# NeuroPSI-Chen Institute Joint Conference on Brain, Behavior & Beyond

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**The Paris-Saclay Institute of Neuroscience** (NeuroPSI) is a joint research unit of the CNRS and the Paris-Saclay University. NeuroPSI scientific project is based on a multidisciplinary and multi-scale approach for studying the nervous system. Our main objective is to understand the anatomical organization and operating principles of neural circuits that control behavior and cognition. A wide range of experimental models are used to capture the diversity of brain architectures and to understand how natural selection drives the evolution of neural design and function. Our experimental approaches aim at determining how cellular interactions lead to neuronal populations, how these populations assemble into functional circuits, and how such circuits generate behaviors in response to environmental cues and internal states. We ask these questions in both physiological and pathological situations to investigate the cell and circuit bases of neuromuscular and neuropsychiatric diseases. Our experimental studies are associated with computational and theoretical approaches to model neural circuits and design brain-machine interfaces.

**Tianqiao and Chrissy Chen Institute** (TCCI) was established in 2016 with the mission to promote holistic brain research focused on three areas - brain discovery, treatment, and development. A primary focus of TCCI is interdisciplinary neuroscience research to understand the brain at the level of the individual neuron and synapse. We support research that will deepen understanding of how the brain gathers, organizes and retains information, and translates perceptions into thoughts, emotions, decisions, actions and memories. We believe that limited understanding of these processes is a bottleneck for new discoveries in both brain treatment and development and we partner with world-leading universities and research institutions to unlock the mysteries of the brain.

**NeuroPSI and TCCI** share the view that understanding brain functions at the molecular, cellular and circuit levels is one of the most exciting goals of science for the decades to come. Integrating different scales of brain organization, analyzing neural networks and their emerging properties during brain development, deciphering the complex interactions between the brain, the body, and the external world are some of the challenging questions that need to be tackled to understand perception, emotion, action, or cognition. We also believe that curing brain diseases or developing neurorehabilitation technologies will not progress without strong research in fundamental neuroscience. Finally, we share the view that the concepts and experimental results of neuroscience research need to be shared with the general public. We thus started a partnership to build an impactful conference program on Brain, Behavior & Beyond that will bring together leading researchers to push further the frontiers of Neuroscience. We are presenting here the first conference of our partnership. Over the next years, we will propose a series of exciting topics at the cutting edge of different fields in brain research.

**This 1st meeting is dedicated to the celebration of the opening of NeuroPSI in Saclay**


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# NeuroPSI Opening Conference in Saclay
# May 11-12, 2023

# Program Booklet

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***Organizers***: *Max Chalabi, Valérie Doyère, Isabelle Ferezou, Edwin Gatier, Tihana Jovanic, Dylan Manceau, Jérôme Roger, François Rouyer, Rose Tatarsky*

# Thursday, May 11

***Chair: Sophie Creuzet***

9:10-9:30 **Introduction**

- **François Rouyer** – *NeuroPSI Director*
- **Anne-Helene Monsoro-Burq** – *Deputy Vice-President 'Life Sciences' of Université Paris-Saclay*

9:30-10:15 **Seth Blackshaw** – *Building and regenerating the vertebrate retina*

Solomon H. Snyder Department of Neuroscience, Johns Hopkins University, Baltimore, USA.
Wilmer Eye Institute, Johns Hopkins University - School of Medicine, Baltimore, USA.
Zanvyl Krieger Mind/Brain Institute, Johns Hopkins University, Baltimore, USA.
Department of Neurology, Johns Hopkins University School of Medicine, Baltimore, USA.

Seth Blackshaw received his B.A. and M.S. in biochemistry in 1991 and his PhD in Neuroscience from Johns Hopkins School of Medicine in 1997, working with Solomon Snyder. He performed postdoctoral research with Connie Cepko at Harvard Medical School, and was appointed Assistant Professor of Neuroscience at Johns Hopkins School of Medicine in 2004, where he is now full Professor. Throughout his career, his research has applied unbiased high-throughput approaches to comprehensively characterize molecular mechanisms controlling neural development and disease. His work has focused on identifying causative genes for retinal dystrophies, gene regulatory networks cell fate specification, injury-induced glial-derived neurogenesis, and aging in the retina and hypothalamus, as well as identification of neural circuitry controlling homeostatic regulation of sleep. His group co-developed the Human Proteome Microarray, which consists of 22,000 full-length unique proteins, and developed splicing-linked expression design (SLED), which enables selective targeting of viral gene therapy vectors to specific cell types and disease states based on patterns of alternative splicing. He is the co-founder of CDI Labs and Boolean Therapeutics, LLC. He has received numerous awards for his research, including the Sloan Foundation Research Fellowship, the W. M. Keck Foundation Distinguished Young Scholar in Medical Research Award, the Stein Innovation Award from Research to Prevent Blindness, and the inaugural Milky Way Research Foundation Award for Rejuvenation Research.

