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Abstract Book

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List of Participants

Oral Presentations

Neural population decoding of hippocampal memory replay

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Résumé

The temporal spiking patterns of cortical neurons convey information about the external environment, including sensory inputs and behavior ("the stimulus"). Single neurons are generally sensitive to a small subset of stimulus features and only by monitoring the concerted activity of many neurons do we obtain a complete picture. Population decoding algorithms offer one approach to study how neuronal ensembles represent information about a stimulus. For example, hippocampal pyramidal neurons display spatial receptive fields ("place fields") as an animal actively explores its environment. The animal's location in the environment can then be accurately inferred from the activity of a representative sample of hippocampal neurons. In this presentation, I will show how decoding approaches can be used to study internally generated hippocampal activity patterns during sleep and rest that reflect recent experience. In addition, I will demonstrate that the usual practice of single cell classification of multi-neuron recordings is not required for the purpose of decoding. Rather, population decoding using spike waveform features directly may make better use of available information in the signal and could lead to optimized algorithms for online, real-time neural encoding and decoding.

*Intervenant

Navigating, cleaning, and analyzing multichannel data

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Résumé

I will present some new approaches to deal with multichannel data (electrode arrays, optical imaging, EEG, ECoG etc). Scalable statistics support navigation and search within very large data sets. Component analysis (PCA, ICA, CCA, DSS, etc.) optimally transforms multichannel data to minimize noise and maximize useful patterns. Non-stationary analysis deals with the severe non-stationarity of certain types of data, due to fluctuations in brain state, artifacts, etc. I'll focus on a class of methods based on joint diagonalization of covariance matrices (known variously as JD, DSS, CSP, KLT) that allow us to discover an optimal analysis matrix to maximize signal-to-noise ratio. These methods can extract extremely weak sources of stimulus-locked, response-locked, condition-specific, oscillatory, etc. activity, that are impossible to observe with other techniques. Many common tasks in electrophysiological data analysis can be addressed by these methods.

*Intervenant

Isletchip for Pancreatic Endocrine Cells: From Bench to Bedside

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Résumé

The pancreatic islets of Langerhans are microorgans composed of different endocrine cell types that regulate glucose homeostasis. The most prevalent of these islet cells are -cells which secrete insulin, the only hypoglycemic hormone. Analogously to the secretion of neurotransmitters by neurons, insulin secretion by -cells is triggered by complex electrical activities resulting from the integration of multiple signals such as nutrients, hormones and cell-cell communications. The ability to record these electrical signals non-invasively with Multielectrode Arrays (MEA) while simultaneously performing real-time analysis is an important step that will open the door for many applications in diabetology. To this end, our multi-disciplinary group consisting of physiologists, microelectronicians, electrochemists and clinicians has developed a first prototype: Isletchip.
Murine and human islets were cultured on MEAs for up to 12 days. Filtered recordings showed the presence of both small action potentials (AP, 600 ms). Pharmacological tools and organ-specific KO mice revealed that APs are single-cell events whereas SWs reflect intra-islet gap-junctional electrical couplings. AP and SW frequencies were dose-dependent to glucose and exhibited hysteretic behavior, with the faster signal decay for declining glucose thought to protect against hypoglycemia. SWs were also modulated by essential hormones, such as the intestinal incretin GLP-1 in the picomolar range and the stress hormone adrenalin. Continuous monitoring demonstrated the enduring stability of SW frequencies over 120 h.

Customized integrated circuits that convert and process APs and SWs in real-time were then designed and tested, a user-friendly interface enabling online analysis. To increase the

*Intervenant

number of working electrodes, electrical fields were generated within MEAs to micropattern islet cells on electrodes by electrophoresis.
As a next stage in its development, Isletchip will integrate microfluidics to facilitate the creation of multiple wells and long-term approaches, notably for drug screening and tissue engineering in diabetology. A clinical program with the goal of applying this technology for pre-transplantation islet quality-control for patients with diabetes has already begun.

On local origins of local-field potentials

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Résumé

We investigated the local field potential (LFP) contribution associated with a single spike in human and non-human-primate cortex. The data were recorded from the temporal cortex of patients who underwent a surgical treatment for the localisation of the epileptic foci [2] and from the motor cortex of macaque monkeys [3]. The LFP and spiking activity were recorded with a 10-by-10 array of intracortical electrodes (Utah array, interelectrode distance 400 m). Spikes of single neurons were discriminated by semi-automatic clustering and the cell type was determined based on a spike waveform [2].
The average of LFP segments triggered on spontaneous spikes (LFP-STA) showed components that were non-causal, i.e. preceding spike occurrence, and non-local, i.e. appearing with no delay at large distances. We show that these properties could be explained by the volume conduction and neuronal correlations.
First, in a simple statistical model of the LFP we demonstrate that the amplitude and width of the LFP-STA depend on the number of contributing neurons and correlations in their firing. Importantly, the jitter in spike times of pairs of correlated neurons will introduce non-causal components to the LFP-STA, while the spatial extension of the correlations will spread LFP-STA in space. Next, we develop a method to correct for the effects of pairwise correlations and volume conduction in experimental data that is based on ongoing LFP correlations. When applied to human and monkey Utah-array recordings, the method allows to disambiguate the local LFP components triggered by a single neuron. Intrestingly, the amplitude and spatial reach of these components were larger for putative inhibitory neurons compared to excitatory neurons possibly reflecting differences in their morphology or synaptic connectivity [1].
In summary, although the contribution of a single neuron is local and does not exceed an area within a radius of 800 m, the LFP and LFP-STA are spatially and temporally extended due to the neuronal correlations and volume conduction.
Work supported by the CNRS and the EC (BrainScaleS, FP7-269921; HBP).

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*Intervenant

Probing resting-state activity with TMS to evaluate under networks properties and virtual brain comparison

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Résumé

First we describe EEG experiments with TMS and then we will show how TVB could help to understand electrical brain activities.
our subjects let freely theirs thoughts without engaging any cognitive task like memory, perception or action, we observe by means of an EEG neural activity. This minimum of neural activity is organized under networks, one of them is called Default Mode Network (DMN) and this peculiar state is designed by reststate activity or resting state. During our work, we record EEG signals when a subject is seated quietly at rest (no visual stimuli : eyes closed, no noise) and we apply a Transcranian Magnetic Stimulation (TMS) and we follow electrical behavior of all electrodes.

As alpha activity is the signature of using DMN we apply TMS when alpha activity is detected. Two areas have been studied : prefrontal cortex which as far as we know is involved in the DMN and a parietal cortex namely area 7 which is not involved in these rest state. We observe an increase of alpha power after TMS mainly in prefrontal area by not in area 7. Moreover we observe an increase of beta power localized mainly in sensory motor areas for both stimulated areas. We conclude that alpha wave are influenced by TMS and that rest state use preferentially prefrontal area.

To validate our experimental measurements, we use The virtual brain (TVB) by looking basic parameters with or without noise a basic alpha behavior could be seen which lead to a better understanding of electrical dynamics into brain.
These results lead to new treatments in order to better characterize the resting state (alpha statistics, micro-states) and to look deeper into TVB by adding criticality to better simulate brain dynamics.

*Intervenant

Using Non-Negative Matrix Factorization for the Analysis of Large Scale Population Spike Trains

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Résumé

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Due to progress in recording technology, the numbers of simultaneously recorded neurons in a typical experiment are ever increasing. This progress calls for new analytical methods to extract from neural responses the features that carry most information about external or internal events of interest. Given that neural responses are known to carry information at a fine time scale[1], these methods need to capture the information carried by the fine temporal structure of neural responses as well as that contained in the cross-cell patterns of neural activity. We report our results on the extraction of information through neural activity using Non-Negative Matrix Factorization[2] (NMF), a technique that decomposes non-negative datasets (such as spike sequences) into a set of non-negative basis functions using non-negative coefficients. In particular, we explored a variant of NMF, which we termed space-by-time NMF, which linearly decomposes single trial neural population responses into trial-independent non-negative temporal and spatial modules and trial-dependent activation coefficients[3]. We tested these methods by applying them to both simulated data and real data recorded from the salamander retina in response to natural images, movies and flashed gratings. We found that space-by-time NMF offers credible spatial and temporal basis functions for neural activity, and capture well the patterns of interacting cells and their temporal modulation. The NMF description of the data provides excellent stimulus decoding performance, and the basis functions generalize well to describe responses to stimuli that were not used for calculating the basis functions.

