATPases (V-ATPases) are highly conserved proton pumps involved in the acidification of intracellular compartments, which allow the accumulation of neurotransmitters in synaptic vesicles. Recent evidence suggests a plausible link between V-ATPase subunits and PD pathogenesis. A new regulatory subunit of *Drosophila* neuronal V-ATPase, VhaAC45RP, was identified in our team and shown to be essential for synaptic vesicle acidification and neurotransmitter release (Dulac et al., eNeuro 2021). The general aim of our work is to better understand the physiological role of VhaAC45RP and its potential involvement in dopaminergic neuron degeneration in *Drosophila* PD models.

Flaven-Pouchon Justin
Team Persing, CSGA, Université de Bourgogne
Behavioral regulation by LAT1-like amino acid transporter minidiscs and glutamate signaling in the *Drosophila* mushroom bodies.

-Authors : **Justin Flaven-Pouchon**, Julie Delescluses, Georges Alves, Yaël Grosjean and Gérard Manière
The *Drosophila* mushroom bodies (MBs) are central to the regulation of complex behaviors, including learning, memory, and social interactions. Although glutamatergic signaling in the MBs is known to contribute to these processes, the specific molecular components involved remain incompletely understood. Here, we investigate the role of minidisc (mnd), a gene encoding an amino acid transporter expressed in MBs, and its putative glutamate receptor interactors, in modulating the behavioral outputs associated with the MBs. We showed that mnd is expressed in distinct MB neuron subtypes and that its loss alters glutamatergic activity within MB circuits. Behaviorally, down regulation of mnd in specific MB lobes increases aggression, suggesting that mnd-dependent glutamate signaling regulates social behavior. Our findings identify mnd as a key modulator of glutamate receptor function in the MBs and uncover its previously unrecognized role in aggression control.

Girard Victor
The Francis Crick Institute
A genetically-encoded method for in vivo tagging and tracing of lipids from cell-to-cell.

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Lipid transport between cells and tissues is important in health and disease. In both mammals and insects, lipids are transported between tissues via circulating lipoproteins. More local lipid transport also occurs between cells within the same tissue. For example, from neurons to glia during excitotoxicity, inflammation, oxidative stress and models of neurodegeneration. Direct evidence for lipid transfer from neurons-to-glia mostly derives from in vitro co-culture models as current in vivo methods are unable to tag fatty acids specifically within a single cell type. To overcome this limitation, we developed conditional cyclopropane fatty acyl tagging (cFAT). cFAT is a bioorthogonal genetically-encoded method for tagging the monounsaturated fatty acyl chains of phospholipids with a 14 dalton cyclopropane group detectable via mass spectrometry. As proof-of-concept in *Drosophila*, we validate the cFAT method, first in S2 cells and then in live animals using the GAL4/UAS system. We find that cFAT activity is non-toxic and does not interfere with growth or development. cFAT can be used to trace inter-organ FA transport in vivo from fat body cells or gut enterocytes into the hemolymph and then on to remote tissues such as the CNS. We also demonstrate how cFAT can be combined with micron resolution mass spectrometry imaging to monitor fatty acid transport between cell types within the CNS. Together, these findings show that cFAT is a powerful method for tracing lipid transport from cell-to-cell that has many potential applications in biomedical research, drug screening and diagnostics.

Issa Raouf

Maintenance of the Nervous System and Behaviour team INSERM UA19

A subset of dopamine neurons persist across distinct life stages to modulate locomotion.