10:15-10:45 **NeuroPSI Short Talks**

- **Julien Leclerq** – *Evolution of gene expression regulation in the developing brain of blind cavefish*

**Abstract:** The nervous system (including the eyes) has evolved different size and morphologies. It is accepted that morphological evolution is mostly driven by changes in gene expression during development, rather than changes in protein function. Thus, understanding changes in gene regulation is critical to understand how new forms arise, and is a major focus of Evo-Devo. Gene expression is regulated through non-coding cis-regulatory elements and trans-acting factors binding them. To disentangle cis- from trans- regulatory divergences in developmental evolution of the brain we use Astyanax mexicanus as a model. This fish has two distinct eco-morphotypes: sighted surface-dwelling fish and blind cave-adapted morphs. The two morphotypes are interfertile, enabling the generation of F1 hybrids. We generated transcriptomes for each morph and F1 hybrids at the onset of neurulation, when extensive variations in gene expression occur to pattern the future brain. We identified 26390 fixed single nucleotide polymorphism (SNPs) on 5573 genes in the two morphs. Comparing allelic expression ratios in F1 hybrids allowed us to identify 108 genes whose change in expression levels are due to changes in cis-regulation. We focused on rx3, a critical gene for eye development, which is down-regulated in cavefish. Using reciprocal transplantation experiments at blastula and gastrula stages, we demonstrated that the level of expression of rx3 is regulated in a cell-autonomous manner. On the contrary, the size of theRx3 expression domain depended on external signaling (Wnt), thus demonstrating the uncoupling of the control of the level and the spatial expression for a single gene.

- **Catherine Hottin** – *Modulating Glycogen Synthase Kinase 3 to preserve photoreceptors from retinal degeneration*

**Abstract:** Glycogen Synthase Kinase 3 (GSK3) is a master regulator of cell signaling processes from development to degeneration of the central nervous system. For decades GSK3 has been a target of interest for the treatment of brain disorders such as Alzheimer's disease. In the retina, recent works showed that GSK3 inhibition with pharmacological compounds preserves photoreceptors from degeneration, although their clinical use might show some limitation. In this context, the goal of this study is to decipher the neuroprotective mechanism of GSK3 inhibition to identify new therapeutic candidates to delay retinal degeneration. To this aim, we took advantage of a conditional mouse line allowing retinal specific deletion of GSK3(Gsk3αand/orGsk3β) in retinal progenitors. In these models, induced-photoreceptor cell death ex vivo and in vivo following MNU injection was significantly decreased compared to controls. To identify candidate genes potentially mediating neuroprotection, we performed RNA-Seq and mass spectrometry analysis in MNU-induced model of degeneration. Out of the 352 deregulated genes identified, most down regulated genes belonged to the phototransduction cascade whereas most upregulated genes identified were mostly related to inflammatory response and cell chemotaxis including relevant secreted factors potentially important to mediate neuroprotection. Furthermore, proteomic analysis identified124 deregulated proteins. Among them, we identified ERK3 as a putative GSK3 direct target. Our transcriptomic and proteomic analysis led to the identification of several candidates which could be relevant to develop new therapies for retinal diseases. As such, functional validation to test the neuroprotective effects is ongoing.

10:45-11:00 ***Break***

***Chair: Sylvie Rétaux***

11:00-11:45 **Sandrine Humbert** – *Huntington disease: from abnormal neurodevelopment to neurodegeneration*

Univ. Grenoble Alpes, INSERM, U1216, Grenoble Institut Neurosciences, Grenoble, France

Sandrine Humbert is a group leader at the Grenoble Institute of Neurosciences (GIN); her lab is currently moving to the Brain Institute in Paris. She began her career at the Institut de Génétique et de Biologie Moléculaire et Cellulaire in Strasbourg, France, where she completed her thesis in the team of Dr. JM Egly, focusing on transcription factors.
As she became interested in brain development and degeneration, Dr. Humbert joined Dr. LH Tsai team in 1996, as a postdoctoral fellow at Harvard Medical School in Boston, USA. After three years, she moved back to France to work with Dr. F. Saudou at the Institut Curie in Orsay, completing her second postdoctoral fellowship.
In 2001, Dr. Humbert secured a position as a research scientist and later, in 2009, became a group leader at Curie Institute. Her current research focuses on Huntington's disease, a late onset neurological condition, exploring its mechanisms and potential therapies. Among numerous scientific achievements, her team made the significant contribution that human brain development is altered in Huntington disease. She is now further elucidating how defects in the developing brain contribute to Huntington disease early alterations in the cortico-derived circuits and adult abnormal connectivity and behavior.

