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## Selected Talks

# A computational model of the healthy and epileptic hippocampus over the sleep-wake cycle

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The hippocampus is a temporal lobe structure which exhibits neural oscillations in different frequency ranges over the sleep-wake cycle, each of them being involved in a cognitive process. For example, theta-nested gamma oscillations (5-10Hz and 30-100Hz) seen during wakefulness are involved in short-term memory and spatial navigation, while Sharp-Wave Ripple complexes (120-200Hz) appearing during slow-wave sleep enable memory consolidation. Understanding the mechanisms underlying the generation and switch between these rhythms is essential to better understand memory processes as well as hippocampal dysfunctions that can alter them.

We developed a computational model of the human hippocampus made of approximately 50000 Hodgkin-Huxley neurons that is able to reproduce both theta-nested gamma oscillations and sharp-wave ripples. The model was imerged in a clinical recording setup, as employed for drug-resistant epileptic patients. More precisely, we took as input the depth (SEEG) signals from several regions projecting onto the entorhinal cortex (the main entry point into the hippocampus), and as output we modeled the LFP recorded by intra-hippocampal SEEG electrodes (using simple dipolar neuron geometry but realistic structure anatomies).

Our results show that Acetylcholine-induced changes in synaptic transmissions control the high frequency component of hippocampal oscillations, while the varying conductance of pyramidal cells' Calcium-Activated Non-specific (CAN) channels governs their low frequency component. Moreover, by including in the model the changes reported in epileptic hippocampi such as mossy fiber sprouting and hippocampal sclerosis, we can obtain pathological rhythms (fast ripples, interictal spikes and seizures) interacting with the sleep-wake cycle.

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\*Speaker

# Dissociation of fear initiation and maintenance by breathing-driven prefrontal oscillations

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Does the body play an active role in emotions? Since the original James/Cannon controversy this debate has mainly been fueled by introspective accounts of human experience. Here, we use the animal model to demonstrate a physiological mechanism for bodily feedback and its causal role in the stabilization of emotional states. We report that during fear-related freezing mice breathe at 4Hz and show, using probabilistic modelling, that optogenetic perturbation of this feedback specifically reduces freezing maintenance without impacting its initiation. This rhythm is transmitted by the olfactory bulb to the prefrontal cortex where it organizes neural firing and optogenetic probing of the circuit demonstrates frequency-specific tuning that maximizes prefrontal cortex responsivity at 4Hz, the breathing frequency during freezing. These results point to a brain-body-brain loop in which the initiation of emotional behavior engenders somatic changes which then feedback to the cortex to directly participate in sustaining emotional states.

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<sup>\*</sup>Speaker



# Task engagement induces population-level behavioral representations in primary auditory cortex

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Primary sensory cortices are classically considered to extract and represent stimulus features, while association and higher-order areas are thought to carry information about stimulus meaning. Here we show that this information can in fact be found in the neuronal population code of the primary auditory cortex (A1). A1 activity was recorded in awake ferrets while they either passively listened or actively discriminated stimuli in a range of Go/No-Go paradigms, with different sounds and reinforcements. Population-level dimensionality reduction techniques reveal that task engagement induces a shift in stimulus encoding from a sensory to a behaviorally driven representation that specifically enhances the target stimulus in all paradigms. This shift partly relies on task-engagement-induced changes in spontaneous activity. Altogether, we show that A1 population activity bears strong similarities to frontal cortex responses. These findings indicate that primary sensory cortices implement a crucial change in the structure of population activity to extract task-relevant information during behavior.

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<sup>\*</sup>Speaker

# Graphene based Nano-Neuroelectronics

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New methods and new technology are required to interrogate neuronal cells by many means and at multi-scale in-vivo, and within model neural networks in-vitro. In particular, to understand how neural circuits operate, we need access to activity of large numbers of neurons at the same time, and record their activity at the single cell level and at the nanoscale regarding the lot of information which relies at the level of synapses and ion channels.

In that race, we will show how graphene based nanoelectronics offers an ideal platform for multifunctional addressing and chronic recording, thanks to its exceptional neural affinity (Veliev 2016), flexibility and optical transparency. Also, the presence of readily accessible surface charges gives the unprecedented possibility to realize an intimate coupling with cells for sensing single neural spikes (Veliev et al. 2017) as well as nanoscale events such as ion channel currents (Veliev et al. 2018).

(Veliev 2016) Veliev, F., Briançon-Marjollet, A., Bouchiat, V., & Delacour, C. (2016). Impact of crystalline quality on neuronal affinity of pristine graphene. *Biomaterials*, 86, 33-41.

(Veliev 2017) Veliev, F., Han, Z., Kalita, D., Briançon-Marjollet, A., Bouchiat, V., & Delacour, C. (2017). Recording spikes activity in cultured hippocampal neurons using flexible or transparent graphene transistors. *Frontiers in neuroscience*, 11, 466.

(Veliev 2018) Veliev, F., Cresti, A., Kalita, D., Bourrier, A., Belloir, T., Briançon-Marjollet, A., ... & Delacour, C. (2018). Sensing ion channel in neuron networks with graphene field effect transistors. *2D Materials*, 5(4), 045020.

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\*Speaker

# Spatiotemporal signature of navigation signals in visual cortex and hippocampus

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When animals navigate, place cells in hippocampus fire selectively when the animal is in a particular place. The firing of these cells depends on self-motion information but also on the location of sensory cues in the environment. Place cells thus rely on sensory information which is processed by sensory areas of the cortex. Previous evidence showed that responses in the primary visual cortex (V1) depends on spatial context during navigation: V1 neurons respond differently to the same visual landmarks in different places and the position encoded by primary visual cortex is intrinsically correlated with the position encoded by hippocampus. Here, we recorded CA1 place cells and V1 neurons simultaneously while mice performed a navigation task in virtual reality. We found that V1 neurons exhibit two major features of spatial coding present in CA1 place cells: 1) their response depends on the distance run in the environment and 2) they tend to fire earlier or later than their preferred position across successive phases of a theta cycle (6-9Hz). In both CA1 and V1, the distance run affected the dependence of response profiles on theta phases. These results thus reveal that, similar to hippocampal place cells, neurons in the primary visual cortex rely on both visual and self-motion information and exhibit spatial coding on timescale of a theta cycle.

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<sup>\*</sup>Speaker

# Prefrontal circuit encoding fear and safety

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Survival critically depends on the ability of animals to select the appropriate behavior in response to threat and safety signals from the external world. However, the synaptic and circuit mechanisms by which the brain learns to encode accurate predictors from noise remain largely ignored. Here, we investigated how the prefrontal cortex and the basolateral amygdala cooperate during learning to mediate successful discrimination between aversive and non-aversive stimuli.

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\*Speaker

# Rich spatio-temporal stimulus dynamics unveil sensory specialization in cortical area S2

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Tactile perception in rodents depends on simultaneous, multi-whisker contacts with objects. To generate internal models of tactile objects, certain reliable features of these multi-whisker contacts must be exploited and encoded along the somatosensory neuraxis. These relevant feature sets have been studied in various conditions in most of the early processing areas in the somatosensory hierarchy up to and including the primary somatosensory cortex (S1), but the secondary somatosensory cortex (S2) has been largely ignored. To address this, we simultaneously and continuously stimulated the 24 caudal macro-vibrissae of rats with different types of Gaussian white noise (GWN) while recording large populations of single neurons in S2. Varying inter-whisker GWN correlations without changing single whisker statistics revealed pronounced supra-linear multi-whisker integration, whereas the same methods applied to S1 showed linear or sub-linear integration. Using novel analysis methods, we show that continuous multi-whisker movements contribute to the firing of S2 neurons over long temporal windows, facilitating spatio-temporal integration. In contrast, S1 neurons encode fine features of whisker movements on precise temporal scales. These results provide the first description of S2's representation during multi-whisker stimulation and outline its specialized role in parallel to S1 tactile processing.

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\*Speaker

# A hippocampus-accumbens tripartite neuronal motif guides appetitive memory in space

Stephanie Trouche \* <sup>1</sup>, Vadim Koren , Natalie M. Doig , Tommas J. Ellender , Mohamady El-Gaby , Vitor Lopes-Dos-Santos , Hayley M. Reeve , Pavel V. Perestenko , Farid N. Garas , Peter J. Magill , Andrew Sharott , David Dupret

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Retrieving and acting upon memories of food-predicting environments are fundamental for survival. Hippocampal pyramidal cells (PYRs) of the mammalian brain provide mnemonic representations of space. Yet, the substrates by which these hippocampal representations support memory-guided behavior remain unknown. By monitoring and manipulating neuronal ensembles in mouse dCA1→Nucleus Accumbens (NAc) pathway, our latest findings identify a circuit that engages PYRs with two postsynaptic partners in NAc for the functional coupling of the neuronal reinstatement of a spatial appetitive memory trace with its behavioral manifestation.

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\*Speaker

# Blitz Poster Abstracts

## **Blitz talks:**

Selma Souihel

Elaine Orendorff

Célian Bimbard

Andrea Alamia

Kevin Berlemont

Wilson Mena

# Alpha oscillations and travelling waves: signatures of predictive coding?

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Predictive coding is a key mechanism to understand the computational processes underlying brain functioning: in a hierarchical network, higher layers predict the activity of lower layers, and the unexplained residuals (i.e. prediction errors) are sent through. Because of its iterative nature, we wondered whether predictive coding could be related to brain oscillatory dynamics. First, we show that a simple 2-layers predictive coding model of visual cortex, with physiological communication delays between layers, naturally gives rise to alpha-band rhythms, similar to experimental observations. Then, we demonstrate that a multi-layer version of the same model can explain the occurrence of oscillatory travelling waves across layers, both feedforward (during visual stimulation) and backward (during rest). Remarkably, the predictions of our model are matched by the analysis of two independent EEG datasets, in which we observed oscillatory travelling waves in both directions.

