GDR Multielectrode Systems & Signal Processing for Neuroscience

4th Congress

Bordeaux 17-18 Oct. 2013

Proceedings

Thursday, October 17, 2013

Time	Event
8:30 am - 9:00 am	Welcome
9:00 am - 12:00 pm	**Development & Methodology - Chair: Sylvie Renaud & Alexander Kuhn**
9:00 am - 10:00 am	**From passive to active electrode arrays: neuroelectronics for large-scale neural interfacing - Luca Berdondini (Genova, Italy)**
10:00 am - 10:25 am	Explore your MEA data with NeuroMap - Florent Bocquelet
10:25 am - 11:50 am	Coffee break / Posters
10:50 am - 11:15 am	Diamond Micorelectrode for Neural Interfacing - Clément Hébert
11:15 am - 11:40 am	DSS: a "swiss army knife" method for multichannel data analysis - Alain de Cheveigné
11:40 am - 12:00 pm	Tuning the porosity of microelectrode arrays to improve extracellular recording of neural networks - Laurent Bouffier
12:00 pm - 1:00 pm	Sponsors - Sponsors
1:00 pm - 3:00 pm	Lunch / Posters
3:00 pm - 6:00 pm	**Motor system & Cognition - Chair: Thomas Boraud & Karine Guillem**
3:00 pm - 4:00 pm	**Reading rat's minds: imagination and decision-making - David Redish (Minneapolis, USA)**
4:00 pm - 4:30 pm	Subthalamic Nucleus Encodes Appetitive and Aversive Reinforcers, Execution Error and Reward Prediction Error, in Rat - Emmanuel Breysse
4:30 pm - 5:00 pm	Coffee break / Posters
5:00 pm - 5:30 pm	Real-time decoding of sensory, cognitive and motor variables from prefrontal population activity: susceptibility to the sensory and cognitive context - Suliann Ben Hamed
5:30 pm - 6:00 pm	Canceling actions involves a race between basal ganglia pathways - Robert Schmidt
6:00 pm - 7:00 pm	General Meeting - GDR
7:30 pm - 10:30 pm	Gala - Reception at Chateau Luchey-Halde Winery

Friday, October 18, 2013

Time	Event
9:00 am - 12:00 pm	**Network Dynamics - Chair: Cyril Dejean & Nicolas Mallet**
9:00 am - 10:00 am	**Network dynamics in psychiatric disease models - Joshua Gordon (New York, USA)**
10:00 am - 10:30 am	LFP and unit recordings in human and monkey: identification and dynamics of excitatory and inhibitory units in relation to LFPs - Alain Destexhe
10:30 am - 11:00 am	Coffee break / Posters
11:00 am - 11:30 am	Large scale imaging of hippocampal network dynamics in the adult mouse in vivo. - Vincent Villette
11:30 am - 12:00 pm	Neuronal signatures of aversive memories - Cyril Dejean
12:00 pm - 1:30 pm	Lunch / Posters
1:30 pm - 4:30 pm	**Neuronal Code - Chair: Cyril Herry & Stéphane Valerio**
1:30 pm - 2:30 pm	**Cell assembly flickering during spatial learning - Jozsef Csicsvari (Klosterneuburg, Austria)**
2:30 pm - 3:00 pm	Operant conditioning of single units in rat motor cortex allows graded control of a prosthetic device - Valérie Stengel
3:00 pm - 3:15 pm	Coffee break / Posters
3:15 pm - 3:45 pm	Reading the population code of the retina - Olivier Marre
3:45 pm - 4:15 pm	Odor discrimination requires proper olfactory gamma oscillations in awake mice. - Gabriel Lepousez
4:15 pm - 4:45 pm	Concluding Remarks - Bernard Bioulac

Thursday October 17th - Morning session

Keynote Speaker:

Luca Berdondini (Genova, Italy)

From passive to active electrode arrays:
neuroelectronics for large-scale neural interfacing

Explore your MEA data with NeuroMap

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Visualizing MEA data is important to understand the detailed dynamics of neural networks. We thus developed NeuroMap, a highly interactive C++/Qt software for spatiotemporal representation of multielectrode (MEA) data, freely downloadable from https://sites.google.com/site/neuromapsoftware/. Neuromap provides several ways to visualize MEA data, including time curves, color-coded spatiotemporal representations, and spatial maps. To construct maps (of either voltage values or surface laplacians estimating current source densities), Neuromap uses thin plate spline interpolation to estimate values between the electrodes. Tools for image registration based on moving least squares allow overlying maps on anatomical images and immunohistochemical labeling. Maps can be further thresholded using simple statistical approaches to visualize only significant activity patterns. Tools are also included for multiple experiments merging by data reinterpolation based on image registration. Data visualization can be exported as single maps, time-series of maps, or movies. The user interface is customizable, allowing resizing, rearranging, or tab-stacking toolboxes and windows.