11:45-12:15 **NeuroPSI Short Talks**

- **Emmanuel Bruet** – *Role of the neural crest-derived meninges and pericytes in cognitive impairment at birth*

**Abstract:** The nervous system (including the eyes) has evolved different size and morphologies. It is accepted that morphological evolution is mostly driven by changes in gene expression during development, rather than changes in protein function. Thus, understanding changes in gene regulation is critical to understand how new forms arise, and is a major focus of Evo-Devo. Gene expression is regulated through non-coding cis-regulatory elements and trans-acting factors binding them. To disentangle cis- from trans- regulatory divergences in developmental evolution of the brain we use Astyanax mexicanus as a model. This fish has two distinct eco-morphotypes: sighted surface-dwelling fish and blind cave-adapted morphs. The two morphotypes are interfertile, enabling the generation of F1 hybrids. We generated transcriptomes for each morph and F1 hybrids at the onset of neurulation, when extensive variations in gene expression occur to pattern the future brain. We identified 26390 fixed single nucleotide polymorphism (SNPs) on 5573 genes in the two morphs. Comparing allelic expression ratios in F1 hybrids allowed us to identify 108 genes whose change in expression levels are due to changes in cis-regulation. We focused on rx3, a critical gene for eye development, which is down-regulated in cavefish. Using reciprocal transplantation experiments at blastula and gastrula stages, we demonstrated that the level of expression of rx3 is regulated in a cell-autonomous manner. On the contrary, the size of theRx3 expression domain depended on external signaling (Wnt), thus demonstrating the uncoupling of the control of the level and the spatial expression for a single gene.

- **Mariagiovanna Russo** – *Investigating Sonic Hedgehog signaling during remyelination*

**Abstract:** In the mature rodent brain, Sonic Hedgehog (Shh) signaling regulates stem and progenitor cell maintenance, neuronal and glial circuitry, and brain repair, including remyelination. Pharmacological inhibition of Gli1, a transcription factor associated with the Shh pathway, enhances remyelination via neural stem cell recruitment (Samanta et al., 2015). We have recently investigated the pro-myelinating properties of GSA-10, a small molecule developed by our group that inhibits Gli1 transcription (Manetti et al., 2016). Using the lysophosphatidylcholine-induced focal demyelination mouse model, we have demonstrated that GSA-10 promotes the recruitment and differentiation of Olig2+ and CC1+ oligodendrocytes into the demyelinated corpus callosum, representing a novel potential remyelinating agent (Del Giovane et al., 2022). By single molecule fluorescent in situ hybridization, we have further identified, for the first time, Shh transcripts in a subset of oligodendrocytes expressing Olig2 and Sox10 mRNAs throughout the mouse brain. Interestingly, using the C9C5 monoclonal antibody, which recognizes Shh peptides, we reported a broad expression pattern of Shh in a subpopulation (11-12%) of CC1+ mature oligodendrocytes. These cells also express Olig2 and Sox10, two oligodendrocyte lineage-specific markers (Tirou et al., 2020), suggesting a role for Shh in myelinating activity. Moreover, we have investigated Shh mRNA and protein during post-natal myelination of the mouse brain, and we identified Shh-C9C5+ cells to be upregulated from P4 to P20, in parallel with the expression of Myelin Basic Protein. Experiments are in progress to further characterize Shh's role and its regulation in primary cultures of rodent oligodendrocytes and during remyelination.

12:15-2:30 ***Break***

***Chair: Alain Destexhe***

2:30-3:25 **Keynote Lecture**:

**Stanislas Dehaene** – *Symbols and rules: Searching for the origins of human singularity*

UNICOG Cognitive Neuroimaging Lab, CEA, INSERM, Université Paris-Saclay, NeuroSpin Center
Collège de France, Université Paris Sciences Lettres (PSL), FR

Student of the École Normale Supérieure and doctorate in psychology at the École des Hautes Études en Sciences Sociales (EHESS), Stanislas Dehaene is a neurobiologist and psychologist currently directing the Cognitive Neuroimaging Unit at INSERM-CEA NeuroSpin in Essonne, where he significantly contributed to understanding the neural basis of cognitive functions like numerical cognition, consciousness, and reading, using cutting edge functional brain imaging techniques.
Dehaene's notable achievements include his membership in the Academy of Sciences since 2005, his position as a professor of experimental cognitive psychology at the Collège de France, and his nomination as chevalier de la Légion d'honneur in 2011. He has also been recognized with the prestigious Brain Prize in 2014 for his groundbreaking research on higher brain mechanisms involved in complex human functions, like literacy, numeracy, motivated behavior and social cognition, and by the American Psychological Association for his Distinguished Scientific Contributions in 2015. Additionally, he has played a prominent role in the scientific community as the chair of the Scientific Council of National Education in France since 2018.