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\*Speaker



# Perceptual decision making: Biases in post-error reaction times explained by attractor network dynamics

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Perceptual decision-making is the subject of many experimental and theoretical studies. Most modeling analyses are based on statistical processes of accumulation of evidence. In contrast, very few works confront attractor network models' predictions with empirical data from continuous sequences of trials. Recently however, numerical simulations of a biophysical competitive attractor network model have shown that such network can describe sequences of decision trials and reproduce repetition biases observed in perceptual decision experiments. Here we get more insights into such effects by considering an extension of the reduced attractor network model of Wong and Wang (2006), taking into account an inhibitory current delivered to the network once a decision has been made. We make explicit the conditions on this inhibitory input for which the network can perform a succession of trials, without being either trapped in the first reached attractor, or losing all memory of the past dynamics. We study in details how, during a sequence of decision trials, reaction times and performance depend on the nonlinear dynamics of the network, and we confront the model behavior with empirical findings on sequential effects. Here we show that, quite remarkably, the network exhibits, qualitatively and with the correct orders of magnitude, post-error slowing and post-error improvement in accuracy, two subtle effects reported in behavioral experiments in the absence of any feedback about the correctness of the decision. Our work thus provides evidence that such effects result from intrinsic properties of the nonlinear neural dynamics.

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\*Speaker

# Functional segregation of the ferret auditory cortex probed with natural and model-matched sounds

Célian Bimbard \* <sup>1</sup>, Agnès Landemard <sup>1</sup>, Sam Norman-Heigneré <sup>2</sup>, Shihab Shamma <sup>3,4</sup>, Yves Boubenec <sup>2</sup>

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Sensory systems are adapted to represent natural stimuli despite their complexity. How auditory cortex encodes this richness of acoustic features into spatially organized patterns of activity remains poorly understood. Here, we combined a novel computational approach contrasting the brain responses to synthetic sounds matching either part or all of natural acoustic features with a cutting-edge high-resolution neuroimaging technique, functional UltraSound. Using this unique combination, we set out to explore functional cortical domains at the basis of natural sound processing.

We first mapped the classical tonotopy of ferret auditory cortex, highlighting core and belt regions. We then used Independent Component Analysis on sound-evoked neural responses to reveal in an unsupervised manner independent spatial sources with specific functional properties. We found independent components spatially and functionally segregated throughout the cortical volume.

In order to pinpoint the respective contribution of each modulation type, we contrasted responses between different model-matched stimuli in individual voxels. We show enhanced responses to full model-matched sounds compared to cochlear-matched sounds in different subregions of core and belt areas. Interestingly, primary regions showed enhanced responses to temporally modulated stimuli, whereas distinct subregions of the belt areas had more diverse selectivity, consistent with functional segregation. Inclusion of an additional modulation feature increased responses in the belt, suggesting mixed selectivity. We found that low-frequency regions were completely explained by the full model, while high-frequency regions in primary and secondary regions had larger responses to original than full model-matched stimuli, as expected from cortical areas sensitive to correlations between modulation filters.

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\*Speaker

# Odor-place coding in cortical circuits

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A major role of olfaction is to guide navigation to find food sources. To do that, animals integrate multisensory information in order to track fragmented odor plumes in a fluctuating spatial environment. However, the cortical mechanisms encoding odor and spatial information have not been identified. The brain structure mediating spatial representation and cognitive maps generation is the hippocampus, who receives one of his inputs from the lateral entorhinal cortex (LEC). LEC has been shown to process information of individual items, locations and object-place memory. One cortical area targeting LEC is the olfactory (Piriform) cortex, where odor perception is thought to emerge, has long been suggested to encode olfactory learning and odor memories. We are studying how the brain represent odor-place association between Piriform Cortex (PCx) and LEC combining state-of-the-art techniques, including: *in vivo* calcium imaging in head-fixed and freely-moving mice, chemogenetics, electrophysiology, computational tools and behavior. This multidisciplinary approach allows us to extract the neuronal coding between PCx and LEC during odor-place representation and memory. We have established mini-endomicroscopy imaging in PCx and LEC. We can routinely image ~120 cells, extract robust odor-evoked signals and decode odor identity using linear classifiers in anesthetized, awake head-fixed and freely-moving mice.

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\*Speaker

# The AII Amacrine Cell as a Target for Vision Restoration with Optogenetics

Elaine Orendorff <sup>\*</sup> <sup>1,2</sup>, Hanen Khabou <sup>1</sup>, Giulia Spampinato <sup>1</sup>, Deniz Dalkara <sup>1</sup>, Olivier Marre <sup>1</sup>

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The progressive loss of photoreceptors in patients with retinitis pigmentosa and other retinal degenerative diseases is a major cause of blindness. Strides have been made recently in applying optogenetics to restore vision in animal models by targeting opsin expression to remaining photoreceptors, intermediate layer bipolar cells, and output layer retinal ganglion cells (RGCs). In later stages of the disease, few photoreceptors remain, and targeting ganglion cells limits the normal visual processing that can be preserved. For example, when an opsin is expressed in ganglion cells, OFF ganglion cells, sensitive to light decrease in the normal retina, will switch polarity and become ON, i.e. sensitive to light increase. Current vision restoration strategies thus only restore a limited amount of retinal processing. Here we present a vision restoration strategy where we target the AII amacrine cell. This interneuron connects the On and Off visual pathways through both sign-preserving and sign-inverting synapses. Our preliminary results, from ex vivo mouse retina multielectrode array recordings, suggest that optogenetic stimulation of AII amacrine cells can generate both ON and OFF responses. Furthermore, by comparing normal light responses of ganglion cells to their responses to optogenetic stimulation, we found that RGCs responsive to light onset or offset remained so under optogenetic stimulation. These results indicate that the AII could be a useful target for vision restoration in the future.

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<sup>\*</sup>Speaker

# A computational study of anticipation in the retina

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Most models of the early visual system, while quite elaborated in their biophysical description as well as their mathematical analysis, consider simple and unrealistic retino-thalamic entries. Studies have shown, however, that the retina is able to perform complex tasks such as motion anticipation to compensate delays in retino-cortical transmission. There exist simplified models of retina anticipation, based on gain control at the level of bipolar cells and retinal ganglion cells (RGCs), able to reproduce several motion features. These models consider 1D receptive field kernels, and thus does not take into account the anisotropy of RGCs receptive fields. Furthermore, they only simulate isolated RGCs whereas these cells are connected in the retina via amacrine cells, or directly through gap junctions.

In this work, we propose an extended GLM model for retina anticipation, allowing us to reproduce responses to several motion features, and sensitivity to orientation. We study the variability of temporal anticipation as a function of both stimulus and model parameters. We then implement a simple model of connectivity, featuring gap junctions between ganglion cells, to further assess the effect of this lateral connectivity on anticipation. Finally we implement receptive field anisotropy through a computation inspired from computer vision and study how elongated receptive field can help correct shape deformation introduced by gain control mechanisms. Finally, we are currently using our retina model as an entry to a V1 model reproducing Optical Imaging measurements, to assess which part of anticipation is performed by the retina and which by the cortex.

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<sup>\*</sup>Speaker

# Poster Abstracts

# Role of biomimetic cortical feedback in a sensorimotor brain-machine interface

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Invasive brain-machine interfaces (BMIs) use single neuron activity to control prostheses, with the long term goal of restoring motor abilities of impaired subjects. So far, these interfaces did not include a somatosensory-like feedback. We hypothesize that sensory feedback will favor rapid and accurate control of movements. We have developed a BMI by combining online recordings of neurons in the motor cortex (M1) and simultaneous real-time delivery of patterned optogenetic feedback over the somatosensory cortex (S1). This is to our knowledge the first invasive motor BMI that includes a short-latency, intracortical, somatosensory-like feedback. Here, our aim is to study the impact of the spatial organization of the S1 feedback on the BMI performance, in order to identify an optimal feedback structure. Towards this aim, we carried out behavioral experiments where a head-fixed transgenic mouse uses M1 activity to bring a one dimensional virtual bar to a rewarded location, while receiving either biomimetic or non-structured patterns of S1 optogenetic feedback. Our data shows that animals perform better under biomimetic feedback versus non-structured feedback. These results emphasize the importance of providing somatosensory-like feedback in the context of a BMI. It also shows for the first time that the structure of the feedback neuronal activity can have an impact on its integration in a BMI task. Ongoing experiments aim to confirm these findings in additional subjects.

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\*Speaker

# Cerebello-cortical coupling via the medial posterior thalamus: role in whisker-dependent texture discrimination.

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Increasing evidence indicates that the cerebellum is involved in complex brain processes, such as sensorimotor integration in active sensory discrimination. Here we focus on the involvement of cerebellum in somatosensory pathways.