Tuning the porosity of microelectrode arrays to improve extracellular recording of neural networks

Heim Matthias [1], Rousseau Lionel [,2], Reculusa Stéphane [1], Urbanova Veronika [1], Mazzocco Claire [,3], Joucla Sébastien [,3], Bouffier Laurent [1], Vytras Karel [,4], Bartlett Philip [,5], Kuhn Alexander [1*], Yvert Blaise [,3*]

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Microelectronics fabrication technologies allow building high-density microelectrode arrays (MEAs). However, decreasing the size of the microelectrodes may become a limiting factor. Indeed, the intrinsic noise level of a microelectrode dramatically increases when the size becomes smaller than typically 20-µm in diameter. In the context of neural activity, we propose to overcome this limitation by using a template-based macro-/mesoporous modification of the microelectrodes, combining the advantages of a small geometric surface with an active surface increased by several orders of magnitude. For this purpose, platinum MEAs were covered with a highly porous platinum overlayer obtained by lyotropic liquid crystal templating possibly in combination with a microsphere templating approach. These porous coatings were mechanically more robust than Pt-black coating and exhibited a noise level ~3 times smaller than that of conventional flat electrodes. This approach can thus be used to build dense arrays of small-size microelectrodes for sensitive neural signal detection.

Diamond Micorelectrode for Neural interfacing

Hébert Clément [1*], Scorsone Emmanuel [1*], Rousseau Lionel [,2*], Mazellier Jean Paul [,3*]

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Several microelectrode materials have been proposed to interface the neural system. Many of those materials have led to impressive neurointerfacing applications. Nevertheless there is still a demand for novel stable and biocompatible materials: the stability of most of the current MEA systems are often affected by inflammatory reactions once they are implanted in vivo.

Diamond is one material that may meet this demand. Indeed in vivo studies revealed very promising biocompatibility properties of the diamond since no major glial layer formation was observed at the diamond surface.
We developed diamond microelectrode arrays on glass for in vitro studies as well as on flexible substrates for in vivo applications. The MEAs were all characterized in PBS in order to evaluate their potential electrochemical windows, impedances and charge injection limits.

We also performed studies exploring surface treatments for the modification of the microelectrodes. They appeared to improve the diamond microelectrode electochemical properties,

Thursday October 17th - Afternoon Session

Keynote Speaker:

David Redish (Minneapolis, USA)

Reading rat's minds: imagination and decision-making

Subthalamic Nucleus Encodes Appetitive and Aversive Reinforcers, Execution Error and Reward Prediction Error, in Rat

Breysse Emmanuel [1], Baunez Christelle [,2*]

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Recent electrophysiological studies have shown that neurons of the subthalamic nucleus (STN) respond differently to predictive cues and at delivery of various rewards (sucrose...) (Lardeux et al, 2009). However, these studies focused on reinforcing agents having only a positive expected value. It was therefore important to assess the responses of STN on the presentation of aversive reinforcing agents like quinine, a bitter compound avoided by rats.
We have thus recorded STN neurons in a behavioral paradigm allowing the recording of neuronal reactivity in expectation and delivery of predicted rewards.
Our results show when quinine replaced sucrose, the specialization in the neuronal response to the cue was reorganized. We have also shown that the STN shares, in part, the encoding function of reward prediction error of dopaminergic neurons. These results consolidate the role of STN in motivation, and provide additional insight on how it contributes to motivational information processing.

Real-time decoding of sensory, cognitive and motor variables from prefrontal population activity: susceptibility to the sensory and cognitive context

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A prerequisite for the success of cognitive Brain Machine Interfaces (interfaces driven by cognitive brain content), is the capacity to access a reliable estimation of cognitive variables, irrespectively of changes in the sensory environment or internal drives and goals. We approach this issue by introducing 1) visual changes in a stable cognitive context and 2) changes in the cognitive demands, in an otherwise stable sensory context, while decoding in real-time visual-, cognitive- and motor-related processes from non-human primate prefrontal neuronal population multi-unit activity (MUA, 48-contacts, in frontal eye fields).
We show that in spite of the fact that changes in both the sensory and cognitive context induce short-term plasticity in the prefrontal sensory, cognitive and motor maps, decoding performance (percentage correct real-time classification) remains well above chance. This study both increases our understanding of dynamical coding within the prefrontal cortex and opens the way to cognitive brain machine interfaces.