3:25-4:10 **Pieter Roelfsema** – *Mechanisms for conscious visual perception and the technology for restoring it in blindness*

Department of Vision & Cognition, Netherlands Institute for Neuroscience (KNAW), Amsterdam, the Netherlands
Department of Integrative Neurophysiology, VU University, Amsterdam, the Netherlands
Department of Psychiatry, Academic Medical Centre, Amsterdam, the Netherlands
Laboratory of Visual Brain Therapy, Sorbonne Université, INSERM, CNRS, Institut de la Vision, Paris, France

Pieter R. Roelfsema is the director of the Netherlands Institute for Neuroscience in Amsterdam since 2007. He is a professor at the Free University of Amsterdam and at the AUMC in Amsterdam. He received his MD degree in 1991 and his PhD degree in 1995. He received an NWO-VICI award (2008) and two ERC-Advanced grants (2014 and 2022). Dr Roelfsema and his team study visual perception, plasticity, memory and consciousness in the visual system of experimental animals, humans, and with neural networks. His focus is to know how neurons in different brain areas work together during seeing and thinking. To achieve that they investigate how networks of neurons work together to perceive and solve cognitive tasks and how they configure themselves during learning. He also develops the neurotechnology for high-bandwidth visual prostheses for blind people, aiming to restore a rudimentary form of sight. Dr Roelfsema coordinates the Dutch neurotechnology initiative NeuroTech-NL. In 2019 he co-founded the start-up company Phosphoenix that aims to develop a visual brain prosthesis.

4:10-4:40 **NeuroPSI Short Talks**

- **Andrea Giorgi** – *Contribution of different populations of V2a reticulospinal neurons to the kinematics of locomotor turning*

**Abstract:** Neuronal circuits underlying locomotion have long been explored for straight-trajectory forward walking, but information on the motor substrates for turning is still elusive. We have recently found, in the mouse, that (1) activating Gi-V2a neurons, a population of excitatory neurons located in the gigantocellular nucleus of the brainstem, induces the expression of multiple motor actions sufficient to steer locomotion, and (2) there exist projection-specific Gi-V2a subsets controlling some of these motor actions, i.e. ipsilateral head rotation followed by a turn (Gi-V2aC2) and locomotor stop (Gi-V2aL2). These findings open to the existence of additional task-specific Gi-V2a subsets, whose orchestrated activity may underlie the kinematics of turning. Here, using advanced multi-marker motion capture recordings in freely behaving mice, we describe the multiple motor actions supporting spontaneous and Gi-V2a induced turnings, including rotations around multiple joints of the body axis, limbs lateralization and cycle, and paws orientation. Then, to further explore the functional heterogeneity of Gi-V2a neurons and causally link their activity to unitary motor components of the turning behavior, we used viral, chemogenetic and optogenetic tools to examine the effect of selectively activating, inhibiting, or ablating different projection-identified Gi-V2a subsets on locomotion and turning. We found that both Gi-V2a neurons projecting to C2 or C7 are sufficient to induce turns, albeit with distinctive kinematics. Overall, this study extends our knowledge about the different kinematic strategies used by quadrupeds for turning, and characterizes the nature, organization and diversity of the underlying descending reticulospinal circuits. This provides new data for integrating turning circuits into the current models of locomotion.

- **Zineb Hayatou/Edouard Ferrand** – *Embodiment of a forelimb neuroprosthesis in the mouse model*

**Abstract:** Current research aims to restore upper limb function through prostheses controlled by brain-machine interfaces (BMI). This research calls for tractable experimental models, such as the mouse, with its unique genetic/molecular toolbox. Thus, there is a strong need to develop a limb neuroprosthesis in the mouse that will allow to test specific motor control and sensory feedback strategies for BMI design. To this aim, we take advantage of a closed-loop BMI that we previously built in the team (Abbasi et al. 2018). Here, we have incorporated a miniature, mouse-scale 3D-printed forelimb prosthesis with four degrees of freedom. The prosthesis position is controlled by the electrophysiological activity of neurons recorded in the primary motor cortex. In preliminary experiments, we successfully trained a mouse to control the forelimb prosthesis in a 2-degrees of freedom space, in order to bring a water reward to its mouth. A major challenge for neuroprosthesis efficiency and acceptance is to achieve embodiment of the artificial limb. To explore this point, we developed a mouse version of the rubber hand illusion. We exposed mice to a static prosthetic paw stimulated in synchrony with their real paw, and analyzed the mice reaction to the threat of the prosthetic paw. In ongoing work, we test whether mesoscopic direct optogenetic activation of the somatosensory cortex could replace peripheral stimulation for successful prosthetic embodiment. In a further development, we will test how the embodiment depends on motor control by training the mice to actively control the neuroprosthetic limb.