We first show using rabies virus injected in the primary somatosensory cortex that this area receives inputs from the cerebellar nuclei, the latency of infection of cerebellar nuclei neurons being consistent with a disynaptic cerebello-cortical pathway. Second, we verified that primary sensory cortex neurons are activated by cerebellar nuclei stimulation, with a short latency similar to the responses observed in primary motor cortex; this is also consistent with the existence of a disynaptic pathway between the cerebellum and primary somatosensory cortex. Third, we sought potential relays between the cerebellum and sensory and motor cortical areas by combining injections of anterograde markers in the cerebellar nuclei and retrograde tracers in the cortical areas. We found abundant cerebellar terminals in areas of the thalamus projecting to these cortices. Notably, we observed that the part of the medial Posterior thalamus containing neurons projecting to sensori-motor cortices received abundant cerebellar afferents. We then examined in slices the functionality of the cerebellar afferents to the Pom and found using optogenetic stimulation that they generate large synaptic currents in Pom neurons, indicating that the cerebellum provides strong inputs to the Pom thalamus.

Altogether, these anatomical and functional results suggest the existence of a disynaptic pathway from the cerebellum to the sensory cortex, notably through the POm, suggesting its potential involvement in sensory modulation.

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<sup>\*</sup>Speaker



# Comparing the effects of adaptation and synaptic filtering on the timescale of recurrent networks

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Neural activity in awake behaving animals exhibits a vast range of timescales that can be several fold larger than the membrane time constant of individual neurons. One possibility is that these large timescales in the neural dynamics are inherited from large timescales of underlying biophysical processes, two prominent candidates being intrinsic adaptive ionic currents and synaptic transmission. How the timescales of adaptation or synaptic transmission influence the timescale of the network dynamics has however not been fully explored.

To address this question, we analyze large networks of randomly connected excitatory and inhibitory units with additional degrees of freedom that correspond to adaptation or synaptic filtering. We determine the fixed points of the systems, their stability to perturbations and the related dynamical timescales. Furthermore, we apply dynamical mean field theory to study the temporal statistics of the activity beyond the bifurcations, and examine how the effects of adaptation and synaptic timescales transfer from individual units to the whole population.

Our overarching finding is that synaptic filtering and adaptation in single neurons have very different effects at the network level. Unexpectedly, the macroscopic network dynamics do not inherit the large timescale present in adaptive currents. In contrast, the timescales of network activity increase proportionally to the time constant of the synaptic filter. Altogether, our study demonstrates that the timescales of biophysical processes have different effects on the network level, so that the slow timescales of different biophysical processes within individual neurons do not necessarily induce slow activity in large recurrent neural networks.

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<sup>\*</sup>Speaker

# Coding with transient trajectories in recurrent neural networks

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Following a stimulus, the neural response typically strongly varies in time and across neurons before settling to a steady-state. While classical population coding theory disregards the temporal dimension, recent works have argued that trajectories of transient activity can be particularly informative about stimulus identity and may form the basis of computations through dynamics. Yet an understanding of the dynamical mechanisms needed to generate a population code based on transient trajectories is still missing. Here we show that a broad class of high-dimensional linear networks of recurrently connected units exhibits the properties needed for transient coding. We first identify a general criterion that distinguishes two classes of networks depending on properties of the connectivity matrix: networks in which all inputs lead to weak, decaying transients, and networks in which specific inputs elicit strongly amplified transient responses and are mapped onto orthogonal output states during the dynamics. For the second class of networks, we provide a procedure to identify transiently amplified inputs and the corresponding readouts for arbitrary connectivity matrices. We then exploit our approach to build the minimal connectivity which robustly implements trajectories that map a specific input onto a specific output state, and we demonstrate that the capacity of the obtained networks increases proportionally with their size.

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<sup>\*</sup>Speaker

# Set-shifting related changes in activity of prefrontal and striatal neuron populations.

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We investigated the dynamics of cell synchrony within and among different functional subregions of STR and PFC from recordings of rats as they performed at criterion levels in two different tasks in an automated T-maze. First they performed a Visual Cue guided task (VC1) then a Turning task (T), then the VC task again (VC2) in the same session. Previous methods employing PCA and ICA were adapted and further developed with a selective shuffling procedure to permit identification of cells participating in synchronous activity. Synchrony was observed among neurons from multiple functional subregions of STR (accumbens shell, and core and dorsomedial STR) and PFC (cingulate, infralimbic and prelimbic areas). Co-active groups could include PFC as well as STR neurons. Synchrony was preserved even when bins were reduced to 10 ms in groups of STR neurons, PFC neurons and both. Different groups of co-active neurons were selectively active at each of the respective steps of the task. They were also selective for the current rule, with differences between synchronous activation in VC1 vs VC2. A Support Vector Machine analyzed STR and PFC population activities and successfully distinguished between tasks, again showing differences for VC1 and VC2 in most sessions. These data show that widespread networks of STR and PFC neurons cooperate and distinguish between tasks as well as reflecting immediate past experience within a single behavioral session.

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\*Speaker

# Complex selectivity to sounds in inferior colliculus and in primary auditory cortex

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The auditory system, as other sensory systems, is thought to be hierarchically organized encoding increasingly complex features from peripheral to more central stages. Yet the precise transformations of auditory representations across stages of the most central auditory system are not fully characterized. To start addressing this question in a systematic manner, we extensively recorded responses in the supragranular layers of the auditory cortex (AC) and the superficial layer of the inferior colliculus (IC) using two-photon microscopy in awake mice. Each of the 148 sounds was presented 15 times. We collected a dataset of 59590 neurons (7 mice, 60 sessions) in the AC. We also obtained activity from 15311 neurons in the IC (31 mice, 101 sessions). Using model-free clustering to organize this rich dataset, we observed many response types, which clustered in a few hundred groups of functionally identical cells. These clusters often displayed non-linearities in both AC and IC, such as non-monotonic intensity tuning. Many of these NL were described previously, but in isolation. In this study, we assess systematically their co-occurrence in the same neurons, and show that some NL are mutually exclusive, others are systematically co-occurring and others are randomly associated with each other. Thus the auditory system encodes selected combinations of non-linear sound features that could serve as building blocks for representing auditory objects. Moreover, surprisingly, we found several groups of cells, in the IC and in the AC, which had identical selectivity to all the presented sounds.

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\*Speaker

# Characterisation of CA1 pyramidal cells according to embryonic birth date

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**Pyramidal neurons** (PNs) in hippocampal **CA1** are classically considered as a homogeneous population. Recent works evidenced PN heterogeneity encompassing dendritic morphology, electrophysiology, connectivity profiles, gene expression and participation in network activity. Several studies converge on the observation that these properties correlate with the cell body location in the depth of the stratum pyramidale (SP). This suggests that PN **segregate functionally** according to their **radial position**, forming a deep and a superficial sublayer with distinct characteristics (reviewed in Soltesz and Losonczy, 2018).

This laminar specification might be **developmentally predetermined**. First, PN **embryonic birthdate** defines the radial location via an "inside first-outside last" migratory scheme. Second, intrahippocampal connections and expression of molecular markers are likely established as a function of the date of neurogenesis (Deguchi et al 2011; Cembrowski et al. 2016). In addition, we showed that early generated CA3 PNs form a separate morpho-functional group, able to synchronize network activity in ex vivo inhibition-blocked preparation (Marissal et al 2012). This raises the question: what defines the physiological identity of a neuron?

Here we aim at determining whether the heterogeneity in CA1 PNs is explained only by their soma location. Furthermore, we investigate whether early generated CA1 PNs form a distinct subpopulation. We use an inducible genetic fate mapping approach to label PNs according to birth date (from E12.5 and E16.5) and study the electrophysiological properties in vitro. This study provides the **first characterisation** of adult CA1 pyramidal cells **as a function of the temporal embryonic origin**.

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<sup>\*</sup>Speaker

# Inferring the function of a recurrent neural network

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A major goal in systems neuroscience is to understand the functions performed by neural circuits. Previous ‘top-down’ approaches tackle this question by first formulating a hypothesis about the function performed by a given neural circuit (e.g. efficient coding/decision making), formalised via an objective function. This hypothesis is then tested by comparing model neural responses, which maximise the assumed objective, with data. However, while this approach has been successful in explaining qualitative aspects of sensory responses, it cannot: (i) predict responses to natural/complex stimuli; (ii) extend to high-level areas, where it is unknown what function neurons perform. We propose a new framework for inferring neural function, based on inverse reinforcement learning (RL). In our work, the function performed by a recurrent neural network is expressed as a reward function, which depends on the network state. Neural responses are assumed to maximise the expected reward achieved by the network. Given specific reward functions, this framework replicates influential top-down models, such as efficient coding, attractor networks, and optimal control. More importantly, it is possible using inverse RL to infer the reward function directly from observed neural responses. Thus, our framework could be used to infer the function performed by recorded neural populations. This contrasts with previous top-down approaches, where experimental data is typically used to confirm/falsify a given hypothesis, specified in advance. Further, we show how the inferred reward function can be used to make testable predictions about how neural dynamics vary depending on contextual changes, such as cell death and/or input statistics.

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<sup>\*</sup>Speaker

# Recording deep cerebellar nuclei during levodopa-induced dyskinesia in parkinsonian mice

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Parkinson's disease is a long-known severe motor impairment caused by a degeneration of the dopaminergic neurons of the substantia nigra pars compacta projecting to different parts in the brain including the striatum. Therefore this neurodegenerative disease has always been associated to the basal ganglia. However, for the past few years, growing evidence have shown an important implication of the cerebellum; in both Parkinson's disease and its associated levodopa-induced dyskinesia.