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*Intervenant

Reversed theta sequences of hippocampal cell assemblies during backward travel

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Résumé

Hippocampal place cells discharge when the animal is located in specific locations (firing fields). As a rat explores its environment, place cells discharge one after the other, representing the ongoing trajectory in real time. However, because firing fields overlap, the spike trains are actually intermingled at a faster timescale: in each cycle of the ongoing theta rhythm (~8 Hz), spike bursts also tend to occur in the same order, representing the past, present and future locations of the rat. These 'theta' sequences also reflect the ongoing trajectory, but at a highly accelerated speed, possibly triggering plasticity processes underlying the formation of initial memory traces. The same sequences are later replayed during rest and sleep, supporting memory consolidation.

At the single-cell level, as the rat moves through a firing field, the corresponding place cell fires earlier and earlier in successive theta cycles: this is known as phase precession. The mechanisms underlying the precise timing of hippocampal cell assemblies are largely unknown, and the functional relevance of phase precession remains debated. We recorded hippocampal place cells and entorhinal head direction cells during backward travel to determine individual cell properties as well as theta sequence dynamics in response to this atypical displacement.

We found that theta sequences were reversed during backward travel, and continued to predict the ongoing trajectory despite the atypical displacement. At the single-cell level, phase precession coded for distance traveled through the firing field, independently of actual locomotor movements. Finally, head-direction cells maintained their preferred firing directions during backward travel, indicating that these cells do not signal travel direction, as assumed by several computational models. Our results should inspire further development of both current and new computational models of hippocampal theta phase precession and theta sequences.

*Intervenant

Modulation of tactile sensory responses during a sensory triggered decision task in mouse forepaw primary motor cortex.

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Résumé

M1 fires action potentials during voluntary movement but also to sensory stimulation. Here we address the function of sensory responses in M1 by developing a sensory triggered reach-and-press task in the awake, head restrained mouse. Mice were trained to respond to a brief vibrotactile stimulus of the forepaw with a quick reaching movement of the same paw ($<$ 500ms) from a "rest" sensor, positioned under the mouse, to a "reach" sensor, positioned in front of the mouse. A "noreach" task was interleaved with the "reach" task where the mouse learnt to withhold reaching after the same stimulus in a different context. Mice learned to perform hundreds of accurate reaches in less than 10 days of training (two 20 min sessions a day). Extracellular polytrode recordings were performed in forepaw M1 an S1 layer V in parallel with forepaw camera tracking at 200Hz. During the task, a large proportion of neurons displayed short latency spiking following the vibrotactile stimulus onset. The strength of firing to the stimulus was often different in reach trials as compared to noreach trials.

*Intervenant

The dorsolateral striatum constrains the execution of motor habits through continuous integration of contextual and kinematic information.

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Résumé

The striatum is required for the acquisition of procedural memories but its contribution to motor control once learning has occurred is unclear. Here we created a task in which rats learned a difficult motor sequence characterized by fine-tuned changes in running speed adjusted to spatial and temporal constraints. After training and extensive practice, we found that the behavior was habitual yet tetrode recordings in the dorsolateral striatum (DLS) revealed continuous integrative representations of running speed, position and time. These representations were weak in naive rats hand-guided to perform the same sequence and developed slowly after learning. Finally, DLS inactivation in well-trained animals preserved the structure of the sequence while increasing its trial-by-trial variability. We conclude that after learning the DLS continuously integrates task-relevant information to constrain the execution of motor habits. This finding provides a new framework to understand the contribution of the basal ganglia to motor learning and control.

*Intervenant

Executive control by human subthalamic nucleus

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Résumé

The subthalamic nucleus (STN) has been shown to be implicated in the control of voluntary action, especially during tasks involving conflicting choice alternatives or rapid response suppression. However, the precise role of the STN during non-motor functions remains controversial.
First, we tested whether functionally distinct neuronal populations support different executive control functions (such as inhibitory control or error-monitoring) even within a single sub-territory of the STN. We used microelectrode recordings during deep brain stimulation surgery to study extracellular activity of the putative associative-limbic part of the STN while patients with severe obsessive-compulsive disorder performed a stop-signal task. Second, 2-4 days after the surgery, local field potential (LFP) recordings of STN were used to test the hypothesis that STN oscillations may also reflect executive control signals.

Extracellular recordings revealed three functionally distinct neuronal populations: the first one fired selectively before and during motor responses, the second one selectively increased their firing rate during successful inhibitory control, and the last one fired selectively during error monitoring. Furthermore, we found that beta band activity (15-35 Hz) rapidly increased during correct and incorrect behavioral stopping.
Taken together, our results provide critical electrophysiological support for the hypothesized role of the STN in the integration of motor and cognitive-executive control functions.

*Intervenant

Hidden Spatial Selectivity of Receptive Fields in Turtle Visual Cortex

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Résumé

As the primary cortical recipient of geniculate afferents, the three-layered dorsal cortex (DC) of turtles can be considered analogous to the primary visual cortex of mammals (V1). At a functional level however, this primary sensory area seems to process visual information in a very different way compared to mammalian V1. One peculiar aspect of turtle visual cortex is that, contrary to mammalian V1, DC neurons have extremely wide receptive fields (RFs), generally covering most of the contralateral visual field. Moreover, thalamic axons projecting to DC appear to lack the localized retinotopic arrangement of mammalian thalamo-cortical projections (Mulligan & Ulinski, J.Comp.Neurol. 296: 531, 1990). Here, we investigated how spatial information is encoded in this visual cortex by recording visually evoked responses of single units with silicon multitrodes in lightly anesthetized (0.5-1% isoflurane) curarized turtles (Trachemys scripta). Most visually driven cells responded to a large variety of visual features irrespective of their position in the visual field but also revealed a prominent adaptation to repetitive stimulation which resulted in a complete extinction of the evoked response after a few repetitions of the same stimulus at interstimulus intervals shorter than several seconds. We found that this adaptation is primarily specific to the location of the stimulus in the visual field: repeated stimulation in one position induced a reduction of the response strength specific to this location, leaving the responses evoked at other positions in the visual field almost unaffected. Turtle dorsal cortex therefore seems to detect changes in the spatiotemporal correlations of the visual stimulus by adapting to the spatial distribution of the sensory inputs experienced over the past tens of seconds. Using two-dimensional white noise stimuli, we also found that a substantial fraction of neurons exhibit localized and spatially structured RF components once the spatially non-selective component of their response is subtracted. Overall, our data suggest that spatial information is indeed encoded across the DC neuron population although it is not mapped across dorsal cortex.

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Towards reproducible data analysis of massively parallel neuronal data during complex behavior

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Résumé

We aim at getting an understanding of the processing in the cortical network during natural behavior. Task related network interaction can only be approached by observing many neurons or populations of neurons simultaneously with behavior. To relate the dynamics of cooperative neuronal processing to behavioral aspects, the data need to be analyzed in a time-dependent, and often trial-by-trial manner under consideration of the statistical features of the neuronal data. The analysis of such massively parallel data is a challenge, in respect to a) the statistical requirements (e.g. avoid combinatorial explosions or massive multiple testing), b) impact and elimination of artifacts, c) the computational effort, e.g., due to the required use of surrogates, and d) the resulting involved and complex analysis workflows. To account for a), we developed a number of statistical methods that enable us to extract the fine temporal correlation structure in massively parallel data, and well as approaches to relate the spike correlations to mesocopic population data (local field potential). Artifact occurrence (b) in such experiments cannot be completely extirpated. However, they may have a considerable impact on the outcomes of the analysis, in particular on (higher-order) correlation analysis. To reliably incorporate additional preprocessing steps (e.g. to eliminate artifacts) and complex analyses in workflows that enable systematic and reproducible analyses, we identified the need for detailed metadata annotation and well-tested analysis software, that includes parallelization (d) to account for c) on compute clusters, as important ingredients. We demonstrate in this contribution the tools that we worked out for solving these tasks, how they integrate into the workflow and present analyses results of such massively parallel recordings.