4:40-4:55 ***Break***

***Chair: Daniel Shulz***

4:55-5:45 **Israel Nelken** – *Auditory cortex activity in freely-moving rats*

The Edmond and Lily Safra Center for Brain Sciences, The Hebrew University of Jerusalem, Jerusalem, Israel, Department of Neurobiology, The Hebrew University of Jerusalem, Jerusalem, Israel

Prof. Israel Nelken is a world-renowned neuroscientist who serves as the director of the Edmond and Lily Safra Center for Brain Sciences (ELSC) at the Hebrew University of Jerusalem and works in the Department of Neurobiology at the Alexander Silberman Institute of Life.

His research has transformed our understanding of the auditory system by utilizing behavioral, electrophysiological, and imaging techniques. He has received various awards for his pioneering work, including the Michael Bruno prize, the Michael Landau prize for Sciences and Research, and the Humboldt research prize. Moreover, he also holds the Milton and Brindell Gottlieb Chair in Brain Sciences at the Hebrew University.

In recent years, he has made significant breakthroughs in understanding the auditory cortex by using animal models to explore the content of past stimulation in unattended sequences of equiprobable tones. His latest publication explores the role of inhibition in the auditory cortex and its contribution to stimulus-specific adaptation (SSA) using targeted cell-attached recordings and optogenetic manipulations in male mice, which is a testament to his groundbreaking research.

5:45-6:15 **NeuroPSI Short Talks**

- **Anindita Das** – *Basal ganglia-cortical dynamics in vocal learning*

**Abstract:** Complex motor skills like speech and playing a musical instrument involve imitation learning via a process of trial-and-error to achieve a sensorimotor 'goal'. Speech is a fundamental behavior involving sensorimotor learning and execution of a sequence of motor commands that generate meaningful vocalizations. Speech learning is attributed to predominantly cortical areas but various degenerative diseases of the basal ganglia (BG)-subcortical circuits are accompanied by deleterious effects on language processing. While the role of BG-cortical circuit in trial-and-error motor learning is well-established, its role in vocal learning or speech acquisition is not fully understood. Our objective is to shed light on the BG-cortical neural dynamics in vocal-motor learning with a focus on the population-level neural dynamics of the highly plastic BG-cortical circuit during sensorimotor learning. For this purpose, we utilize songbirds as the experimental model as they exhibit the closest resemblance to humans in terms of their ability to acquire syntax-specific vocalization via imitation. Zebra finches learn their song from the adult male (typically the father in the nest) through a process of trial-and-error learning. The avian BG-cortical circuit is crucial for this purpose. We use dense silicon probes to record simultaneously from the avian BG and the 'cortical' forebrain area in juvenile zebra finches that are undergoing sensorimotor learning to investigate learning-related changes in both the population-level spiking activity and the subthreshold local field potential. These recordings provide a unique window into the concerted circuit dynamics during a natural sensorimotor learning behavior and identify BG-cortical neural interactions underlying vocal-motor learning.

- **Andrea Thiebault** – *Acoustic foraging network in African penguins*

**Abstract:** African penguins Spheniscus demersus are Endangered seabirds endemic to Southern Africa. They feed on pelagic fish, diving to 30m depth within 40km from the coast. They actively coordinate their feeding behaviour and they benefit greatly from feeding in groups. The mechanisms by which they regulate these group activities remain unknown. We hypothesized that acoustic signals could play an important role for foraging coordination in these non-flying seabirds. We deployed miniature acoustic recorders and accelerometer/depth loggers simultaneously on African penguins to study their vocal activities in relation to their three-dimensional movements (e.g. depth and prey pursuits). We confirmed the existence of three main types of sea-surface vocalisations, and revealed the existence of other types of vocalisations. Vocalisations were all produced in specific contexts along the foraging trip, suggesting specific functions. In addition, we conducted acoustic experiments at sea to test the function of vocalisations. Using propagation experiments, we demonstrated that sea-surface vocalisations can be used for penguins to communicate over a few hundred kilometres. Using playback experiments, we showed that these vocalisations were used by penguins to maintain "contact" with distant conspecifics at sea and to "recruit" them on foraging grounds. Our results confirmed that African penguins form a network based on acoustic signals when foraging at sea. Such communication system could be crucial for them to be able to forage efficiently.