Canceling actions involves a race between basal ganglia pathways

Schmidt Robert [1,2], Leventhal Daniel [3], Mallet Nicolas [1], Chen Fujun [1], Berke Joshua [1]

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Salient cues can prompt the rapid interruption of planned actions. It has been proposed that fast behavioral inhibition involves specific basal ganglia pathways, and we tested this by comparing activity in multiple rat basal ganglia structures during performance of a stop-signal task. Subthalamic nucleus (STN) neurons showed low-latency responses to Stop cues, irrespective of whether actions were successfully canceled or not. By contrast, neurons downstream in the substantia nigra pars reticulata (SNr) responded to Stop cues only in trials with successful cancellation. Recordings and simulations together indicate that this sensorimotor gating arises from the relative timing of two distinct inputs to neurons in the SNr dorsolateral «core» subregion: cue-related excitation from STN and movement- related inhibition from striatum. Our results support race models of action cancellation, with successful stopping requiring Stop cue information to be transmitted from STN to SNr before increased striatal input creates a point of no return.

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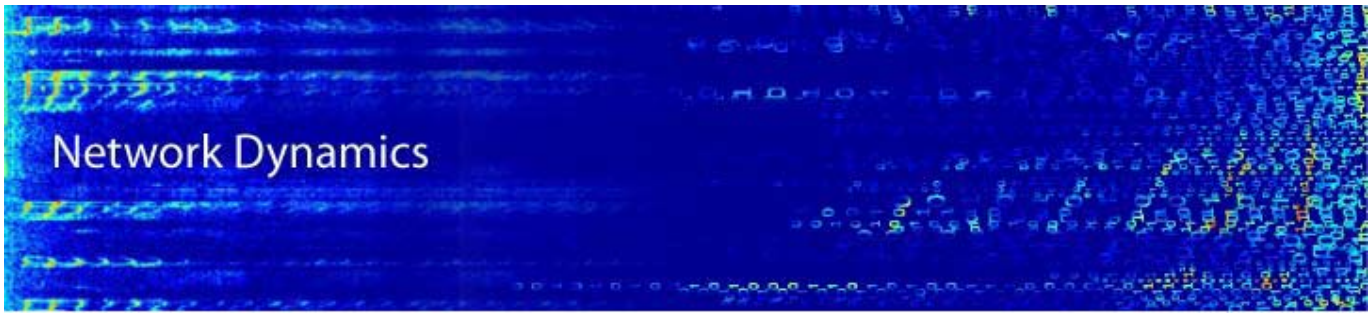

Keynote Speaker:

Josh Gordon (New York, USA)

Network dynamics in psychiatric disease models

LFP and unit recordings in human and monkey: identification and dynamics of excitatory and inhibitory units in relation to LFPs

Destexhe Alain [1], Telenczuk Bartosz [1], Dehghani Nima [,2], Le Van Quyen Michel [,3], Cash Syd [,4], Halgren Eric [,5], Hatsopoulos Nicho [,6]

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We report results from an analysis of Utah array (NeuroPort) recordings in human temporal cortex and monkey motor cortex. The high density of the arrays permits to identify direct connections between pairs of units, proving their excitatory or inhibitory nature. We followed the dynamics of excitatory and inhibitory neurons, which were tightly balanced in all states, from wakefulness and sleep. The firing of inhibitory neurons was particularly related to oscillatory behavior, with many interneurons firing phasically with beta and gamma oscillations. Sleep delta waves were associated with "Up" and "Down" states in both cell types. In some cases, it was possible to see the effect of single units on the LFP, which we compare to the "unitary LFPs" identified in vitro. We conclude that, because of their high density, Utah arrays are a unique tool to distinguish excitatory and inhibitory neurons, and infer their dynamics during wake and sleep states.

Large scale imaging of hippocampal network dynamics in the adult mouse in vivo.