*Intervenant

ECOG signature of large-scale functional connectivity in the brain

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Résumé

Reading sentences involves a distributed network of brain regions acting in concert surrounding the left sylvian fissure. The mechanismsof neural communication underlying the extraction and integration of verbal information across subcomponents of this reading network are still largely unknown.Werecorded intracranial EEG activity in 12 epileptic human patients performing natural sentence reading and analyzed long-range corticocortical interactions between local neural activations. During a simple task contrasting semantic, phonological, and purely visual processes, we found process-specific neural activity elicited at the single-trial level, characterized by energy increases in a broad gamma band (40 –150 Hz). Correlation analysis between task-induced gamma-band activations revealed a selective fragmentation of the network into specialized subnetworks supporting sentence-level semantic analysis and phonological processing. We extend the implications of our results beyond reading, to propose that gamma-band amplitude correlations might constitute a fundamental mechanism for large-scale neural integration during high-level cognition.

*Intervenant

The cerebellum, an actor of sensorimotor integration in the control of voluntary movement.

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Résumé

Sensorimotor integration is crucial to perception and motor control. How and where this process takes place in the brain is still largely unknown. Here we analyze the cerebellar contribution to sensorimotor integration in the whisker system of mice. We identify an area in the cerebellum where cortical sensory and motor inputs converge at the cellular level. Optogenetic stimulation of this area affects thalamic and motor cortex activity, alters parameters of ongoing movements and thereby modifies qualitatively and quantitatively touch events against surrounding objects. These results shed light on the cerebellum as an active component of sensorimotor circuits and show the importance of sensorimotor cortico-cerebellar loops in the fine control of voluntary movements.

*Intervenant

Two types of asynchronous activity in networks of excitatory and inhibitory neurons

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Résumé

Balanced networks of excitatory and inhibitory neurons are believed to play the role of fundamental units of computation in the cortex. Asynchronous activity in such networks constitutes the primary medium for the propagation and the processing of information.

In this theoretical work, we show that an unstructured, sparsely connected network of model neurons can display two fundamentally different types of asynchronous activity. For weak synaptic couplings, the network at rest is in the well-studied, classical asynchronous state in which individual neurons fire irregularly at constant rates. For strong couplings, we find that the network at rest displays a novel type of heterogeneous asynchronous activity, in which the firing rates of individual neurons fluctuate strongly in time and across neurons.

The two types of asynchronous resting states may possess vastly different computational properties. In the classical asynchronous state, temporally varying inputs lead to a highly redundant response of different neurons that favors information transmission but strongly limits the computational capacity of the network. In the heterogeneous asynchronous state, the incoming stimulus interacts with the internal dynamics, so that the response of different neurons to
the input strongly vary. This variability in the population deteriorates the transmission of information, but provides a rich
substrate for non-linear processing of the stimuli as performed in decision-making and categorization.

The difference between the two states is most apparent at the level of the population activity rather than in individual neurons. Multi-electrode recordings would therefore allow to distinguish between the two types of activity.

*Intervenant

Neuronal population correlate of asymmetric auditory perception in mice

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Résumé

Natural sounds display strong intensity fluctuations over time. However, we currently understand better auditory processing in the frequency domain than in the temporal domain. Recently, auditory psychophysics showed that humans perceive a sound whose intensity increases as louder than a sound whose intensity decreases over time, although the overall intensity of the sounds are the same. The underlying neuronal mechanisms of this striking perceptual asymmetry are still elusive. To test if the direction of intensity variation is asymmetrically processed by the auditory system, we have recorded the activity of large populations of neurons in the auditory cortex of awake mice while playing sounds of ramping-up and ramping-down intensities with various durations. We observed that long ramps ($>$ 250ms) produce complex cortical population dynamics with different sets of neurons firing at the beginning compared to the end of the ramps. This indicates that the coding of intensity variations coding is strongly distributed in the auditory cortex. More interestingly, we observed that population firing rate is overall larger for increasing ramps than for decreasing ramps, suggesting that, also for mice, sounds ramping up could be perceptually more salient than sounds ramping down. To test this hypothesis, we performed behavioral experiments in which the saliency of a sound is measured through associative learning speed. We observed that increasing ramps are more rapidly associated to a correct behavior than decreasing ramps, showing that increasing sound intensities are more salient than decreasing sound intensities for mice. Altogether, these novel observations indicate that strongly non-linear processes in the auditory system shape both the perception and the cortical representation of time-varying sounds, to eventually reinforce rising and thus potentially approaching sound sources.

*Intervenant

Dissection of oscillatory dynamics in entorhino-hippocampal circuits or how to know that we know nothing

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Résumé

Hippocampal function in learning and spatial navigation relies on complex dynamic interplay between multiple afferents and local networks. Activation of each of these networks is associated with transient high frequency oscillation (HFOs) events covering gamma (20-100 Hz) and epsilon (100-200 Hz) frequency ranges. HFO generators generally exhibit distinct frequency content and give rise to LFP signals with specific anatomical localization dictated by axonal projections of its constituent neuronal populations and morphological and physiological properties of the target neuronal populations. This implies that objective characterization of HFO generators should rely on detection of anatomically and spectrally limited transient oscillatory events. Conventionally used statistics, such as average spectrum or phase-amplitude modulation measures for a single channel LFP derived from cell body layer do not capture the complete picture and introduce various biases into characterization of HFO generators and detection of respective HFO events. Novel analysis of multichannel LFP recordings across all HPC, MEC and LEC lamina and multiple single unit recordings uncover a much more complex picture of the entorhino-hippocampal dynamics than previously thought. All of the HFO were associated with distinct physiological frequency bands, anatomical distribution related to specific afferent projections to the hippocampus and had well defined relationship to theta oscillation. However, both signal and current generators giving rise to many of the HFO are leaving wide room for interpretation. I will give physiological and functional consequences of our interpretation of the observations.

*Intervenant

Variability statistics of spiking activity in motor cortical neurons during wait and movement

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Résumé

Variability of neural activity is apparent throughout the central nervous system. Understanding its nature and origin is essential for our understanding of information processing in cortical networks. To analyze variability in spiking activity we used two measures: (i) The coefficient of variation (CV) of inter-spike intervals (ISIs) measures the (ir)regularity of a sequence of spikes. Because it overestimates irregularity in case of firing rate changes, we use a local measure, the CV2 (Holt et al. 1996), averaging individual measures, each calculated over two consecutive ISIs. The CV signifies intra-trial variability in the range of tens of milliseconds. (ii) The Fano factor (FF), computed as the variance of spike counts divided by their mean, expresses the spike count variability across trials of the same experimental condition. Thus, the FF signifies inter-trial variability, on a longer time scale in the range of seconds.
We recorded simultaneously the spiking activity of 80 to 160 neurons using Utah arrays chronically implanted in motor cortex of three monkeys. We analyzed the data recorded during a wakefulness resting-state condition (160 neurons recorded in one 15 minutes session) or a delayed reach-to-grasp task (Riehle et al. 2013; 1929 neurons recorded in 21 sessions and 544 neurons in 140 sessions, respectively).

We found across all neurons and conditions a strong negative correlation between mean firing rate and mean CV2. However, if correlating for each neuron rate and CV2 in sliding windows, correlation is not significant in ~50% of the neurons, negative in ~40% and positive in ~10% of them. There is a positive correlation between CV2 and the spike width. FF is negatively correlated with firing rate and positively with CV2. When separating data recorded during motor behavior in periods of wait and of movement, CV2 and firing rate are significantly lower and FF is significantly higher during wait than movement. The relation between the squared CV2 and FF depends strongly on the behavioral context. In our data is the renewal prediction (CV2 = FF) almost fulfilled during movement, but not during the waiting period where the FF is by far larger than the CV2. We will discuss how these variability measures are related to behavior and the functional organization of motor cortical networks.