# Friday, May 12

***Chair: Jean René Martin***

9:30-10:25 **Keynote Lecture**:

**Michael Rosbash** – *Using circadian neurons to help understand the brain*

Department of Biology, Howard Hughes Medical Institute, Brandeis University, Waltham, MA, USA

Michael Rosbash is a renowned scientist whose groundbreaking work has transformed the study of circadian rhythms. With a background in both chemistry and biology, he completed his PhD in Biophysics at MIT and then pursued a fellowship in genetics at the University of Edinburgh. He has been a professor and researcher at Brandeis University for decades, and is also affiliated with the Howard Hughes Medical Institute and Massachusetts General Hospital. Though Rosbash began his career studying RNA processing, he soon became fascinated by the genetic aspects of behavior, particularly in fruit flies.

In 1984, he and colleague Jeffrey Hall successfully cloned the first Drosophila circadian clock gene, period, paving the way for further groundbreaking discoveries. Over time, Rosbash identified additional fundamental genes and proposed the Transcriptional Translational Negative Feedback Loop as the mechanism behind circadian clocks, which holds up today and has been found to be applicable not just to fruit flies, but to all other living organisms, including humans. Today, Rosbash continues to focus on his two primary research areas: RNA processing and the genetic mechanisms underlying biological rhythms. His contributions to molecular genetics have earned him numerous awards and honors, including the Nobel Prize in Physiology or Medicine in 2017, election to the American Academy of Arts and Sciences in 1997, and election to the National Academy of Sciences in 2003.

10:25-10:55 **NeuroPSI Short Talks**

- **Ajay Sunilkumar** – *Ocelli-mediated light input to the circadian clock in Drosophila*

**Abstract:** Light is the most critical environmental cue responsible for entraining the circadian clock in most animals. In Drosophila melanogaster, the brain clock that controls rest-activity rhythms synchronizes with light/dark (LD) cycles through Rhodopsin-mediated visual input pathways and by a circadian photoreceptor Cryptochrome (CRY) located in most clock neurons. The rhodopsin-mediated pathway can be again subdivided into compound eye pathway and HB-eyelet pathway, where the light information reaches clock neurons via compound eyes and HB-eyelets, respectively. It is unknown whether ocelli, another visual organ in Drosophila, which possesses only Rhodopsin 2 (Rh2), can contribute to the photoentrainment of clock neurons. In the present study, we investigated whether ocelli are involved in photoentrainment and, if so, to decipher the underlying neuronal circuitry. Our behavioral studies conclusively establish the involvement of Rh2 photoreceptors in circadian light input, and physiological investigations revealed a functional connection between Rh2-expressing photoreceptors and most of the clock neurons. We then characterized the complete neural circuit connecting ocelli to clock neurons with the available connectome analysis tools and anatomical studies. The 5th s-LNv and three CRY+ve LNds, clock neurons that are primarily engaged in regulating evening peaks in light/dark cycles, were discovered to be the primary recipients of ocelli-mediated inputs. Unlike compound eyes, which use ORT and HisCl1, histamine receptors in the ocelli-mediated light input pathway were identified as ORT exclusively. Taken together, this study unravels a novel circadian light input pathway and its underlying circuit for the fine-tuning of circadian rhythms.

- **Nastasia Mirofle** – *Neurobiological markers of social variability in congenic mice: emergence of individual personality traits*

**Abstract:** Origin of individual variability has not yet been fully defined in healthy individuals and yet its emergence could serve an evolutive advantage. We previously showed the existence of 3 profiles regarding choice strategies in a mouse gambling task, matching with prefrontal monoamine contents. We now wonder whether 1) such profiles exist in a social context, 2) if yes, whether they are stable throughout development -from adolescence to adulthood-, and 3) if early social markers could predict the emergence of other behavioral traits. Indeed, our aim was to study behavioral variability through development to determine individual profiles. This would allow us to question whether early behavioral markers could predict the development of decision-making strategies at adulthood. Methods: We focused on the influence of environmental enrichment on the development of social repertoire diversity. For that, we assessed from adolescence to adulthood several social variables (social interaction and motivation), acoustic communication, reward preference (anhedonia test) and defensive reaction to a stressful event (looming task). Results: Our results showed the existence of 3 distinct social profiles in adolescence, distinguished by social dominance and communication that remain stable while others -associated to social motivation and interaction- evolve with time. We also showed how living in a naturalistic environment within a large group benefits differently to the two genders, enhancing social motivation in females, and decreasing dominance in males. Behavioral investigations will be completed with identification of neurobiological markers with RT qPCR and HPLC methods targeting monoamine regional contents.