Levodopa is the main used therapy for Parkinson's disease. However, after several years of treatment, patients develop abnormal involuntary movements called levodopa-induced dyskinesia. Both the disease and the treated states induce major brain modifications. Because the basal ganglia and the cerebellum are important motor brain region, our interest is to study what are the changes occurring in this circuitry. To do so, we combine *in vivo* electrophysiological recordings and optogenetic stimulations of the cerebellum in transgenic mice expressing ChR2 in Purkinje cells to study the involvement of this pathway in the motor impairments of Parkinson's disease and dyskinesia.

Our experiments tend to show that cerebellar stimulations are able to decrease levodopa-induced dyskinesia and corroborate the importance of the cerebellum in this pathology.

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\*Speaker

# Impact of 22-kHZ ultrasonic vocalizations on theta and gamma oscillations in the neural network underlying fear expression in rats

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Fear behavior is known to depend on the interaction between the prefrontal cortex (PFC) and the basolateral amygdala (BLA), and the expression of fear involves synchronized activity in Theta (4–12 Hz) and Gamma (30–120 Hz) frequency oscillations. Recent studies showed that freezing, a behavioral expression of fear, temporally coincides with the development of sustained 4-Hz oscillations in prefrontal–amygdala circuits. During fearful states, rats also emit 22-kHz ultrasonic vocalizations (USV) that are considered to be part of the animal’s defensive repertoire. The present study was aimed at assessing the impact of USV emission on oscillatory activities in the Theta and Gamma bands.

Rats were trained in an odor fear conditioning paradigm while local field potential in their BLA, PFC and olfactory cortex were monitored, together with USV, freezing behavior and respiration.

We observed a clearcut impact of USV’s emission on oscillatory activities. Indeed USV emission induces a significant decrease in Theta activity while an increase in Gamma activity is observed associated with a narrowing of the frequency band. Interestingly, USV emission strongly alters the animal’s respiratory rate (3-8 Hz), thus potentially affecting respiration-locked rhythm that has been recently suggested to play a role in the organization of prefrontal network activity. Therefore, we are currently investigating whether the effect of USV might be explained by changes in respiration-locked brain rhythm.

The present data suggest that sequences of USV calls could result in a differential gating of information within the network of structures sustaining fear behaviour.

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\*Speaker



# Inferring the dynamics of neural populations from single-trial spike trains using mechanistic models

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Multi-neuronal spike-train data recorded in vivo often exhibit rich dynamics as well as considerable variability across cells and repetitions of identical experimental conditions (trials). The interpretation of such data often relies on abstract statistical models that allow for principled parameter estimation and model selection; however, the interpretive power of these models is limited by the low extent to which prior biophysical constraints are incorporated. Here we present a statistically principled approach based on a population of doubly-stochastic integrate-and-fire neurons, taking into account basic biophysics. This model class comprises an idealized description for the dynamics of the neuronal membrane voltage in response to fast independent and slower shared input fluctuations. We efficiently compute the likelihood of observed spike trains by leveraging analytical methods for spiking neuron models combined with inference techniques for hidden Markov models, which allows us to reconstruct the shared input variations, classify their dynamics, obtain precise spike rate estimates, and quantify how individual neurons couple to the low-dimensional overall population dynamics, all from a single trial. Extensive evaluations on simulated data, and validations on ground truth recordings in vitro demonstrate that our method efficiently yield accurate results, and simpler phenomenological models are outperformed. Finally, we apply the method to a neuronal population recorded in vivo, for which we assess the contributions of individual neurons to the overall spiking dynamics. Altogether, our work provides statistical inference tools for a class of reasonably constrained, mechanistic models and demonstrates the benefits of this approach to analyze measured spike train data.

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<sup>\*</sup>Speaker

# Combined two-photon imaging and modeling of endogenous and evoked dynamics in the auditory cortex of awake mouse

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The adult brain is characterized by a prominent ongoing activity even in the absence of clear sensory inputs. In auditory cortex, spontaneous activity has been shown to contain population events of random size occurring at relatively random time intervals. To investigate the spatial structure and the network machinery that drives these auditory cortex (AC) endogenous dynamics, we used chronic two-photon Ca<sup>2+</sup> imaging of large populations of neurons in superficial and deep layers in awake and anesthetized head-fixed mice. Spike trains of up to 1000 neurons recorded in parallel over a 1x1 mm fields of view were estimated from calcium signal thanks to the new MLSpoke algorithm.

Consistent with electrophysiological measurements, we found that, in the awake state, populations of neurons in AC display synchronous spontaneous events of a duration of about 200 ms and frequency of 0.35 Hz. Under isoflurane anesthesia, population events were even more prominent and inter-event activity was strongly diminished.

In general, not only the size but also the location of spontaneous events was highly variable. Comparison of consecutive events demonstrated a non-monotonic relationship between spatial overlap of the events and inter-event intervals with a peak of spatial overlap for the events separated by 3s intervals. This indicates that spontaneous events interact with each other, excluding or promoting one another depending on elapsed time.

Sound-evoked responses were as variable as spontaneous event but included a core of robustly responding neurons. Thus, in AC, complex stochastic population dynamics interplays with an evoked activity to generate auditory representations.

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\*Speaker

# Beta oscillations in a large network during an olfactory discrimination task: what do they signal?

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When dealing with the question of information transfer across brain regions, beta rhythm often appears as a good candidate for supporting functional coupling of neurons over long distances. In the olfactory system, beta activity is a major rhythm. Several studies converge towards the idea that beta expression goes well beyond the olfactory areas, suggesting it could represent widely coherent states.

In an attempt to get a more unified view of the conditions of beta expression in a large network, we analyzed its expression in brain areas suspected to be task-related when rats performed a two-alternative odor choice task. These areas involved sensory, limbic and sensorimotor regions. Beta expression was analyzed during a simple discrimination, rule transfer, short- and long-term tests, and reversal tasks.

We observe that beta amplitude is correlated with the level of expertise of the animals: maximal when rats reach learning criterion, it collapses when a new odor pair discrimination is introduced and increases again with performance. However, reversal test and intra-session analyses reveal that beta is not correlated with the performance but with the level of certainty the animal has towards the experimental context. Interestingly, we show that a new discrimination cannot be achieved as long as beta expression has not decreased. This is striking during reversal learning. Coherence analysis indicate that, when expressed, beta appears in a large network including olfactory areas and striatum, but neither hippocampus CA1 nor cerebellum.

Overall, our data suggest that beta rhythm signals a consolidated, unyielding and widely coherent state.

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<sup>\*</sup>Speaker

# Tridesclous and pyacq: a real time spike sorting engine

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tridesclous is a new package for spike sorting. It is both online and offline. tridesclous propose a new approach for spike sorting based on template matching. Furthermore this approach resolve the problem of spike collision. The package include the method itself but also a user interface specifically design for the methods. Tridesclous is quite fast and some part of the processing chain is written with OpenCL (GPU computing). So tridesclous make possible to computing efficiently the spike sorting for high channel count ( $> 100$ ).

pyacq is a framework for distributed acquisition/processing/visualzation. It allow to distribute some processing "Nodes" accross machines. Pyacq interface several devices in the field of multi electrode electrophysiology (Blackrock, Multichannel, mesasurement computing, nation instrument, and soon Intantech board). So pyacq make possible to grab in real time multi channel signal chunks, distribute then across an dedicated network and sort them with the tridesclous in real time.

This two packages togoether propose for experimentalist a customisable system for real time spike sorting wihtout sacriying the sorting quality.

<https://github.com/tridesclous/tridesclous>

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\*Speaker

# An online service for statistical validation of data-driven neuroscientific models

Pedro Garcia-Rodriguez <sup>\*</sup> <sup>1</sup>, Shailesh Appukuttan <sup>1</sup>, Lungsi Sharma <sup>1</sup>,  
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Validating increasingly complex models of neural systems with respect to experimental data is both a scientific and a technical challenge. Scientific challenges include the choice of appropriate statistical tests for quantifying the differences between model predictions and experimental results, reconciling conflicting experimental findings, and deciding on the weighting to be given to different validations. Technical challenges include interfacing validation test definitions with model implementations, tracking model/test versions, and automation of the validation process. We have developed a framework, part of the Human Brain Project (HBP) Brain Simulation Platform, to meet the technical challenges and assist neuroscience researchers in meeting the scientific challenges. The validation framework comprises a RESTful web service for keeping track of models, test definitions, and validation results. This service can be accessed through web apps in the HBP Collaboratory and with a Python client. Users can search a catalog of models, tests and results, register new entries, visualize comparisons of model performance, and explore details of individual simulations. Model and test definitions are expected to use the SciUnit interface, which decouples test and model, allowing the same test to validate different models of the same structure. A commenting feature allows experts to discuss the appropriateness of different tests and the quality of the underlying data.

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<sup>\*</sup>Speaker

# Selection and oscillations in a spiking model of the Basal Ganglia

Benoît Girard \* <sup>1</sup>, Jean Liénard <sup>2</sup>, Hugo Chateau Laurent <sup>1</sup>, Kenji Doya <sup>2</sup>

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From a mean-field model of the Basal Ganglia based on extensive anatomical and electrophysiological primate data (Liénard & Girard, 2014), we have derived an IaF-based spiking model. We show that this model keeps the biological plausibility properties of the mean-field model. While it was not parameterized to fulfill any specific function, it is able to select among competing channel and to oscillate in the beta band in simulated Parkinson disease. Liénard, J. & Girard, B. (2014). A Biologically Constrained Model of the Whole Basal Ganglia Addressing the Paradoxes of Connections and Selection. *Journal of Computational Neuroscience*. 36(3):445-468.