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Temporal expectancy in fear conditioning: an analysis of local field potential in the amygdalo-prefronto-striatal network early in training

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Résumé

In Pavlovian fear conditioning, the animal learns the association between a conditioned stimulus (CS) and an unconditioned stimulus (US) but also that the CS predicts the time of arrival of the US. While temporal expectancy is expressed behaviorally after overtraining, the CS-US time interval is learned in a few trials (Diaz-Mataix et al., 2013). The prefrontal cortex and the striatum are believed to play a role in processing interval timing, whereas the amygdala is essential for learning the CS-US association and may also have a role in CS-US interval processing as well. Here we assessed the time-related functional connectivity between these interconnected structures during the CS after fear conditioning. We used a conditioning paradigm in which the US (footshock) is presented in the middle of a 60-s auditory CS (i.e. 30s after tone onset); this paradigm allows differentiation between the time of arrival of the US and the onset and offset of the CS. We recorded local field potential (LFP) during trials without shock in the basolateral amygdala, the dorsomedial striatum and the prelimbic cortex in behaving rats before and after conditioning. We analyzed the synchrony in oscillatory activity in the LFP (coherence) between these structures in different frequency ranges (theta and gamma) for which specific increases in coherence had previously been observed overtrained animals. Our results suggest an involvement of the amygdalo-prefronto-striatal circuit as a whole in processing CS-US interval in an aversive conditioning protocol.

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The ups and downs of beta oscillations in monkey motor cortex

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Résumé

Since the first descriptions of sensorimotor rhythms by Berger (1929) and by Jasper and Penfield (1949), the potential role of beta oscillations (~ 13-30 Hz) in the brain has been intensely investigated. Sensorimotor beta power is low during movement, transiently increases after movement end and tonically increases during object grasping. Beyond these robust observations, the reported beta modulations are rather heterogeneous across studies. Many potential roles in cognition and motor control were therefore proposed for these oscillations, ranging from postural maintenance to signal expectancy and sensorimotor integration. We have studied motor cortical local field potential beta oscillations in macaque monkeys performing complex visuomotor tasks. We find systematic modulations of these oscillations in relation to the behavioral context, in particular comparing epochs of visual cue expectancy, visuomotor integration and movement preparation. Importantly, we find that not only beta power, but also beta frequency modulates systematically with behavioral context, suggesting the existence of several beta bands. This is supported by recent results demonstrating distinct locations of beta bands involved in different aspects of the visuomotor task. Thus, our results reconcile the disparate roles proposed for sensorimotor beta oscillations in cognition and motor control, evidencing the existence of multiple co-active beta band networks involved in either signal expectancy or motor maintenance.

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Brain networks and functional connectivity in benign childhood epilepsy

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Résumé

We investigated whether functional brain networks are abnormally organized in epilepsy's disease. Using high density and resolution electroencephalography (EEG) data from nine healthy adolescents and eight patients of the same age group with benign childhood epilepsy with centrotemporal spikes (BCECTS). In this study we characterized how the dynamics of the healthy brain differed from the state of the brain of epilepsy patients with and without spikes in the context of resting state. All patients had epileptogenic focus in the right hemisphere. To this end, graph metrics, cluster coefficient and characteristic path length were applied to matrices of functional connectivity of EEG channels. Correlations between all pairwise combinations of EEG channels were determined with phase-locking value for different frequency bands. The matrices were converted to graph by applying a threshold and graph metrics were computed as a function of network density. The theta (4-8 Hz) and alpha (9-13 Hz) bands showed the largest deviations from healthy controls across various measures with robust statistics significance within the groups. In particular, patients with BCECTS demonstrated significantly higher asymmetric phase-locking value. In addition, differences between controls and patients in graph metrics revealed deviations from healthy controls. These findings show that, despite the focal nature of BCECTS, the epileptic brain differs in its global network characteristics from the healthy brain and that deviation in epilepsy brain dynamics is frequency dependent.

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Poster Presentations

Sleep-scoring in mice using gamma frequency in the olfactory bulb

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Résumé

The growing interest in the physiology of various behavioral states demands reliable and systematic methods of wake and sleep stage scoring. Traditional methods identify sleep by monitoring movement or muscular activity, however if sleep and wake are truly different brain states the two should be identifiable using information on neuronal activity alone.

It has been shown that gamma oscillations in the olfactory bulb (OB) of the mouse are strongly reduced during sleep (Manabe et al. 2013). Here, we show that low gamma power in the 50-70Hz band recorded from the OB shows a bimodal distribution that allows to separate sleep and waking states. Moreover rapid-eye-movement (REM) and non-REM (NREM) sleep can be distinguished using theta-band power (6-10Hz) recorded in the hippocampus (HPC). We therefore present a method of constructing a two-dimensional phase space allowing to distinguish between waking, REM and NREM sleep that relies exclusively on LFP recordings from the HPC and the OB and can be automatically calibrated. This technique allows for identification of brief periods of arousal and dozing and is therefore a promising tool for the fine study of sleep microstructure.

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Visual cortical representations are enhanced by cross-modal auditory interactions in mice

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Résumé

Perception relies importantly on multi-modal integration. In particular, the interaction between vision and audition is the source of multiple crossmodal illusions in humans (e.g. Mc Gurk effect, double flash illusion, ventriloquism), in which one modality influences perceptions in the other. The neural mechanisms of such cross-modal interactions remain elusive. To test how sounds can modulate representations in the primary visual cortex (V1) of awake mice, we used 2-photon microscopy to record the activity of large populations of neurons while playing uni- or bi-modal sequences, consisting of visual stimuli generating apparent motion towards or away from the animal, and auditory stimuli of increasing and decreasing amplitude or frequency. We observed that a small fraction of the neurons inside V1 responded to sounds and even displayed auditory tuning. An even larger fraction of neurons had their responses to a visual stimulus modified by the sounds played simultaneously. At the level of the whole neuronal population, the main effect was that responses to visual sequences appeared to be more reproducible when accompanied by auditory sequences than when played in silence. These observations suggest that an auditory input can improve the cortical responses to visual stimuli, and hence their perception. We will perform behavioral experiments to test this hypothesis.

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Auditory processing and attentional brain states

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Résumé

Auditory responses are known to be shaped by attentional and conscious states (1). A newly designed oddball paradigm designed for use in humans has shown that cortical and subcortical responses to a deviant tone are dependent on the attentiveness and the conscious state of the subject (2).
However, auditory responses were observed through EEG and LFP recordings, which do not allow to address the question at the neuronal level. We aim to develop this paradigm in rodents, with extracellular recordings in several brain structures involved in auditory and attentional processes.

Moreover, explicit instructions were given to human subjects in order to control attentional load, which cannot be directly adapted to rodent subjects. Here we designed a new attentional paradigm for mice, coupled to the oddball task and extracellular recordings.

In this task, additionally to successive presentation of standard and deviant tones with local and global irregularities, we add random presentations of a third tone with a specific rewarding value. At the presentation of this tone, the animal may obtain a cerebral rewarding stimulation by doing a nose poke. Attentional states were then identified by positive responses to the rewarding predicting sound. As in the human paradigm, this paradigm forces the animal to focus its attention on auditory stimulus, and allows us to differentiate attentional from non-attentional states. In this study we present both the behavioral task assessment, and the analysis of standard and deviant neuronal/LFP responses within these different attentional states.

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Dynamics of hippocampal theta sequences and their reactivations during subsequent sleep in freely moving rats

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Résumé

Hippocampal 'place cells' code for the position of the animal in space. As a rat explores its environment, the activity of hippocampal place cells is temporally organized by theta oscillations (~7 Hz). At the single cycle timescale (~100ms), stereotyped spatio-temporal spike sequences called 'theta sequences' represent the animal's ongoing trajectory. Subsequently, these behavioural episodes are replayed in a temporally condensed form during sharp-wave-ripple (SWR) events, during both sleep and quiet awake states. These reactivations are believed to play a crucial role in spatial learning, planning and memory. Notably, trajectories are replayed in the same order as during exploration when the animal is sleeping or about to start a journey (forward replay), but in reverse order at the end of a trajectory (reverse replay). In humans, memory performance is better for forward than backward associations and sleep enhances forward but not backward associations. However, while correlations have been documented between theta sequences during behaviour and replay during SWRs, a causal link between these two hippocampal activity patterns remains elusive. Do the dynamics of hippocampal place cells during behaviour influence those of replay events during SWRs? We have recently shown that theta sequences are reversed when the animal travels backward in the environment (Cei et al., 2014). To test if the travel direction of the animal influences the direction of replay during subsequent sleep, we now transport rats on a miniature treadmill mounted on a model train around a 6 m-long elliptical track. We record hippocampal place cells and interneurons as rats are transported either in the forward or backward direction, then during sleep. Coupled train and sleep sessions are repeated, alternating between forward and backward travel directions. We quantify the proportion of replay events in the same vs opposite direction compared to preceding travel direction.