Villette Vincent [1], Malvache Arnaud [1], Tressard Thomas [1], Cossart Rosa [1]

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The main functions of the hippocampus are to support navigation and memory. It is hence well established that the activity of single hippocampal neurons is modulated by spatial location. However, how the functional organization of spatially modulated neuronal assemblies evolves when changing external cues remains unknown. Here, we have adapted a previously described chronic window on the brain (Dombeck etal. 2010) to allow for large scale calcium imaging from hundreds of CA1 neurons simultaneously in head restrained adult mice. Mice are free to run on a treadmill allowing for self-paced changing of tactile cues while network oscillations are simultaneously recorded.. The number and type of tactile cues provided on the treadmill were sequentially changed while imaging network dynamics with a genetically encoded calcium indicator (GCaMP5G). We show that the activity of CA1 neuronal assemblies is modulated by time, location / distance depending on the external cues provided on the treadmill.

Opiate dependence induces network state shifts in the limbic system.

Dejean Cyril [1,2], Boraud Thomas [3,4], Le Moine Catherine [1,2]

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The hedonic homeostasis dysregulation theory of addicion predicts that brain reward systems, particularly the mesolimbic dopamine system, switch from a physiological state to a new «set point». In opiate addiction, dopamine system principal targets, prefrontal cortex (PFC), nucleus accumbens (NAC) and basolateral amygdala complex (BLA) also adapt to repeated drug stimulation. We investigated the impact of chronic morphine on the PFC-NAC-BLA network dynamics with simultaneous electrophysiological recordings in freely-moving rats subcutaneously implanted with continuous-release morphine pellets. Chronic morphine produced a shift in the network state correlated with behavioral changes. Network activity and state appeared to normalize after two days. Blockade of μ opioid receptors was nonetheless sufficient to disrupt this acquired stability. In line with the homeostatic dysregulation theory of addiction, we show that the PFC-NAC-BLA network of the dependent brain is characterized by a de novo balance for which the drug of abuse becomes a main contributor.

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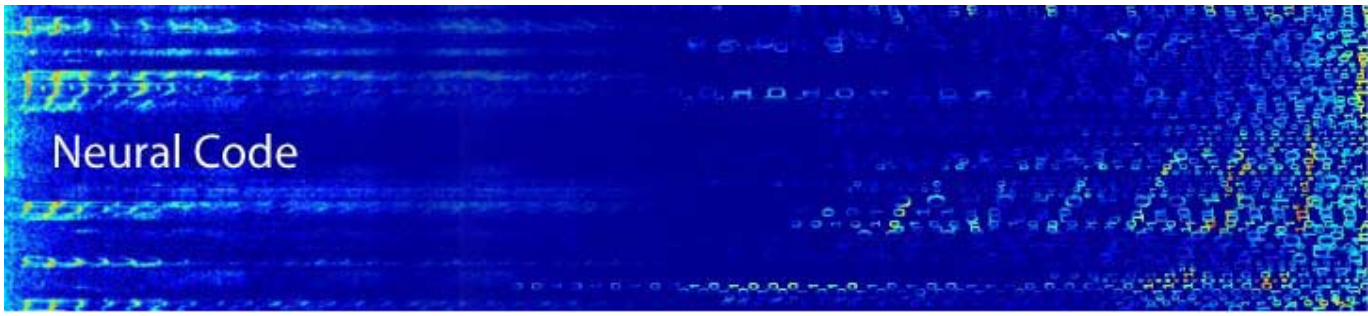

Keynote Speaker:

Josef Csicsvari (Klosterneuburg, Austria)

Cell assembly flickering during spatial learning

Operant conditioning of single units in rat motor cortex allows graded control of a prosthetic device

Stengel Valérie [1], Arduin Pierre-Jean [1], Shulz Daniel [1*], Frégnac Yves [1*]

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Brain-machine interfaces use neuronal activity to control prostheses, with the long term goal of restoring motor abilities to impaired subjects. Here, several motor cortex neurons were recorded simultaneously in head-fixed awake rats and were trained, one at a time, to modulate their firing rate up and down in order to control a one-dimensional actuator carrying a water bottle. The goal was to maintain the bottle in front of the mouth, allowing the rat to drink. All conditioned neurons adapted their firing rate to the instantaneous bottle position so that the drinking time was increased relative to chance. The mean firing rate averaged over bottle trajectories depended on position. The conditioned neuron reacted faster and led to a better control than if bottle trajectories were simulated using the activity of simultaneously recorded surrounding neurons. Our study demonstrates that conditioning single neurons is a suitable approach to control a prosthesis in real-time.