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\*Speaker

# Serial order of elements versus grammatical structure: neuronal encoding in a high-level auditory area of the songbird brain

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Sensitivity to the temporal order of communication sounds is fundamental not only for language comprehension in humans but also for song recognition in songbirds. Encoding the serial order of items within a sequence may help recognition of relationships between adjacent items and learning the underlying structure of the sequence. Taking advantage of the stimulus-specific adaptation phenomenon (repetition-induced suppression) observed in a high-level auditory region of the zebra finch brain, we show that neurons in this region encode serial ordering of elements in conspecific songs. Rearranging the order of elements reinstated the initial robust neuronal responses. The clear sensitivity to serial order of syllables cannot, however, be extended to song structure. Changing the structure of artificial songs from the ABAB to the AABB pattern did not reinstate robust responses. Our results therefore contribute to the ongoing debate about the ability to learn grammatical structure in songbirds.

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\*Speaker

# Large-scale synchronization in the brain depends on respiratory regime

Baptiste Girin <sup>\*</sup> <sup>1</sup>, Samuel Garcia <sup>1</sup>, Nathalie Buonviso <sup>1</sup>

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Inter-area communication requires the different brain rhythms to be coordinated across areas. As others, we hypothesized respiratory rhythm could act as a central clock for cerebral rhythms coordination. If true, one can expect neuronal activity to be influenced by respiration in a large brain network. We tested that by recording respiration and neuronal activity in different brain areas in the freely-moving rat during different vigilance states. In agreement with recent publications, we observed that all structures could be modulated by breathing. We provided the additional observation that such a modulation varies according to the vigilance state, each state being associated with a specific respiratory regime. Particularly, we observed a large-scale synchronization across areas on the breathing rhythm during quiet state, where animal's breath is around 2Hz. We then sought to decorrelate brain state from respiratory regime. Animals were thus recorded while breathing a CO<sub>2</sub>-enriched air, which changes the respiratory regimes. We observed the across-areas respiratory synchronization observed in quiet state can be extended, under CO<sub>2</sub> condition, to other vigilance states (REM and non-REM) and to higher respiratory frequencies (3-4 Hz). Finally, data from double-tracheotomized rats show that amplitude and spatial extent of breathing-related modulation correlate with air volume in the nasal cavity. We concluded that large-scale synchronization of brain areas on respiration is mostly dependent on the respiratory regime (volume).

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<sup>\*</sup>Speaker



# Critical revision of the neurophysiology of tracking eye movements

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During the last five decades, multiple studies supposed that kinematic parameters of tracking eye movements were encoded in the neuronal processes underlying their generation. From time series of measured angular deviations, magnitudes such as movement amplitude, duration and their ratio (speed) were calculated and models proposed the existence, in the brain, of processes which would reduce a difference between gaze and target directions (for guiding the saccade) or between the eye and target speeds (for accelerating the slow eye movement), and maintain the eye speed despite target stabilization within the central visual field. This parallelism made between the relative motions of rigid bodies (eyeball and target) and hypothetical processes led neurophysiologists to search for correlations between the neurons' activity and kinematic parameters (position, speed and acceleration) and to propose that their firing rate could be predicted by their linear combination. Such a "neuronalization" of behavioral parameters is questionable for a safe advancement of the neurophysiology of visually-guided movements (Goffart, Bourelly and Quinton 2018). Instead of plunging within the brain medium, notions which were actually designed to quantify the motion of rigid bodies in the physical world, we propose to use principles that are intrinsic to the brain functioning (parallel flows of activity constrained by the connectivity, population coding, multiplicity of transmission delays, synchrony of neuronal discharges, heterogeneity of neurons, etc.).

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\*Speaker

# Expectancy signals in the barrel cortex revealed by highly predictable multi-whisker deflections

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Sensory information processing depends on the nature of the input but is also determined by previous stimulation history. A violation of an expectation can trigger neuronal responses that show the preparedness of the nervous system for an expected input. Within the predictive coding hypothesis (Friston 2005), these expectancy signals are determined by the mismatch between sensory input and a prediction coming from higher cortical areas. However, in a primary sensory cortex it still needs to be determined if they can appear in a pre-attentive manner. In this work, we used the rat whisker system to study the effect of repetitive spatio-temporal stimulation patterns that provide strong predictability in space and time. We used a multi-whisker stimulator that delivers controlled micrometric displacements to the 24 caudal whiskers of the snout of the rat (Jacob et al. 2010), while simultaneously recording using multielectrode silicone probes in the primary somatosensory cortex of animals anesthetized with isoflurane. Our stimulation patterns converge into a whisker and we measure in its corresponding cortical column. Complete patterns were delivered in a training phase while truncated patterns were given in a pre- and post-test phase. Random occurrences of truncated sequences with a 10 % chance were also present during the training. Analysis performed on multi-unit and single-unit activity, showed advanced and delayed signals to the truncated patterns. These results provide evidence of the existence of expectancy signals in a pre-attentive manner in a primary somatosensory cortex.

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<sup>\*</sup>Speaker

# A closed-loop brain-machine interface for probing the role of variability during motor learning

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Motor variability, that is variations between repetitions of a limb movement, arise notably from neural variability in the motor cortex. It is often seen as a by-product of network activity and mostly detrimental to precise motion. However, recent works suggest that motor variability may be useful during learning by facilitating exploration of the motor space.

To causally probe the role of motor variability in producing motor output, we built a fast, closed-loop brain-machine interface in mice including an optogenetically-delivered, intra-cortical feedback. It allows mice to control a virtual arm by modulating neurons's activity in the motor cortex. This system gives us complete control over both motor outputs and sensory inputs, along with a novel sensorimotor contingency to explore.

Mice have to learn to move a single rotational joint of the virtual prosthesis to a particular angle to obtain a reward. During the learning and until a performance plateau is reached (exploration phase), we inject random bursts of spikes in the motor signal to artificially increase the trial-to-trial variability. After the plateau, we remove the variability and allow further training (exploitation phase).

We expect that injecting variability during learning of a novel motor task will improve learning speed by facilitating motor exploration, at the cost of suboptimal performance once the learning phase is over. We moreover expect that removal of added variability in the exploitation phase will further increase performance. This protocol has been successfully applied on 2 mice, and 4 more are ongoing.

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<sup>\*</sup>Speaker

# Anatomo-functional regionalisation of the nodulo-uvular complex in freely moving rat

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Orientation and navigation are based on body representation in space, fed and updated by the vestibular system that measures head movements. It collects two types of information, the rotation and the translation of the head. However, these signals contain ambiguities that the central nervous system must lift as soon as they enter in the vestibulo-cerebellum (VC) and in the vestibular nuclei (VN). First, previous electrophysiological recordings in the team show that median Purkinje cells are widely sensitive to rotation and gravity. However, it is also necessary to extract the acceleration of the head from vestibular inputs. So, we first verified that receptive fields of lateral Purkinje cells present a sensitivity for acceleration. These results are consistent with the existence of an extraction of gravity in a medio-lateral axis in the VC. Second, according to the literature, we know that the rotational and translation inputs are segregated in the cerebellum, in the nodulus and in the uvula respectively. But, reciprocal projections from those two structures via the vestibular nuclei allow to merge them since projections from one project back to the other. Anterograde injections in the VC, suggest that there is a regionalization of the Purkinje cells projections depending of their localisation in the VC. Thus, another integration in the rostrocaudal axis allows the extraction of the gravity from the acceleration signal. Altogether, these anatomical and electrophysiological results suggest the existence of a double integration of the vestibular signal along the rostrocaudal axis via the VN and along the mediolateral one in the VC.

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\*Speaker

# Dynamic causal modeling of cortico-cortical evoked potentials

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Epilepsy surgery procedures may use focal intracortical electrical stimulation using depth electrodes. These local stimulations propagate through white matter fibers and generate cortico-cortical evoked responses (CCEP) at distant sites.

In this study, we aimed at developing a biophysical modeling approach allowing to precisely estimate CCEPs features. Using dynamic causal modeling, a CCEP was considered as the activity generated by a transient stimulus entering the stimulated region, which in turn was directly connected to the recording region. Both regions were modeled with neural mass models. Neuronal parameters of the model were estimated from the first CCEP component, occurring before 80 ms. This methodology was applied to 5330 bipolar stimulations from 180 epileptic patients (F-TRACT database), representing a total of 60700 CCEPs. We focused the group analysis on the estimation of the axonal conduction delays between cortical regions and local synaptic (excitatory and inhibitory) time constants. The cortical mapping of these neuronal parameters was obtained at the group level using anatomical-based averaging procedures.

We found that the axonal delays between regions were globally very short (median=1.8ms) and only 13% (resp. 3%) were longer than 10ms (resp. 20ms). This was associated to a median velocity of 16 m/s. Moreover, fastest synaptic dynamics were found in sensory-motor and latero-temporal regions.

To our knowledge, this study is the first to propose an in vivo and local estimation of axonal conduction and synaptic delays across the whole human cortex. Importantly, these results will be available to the scientific community as part of the F-TRACT atlas ([ftract.eu](http://ftract.eu)).