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Spatio-temporal structure of motor cortical spiking activity during reach-to-grasp movements

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Résumé

Extracellular recordings in awake behaving monkeys have shown that the primary motor cortex (M1) is not only active during movement execution but also during motor preparation. However, it is not known how this preparatory activity is spatially distributed in M1 and in particular, how it relates to the movement-related organization of this cortical area. To address this issue, we used 100-electrodes Utah arrays (Blackrock Microsystems) chronically implanted in the arm and hand representation of M1 of two monkeys performing a delayed reach-to-grasp task. The monkey had to grasp and pull an object using one of two different grips: a side grip or a precision grip. In each trial, a cue was briefly presented to instruct about the grip type to be performed 1 s later, at the end of a preparatory delay.

In the two monkeys, single unit activity was recorded from a large number of electrodes uniformely distributed across the array. We sorted the neurons in disctinct functionnal classes based on their firing rate modulations at each task event: the cue presentation, the early and late part of the preparatory delay, the movement execution and the object release. Neurons selectivity for the two grip types was also used to characterize in more details the functional properties of the different classes of neurons.
We found that neurons belonging to these different classes are not distributed uniformly over the array. Neurons with movement-related properties are grouped in relation to the proximal and distal representation of the upper limb. In contrast, neurons active during the preparatory delay dominate in cortical zones located at separate M1 locations. These observations suggest that the functionnal organization of M1 is not only linked to the topographic organization of the descending motor output but may be defined in part, by more complex cognitive motor functions.

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Smell's melody: Brain processing of odor and sound interactions

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Résumé

The interplay between different senses is a very efficient strategy for amplifying behaviorally relevant stimuli. Cross modal integration is often studied in multisensory associative brain regions. However, recent studies have shown that integration could also occur in primary sensory cortices, previously considered to be unimodal. This finding has modernized our view of brain organization and suggests that the entire brain is multisensory. The goal of this project is to understand whether the establishment of neuronal oscillations can functionally connect sensory regions, and how these connections are built up by learning. We examine changes in the cortical network involved in the acquisition of a multisensory association between a sound and an odor in rats through the analysis of the local field potentials' oscillations. The originality of the project is to sample a large network of brain structures including primary sensory structures (primary auditory cortex, olfactory bulb) and multimodal areas towards which converge these two senses: the piriform and perirhinal cortices. We have developed a behavioral test in which the rat must combine simultaneous auditory and olfactory informations. Preliminary data of brain activity obtained in this task suggest that phase locking of low frequency oscillations ($<$ 35 Hz) between distant areas could be involved in the cross modal association.

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Subthreshold Information Decoding at the Granule Cell to Purkinje Cell Synapse

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Résumé

Temporal coding in Purkinje cells (PCs), the sole output of the cerebellar cortex, plays a major role in motor control. Alteration of PC discharge leads to movement disorders such as ataxia. Each PC receives 170000 inputs from granule cells (GCs), the relay of the mossy fibers. GCs also provide a feedforward inhibition on PCs through activation of molecular layer interneurons.
Since PCs are spontaneously active, we asked whether and how burst of subthreshold GCs inputs combined with molecular layer interneuron feedforward inhibition could modify PC discharge thereby influencing cerebellar cortex output.

On acute cerebellar slices, burst stimulations (3 to 7 stims, 200 Hz) were elicited on a few GCs using extracellular stimulation and PC discharge was monitored in juxtacellular recordings. At the end of the experiment, PCs were whole-cell patched and both excitatory and inhibitory synaptic charges were determined. In order to mimic physiological conditions, we used Thy1-Channelrhodopsin2 mice combined with optogenetic illumination to reproduce "in vivo-like" level of synaptic background activity. This was assessed by calculating the instantaneous coefficient of variation (CV2) between two adjacent spikes.
We then analyzed the trains of spikes of PC and found that the structure of the train was correlated with the balance between excitation and inhibition. We also observed that the number of stimulations in the burst influences the net effect of GCs inputs on PC discharge. Our results demonstrate that the organization of local microcircuits and the temporal organization of GCs inputs may control the output of the cerebellar cortex.

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Neural coding of variable song structure in the songbird.

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Résumé

Songbirds are an excellent model for exploring the neural coding of variable sequences of categorical acoustic elements.
The domesticated canary, for instance, produce higly variable songs with complex transition rules between two consecutive acoustic elements. These transition rules are non-Markovian (i.e. the next acoustic element to be sung is dependent on several previous elements, not only the last one) (Markovitz et al., PLoS Comp. Bio. 2013).
Our aim is to understand how complex song sequences produced by canaries are coded in a sensorimotor area, the HVC nucleus.
The HVC (somehow analogous to vocal premotor cortical areas) participates in generating temporal organization of acoustic elements within songs (Hahnloser et al., Nature 2002).
In the HVC of canaries, most of cells show auditory responses and are selective for the bird's own song (BOS) over its temporal variants (with a different order of acoustic elements) (Lehongre & Del Negro, Neurosci. 2011), but how the sequential structure (ordering of acoustic elements) is coded is poorly understood.

In our study, we recorded auditory responses in HVC of anesthetized canaries using multi-electrods arrays (8 or 16). We used as auditory stimuli the bird's own song (BOS) and modified versions of the BOS, in which we manipulated either the local or global structure. We reversed the position of two consecutive elements (local) or reordered parts of the song. We are currently quantifying responses of single units according to methods used in recent studies performed on bird species with less variable song structures (Fujimoto et al., J. Neuro 2011 ; Bouchard & Brainard, J. Neuro. 2013). We are assessing, for instance, the influence of transition probabilities between acoustic elements on neuronal responsiveness. We are also exploring the distributed representation of the BOS. To this end, after gathering all single-unit recordings, we are examining the multi-dimensional representation using, in particular, reduction methods (e.g. PCA) (Machens et al. J. Neuro., 2010). Preliminary results will be presented.

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Associative learning and network plasticity in the mouse barrel cortex

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Résumé

Neuronal circuits in primary somatosensory cortices exhibit plastic changes to reflect recent sensory experiences and learning. We are interested in the effects induced by associative learning on the sensory maps in barrel cortex, a region of the primary somatosensory cortex dedicated to whiskers.
We developped a new learning paradigm where mice are freely moving and their whiskers are stimulated remotely. We also present our strategy for mapping the whisker cortical representation with multi-electrode recordings and for investigating the effects of learning on cortical networks.

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Role of astrocytes connexins in the regulation of sleep oscillatory pattern.

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Résumé

Coordination across brain structures is thought to be crucial for the appropriate consolidation of memory trace. Cortical slow oscillations orchestrate the timing of hippocampal ripples (supporting neuronal reactivations), cortical delta waves and cortical spindles.
Our project aims at challenging the classical "neurocentric" view of brain rhythms regulation during sleep. Indeed, recent evidences showed that astrocytes regulate cortical slow oscillations during sleep and are involved in brain processes related to memory deficits induced by sleep deprivation (Halassa et al. 2009). We therefore investigated the role of astrocytic connexins (main constituent of gap junctions and hemichannels) in the regulation of network oscillations, by multisite recordings in mice double knockout for astrocytic connexins Cx43 and Cx30 (dKO) (Wallraff et al. 2006).
Our results show that sleep slow oscillations are decreased in cortical structures and that the coordination between spindles and ripples are impaired in this dKO model. Moreover, we found that the slow rhythm associated to breathing was also impaired in the olfactory bulb of dKO mice, confirming the results obtained in vitro by Lisa Roux. Olfactory bulb slices indeed exhibit spontaneous oscillations very similar to the slow oscillations recorded during sleep in cortical cells, and those oscillations are impaired in dKO mice. Therefore here we suggest that astrocytes are involved in the fine regulation of sleep oscillatory patterns.