-Authors : Agathe Konuita, Lauren Bisse, Elodie Farineaux, Cai Rioqui, Nikos Konstantinides, **Raouf Issa**

Locomotion is an evolutionarily conserved behaviour that is essential for an animal's survival and interaction with its environment. The neuronal circuits that support it emerge during development and are refined as the nervous system undergoes structural and functional changes throughout life. However, it remains unclear whether and how the modulation of locomotion across life stages relies on a shared neuronal circuit despite the animal kingdom. To address this question, we conducted a longitudinal study focusing on dopaminergic neurons (DANs), which are key regulators of locomotion across species. Our investigation focused on a specific subset of the fly ventral nerve cord (VNC), the functional analogue of the human spinal cord. Our research revealed that the VNC DANs, which have previously been shown to support adult locomotion (specifically flight), originate during embryonic development and persist through metamorphosis. Using optogenetics, we established that VNC DAN activity is required to modulate movement speed at distinct developmental stages of the fly, including embryo, larva, and adult. Furthermore, we observed that the functioning of these neurons, from embryonic to adult nervous systems, is followed by a significant architectural remodelling, involving a transition from dense neurite arborisations in early development to more refined, extended axonal projections in adulthood. At the molecular level, transcriptomic and immunolabeling analyses revealed that adult VNC DANs maintain the expression of conserved developmental transcription factors (TFs), including Antennapedia (Antp)/Hox6-8 and Pdm2/Oct-2. Functional experiments confirm that continued expression of Antp and Pdm2 in these neurons is essential for normal locomotion in adulthood. Together, our findings demonstrate that DANs responsible for adult locomotor control emerge early during development and maintain key molecular features throughout life. This work provides programmes that sustain neuronal function across the lifespan, and how early disruptions to these programmes may contribute to late-onset neurological diseases.

Jauffret Benjamin
Laboratoire d'Ethologie Expérimentale et Comparée (LEEC)
Does environmental enrichment impact ants' learning abilities?

In recent decades, laboratory practices for housing animals have gradually shifted. For example, mammals such as rodents are typically kept in enriched environments, as several studies showed that this improves welfare by promoting natural behaviours and reducing anxiety. Beyond welfare, under-stimulation can impair brain development and reduce cognitive abilities — an effect well documented in rodents. Experimental studies comparing behaviour in enriched and non-enriched environments remain surprisingly rare in invertebrates. To start addressing this gap, we conducted a small-scale experiment testing whether enriched housing affects learning in Formica fusca ants. Six sub-colonies of 60 workers each were housed for one week in either (1) an enriched environment designed to stimulate the ants' senses by mimicking aspects of their natural habitat, or (2) a standard, non-enriched plastic box lacking sensory or structural stimulation. During this period, we recorded overall group activity. Afterwards, individual ants were tested on two learning tasks: a spatial maze (with one rewarded arm) and an olfactory discrimination task (with one rewarded odour out of three). We found no clear evidence for a difference in learning performance between the two groups. While a larger sample size would be needed to draw firmer conclusions, our results raise the possibility that one week of enrichment may be insufficient to induce detectable cognitive effects. Future studies using longer enrichment periods, or directly comparing lab-reared and wild ants, could help clarify how rearing conditions affect the ecological validity of laboratory results.

Jia Zihao
Functional and Adaptative Biology Unit, CNRS UMR 8251, Université Paris Cité
Investigating the role of LRRK2 and its phosphorylation in the gut-brain axis in Parkinson's disease using *Drosophila*.

Parkinson's disease (PD) is second only to Alzheimer's disease in the list of the most common neurodegenerative disorders. 5-10% of PD cases can be related to mutations in about 20 risk genes, such as SNCA (encoding α-synuclein), LRRK2, PRKN (encoding Parkin), PINK1, and DJ-1. LRRK2 is one of the major genes contributing to familial PD, with the G2019S mutation being the most prevalent one. Recent researches suggest that LRRK2 may be involved in the mechanisms by which the gut-brain axis regulates PD pathogenesis. LRRK2 is a ubiquitously expressed multidomain protein that functions as a kinase, and the pathogenicity of the G2019S form may result from its kinase hyperactivity. To better understand the role of LRRK2 in the gut-brain axis, we express wild-type (WT) or mutant (G2019S) human LRRK2 ubiquitously, and then selectively in neurons or gut enterocytes, in order to characterize specific defects associated with the mutation.

Mariana Da Silva Malheiro
Centre de Recherche sur la Cognition Animale (CRCA)
Does the social environment influence behaviour in a *Drosophila* model of Alzheimer's disease?