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\*Speaker

# Cellular basis of vestibular signal processing in the cerebellum

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The vestibular system receives raw ambiguous input from 5 peripheral sensors in the inner ear (3 semicircular canals and 2 otolithic organs), that need to be transformed in order to perform its functions (balance, orientation...). The mechanisms and the sites of these transformations are not known. Compared to the rest of the cerebellum, the vestibulo-cerebellum, the part of the cerebellum receiving massive input from the vestibular nerve, contains in abundance a cell called Unipolar Brush Cell (UBC). UBC's exist in many subtypes and generate prolonged responses to brief inputs owing to the peculiar architecture of the mossy fiber-UBC synapse.

To understand the function of each UBC subtype in this microcircuitry, we designed a numeric model of UBC-mossy fiber synapse and a monosynaptic retrograde tracing experiment from UBCs.

After release of glutamate simultaneously at all synaptic junction, our model of mossy fiber-UBC synapse showed a rapid equilibrium, with glutamate remaining in the synapse for tens of milliseconds. When combined with a model of AMPA receptor, our model also reproduces the resurgence of the AMPA tail current observed in UBC's. Finally, it predicts that the synapses probably exhibit low pass filter and phase shifting properties; these phenomena probably underlie the processing of vestibular information.

Tracerization experiments showed that the antibodies tested are compatible with the Idisco protocol, and can reveal branches of vestibular nerve. We also found that the tissue autofluorescence signal is sufficient for observing at high resolution and reconstructing three dimensional structures of the inner ear.

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<sup>\*</sup>Speaker

# What is the function of medial entorhinal cortex in a distance estimation task?

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Path integration is a navigational strategy based on self-motion cues that requires the animal to estimate the distance and orientation relative to a starting location. Based on their firing properties, grid cells in the medial entorhinal cortex (MEC) have been hypothesized to represent the neural substrate of path integration. Grid cells display a striking hexagonal grid-like firing pattern within an open field. Their activity is modulated by running speed and heading direction suggesting that they integrate self-motion cues to signal distance and direction information necessary for path integration. Animal and human studies point to a role of the MEC in distance estimation. However, how MEC cells participate to such process remain largely unknown. In this study, we recorded MEC neurons while animals were trained to estimate three distances on a linear track (30, 60, and 90 cm) in darkness. We found that both grid cells and non-spatially tuned cells in the MEC show a spatial activity that is located at the three distances learnt by the rat. Overall, these results indicate that the MEC hosts a population of neurons that works as an internal odometer, signaling discrete distances during self-motion-based navigation.

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<sup>\*</sup>Speaker

# Directional selectivity across macaque motor cortical layers during reach planning and execution.

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Directional selectivity during arm reaches has been extensively studied in motor cortex, yet we still know very little about how it is distributed and dynamically modulated across cortical depth.

We explored directional selectivity in a macaque monkey during pre-cued center-out reaching. The target location was cued visually several seconds before the go-signal. Recordings were made simultaneously from superficial and deep cortical layers with multi-contact linear array (laminar) probes, in arm regions of dorsal premotor cortex (PMd) and primary motor cortex (M1).

Following the cues, the neuronal population in superficial PMd had an earlier phasic response than deep PMd and M1. Post-cue directional selectivity was maximal subsequent to this early phasic response, but also stronger in superficial PMd. Around movement execution, selectivity was overall stronger in PMd than M1. In addition, selectivity was stronger in superficial PMd and M1 just before movement onset, while deep layers increased their selectivity towards movement end.

These different dynamics of directional selectivity might be related to the different predominance of cortico-cortical vs. sub-cortical projections of superficial vs. deep cortical layers, respectively. Early cue-related information seems to be preferentially elaborated in superficial PMd, and the stronger selectivity here might suggest a more categorical or goal-related representation of the motor plan.

The delayed and weaker selectivity of deep PMd and of M1 might suggest a stronger relationship to the less categorical muscular implementation of the motor plan, and towards the movement end also online motor command adjustments to successfully enter the peripheral target.

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\*Speaker



# Inferring and validating mechanistic models of neural microcircuits based on spike-train data

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The interpretation of neuronal spike train recordings often relies on abstract statistical models that allow for principled parameter estimation and model selection but provide only limited insights into underlying microcircuits. In contrast, mechanistic models are useful to interpret microcircuit dynamics, but are rarely quantitatively matched to experimental data due to methodological challenges. To date, model selection methods based on spike-train data are much more advanced and principled for abstract, phenomenological models than for mechanistic circuit models. Here we present analytical methods to efficiently fit spiking circuit models to single-trial spike trains. Using the maximal-likelihood approach, we statistically infer the mean and variance of hidden inputs, neuronal adaptation properties and connectivity for coupled integrate-and-fire neurons. Evaluations based on simulated data, and validations using ground truth recordings in vitro and in vivo demonstrated that parameter estimation is very accurate and efficient, even for highly sub-sampled networks. We finally apply our methods to recordings from cortical neurons of awake ferrets and reveal population-level equalization between hidden excitatory and inhibitory inputs. The methods introduced here enable a quantitative, mechanistic interpretation of recorded neuronal population activity.

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<sup>\*</sup>Speaker

# A reassessment of stimulus dependence of receptive fields in primary visual cortex

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Estimation of a receptive field (RF) model based on an ensemble of visual stimuli and associated neural responses is a common approach for studying neuronal coding in the primary visual cortex (V1). The interpretability of such models has, however, been regularly challenged due to the stimulus dependence of their fits, i.e. their failure to generalize between different stimulus statistics. However, the compared stimulus sets were often insufficiently controlled for a number of basic parameters, putting in question the interpretation of these generalization results. In this study, we used a carefully designed set of visual stimuli to characterize short-term RF stimulus-dependence phenomena with unprecedented accuracy.

We performed dense multi-electrode extracellular recordings of neuronal responses in area 17 (V1) of anesthetized cats during presentation of various types of commonly used stimuli (white noise, flashed natural images and natural movies), as well as matched counterparts in which only one parameter (temporal correlation, high-order spatial statistics) had been modified. We then estimated various common RF models for each stimulus type and computed cross-prediction performances. Our preliminary analysis suggests that generalization abilities of common RF models might have been underestimated in previous studies. This discrepancy might be due to differences in both methodology and interpretation. In accordance with previous findings, we nevertheless observed a clear difference in RF temporal kernel shapes between natural movies and their temporally randomized counterparts. Overall, these results suggest that temporal correlation is the main factor of RF stimulus dependence, while the impact of spatial statistics has been previously overestimated.

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\*Speaker

# A real-time spike sorting software for thousand electrodes

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Recent technological advances allow to record simultaneously from tens to thousands electrodes packed with high density. To analyze these extracellular data, scalable, accurate and semi-automated algorithms have been proposed to sort spikes from hundreds of recorded cells. However, these algorithms do not allow tracking the activity of individual neurons during the experiment, since the entire processing is run offline. This is a limitation for some experimental decisions which could be guided by the recent activity of the recorded cells, and more generally for the design of closed loop experiments.

To address this issue we designed an online spike sorting software that accurately sorts spikes in real time for up to a thousand of electrodes. Our algorithm identifies the template waveforms and their spike times by combining a clustering algorithm and a greedy template matching algorithm. It handles well-known spike sorting issues such as misalignments in the spike detection or overlapping spike waveforms. The online clustering procedure allows dealing with slow changes of the templates over time (e.g. drifts).

We validated that our software could sort spikes in real time for an increasing number of electrodes on simulated datasets. We assessed the accuracy of the results with both in vitro and in vivo ground truth datasets. Our software thus enables optimal experimental design and closed loop experiments, where the choice of the stimuli to present depends on the data acquired recently. It will also be a valuable tool for experimentalists to monitor their large-scale recordings during the experiment.

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<sup>\*</sup>Speaker

# Curation and reuse of neural activity data

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This poster will present the Neural Activity Resource (NAR) as a collection of tools and documents for the management, the curation and use of datasets containing recordings of neural activity.

Developed by the Human Brain Project to organize experimental and simulated neuronal activity data, the Neural Activity Resource extends the initial data curation performed in the Data Workbench with workflows to provide additional metadata, specific to a given recording technology.

To extend the core components of the HBP Neuroinformatics Platform, metadata schemas for the HBP Knowledge Graph are collaboratively developed through the Neuroshapes project, which is currently supported by five entities: International Neuroinformatics Coordinating Facility (INCF), Blue Brain Project, EPFL, the Krembil Centre for Neuroinformatics and Unité de Neurosciences Information et Complexité (UNIC, CNRS). The schemas are written in SHACL (Shapes Constraint Language), a language for validating semantic graphs. The main goal is the development of use case driven and shared validatable data models to enable the F.A.I.R. principles (Findable, Accessible, Interoperable and Reusable) for basic, computational and clinical neuroscience (meta)data.

This poster will present the current status of schema development, with two examples: for whole-cell patch clamp recording and two-photon calcium imaging. The Neural Activity Browser will also be introduced, a Collaboratory app for browsing and visualizing activity datasets stored in the HBP Knowledge Graph.