10:55-11:10 ***Break***

***Chair: Sylvie Granon***

11:10-11:55 **Carmen Sandi** – *Mitochondria regulate brain circuits for anxiety and motivation*

Brain Mind Institute, School of Life Sciences, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland

Carmen Sandi is Professor at the Swiss Federal Institute of Technology Lausanne (EPFL). She has done seminal contributions to understand how stress affects brain function and behavior. Currently, her lab investigates the factors and mechanisms that define individual differences in stress effects, focusing on how brain mitochondria and metabolism regulate behavior, and using integrative approaches in rodents and humans. She did her PhD at the Cajal Institute (Madrid), followed by postdocs at the University of Bordeaux and the UK Open University. Following a tenured professor position at UNED Madrid, she was recruited at the EPFL in 2003, where she has served as the Director of the Brain Mind Institute (2012-2019).
She has published over 260 articles and several books, and received numerous awards and honors, including the Ron de Kloet Prize for Stress Research, the John Paul Scott Award for Research on Aggression, and the Agora Prize from the Swiss National Science Foundation. She has received honorary appointments in several Universities, including the Valkhof Chair at Radboud University, Distinguished Visiting Scientist at the Hungarian Academy of Sciences, and Sabbatical Professor positions at Bern and Rockefeller Universities. She is founder and co-President of the Swiss Stress Network and co-Director of the Swiss Center for Competence in Research Synapsy. She has served in several editorial and institutional boards, and has been President of several organizations, including the European Brain and Behavior Society (EBBS), the Federation of European Neuroscience Societies (FENS), the Cajal Advanced Neuroscience Training Program, and ALBA Network.

11:55-12:25 **NeuroPSI Short Talks**

- **Dylan Manceau** – *Feeding state-dependent modulation of neuronal circuit activity and behavior by neuropeptidergic signaling*

**Abstract:** Animals respond to the environment differently depending on the context/state. Neural circuit mechanisms underlying this behavioral flexibility remain unknown. Drosophila larva offers means of studying the mechanisms of this modulation of behavior at neural circuit level thanks to the ongoing reconstruction of its whole CNS connectome that allows to map circuits at the synaptic scale and powerful genetic tools allowing for manipulations of neuronal activity and molecules with single-cell resolution. Ongoing work from our team has shown that changes in feeding states modulate sensorimotor decisions in response to an air-puff by differentially modulating reciprocally connected inhibitory interneurons in a decision circuit that drive opposing actions. In order to decipher whether and, if so, how neuropeptidergic transmission is involved in this modulation, first, we have been studying two neuropeptides: NPF and sNPF, respectively orthologue and functional homolog of the mammalian NPY. Using antibody labeling and genetic approaches, we have shown that sNPFR is expressed in mechanosensory neurons and both sNPFR and NPFR in inhibitory interneurons in our decision circuit. Combining behavior analysis and calcium-imaging in different feeding states, we found that downregulating sNPF or NPF signaling could influence inhibitory neurons activity and behavior in a state-dependent manner. Moreover, preliminary data suggest leucokinin, a neuropeptide involved in water homeostasis and feeding, is instrumental in modulating behavior in larvae fed on sucrose.

Altogether, our data suggest this pair of interconnected inhibitory interneurons could be a hub for the integration of physiological state information carried by a combination of neuropeptides.

- **Emre Baspinar** – *Modeling reward-driven decision making using biophysically realistic AdEx mean-field models*

**Abstract:** The Adaptive Exponential (AdEx) mean-field framework describes the averaged neuronal population behavior modeled by AdEx network. In the case of cerebral cortex, AdEx networks are used to model two cell types: Regular Spiking (RS) neurons, displaying spike-frequency adaptation as observed in excitatory pyramidal neurons, and Fast Spiking (FS) neurons, with no adaptation, as observed in inhibitory interneurons. AdEx networks are high dimensional, complex and difficult to analyze. AdEx mean-field models are low dimensional, simpler and easier to analyze compared to networks, yet they approximate closely the network dynamics, motivating our choice of model. Here, we extend the AdEx mean-field framework to model two networks of excitatory-inhibitory neurons, representing two cortical columns, and interconnected with excitatory connections contacting both RS and FS cells. Thus, this connection scheme introduces bicolumnar competition. Each column represents a pool of neurons making the decision in favor of one of two choices represented by two partially filled bars on screen. Task is based on maximizing total reward provided at the end of each episode consisting of a number of trials. The total reward depends on the coherency between choices of the subject and implemented strategy. A reward-driven learning mechanism allows the model to capture the implemented strategy, as well as subject exploratory behavior. We compare simulation results to performance data obtained from human subjects. Finally, this model provides a biophysical ground for simpler phenomenological models proposed for similar decision-making tasks and can be applied to neurophysiological data obtained from the monkey brain.