Alzheimer's disease (AD) is a neurodegenerative disorder that leads to behavioural deficits in some patients, including reduced motor skills. This disease is characterised by the accumulation of the Aβ protein, the most toxic form of which is the Aβ42 peptide. Studies have shown that loneliness increases the risk of developing AD, while staying mentally active and participating in social activities may help prevent cognitive decline and delay the onset of the disease. Currently, no medication has been shown to be effective in preventing the progression of AD. It is therefore important to identify factors that may delay certain behavioural symptoms. Using an animal model of AD, we aim to understand the effect of Aβ42 at the cellular level in relation to

locomotor activity, and to show how this effect may be mediated by the social environment. *Drosophila* provides an effective model for this study, with a wide range of behaviours that are easy to study, and numerous genetic tools that allow the manipulation of gene expression and neuronal activity. In addition, *Drosophila* has already been used to study the relationship between Aβ42, amyloid plaques and memory, making it a particularly relevant model. Our results show that the expression of Aβ42 in the mushroom bodies, the main center of learning and memory in insects, reduces locomotor activity when *Drosophila* males are tested alone, but increases locomotor activity when they are tested in groups with conspecifics. Our results indicate that social conditions may interact with the Aβ42-mediated locomotion deficit.

Paoli Marco
Centre des Sciences du Goût et de l'Alimentation (CSGA)
Statistical olfactory learning in honey bees.

Statistical learning is a key mechanism for detecting regularities in sensory inputs. Among its functions is the ability to extract regularities from sequences (of sounds, objects, odors, etc.), enabling species to predict future events and guide behavior. This capacity has been demonstrated in vertebrates, including human infants, non-human primates, and birds. However, the minimum computational architecture required for statistical learning remains unclear. To address this issue, we studied statistical learning in the honey bee (Apis mellifera), an invertebrate model for learning studies. We show that bees learn and recall the temporal structure of sequences of odorants, suggesting that statistical learning is a fundamental component of a conserved cognitive toolkit present even in invertebrates.

Montgomery Stephen
University of Bristol, School of biological sciences, Bristol, United Kingdom
Evolution of expanded learning and memory centres in *Heliconius* butterflies.

How animals perceive, process and respond to environmental cues is tightly tuned to the species-specific demands imposed by their ecology and life history. This specialisation is likely reflected in neural systems that support cognitive processes, as well as the behaviours expressed by those systems. In Heliconius butterflies the mushroom bodies - insect learning and memory centers - are significantly expanded relative to all other butterflies, with 8-times more Kenyon cells than their close relatives. Mushroom body expansion in Heliconius coincided with the evolution of a novel dietary shift towards active pollen feeding, and a spatial foraging behaviour, trap-lining, which is thought to require long-term spatial memory of visual scenes. I will discuss evidence that selection for trap-line foraging has reshaped Heliconius cognition along specific lines, reflected in both neuroanatomical specialisations and shifts in a restricted range of learning and memory traits. By following the neural pathways that lead to and from the mushroom bodies, a mosaic pattern of neural adaptations is apparent, with shifts in cells and structures supporting visual and sparse coding within the mushroom body. Behavioural experiments closely mirror these changes, with improved performance in non-elemental learning and long-term memory in Heliconius, but specifically within a visual context. These results are consistent with visual specialisation of the Heliconius mushroom body facilitating a specific enhancement of visual memory, likely due to the requirements of long-term foraging efficiency, and illustrate the precision with which selection can reshape animal cognition. Finally, I will discuss the early stages of our work aiming to understand the cellular and developmental basis of these neural adaptations, and the potential role of novel intermediate progenitor cells in amplifying Kenyon cell production.

Pavlowsky Alice
Laboratoire de Plasticité du Cerveau UMR8249 CNRS ESPCI-PSL, Equipe : Energie et Mémoire
Neuronal fatty acid oxidation fuels memory after intensive learning.