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Time estimation and neural coding in the striatum

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Résumé

The ability to estimate temporal intervals in seconds-to-minutes range is necessary for a number of behaviors both in humans and animals. However, the neural mechanisms underlying such function are largely unknown. The implication of the basal ganglia in the estimation of temporal intervals was identified through the study of patients suffering from Parkinson's disease and has been confirmed in rodents using pharmacological perturbations of the dopaminergic system. But this subcortical network also plays an important role in motor control and its activity can be modulated by reward expectation and sensory stimuli. For this reason, it is challenging to isolate the contribution of basal ganglia to time estimation from a number of co-varying behavioral variables. To address this issue we designed a new behavioral paradigm in which rats are trained to estimate a 7 seconds interval while running on a motorized treadmill. We found that rats were capable of estimating such interval even if they had to run for several seconds while maintaining a fixed position on the treadmill. Tetrode recordings in the dorsolateral striatum were realized while rats performed the task. We observed that a significant fraction of striatal cells displayed linear correlation between firing rate and elapsed time. Further statistical and experimental work is ongoing to determine the specificity and functional relevance of these representations.

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Neuronal networks with controlled architectures

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Résumé

Understanding the propagation of mechanical signals within the human brain requires observing the activity of interconnected neurons and their interactions in response to mechanical loads. To address this question, we have designed a new method to create in vitro neuronal networks of controlled architectures. The functional parameters of these neuronal networks include the control of the total number of interconnected neurons, their positions and the length of the connection between neuron aggregates. By confining soma location and neurite elongation to a predefined pattern, the global architecture of the neuronal networks open a way to conduct mechanical experiments on well-controlled artificial neuronal circuits. The spatial control of neurons is obtained by using a microcontact printing technique to form two-dimensional laminin architecture on culture substrates of tunable rigidities. Our results demonstrate that neuronal networks form spontaneously in vitro by cell migration leading to the localization of somas on circular islands and the growth of neurites on laminin tracks. By combining fluorescence microscopy and the use of pharmacological inhibitors, we demonstrate that microtubules play a key role in the process of neuronal migration. Furthermore, we used low-modulus hydrogels to investigate the influence of the substrate rigidity on the dynamics of network formation. Our results indicate that the speed of formation is significantly higher on soft hydrogels, suggesting that the motility of cortical neurons is a matrix stiffness dependent process and may be used to control the formation kinetics of neuronal circuits. Finally, immunochemistry reveals that cortical neurons form functional synapses in long-term networks.

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Contribution of cerebellar PF-PC LTP to spatial map stability

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Résumé

Several plasticity sites have been described in the cerebellar cortex, among which the Parallel Fiber–Purkinje Cell synapse, displaying both Long Term Depression (LTD) and Long Term Potentiation (LTP), has received most interest. We previously showed that a lack of PF-PC LTD altered self-motion processing and subsequent dependent hippocampal processes, i.e. maintaining a cognitive representation of space using self-motion information and using it for optimal goal-directed behavior. However, it remains unclear if these navigation processes specifically depend on cerebellar LTD per se or ensue from a general disruption of cerebellar circuitry. To test this we investigated the functional consequences of a deficit of LTP at PF-PC synapses using L7-PP2B mice model. Hippocampal place cell properties of L7-PP2B mice were characterized during free exploration of a circular arena. In contrast to mice lacking cerebellar LTD, place cell properties of L7-PP2B mice were not impaired when mice had to rely on self-motion cues. Surprisingly, L7-PP2B place cells displayed instability in the absence of any proximal cue manipulation in 20 % of the recording sessions, characterized by a coherent angular rotation of the whole set of recorded place cells. During these events, in which the spatial relationships between the object and the mouse spatial representation are changed, mice displayed an increased exploration of the object, suggesting that for the mouse the object was located at a new position. These data suggest that, in the absence of cerebellar LTP, hippocampal spatial representation cannot be reliably anchored to the prominent external cue. These results along with those from L7-PKCI mice, indicate that the cerebellum contributes to both hippocampal representation and subsequent navigation abilities and that LTP and LTD are likely to play different roles in these processes.

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Large-scale sensory integration during a sensory detection task in the mouse

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Résumé

Sensory perception leading to adapted behavior requires the integration of sensory signals across multiple inter-connected cortical areas, with primary sensory areas that should signal the nature of the sensory stimulus, motor area the motor output and higher-order areas the valence of the stimulus. To better understand the integration of sensory signals across cortical areas, we have recorded sensory evoked potential (SEP) using simultaneous local field potential recordings from the barrel field of the primary somatosensory area (S1), the secondary somatosensory area (S2), the primary motor area (M1), the parietal area (PtA), the medial prefrontal cortex (mPFC) and the dorsal hippocampus (dCA1). SEPs were recorded in mice during the learning and the execution of a whisker-based sensory detection task. The mice were water-restricted and trained to lick a water spout in response to a small passive whisker stimulation in order to obtain a drop of water as a reward. Mice could learn this task within 7-10 days of daily training session. We found that SEPs could be recorded in all cortical areas under investigation with increasing latencies from S1, S2, M1, PtA, dCA1 and mPFC. When comparing successful (Hit) with unsuccessful (Miss) trials in animals that have learned the task, we found higher amplitude of the early sensory response for Hit trials in mPFC, dCA1 and to a lesser extend M1, but little difference in S1, S2 or PtA. The same comparison during the first training days, when the mice are not yet performing, yielded to little or no difference in any cortical area. As the mice learn the task, we observed a pronounced increase of the SEP for Hit trials in mPFC and dCA1. Our results suggest that mPFC and dCA1 could signal the relevance of the sensory stimulus in the context of a well define behavior, whereas S1 and S2 responses would be more constrained by the nature of the stimulus.

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Functional plasticity in the cerebello-cortical pathway in experimental Parkinson's disease

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Résumé

The cerebellum, together with the basal ganglia, constitutes a major subcortical afferent structure of the motor cortex. In Parkinson's disease, a classical basal ganglia disorder, major functional changes take place in the basal ganglia-thalamo-cortical pathways in patients. In contrast, alterations of the cerebellum and of the cerebello-cortical pathway have been less studied in this disease. In our study, we analyzed the neuronal activity of the cerebellar nuclei, which form the output gateway of the cerebellum, and of the motor cortex, and we examined the influence of the cerebellum on motor cortex activity in a 6-hydroxydopamine (6-OHDA) animal model of Parkinson's disease. Extracellular recordings of the cerebellar nuclei units revealed a mild decrease in the firing rate of cells in 6-OHDA-lesioned rats, but no significant change in cerebello-thalamic projections neurons. In contrast, we observed a clear reduction in neuronal activity in the motor cortex in these animals. Unexpectedly, this reduction was reversed by pharmacological inactivation of the cerebellum, thus revealing an abnormal inhibitory effect of the cerebellum on motor cortex activity in 6-OHDA-lesioned rats. Altogether, these results demonstrate that the cerebello-cortical pathway is the site of major functional remodelling following the loss of midbrain dopaminergic neurons.

*Intervenant

Integration of silicon-based probes and micro-drive array for chronic recordings of large populations of neurons in behaving animals

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Résumé

In the 1940's, Donald Hebb hypothesised that neuronal assemblies distributed across multiple brain structures are the functional units of processing in the mammalian brain. This proposition has led to the challenge of recording the activity from neuronal populations to study neural circuit functions in relation to behaviour. Extracellular recordings of action potentials is a major technique used in neuroscience and it has led to major discoveries, including the orientation selectivity of neurons in the primary visual cortex and the identification of place cells in the hippocampal formation. In the last decades, new approaches have been developed to record from an increasingly larger number of neurons simultaneously in behaving animals. Among these approaches, the use of micro-drive arrays has proven efficient for reliable chronic recordings of groups of neurons from one or multiple brain structures with wire electrodes. More recently, the emergence of electrode-dense silicon probes gives the opportunity for larger scale recordings. Our aim is to develop a new system for chronic large scale distributed recordings by combining the advantages of the micro-drive array and silicon probe approaches. The system is based on a new design of silicon probe that is long and flexible, which allows it to be inserted in a custom-made micro-drive array. The array can carry up to 16 individually movable probes with 16 recording sites each. The complete device can be chronically implanted in rats and is easily recycled. We present the advancements in the development of this system and the first recordings that were acquired from the hippocampal formation in a freely moving rat.