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\*Speaker

# Loop-like bidirectional interactions between place-cells and grid-cells in a vision- and self-motion driven spatial representation model

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Hippocampal place cells and entorhinal grid cells are thought to form a representation of space by integrating internal and external sensory cues. Experimental studies show that different subsets of place cells are controlled by vision, self-motion or a combination of both. Moreover, recent studies in environments with a high degree of visual aliasing suggest that a continuous interaction between place cells and grid cells can result in a deformation of hexagonal grids or in a progressive loss of visual cue control. The computational nature of such a bidirectional interaction remains unclear. In this work we present a neural network model of a dynamic loop between place cells and grid cells. The model is tested in two recent experimental paradigms involving double-room environments that provide conflicting evidence about visual cue control over self-motion-based spatial codes. Analysis of the model behavior in the two experiments suggests that the strength of hippocampal-entorhinal dynamical loop is the key parameter governing differential cue control. Construction of spatial representations in visually identical environments requires weak visual cue control, while synaptic plasticity is regulated by the mismatch between visual- and self-motion representations. More generally our results suggest a functional segregation between plastic and dynamic processes in hippocampal processing.

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<sup>\*</sup>Speaker

# Behavioral state-dependent modulation of CA1 pyramidal cells' membrane potential in mice navigating a virtual reality environment

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Spontaneous locomotion strongly influences the state of the hippocampal network and is critically important for spatial information coding. However, the intracellular determinants of CA1 pyramidal cells (PCs) activation during locomotion are poorly understood. Here we recorded the membrane potential (Vm) of CA1 PCs while non-overtrained mice spontaneously alternated between periods of movement and immobility during a virtual spatial navigation task. We found opposite membrane polarization between bursting and regular firing CA1 PCs during movement. Regular firing CA1 PCs were more depolarized and fired at higher frequency during movement compared to immobility while bursting CA1 PCs, located deep in the CA1 pyramidal cell layer and preferentially inhibited during sharp wave ripples, were hyperpolarized during movement. We propose that the selective suppression of a subpopulation of CA1 PCs during locomotion enhances signal to noise ratio for efficient spatial information coding.

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\*Speaker

# DIFFERENTIAL CODING STRATEGIES IN GLUTAMATERGIC AND GABAERGIC NEURONS IN THE MEDIAL CEREBELLAR NUCLEI

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The cerebellum drives motor coordination and sequencing of actions at the millisecond timescale through the adaptive control of cerebellar nuclear output. Cerebellar nuclei integrate high frequency information from both the cerebellar cortex and the two main excitatory inputs of the cerebellum, the mossy and the climbing fibres. However, how nuclear cells process rate and temporal codes carried by these inputs is not well understood. Here, we investigate the influence of the cerebellar cortical output, the Purkinje cell, on identified cerebellar neurons in anesthetized mice. Using transgenic mice expressing the Channelrhodopsin2 either in Purkinje cells, in glutamatergic or in gabaergic nuclear neurons we demonstrated that the action potential waveforms extracted from extracellular recordings can reliably discriminate between glutamatergic and gabaergic neurons. We could then show that glutamatergic neurons fire at high frequency and multiplex rate and temporal code from Purkinje cells while the gabaergic neurons are exclusively gradually inhibited. Our results suggest that Purkinje cells operate a target cell specific control dependent contraglutamatergic projection cells can be dynamically entrained at a wide range of frequency mediated by Purkinje cell.

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\*Speaker

# Subcortical Pain Processing in rodent models of Parkinson's Disease

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Parkinson's disease (PD) is characterized by a progressive degeneration of dopaminergic neurons (DA) located in the substantia nigra pars compacta (SNc). The main consequence of this DA loss is a dysfunction of a group of structures called the basal ganglia (BG). This disease is classically associated to motor symptoms, however, it is increasingly recognized that numerous non-motor symptoms, including pain are also present. Up to 60 % of PD patients describe bizarre and unexplained transitory painful sensations such as painful burning, stabbing, aching, itching or tingling sensations. Sensitivity to pain is also increased in patients with PD, with or without pain and their pain threshold is altered. The origin of these pain symptoms as well as the functional state of central nociceptive structures in the context of PD has never been explored. Here, we investigated pain processing in a network linking the parabrachial nucleus (PBN), a key sensori-motor structure processing low level pain information, and two structures of the BG known to dysfunction in PD and animal models of PD, the subthalamic nucleus (STN) and substantia nigra pars reticulata (SNr), using in vivo electrophysiology.

The purpose of the present electrophysiological study was to investigate in the anaesthetised 6-OHDA lesioned rats :

- i) STN, SNr and PBN pain processing following noxious stimulations.
- ii) The presence of neuroplasticity in PBN nociceptive stimulation activated neurons that could explain abnormal pain sensations in PD patients.

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\*Speaker



# Characterizing the roles of parvalbumin interneurons requiring cdhr15 and cdhr23 during development in the excitatory-inhibitory balance of the auditory cortex

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A key principle of brain function is the balance between neuronal excitation and inhibition (E/I). In the auditory cortex (AC), this balance sharpens the frequency tuning of the neuronal response, and the temporal E/I relationship allows a submillisecond precision of the response, two features essential to hearing. However, the excitatory and inhibitory neuronal populations constituting the AC and the molecular framework underlying the development of E/I balance remain largely unknown. To address these issues, we use mouse lines that carry deafness gene mutations and are susceptible to audiogenic seizures, reflex seizures elicited by loud sounds that are a hallmark of E/I balance deficits. In hearing sensory cells, the cadherin-related (cdhr) proteins cdhr15 and cdhr23 form the tip-links responsible for conveying sound-evoked mechanical forces to the mechanoelectrical transduction channels. Based on the susceptibility to audiogenic seizures of heterozygous Cdhr23+/- and Cdhr15+/- mutant mice, which have normal peripheral hearing, a role for cdhr15 and cdhr23 in the embryonic brain was recently discovered. Many GABAergic interneuron precursors express cdhr15 and cdhr23 in the medial ganglionic eminence, during embryogenesis. Deficiencies of either of these proteins results in a 50% reduction of parvalbumin-expressing interneurons in the AC. This deficit can be explained by the defective entry into the neocortex of interneuron precursors that would normally express Cdhr23 and Cdhr15. Thus, a population of newly born interneurons is endowed with specific cdhr proteins involved in its addressing to the developing AC. In this study we will characterize the function of parvalbumin interneurons requiring cdhr15/cdhr23 during development.

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<sup>\*</sup>Speaker

# Piriform cortex network activity during natural sleep and wake state

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The topographical organization of the olfactory bulb circuits is not preserved at the level of the piriform cortex (PIR) as the output of individual glomeruli presents widespread projections throughout the PIR and individual PIR pyramidal cells receive inputs from multiple glomeruli. These features suggest that PCIR neurons "bind" information coming from different channels of information and therefore collectively code for odor "objects". Our work is based on the hypothesis that such binding is dictated by learning and experience: these latter would modify the synaptic weights from the main olfactory bulb to PIR neurons, as well as between PIR neurons, resulting in a change in the functional connectivity of the PIR network. We hypothesized that such modifications are reflected in the correlation structure of the PIR network in its "default" state, particularly during sleep when interference from external sensory inputs is minimal. To test this hypothesis, we conducted in vivo silicon probe recordings of large neuronal ensembles of anterior PIR combined with precise monitoring of the sniff cycle in freely moving mice undergoing an olfactory learning task. The combination of these advanced methods allowed characterizing PIR network activity and the dynamic relationships between single units' activity and the sniff cycle during both natural sleep and behavior. These results will serve as a basis to test the impact of learning on PIR network activity.

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\*Speaker

# Electrophysiological study of audio-visual integration in Shank3C mice model of ASD.

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Abnormal sensitivity to sensory information is a key feature of clinical presentation of autism spectrum disorders (ASD). Because sensory information processing drives adapted cognitive functions, our working hypothesis is that alterations in sensory responsiveness in ASD could trigger other autistic symptoms. To understand the integration processing alteration of sensory information in ASD, we performed *in vivo* electrophysiological recordings in the primary visual cortex (V1) of Shank3C mice. The goal is to study cross-activation of V1 by an auditory modality. Previous studies have demonstrated that, in WT mice, activation of auditory cortex by a brief noise stimulus recruit inhibitory circuits in primary visual cortex (V1) originating from infragranular layers of V1. This acoustic-driven inhibition reduces visual synaptic and spike responses in supragranular layers of V1. Consistently, we show here that *in vivo* recordings of LFP and multi-unit activities responses in V1, using laminar probe in WT mouse, showed evoked response potential (ERP) in different layers after a visual stimulation. A concomitant sound burst is able to modulate these ERP. We hypothesize that a modification of the sound's threshold that modulates ERP in Shank3C mouse would be involved in abnormal sensory-based behaviors. In a classical fear-conditioning paradigm, pairing a visual stimulus with a mild electric foot-shock causes the emergence of a conditioned motor response, in both WT and Shank3C mice. Our data show that the noise burst degrade Shank3C mice (but not WT) behavioral response.

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\*Speaker

# Neural trajectories in realistic cortical neural network model

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Cardinal cognitive functions ubiquitously imply sequential spatiotemporal patterns of neural activity in many cortical recurrent networks, such as navigation (Fujisawa et al., 2008), motor planning and execution (Churchland et al., 2012), perception (Crowe et al., 2010), working memory (Baeg et al., 2003), and memory consolidation during sleep (Euston et al., 2007). In the awake brain, these neural trajectories operate within a global asynchronous state of activity. Previous theoretical studies provide important clues for explaining the learning and emergence of neural trajectories, through feedforward structures (Clopath et al., 2010; Liu and Buonomano, 2009) or sequences of Hebbian Assemblies (Chenkov et al., 2017) embedded within recurrent networks. However, the question remains largely unanswered of how they robustly emerge in the awake state in animals and human beings. We simulate a cortical neural network model of Integrate-and-Fire neurons with synaptic currents and induce learning of an example trajectory through biologically realistic STDP. Amidst chaotic spontaneous background activity, we obtain neural trajectories in physiological conditions, and quantify how robust they are to the inherent variability of biological systems.