-Authors: **Alice Pavlowsky**, Bryon Silva, Lydia Danglot, Pierre-Yves Plaçais, Thomas Preat
Metabolic flexibility allows cells to adapt to different fuel sources, which is particularly important for cells with high metabolic demands. In contrast, neurons, which are major energy consumers, are considered to rely almost solely on glucose and its derivatives to support their metabolism. Here, using *Drosophila Melanogaster*, we show memory formed after intensive massed training is dependent on mitochondrial fatty acid (FA) b-oxidation to produce ATP in neurons of the mushroom bodies (MB), a major integrative center in insects' brain. We then determine that the surrounding glia provide the FA to the neurons and identify the key actors of the FA's transfer from glia to neurons, which is required to support memory formation after intensive learning. Furthermore, we demonstrate that this intensive massed training is associated with mitochondria network remodeling in the soma of MB neurons, resulting in increased mitochondrial size. Artificially increasing mitochondria size in adult MB neurons increases ATP production in their soma and, at the behavioral level, strikingly results in improved memory performance after massed training. These findings challenge the prevailing view that neurons are unable to use FAs for energy production, and importantly revealing on the contrary that in vivo neuronal FA oxidation has an essential role in cognitive function, including memory formation.

Ponte Giovanna
Department of Biology and Development of Marine Organisms Stazione Zoologica Anton Dohrn, Naples, Italy.
Exploring the Complex Neural Networks of Octopus.

After more than a century of studies on the evolutionary diversity and novelties of cephalopods among molluscs and other invertebrates, these organisms continue to inspire and sustain advanced scientific endeavours. Cuttlefish, squid and octopus are endowed with a highly intricate nervous system, with octopus having over 500 million nerve cells. More than 40% of these cells contribute to the formation of a multilobular brain, originating from the fusion and condensation of ganglia of molluscan origins. Octopus vulgaris is an iconic species serving as a model of a brain and continues to solicit significant interest in the exploration of sentience and primary consciousness among invertebrates. I aim to reveal how neuromodulators and genomic innovations shape neural circuits. Here I will explore some key features of the complex neural network characterizing the octopus brain.
First, I will briefly describe the organization of cephalopod brains and their diversity among species. Through a comparative analysis across over 50 species, we identified distinct cerebrotypes. PCA followed by hierarchical clustering suggested that brain organization in these species is related not only to evolutionary history of the taxa considered but also to taxon-specific lifestyles and other adaptations. Overall, our data suggest that brain composition reflects ecological adaptations, thus further supporting recent evidences of the existance of genomic innovations within the clade. The findings of cephalopod cerebrotypes also complement our analysis of the functional analogies of cephalopod neural areas with mammalian brains.
In addition, I will overview our studies on the characterization of the neural circuitry of Octopus vulgaris. Building on the body of work by J.Z. Young, we applied a neural-network approach to octopus brain architecture and connectivity. Neuromodulatory fingerprints identify distinguished areas of a given complexity. By mapping over 350 neural pathways connecting over 30 octopus brain regions in the supra- and sub-oesophageal masses and the optic lobes, we carried out a macroscale analysis resulting in small-world properties, multiscale modularity, the existence of hubs, and segregation-integration neural dynamics.

Overall, our work is consistent with the idea that a mollusc brain resolved similar principles characterizing of mammalian neural systems.

Pred'homme Maureen
MERSEA laboratory (Marine Ecosystems and oRganisms reSEArch Lab), Université de Caen Normandie
Post-reproductive Neurodegeneration in Cuttlefish: Unveiling an Alzheimer's-like Tauopathy?