*Intervenant

Etude de l'activité des cellules pyramidales de CA1 de l'hippocampe chez la souris naviguant dans un environnement virtuel.

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Résumé

En 1971, O'Keefe & Dostrovsky découvre dans l'hippocampe des neurones qui modulent leur fréquence de décharge en fonction de la position de l'animal dans son environnement. Ils les appellent " cellules de lieu " car la localisation de l'animal dans l'environnement est le meilleur corrélat de leur décharge. Lorsqu'un environnement familier est modifié certaines cellules de lieu activées avant les changements deviennent silencieuses, et d'autres anciennement silencieuses deviennent actives. Nous ignorons quelles sont les propriétés intrinsèques et les entrées synaptiques permettant de définir si une cellule va être active dans un environnement donné.
On ne peut pas répondre à cette question en utilisant des techniques d'enregistrements extracellulaires car elles ne permettent d'enregistrer que les potentiels d'action émis par plusieurs neurones. C'est pourquoi il est nécessaire d'effectuer cette étude avec une technique d'enregistrement intracellulaire. Les enregistrements intracellulaires sont très difficiles à obtenir sur des animaux en comportement. Cependant il existe depuis peu une approche consistant à effectuer ce type d'enregistrement électrophysiologique sur des animaux ayant la tête fixée naviguant dans un environnement virtuel. Le travail que j'ai effectué au cours de de mon stage de M2 avait pour objectif de mettre en place un protocole expérimental utilisant la réalité virtuelle pour obtenir des enregistrements électrophysiologiques intracellulaires de la couche des cellules pyramidales de CA1 de l'hippocampe.

Nous montrons ici que les souris sont bien capables d'apprendre à courir dans un environnement virtuel tête fixée, en augmentant le nombre de récompenses récupérées et en augmentant leur vitesse de déplacement dans l'environnement virtuel. Nous montrons aussi que nos conditions expérimentales permettent l'obtention de différents enregistrements extracellulaires et intracellulaires de cellules dont la fréquence de décharge est modulée spatialement. Nos résultats suggèrent qu'il est possible que les souris codent l'environnement en s'appuyant plus sur les informations proprioceptives que sur les informations visuelles.
Mon projet de thèse serait d'utiliser et améliorer ce Protocol afin d'étudier les propriétés intrinsèque et synaptique des cellules pyramidales de la couche CA3 de l'hippocampe.

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Multichannel optogenetic stimulation for the study of cortical representations underlying sensory discrimination in mice

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Résumé

The development and refinement of multichannel stimulation techniques will allow the investigation of the causal role in behavior of the activation of specific subgroups of cells within a larger network. We have built a patterned photostimulation rig using an LED-based videoprojector. The optical system projects an 1280x800 pixel screen onto an area of about 2-by-3 mm, with a maximum intensity of 40 mW/mm2 for the blue LED (455 nm). Mice expressing ChR2 in excitatory cortical neurons can learn to discriminate between the activation of two different regions of auditory cortex with this system, as reported by a Go-No Go licking task. We are currently investigating how different stimulation parameters influence the rate of acquisition of this task. We plan to use this approach to study which aspects of the cortical representation of sounds are relevant for acquiring and expressing behavioral discrimination.

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Two Statistical Tests Built From Peri-Stimulus Time Histograms

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Résumé

The peri-stimulus time histogram (PSTH) is the most commonly used representation of the mean response of a given neuron to repeated stimulus presentations (Perkel, Gerstein & Moore, 1967, Neuronal spike trains and stochastic point processes. I the single spike train. Biophys J, 7:391-418). Several smoothing techniques have already been proposed to improve the statistical properties (essentially the expected root mean square error) of the estimated PSTH (e.g., Kass, Ventura & Cai, 2003, Statistical smoothing of neuronal data. Network: Computation in Neural Systems, 14(1):5–15) and methods for constructing pointwise confidence intervals have been presented (Pouzat and Chaffiol, 2009, Automatic Spike Train Analysis and Report Generation. An Implementation with R, R2HTML and STAR. J Neurosci Methods 181:119–144), but rigorous tests addressing the following two questions are, to our knowledge, still lacking:
- Is a given neuron responding to a given stimulus, that is, is the PSTH significantly non-flat?
- Are the responses of a given neuron to two different stimuli different?
We propose to address the first question by constructing a confidence band around the estimated PSTH, that is a region within which the true PSTH (the one we would estimate if we could repeat our stimulation an arbitrarily large number of times) will be entirely contained with a probability we can choose (e.g., 0.95 or 0.99). We propose to address the second question by looking at the difference between the PSTHs obtained with two different stimuli. We show that this difference, once properly scaled, convergences towards a Brownian motion under the null hypothesis that the two responses are identical. We then test the observed scaled difference against a standard Brownian motion.
The proposed method are easily implemented and our own implementation in Python will be used to analyze data from the first olfactory relay of an insect, the cockroach Periplaneta americana.

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SPySort

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Résumé

Neuroscientists use extracellular recordings to monitor many neurons while keeping tissue damage at a minimum. But the collected raw data are then mixtures of activities—from many neurons—that have to be separated or sorted before most physiologically relevant questions can be addressed. Sev- eral spike sorting methods have not surprisingly been proposed over time and we implement here, as a Python package, an extension of the method described in [1]. The SPySort package takes advantage of the Numpy arrays and statistical tools, Matplotlib plot functions, Scipy signal processing and statistical modules and the Scikit-learn k-means and Gaussian Mixture model. In addition, some of the Pandas methods are used to provide some robust statistical tools. By exploiting all the aforementioned Python packages, SPySort is a flexible and easy-to-use environment for spike sorting. SPySort consists of five modules. The first module provides methods for reading, normalizing, subset- ting raw data—i.e. selecting specific recording channels—as well as a summary method returning all the important statistics of the raw data. The second module takes care of spikes detection and also includes methods for filtering the data. The third module extracts events—i.e. makes cuts on the raw data around the locations of the detected spikes. The next module performs clustering after an optional dimension reduction using PCA. The user can choose among three presently implemented clustering al- gorithms: k-means; Gaussian Mixture model; Bagged clustering. The end result of this clustering stage is a set of waveforms associated with the different identified neurons. The last stage goes back to the raw data (or to the next chunk of recorded data) and resolve all detected events including the superposed ones. A new fast and efficient sampling jitter correction algorithm is used at that stage. SPySort has its own github place at: https://github.com/gdetor/SPySort

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Characterisation of the interaction between the nucleus reuniens and the hippocampus in anaesthetised rats

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Résumé

The nucleus reuniens (RE) is a thalamic nucleus relaying the information between the prefrontal cortex and the hippocampus (HPC). Although numerous anatomical and lesional studies suggest that the RE displays a key role in memory functions in which the HPC and prefrontal cortex are involved, its functional interactions with both structures are poorly understood. In order to bridge the structural and functional levels of integration, we recorded the interaction (LFPs and uniti activities usung 32-sites silicon probes) between the RE and the HPC in anesthetized rats during two brainstates: theta (THE) and slow oscillations (SO) episodes.

Our results show a brainstate-specific interaction between both structures: (1) during SO episodes, RE neurons fire high-frequency bursts of spikes and gamma oscillations in the RE appear comodulated with the ripple band in the stratum pyramidale of the HPC; (2) during THE episodes, a portion of RE neurons are entrained by hippocampal theta oscillations. Moreover, we observed a clear 9 Hz oscillation in the RE, which is highly coherent with the strata oriens and pyramidale of the HPC, whereas the RE projects in the lacunosum moleculare. This 9 Hz oscillation entrains the RE neurons and a portion of the CA1 neurons (putative principal cells and interneurons targeting the soma).