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<sup>\*</sup>Speaker

# Local modification of the grid cells firing pattern in a goal-directed navigation task

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Entorhinal grid cells are spatially selective neurons whose firing fields form a regular triangular pattern across an environment. This activity is thought to form an euclidian map-like representation of the rat's location and orientation based on movement-related information. So far, grid cells properties have never been analyzed in a goal directed navigation behavior. In this study, we recorded grid cells while rats performed a continuous goal-directed navigation task in a circular arena polarized by a visual cue card. In this task, animals learn to reach and stay for two seconds in an unmarked area, in order to receive sugar pellets that are randomly scattered on the floor. Animals successively performed the task in light-dark-light sessions. We aimed at understanding whether the presence of a spatial goal influences the spatial activity of the grid cells. Results shown that grid cells firing pattern is modified around the goal zone. In particular, field spacing expanded at the proximity of the goal . Furthermore, we observed that the grid maps of all grid cells recorded during successive days had the same orientation. Finally, grid cells spatial selectivity and regularity strongly decreased in darkness. This decrease was proportional to the reduced performance of the animals, compared to light sessions. These results demonstrate that the grid cell firing pattern is not uniform but locally modifies around non-physical boundaries, such as an unmarked goal area.

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\*Speaker

# Burst firing and spatial coding in subicular principal cells

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The subiculum is the major output structure of the hippocampal formation and is involved in learning and memory as well as in spatial navigation. Little is known about how the cellular diversity of subicular neurons relates to function. Previously, *in vitro* studies have identified distinct bursting patterns in subiculum. Here, we asked how burst firing is related to spatial coding *in vivo*. Using juxtacellular recordings in freely moving male rats, we analyzed the bursting behavior of 102 subicular principal neurons and distinguished two populations, i.e. sparsely bursting (~80%) and dominantly bursting neurons (~20%). The two populations had distinct spatial properties, sparsely bursting cells being better tuned to the animal's position than dominantly bursting cells. In ~60% of spatially tuned neurons, bursts defined sharper place fields than isolated spikes. We conclude that burst firing is relevant to subicular spatial coding, possibly by serving as a mechanism to transmit spatial information to downstream structures.

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<sup>\*</sup>Speaker

# From serial to parallel: predicting the activity of neural populations from sequential recordings

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A major goal in sensory neuroscience is to understand how populations of neurons code for stimuli. While the number of neurons that can be recorded simultaneously is increasing at a fast pace, in most cases these recordings cannot access a complete population. Recent progress allow to profile each recorded neuron thanks to genetic and physiological tools, and to pool together recordings from neurons of the same type across different experimental sessions. However, it is unclear how to infer the activity of a full population of neurons of the same type from these sequential recordings. Neural networks exhibit collective behaviour, e.g. noise correlations and synchronous activity, that are not directly captured by a conditionally-independent model that would just put together the spike trains from sequential recordings. Here we present a method to build population activity from single cell responses, which requires pairwise recordings only to train the model. Our method combines copula distributions and maximum entropy modeling, and it can predict the activity of whole populations using only sequential recordings of single cells. We applied this method on a population of retinal ganglion cells all belonging to the same type. From just the spiking response of each cell, we could predict the full activity of the population. More surprisingly, we could generalize and predict the population responses in different experiments. We predicted synchronous activity accurately and showed it grew with the number of neurons. This approach is a promising way to infer population activity from sequential recordings in sensory areas.

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\*Speaker

# Etude de la FCR-A par l'analyse numérique : cas de la maladie neurodégénératives

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Les maladies neurodégénératives, sont des maladies chroniques invalidantes à évolution lente et discrète. Elles provoquent généralement une détérioration du fonctionnement des cellules nerveuses, en particulier les neurones, pouvant conduire à la mort cellulaire (ou neurodégénérescence).

Les troubles induits par les maladies neurodégénératives sont variés et peuvent être d'ordre cognitivo-comportemental, sensoriel et moteur.

Au fur et à mesure que la recherche progresse, de nombreuses similitudes apparaissent reliant ces maladies les unes aux autres. La découverte de ces similitudes offre l'espoir d'avancées thérapeutiques qui pourraient améliorer simultanément de nombreuses maladies.

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\*Speaker



# Study of prediction in cortico-cerebello-cortical loop.

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The cerebellum is a structure showing reciprocal connections with the cerebral cortex. Indeed, part of the cortex projects on the cerebellum through the pons, and in return the cerebellum projects via a set of thalamic nuclei on restricted cortical zones.

The functional connection between the cortex and the cerebellum was studied by the application of optogenetic stimulation and electrophysiological recordings of the extracellular activity of the cortico-pontic neurons in freely-moving mice. The specific stimulation of these neurons was obtained by the combination of injection of retrograde virus into the pontine nuclei of transgenic mice producing a CRE-dependent expression of Channel Rhodopsin.

Optogenetic stimulation at the implantation site of the extracellular electrodes, allowed us to record an "echo"-response of the cerebellum propagated through the cortico-cerebello-cortical loop. The ability of the cerebellum to establish a prediction based on the temporal recurrence of the information from the cortex was studied by the implementation of a protocol comprising a series of regular stimulations in which, in a totally unpredictable manner, certain stimuli were omitted. This experimental paradigm allows us to see the trace of a cerebellar feedback to the cortex soon after the omission of the stimulation.

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\*Speaker

# How does the cerebellum modulate hippocampal coding?

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The cerebellum is known to interact with the hippocampus. However, little is known about the organization and functioning of the circuits supporting such interactions.

By using a retrograde tracing strategy the team has recently identified three polysynaptic pathways from the cerebellum to the hippocampus (HPC) involving lobule VI, Crus I and paraflocculus. By simultaneously recording the local field potentials from the HPC and the cerebellar cortex in behaving mice we have found higher levels of coherence in the theta range (6-12 Hz) between lobule VI and/or Crus I and the HPC compared with a control (lobule II/III). In particular, Crus I-HPC coherence dynamically changed depending on the behavioral and sensorial context, being maximal during goal-directed behavior.

Now, we are using transgenic mice expressing channelrhodopsin specifically in the cerebellar Purkinje cells (L7-ChR2 mice), the only output of the cerebellar cortex, in order to optogenetically control the activity of discrete cerebellar circuits. Using a virtual reality (VR) setup, we are now performing acute-like experiments in head-fixed mice using silicon probes to record the laminar profile of LFPs and units in the dorsal HPC while we stimulate precise spots on the cerebellar cortex with an optic fibre. Stimulation at specific hotspots generates heterogeneous hippocampal responses, either inhibitory or excitatory, at single cell level. Using this strategy we aim to explore to which extent and through which sensory information cerebellar manipulation can affect the hippocampal place code.

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<sup>\*</sup>Speaker

# Song related activity in the avian cerebellum

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Songbirds feature a neural circuit dedicated for song learning and production and is thus used as an animal model for studying acquisition and plasticity of complex motor programs. The cerebellum is known to be implicated in fine control of movements. Recently, it was shown that the cerebellum is connected to the song-related basal ganglia nucleus through the thalamus in songbirds. In this study, we extracellularly recorded the neural activity of cerebellar neurons in awake and singing birds. The recordings were performed in the lobule 3 of the cerebellar cortex and in the lateral Deep Cerebellar Nucleus (DCN). We found that the activity of the neurons of the cerebellar cortex is strongly modulated during singing. Moreover, we present anatomical evidence for a putative connection between the ventral basal ganglia circuits, known to receive song-related information, and the cerebellum via the pons. Such circuit could mediate song-related input to the cerebellum and participate to the observed responses.

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\*Speaker

# Membrane potential slow oscillations related to respiration as a gating system for fast intracellular oscillations in rat mitral cells in vivo

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We previously evidenced, in anesthetized rats, a slow dynamic in Mitral/Tufted (M/T) cells characterized by membrane potential slow oscillations (MPSO) related to respiration. In another hand, at the extracellular level, we showed, in local field potentials (LFPs), that slow respiratory modulation shapes the occurrence of beta (15-35Hz) and gamma (35-100Hz) fast oscillations, alternating beta and gamma waves along the respiratory cycle.

Then, we wondered to what extent the two fast regimes (gamma and beta) of membrane potential subthreshold oscillations (STOs) could co-exist in *in vivo* M/T cells, and especially how fast STOs could interact with the MPSO i) in their reactivity to odor stimulation, ii) in their relation with respiratory cycle, and iii) in their relation with spiking activity.

We demonstrated for the first time *in vivo* that 1) fast STOs in both beta and gamma ranges co-exist in a single M/T cell, 2) the presence of an MPSO shaped the occurrence and dynamics of intracellular STOs. 3) the presence of an MPSO favored the phase-locking of STOs with the respiratory rhythm at respiratory phases similar to what is observed for fast LFP oscillations, 4) STO frequency and the spike rate are better correlated in cells with an MPSO. We concluded that most of M/T cells can exhibit STOs in both frequency ranges and MPSOs appear as a gating system for STOs allowing them to interact with fast rhythms at LFP and spike levels.

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