-Authors : **Maureen Pred'homme**, Céline Zatylny-Gaudin, Joël Henry
The common cuttlefish (Sepia officinalis) is a short life-span cephalopod (20–22 months) that exhibits rapid post-reproductive decline which appears to be linked to neurodegeneration. This phenomenon, characteristic of semelparous species (single reproductive event), manifests through behavioral and physiological alterations: sensory loss, impaired bathymetric regulation, motor decline, and instinctual feeding disturbances. These observations suggest the involvement of neural aging biomarkers in the central nervous system (CNS). To test this hypothesis, new CNS transcriptomes from cuttlefish were sequenced (NGS) at different life stages. In silico analysis revealed the expression of molecular markers associated with Alzheimer's disease, including amyloid-β peptide precursor (APP), Tau protein (implicated in neurofibrillary tangles), and APP-cleaving enzymes (ADAM, BACE-1, PSEN). Specific antibodies targeting these biomarkers were developed based on cuttlefish-derived sequences. The Aβ42 peptide inferred from the neurotranscriptome was also synthesized. Immunostaining demonstrated variable distribution and abundance of these biomarkers in the CNS across life stages, correlating with post-reproductive decline. Concurrent in vitro assays revealed spontaneous aggregation of the synthetic peptide into amyloid polymers, visualized via transmission electron microscopy (TEM). These aggregates exhibit significant structural homology with amyloid plaques observed in vertebrates. These results support the hypothesis of a shared neurodegenerative mechanism between cuttlefish and vertebrates, involving molecular pathways analogous to Alzheimer's disease. The spontaneous aggregation of Aβ peptides in cuttlefish, combined with the spatiotemporal expression of identified biomarkers, establishes this species as a key model for studying neurodegenerative processes.
Key words: Neurodegeneration; Cuttlefish; IHC; -Omics; in silico.

Prévot Héloise
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Understanding Circuit Function Through Dynamics-Based Comparison of Neural Motifs in the *Drosophila* Larva Connectome.

Recent advances in connectomics now allow us to reconstruct entire neural circuits at synaptic resolution in small model organisms like *Drosophila Melanogaster* larvae [Winding 2023, Bénichou 2023]. Combined with powerful genetic tools and large-scale behavioral recordings [Jovanic 2016, Masson 2020], these datasets offer a unique opportunity to reverse-engineer the physical basis of behavior. However, translating the structure of a connectome into a functional understanding of behaviorally relevant neural computations remains a major challenge. In network theory, the functions of biological networks are often hypothesized to be governed by an ensemble of regularly repeated, small subgraphs termed motifs [Milo 2002]. These motifs are typically identified through their statistical over-representation within a network. Yet this approach overlooks the dynamics they support—how activity propagates through them or how they process information—features that are essential to understanding their role as functional units. To move beyond purely structural comparisons, we develop dynamics-based dissimilarity measures between candidate network motifs, revealing functional relationships that are not apparent from topology alone (fig.1.). Using the Kuramoto model as a biologically inspired example, we quantify how motifs synchronize in response to inputs, enabling us to group them by functional outputs rather than wiring pattern alone

[Riascos 2024]. We aim to apply these tools to motifs identified in the *Drosophila* larva connectome—particularly those involved in sensory integration and motor control—by combining synaptic-resolution structural data with large-scale behavioral recordings from optogenetically stimulated larvae.

Seugnet Laurent
Centre de Recherche en Neurosciences de Lyon, WAKING team
Amino acids and the Regulation of the Sleep-wake cycle in *Drosophila*

-Authors : Sandrine Parrot, Jacob Crehan, Chloé Aman, Philippe De Deurwaerdère, Matthew Thimgan, **Laurent Seugnet**
A comprehensive view of whole-brain amino acid levels hold the potential to provide valuable insights into the brain's state, given the mutual interconnections through metabolism, food intake, and neurotransmission. We tested this concept by evaluating free amino acid levels in single Drosophila brains across 24h and at two different ages. A large proportion of these amino acids displayed time-of-day variations, and a subset exhibited age-dependent variations. Cross-correlation analysis of the datasets confirmed broad time-of-day and age dependent interconnections between amino acids. Factor Analysis of Mixed Data revealed further data structuration along key amino acids. For example, 50% of the variance could be accounted by an inverse coupling between gamma-aminobutyric acid and several essential amino acids during the active phase, linking food intake and sleep. This proof of concept emphasizes the value of combining multivariate analysis to whole-brain amino acid levels evaluation, shedding potentially new light on sleep-wake regulation and aging. I will also present some data emphasizing the role of branched chain amino acid in this context.