12:25-2:30 ***Break***

***Chair: Tihana Jovanic***

2:30-3:15 **Gero Miesenböck** – *The Pressure to Sleep*

Centre for Neural Circuits and Behaviour, University of Oxford, Oxford, UK

Gero Miesenböck is Waynflete Professor of Physiology and Director of the Centre for Neural Circuits and Behaviour at the University of Oxford and a fellow of Magdalen College, Oxford. Gero studied medicine at the University of Innsbruck in his native Austria and did postdoctoral research at Memorial Sloan-Kettering Cancer Center in New York. He was on the faculty of Memorial Sloan-Kettering Cancer Center and Yale University before coming to Oxford in 2007. Gero is known as the founder of optogenetics. He was the first scientist to modify nerve cells genetically so that their electrical activity could be controlled with light. He has been a pioneer in the use of flies to study neural circuits. His work has revealed how sensory information is represented and associated with behavioural consequences; how such associations are stored at selectively addressable memory locations; how sex-specific behaviors are expressed; how decisions form; and how sleep deficits are sensed and corrected. For his foundational work on "the development of optogenetics, a technology that has revolutionized neuroscience," Gero received, among other accolades, the Shaw Prize in Life Sciences and Medicine, the Louisa Gross Horwitz Prize, the Japan Prize, the Massry Prize, and the Brain Prize.

***Chair: Cyrille Vaillend***

3:15-4:00 **Anne Joutel** – *Small vessels, big problems: new insights into the mechanism of cerebral small vessel diseases*

Institute of Psychiatry and Neurosciences of Paris, INSERM UMR1266, University of Paris, F-75014 Paris, France.
Groupe Hospitalier Universitaire Paris psychiatrie & neurosciences, Hôpital Sainte Anne, Paris, F-75014 Paris, France.

Anne Joutel is a French neurologist and neuroscientist known for her groundbreaking work in the field of cerebral small vessel diseases (SVD). She received her medical degree from Paris Diderot University and her PhD in neuroscience from Pierre and Marie Curie University. She is currently INSERM Research Director at the Institute of Psychiatry and Neuroscience of Paris (IPNP).
Joutel's research focuses on understanding the pathogenic mechanisms of SVD, particularly in CADASIL, a monogenic form of SVD caused by mutations in the Notch3 receptor. Joutel's seminal work has shed light on multiple novel mechanisms underlying cerebrovascular dysfunction, including the establishment that aggregation/accumulation of the extracellular domain of Notch3 in brain vessels is a central event in CADASIL. In addition, her laboratory investigates the therapeutic potential of treatments such as passive immunization against Notch3, with the goal of advancing these treatments towards clinical trial readiness.
Anne Joutel has received numerous awards for her contributions to neuroscience, including the prestigious Brain Prize in 2019. She is also a recipient of the INSERM-Assistance Publique des Hôpitaux de Paris award for translational research, and the Anita Harding Prize from the European Society of Neurology, as well as multiple additional honors and awards.

4:00-4:15 **NeuroPSI Short Talk**

- **Thomas Deneux** – *AI education meets metacognition*

**Abstract:** We will present an educational robot developed at NeuroPSI to teach "how AI works" trough manipulation and visualization of artificial neural networks. The spin-off company "Learning Robots" now commercializes this solution. We will also introduce an ongoing doctoral research project on the benefits of teaching machine learning to allow pupils better understand their own learning strategies.

4:15-4:25 **Yan Li** – *Tianqiao and Chrissy Chen Institute*

4:25-4:40 **Concluding Remarks**

- **André Le Bivic** – *Director of the Institute of Biological Sciences of the CNRS*

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Driven by their intense desire to understand how perceptions are formed and impact our behavior, husband and wife Tianqiao Chen and Chrissy Luo established the Tianqiao and Chrissy Chen Institute in 2016 with the mission to benefit humanity. Through promoting a holistic and interdisciplinary approach, the Chen Institute drives fundamental brain research through three key areas – brain discovery, brain treatment, and brain development.

TCCI® partners with world-leading universities and research institutions to uncover the mysteries of the human brain and how informational input translates into behavioral output. Founders Tianqiao and Chrissy Chen are long-time philanthropists who contributed to children's medical funding programs in China and Inner Mongolia, supported education for underprivileged families, and donated to disaster relief and rebuild efforts.

## DIM C-BRAINS:
## Cognition and Brain Revolutions: Artificial Intelligence, Neurogenomics, Society

The objective of the DIM C-BRAINS is to remove the technological, conceptual and organizational barriers that are hindering progress in research to resolve the complexity of the brain and make our region a major focus for innovation in health and beyond.