Reading the population code of the retina

Marre Olivier [1], Tkacik Gasper [,2], Mora Thierry [,3], Simmons Kristy [,4], Berry Michael [,5]

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We recorded a large population of the retinal output while displaying a bar moving randomly. We show that the bar position can be reconstructed from retinal activity with a precision in the hyperacuity regime using a linear decoder acting on 100+ cells. Instead of a moving hill of activity, ganglion cells employed a sparse and distributed code to represent the object's trajectory, with both ON and OFF cells contributing significantly and cells responding to motion far in their surround. As a result, decoders based on the receptive field did not perform as well, in part because the classical receptive field did a poor job predicting ganglion cell responses. Population redundancy was high, but could be predicted from the information conveyed by individual cells. This uniform redundancy allowed for diverse collections of ganglion cells to represent high-accuracy motion information in a form easily read out by downstream neural circuits.

Odor discrimination requires proper olfactory gamma oscillations in awake mice.

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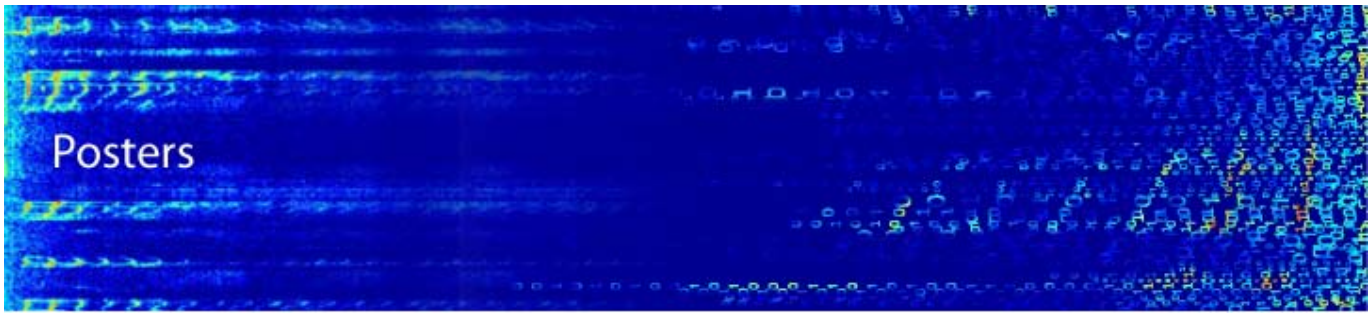
Gamma oscillations are commonly observed in sensory brain structures, notably in the olfactory bulb. The mechanism by which gamma is generated in the awake rodent and its functional significance are still unclear. We combined pharmacological and genetic approaches in the awake mouse olfactory bulb to show that that gamma oscillations required the synaptic interplay between excitatory output neurons and inhibitory interneurons. Gamma oscillations were amplified or abolished following optogenetic activation, or selective lesions to the output neurons of the olfactory bulb. In response to a moderate increase of the excitation/inhibition ratio in output neurons, long-range gamma synchronization was selectively enhanced while the mean firing activity and the amplitude of inhibitory inputs both remained unchanged in output neurons. Nevertheless, enhancing olfactory bulb gamma synchronization during an olfactory learning task impaired odor discrimination. Thus, an optimal level of neuronal gamma synchronization is necessary for the correct discrimination of similar sensory stimuli.


Posters

Surprise Decoding in the Retinal Activity

Deny Stéphane [1*], Picaud Sege [1], Macé Emilie [1], Tkacik Gasper [,2], Mora Thierry [,3], Marre Olivier [1]

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A fundamental task of the brain is to make predictions about the future, and thus to signal any violation of this prediction. Electroencephalogram recordings have indeed shown a brain response to unexpected changes among repeated stimuli. While this signaling of surprise was first measured in the cortex, recent work has shown that the retina might already be involved in surprise detection. In this work, we compared different decoding techniques to obtain a surprise representation from the retinal activity, while submitting the retina to a complex visual scene. Experimentally, we projected the movie of a bar animated by a natural motion on a rat retina. We recorded the ganglion cells of the retina with a multi-electrode array (60 microns spacing, 252 electrodes) in order to obtain a nearly complete representation of the retinal output. We eventually showed that surprise could be very well decoded from the retinal activity with linear decoding.