Sillon Léo
TPI team, CSGA
Taste regulation of immunity.

Animals rely on their sensory systems to detect environmental cues, which are then processed and integrated by the nervous system to trigger specific responses. Taste is a crucial sensory modality that allows animals to assess their environment and can influence various aspects of behaviour and physiology. One major challenge animals face is the constant need to detect and respond to pathogens in their environment. However, the mechanisms linking sensory detection, especially taste, to immune responses remain largely unexplored. Here, we demonstrate that *Drosophila* larvae detect bacterial cell wall components via their gustatory system and respond by modulating cellular immune activity. This response involves specific gustatory neurons that act as early sentinels of infection, linking environmental detection to immune priming. Our results suggest that taste not only informs feeding decisions but also plays a previously unrecognized role in pathogen surveillance. Our findings reveal a novel sensory-immune axis and highlight the protective role of gustatory cues against infection, expanding current understanding of neuroimmune crosstalk.

Stoclet Lydie
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Sleep and neuroglial interactions in a critical period of the *Drosophila* olfactory system

During development, some neuronal circuits can be remodeled by experience and the environment only during specific temporal windows, known as critical periods (CP). Sleep is more abundant during these CP and promotes plasticity. Its disruption can have long-term consequences on neuronal functioning. The mechanisms involved in CP remain enigmatic. We already know that synapse-astrocyte cell contacts regulate

neurotransmission and synaptogenesis as a function of sleep. In mammals and insects alike, neuroglial interactions have recently been shown to play a central role in CP, but the underlying mechanisms are poorly described.
This project aims to clarify the relationship between sleep, neuroglial interactions and CP, by exploiting the potential of a simple, well-characterized and flexible model: long-term habituation (LTH) to CO_2 in the olfactory system of Drosophila with CP that ends in early adulthood.
This LTH results in a persistent increase in the volume of the CO_2-specific glomerulus (V glomerulus) and reduced behavioral responses to this odor, due in part to enhanced inhibition by GABAergic local interneurons (LN). These changes can only occur if exposure to CO_2 began in the first 48 hours of adult life, a period during which flies sleep a lot.
Using the GRASP (GFP Reconstitution Across Synaptic Partners) technique, we observed that CO_2 exposure during CP significantly modifies contacts between LN presynapses and astrocytic membranes, suggesting an important role of these interactions in this context. In the remainder of the project, we will further investigate neuroglial interactions and the molecular mechanisms underlying these processes, focusing on cell contact between astrocytes and interneurons, which appears to be essential in this context. We will also examine the influence of sleep on LTH and CP by modulating, mechanically or thermogenetically, sleep quotas both upwards and downwards.
The findings of this project could help decipher the importance of astrocyte-interneuron contact in brain plasticity, as well as highlighting the importance of sleep and the need to protect it, particularly during CP.

Turrel Oriane
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Diversity of the roles of Mushroom Body's Active Zone proteins in memory formation.

-Authors : **Oriane Turrel**, Sabrina Putignano, Stephan Sigrist
In *Drosophila*, associative memory formation occurs in the Mushroom Body (MB). It has been shown that the synaptic connection between the MB neurons and the MB-Output Neurons (MBONs) are the crucial site in which plasticity occurs, underlying memory formation. This connection is modulated by Dopaminergic Neurons (DANs) coding for the value of the experience (punition, reward for example). The MB are composed of 3 lobes: 1 horizontal γ, and 2 horizontal and vertical αβ and α'β'. Those lobes are subdivided into smaller micro-circuits determined by their innervation by DANs and MBONs. Interestingly, it has been shown that each of the MB lobes is involved in different memory phases, with specific DANs and MBONs involved. Diversity in the composition of proteins of the presynaptic Active Zone (AZ) is known to be implicated in the variety of plasticity rules and could explain the different roles of each MB lobe relating to memory formation. We have previously shown that there is an increase of certain AZ proteins after aversive olfactory conditioning during memory consolidation. Those changes and their dynamic are specific for each MB lobes. These results could underline the role of each MB lobe in memory phases due to different plasticity rules. To test this hypothesis, we are describing the AZ proteins diversity with super-resolution imaging (STED) and testing the role of specific AZ proteins in each of the MB lobes.