Altogether, our results suggest that the RE could provide a modulation of the HPC networks and could participate (1) to the expression of CA1 ripples during SO and (2) would bring an extra modulation of CA1 neurons during theta-related mechanisms. These results must now be confirmed in freely-moving animals in order to test the functional significance of such interaction.

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Neurons of the nucleus accumbens encode aversion and preference through specific gamma oscillations

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Résumé

Addiction can be viewed as a pathology of learning and memory, with the formation of persistent maladaptive memories. The main problem in treating addiction is the recurrent risk of relapse that greatly relies on drug-associated memories. In opiate addicts, the early aversive state of withdrawal motivates drug seeking and strengthens this pathological link and its well-known negative consequences. Hence, in abstinent individuals withdrawal memories is suggested to motivate drug seeking and relapse. Here we investigated the encoding and retrieval of these withdrawal memories. We used a conditioned placed aversion (CPA) protocol combined with chronic electrophysiological recordings in rats. We focused here on the nucleus accumbens (NAC) since it is the most sensitive structure for the acute withdrawal effects and reactivation of opiate withdrawal memories. Morphine dependence was induced by subcutaneous implantation of morphine pellets. Conditioned place aversion (CPA) took place in an unbiased Y-maze and withdrawal conditioning was performed by s.c. injections of naloxone 15μg/kg. Electrophysiological recordings were performed daily during the protocol. Local field potentials and single units have been analyzed through different methods (frequency-space position maps, phase locking, spindles extraction with wavelets transforms, time-frequency analyses). The NAC show prominent gamma range oscillations under the form of segregated spindles: low gamma (60Hz) and high gamma (90Hz). In the CPA paradigm, the behavioral responses showed a typical place aversion for the compartment associated with opiate withdrawal and a preference for the compartment associated with saline. Interestingly the contexts respectively associated with withdrawal (aversive context) or the absence of withdrawal (preferred context) present different gamma profiles. Aversive memory retrieval is associated with high gamma whereas safety is linked to low gamma. Conditioning results in an increase in context related information content at the level of single NAC neurons. We demonstrate here that NAC neurons differentially encode aversion and preference through specific gamma oscillations.

*Intervenant

Acute deprivation preserves diffuse thalamocortical connectivity in the developing barrel cortex

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Résumé

During development sensory cortex is formed as an array of columns each receiving, via thalamus the sensory input from the discrete region of sensory space. Classical model for the thalamocortical development is rodent's barrel system, where each whisker of the snout is represented by single cortical column, so called 'barrel' that gives the name for the corresponding part of somatosensory cortex – 'barrel cortex'. Early postnatal period in rodents is known as "criticial" period, during which formation of the topographic thalamocortical synapses critically depends on sensory input, and sensory deafferentation as well as manipulations with cortical activity result in formation of aberrant cortical maps. This means that sensory driven activity is extremely important in formation of cortical whiskers' representations. However, physiological activities which underlie this sensory-driven plasticity in the developing synapses during the critical period are still poorly understood. To answer this question we use deprivation model in the developing barrel system, when one or few whiskers were trimmed (acute deprivation) at the beginning of the critical period. Preliminary results demonstrate that acute deprivation is associated with persisted diffuse connectivity at the cortical level, meaning that single whisker evokes short latency cortical response both in the corresponding and in the deprived cortical columns. However, stimulation of the originally trimmed whisker (because of its physiological regrow) also evokes short latency cortical response in its corresponding cortical column. Thus in contrast to control animals, where end of critical period is associated with establishment of the adult like pattern of neuronal connectivity with precise thalamocortical connections (Mitrukhina, Suchkov et al., 2014), acute deprivation preserves 'diffuse' state of thalamocortical connectivity, where thalamic inputs overlap and compete for the cortical territories.

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Neural and behavioral discrimination of very brief acoustic vowels

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Résumé

The timbre of a sound plays an important role in our ability to discriminate between behaviorally-relevant auditory categories, such as different vowels in speech. Here, we investigated the neural representation of vowels in the primary auditory cortex (A1) of anaesthetized guinea-pigs, but with severely-impoverished timbre cues. Five different vowels were presented at durations ranging from 2ms to 128 ms. A psychophysical experiment involving human listeners showed that identification performance was near ceiling for the longer durations and degraded close to chance level for the shortest durations. This was likely due to spectral splatter, which reduced the contrast between the spectral profiles of the vowels (the main timbre cue here) at short durations. Using mutual-information estimates to analyze the neural recordings, we found that auditory cortical neurons of A1 could be used to reliably identify several vowels for all durations. Information carried by individual cortical sites was low on average, but the population code was accurate even for durations where human behavioral performance was poor. These results suggest that a placpopulation code is available at the level of A1 to encode spectral-profile cues for very short sounds. But, at least for vowels and for human listeners, some of this information may be disregarded, perhaps in the interest of categorical perception.

*Intervenant

Role of the Cerebellum in sensory prediction during voluntary movement : the case of the vestibular system

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Résumé

The ability to orient and move in space (navigate) is underpinned in mammals by a complex network of brain structures integrating information from different modalities. Extensive evidence from inner ear injury have emphasized the role of the vestibular system in mammalian navigation. However most neurophysiological studies of vestibular function have failed to adequately understand phenomena observed in the context of active movements such as sensory anticipation. Other evidence suggests the existence of an inhibitory prediction signal received by vestibular neurons of the pons during self-generated movements (Roy and Cullen, 2004). The vestibulo-cerebellum might ideally fullfil the role of generating such prediction signals. The aim of our work is to identify the nature of transformations taking place in the vestibulo-cerebellum during spontaneous movements in awake animals. We designed an implantable headstage allowing us to monitor head movements while recording multiunit activity in the vestibulo-cerebellum. Linear acceleration and angular velocity of the head are measured using a 6-axis microelectromechanical system (MEMS), providing a direct quantification of inertial signals transduced by the animal's inner ear. The activity of groups of Purkinje cells is recorded using tetrodes implanted in the nodulus, the vermal part of the vestibulo-cerebellum.

*Intervenant

Characterisation of an anatomical and functional circuit between the cerebellum and the hippocampus underlying navigation in mice

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Résumé

Our ability to navigate efficiently in an environment requires the use of a reliable internal representation of the external world. Such a cognitive map is formed in part in the hippocampal system. The hippocampus contains specialized pyramidal neurons (named place cells) that fire at specific location of the environment and gives dynamic information about self-location relative to the external world. The activity of these cells is controlled by multi sensory inputs combining external information (such as visual, auditory, olfactory and tactile cues) and inputs generated by self-motion (i.e. optic flow, proprioceptive and vestibular information), involving a large network of structure that interact with the hippocampus to optimize spatial coding. Our recent data suggest that the cerebellum belongs to such network. Indeed, a lack of plasticity in the cerebellum leads to a deficit in hippocampal spatial coding, specifically when mice have to rely on self-motion cues (Rochefort et al., 2011). Although this strongly suggests that the cerebellum interacts with the hippocampus to optimize spatial representation and navigation, the anatomo-functional substrate of this interaction remains unknown. In our current work, using transynaptic tracers, we have identified an anatomical pathway that links the cerebellum to the hippocampus. Moreover, we have designed a new behavioral task enabling to record electrophysiological activity during both foraging and goal-directed behavior. We have investigated synchronized oscillations between the cerebellum and the hippocampus in normal condition as well as in L7-PKCI transgenic mice lacking long-term depression at cerebellar parallel fiber-Purkinje cell synapses.

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VINCENT	Marion	INRIA, Sophia-Antipolis
WATSON	Thomas	
WESTPHALEN	Rikke	Lundbeck, Denmark
WIEBE	Sherman	EXHIBITOR – Plexon
WILLIAMS	Mark	ICM, Paris
XU	Hao	Collège de France, Paris
ZHANG	Lu	IBPS, Paris
ZUGARO	Michaël	Collège de France, Paris