Vey-Payre Hugo
Centre de Recherche sur la Cognition Animale
Behavioral flexibility comparison in social and solitary bees.

Sociality is present in all lineages, from undifferentiated aggregates to highly integrated societies. Living alone or in a group is predicted to shape the level of behavioral flexibility as the social context is likely to impose different cognitive challenges on individuals. We hypothesize that the decoupling between reproductive and non-reproductive activities in eusocial species was accompanied by a reduced need for behavioral flexibility in comparison to solitary individuals. Behavioral flexibility, defined as the ability for an

animal to adapt its behavior to changing environmental contingencies, can be assessed under controlled laboratory conditions, using appropriate tasks such as reversal learning. The aim of my PhD is to compare the levels of behavioral flexibility between Apis mellifera, a well-studied eusocial species used as a model for studies on cognition, and Osmia bicornis, which is used as a pollination aid and whose cognitive abilities have been much less studied. In addition, we compare the cognitive performance of males and females in solitary bees, an aspect that has not received much attention. Both species are tested in visual

Vittet Julie
Centre des Sciences du Goût et de l'Alimentation (CSGA) / PERception Sensorielle, Interaction Neurone-Glie (PERSING)
Behavioral Effects of Volatile Compounds on *Drosophila* Species: Towards Ecological Solutions for Managing Invasive Pests in Fruit Crops.

Global warming, together with international trade and movements, has contributed to the spread of insect pests, such as *Drosophila* suzukii, in France. In this context, we have recently observed remarkable effects of two odorant compounds, propanoic acid and butyric acid, not only on the behavior of this invasive species, but also on the model species *Drosophila Melanogaster*. While these acids are attractive to larvae, they exert a repulsive effect on adults, significantly altering their courtship behavior and leading to the complete abolition of copulation. At higher concentrations, these molecules also induce anesthesia in adults (patent PCT/EP2020/075386). However, the mechanisms underlying the recognition and action of these compounds remain to be fully elucidated. Recent research has suggested the possible involvement of an as yet unidentified organ in olfaction. Our objective is to understand these mechanisms of action in order to propose ecological and non-toxic solutions for the management of fruit crops, while preserving biodiversity and human health.

Yue XiaoJing
Laboratoire de Biologie et Modélisation de la Cellule, ENS de Lyon, Bertrand Mollereau team
Understanding the Role of Lipid Droplets and α-Synuclein in Parkinson`s Disease.

Parkinson's disease (PD) is characterized by the accumulation of alpha-synuclein (α-Syn) aggregates in dopaminergic neurons (DAs), which is associated with DAs loss. It was found recently that lipid dysregulation is central in PD progression. Lipid droplets (LDs) are organelles that regulate the storage and hydrolysis of neutral lipids. α-Syn can bind to the phospholipid membrane of LDs. However, the function of this interaction is poorly understood. In this project, we overexpressed dPlin2 (*Drosophila* Plin2) and α-Syn in *Drosophila* DAs to investigate their role on LD metabolism on DAs function in PD. Although LDs accumulation in DAs is hard to detect, we observed that dPlin2 overexpression induces severe climbing defect of flies, which can be rescued by the overexpression of lipase brummer and pharmacological L-Dopa feeding. This indicates that the inhibition of LD lipolysis causes DAs dysfunction and a subsequent climbing defect. Surprisingly, α-SynWT or α-SynA30P mutant could rescue this climbing defect as well, suggesting that α-Syn could restore lipolysis and DAs function. Our data show that dPlin2-induced DAs dysfunction and climbing defects could be due to mitochondrial dysfunction, which needs further investigation.