Expicit memory creation during sleep: a causal role of place cell on navigation

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It is now widely accepted that sleep is important for the consolidation of preexisting memory traces. Here we show that a place preference task can be learned during sleep without prior waking experience. We design a protocol to trigger during sleep, intracranial rewarding stimulations by the action potentials of a unique hippocampal place cell. After awakening, animals went and stayed within the associated place field. These results show that it is possible to create an artificial explicit memory during sleep and that this memory trace is used during subsequent waking period to drive a goal directed behavior. Moreover, it demonstrates the causal role of place cells on the mental representation of space as hippocampal cell assemblies still thus conveyed the same spatial information during sleep and wakefulness.

Generation of locomotor-like activity in the isolated rat spinal cord by electrical microstimulations driven by an artificial CPG

Joucla Sébastien [1], Ambroise Matthieu [1,2], Levi Timothée [1,2], Lafon Thierry [1], Chauvet Philippe [1], Rousseau Lionel [1,3], Lissorgues Gaëlle [1,3], Saighi Sylvain [1,2], Bornat Yannick [1,2], Lewis Noëlle [1,2], Renaud Sylvie [1,2], Yvert Blaise [1]

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Neural prostheses may restore functions following lesions of the central nervous system (CNS). Here, we address this challenge in the neonatal rat spinal cord isolated ex vivo. Microelectrode arrays were inserted in the lumbar region to determine optimal stimulation sites to elicit elementary bursting patterns on L2/L5 ventral roots. An artificial CPG implemented on FPGA was built to generate alternating activity and was hybridized to the living spinal cord to drive electrical microstimulation on pre-identified sites. Using this strategy, sustained left-right and flexor-extensor alternating activity on bilateral L2/L5 ventral roots could be generated, comparable to locomotor-like activity elicited by pharmacological application. These results are a first step toward hybrid artificial/biological solutions for the restoration of lost functions in the injured CNS.

From learning-set to task-set in macaque monkeys

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In our changing environment, it is necessary to behave in a flexible manner to produce optimal outcomes given changing contingencies. How is this flexibility implemented, and what are its neural correlates? We developed a monkey equivalent of the 'Task-Set Manipulation' task (Collins & Koechlin,2012). In the training phases of the task, 3 monkeys learned by trial and error stimuli-targets associations in a stochastic environment (invalid feedback given in 10% of trials). This means that transitions between exploration and exploitation can only be triggered by a continuous checking of environmental information, and not solely by a single feedback, promoting flexibility of behaviour.
Monkeys adapted their responses to this environment and showed the formation of a learning-set, a strategy that allows efficient learning of problems. We also show the level of transfer of this learning-set to the 'task-set' version of the task in which mappings but not stimuli are changed.

Interaction between the basal ganglia and the cerebellum in songbirds.

Pidoux Ludivine [1], Leblois Arthur [1*]

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Vocal learning involves the basal ganglia (BG)-thalamo-cortical and the cerebello-thalamo-cortical network in humans. These loops interact together in mammals, but the role of their interaction during sensorimotor learning remains undetermined.
Songbirds have a BG-thalamo-cortical circuitry dedicated to song learning. A cerebellar projection to the thalamic region adjacent to the song-related thalamic nucleus receiving BG input (DLM) suggests that the BG and cerebellum interact during song learning. We are studying this interaction.
We confirmed the anatomical connection from the deep cerebellar nuclei to the song-related BG nucleus via a thalamic region adjacent to DLM. We show that this pathway is functional: electrical stimulation in the deep cerebellar nuclei evoked fast excitatory responses in pallidal neurons, consistent with a disynaptic pathway.
Our results suggest that the cerebellum is involved in song learning through its interaction with the song-related BG, providing a unique model to study the interactions between cerebellum and BG.

Uncertainty and checking for reward: monkey behaviour and prefrontal neurophysiology

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Understanding how we monitor uncertainty and decide between alternatives is a crucial aspect of assessing the question of adaptive and flexible behaviour. Reducing uncertainty requires searching and verifying for new or additional information. The underlying neurobiological bases of such monitoring process are as yet poorly understood.
Here, we used a double-task design to investigate behavioural and neurophysiological aspects of monitoring performance and checking. Monkeys had to perform a 2 forced-choice categorization task in which uncertainty (i.e. difficulty) is manipulated from trial to trial. In parallel, they were also offered the opportunity to track the imminence of the future delivery of a bonus reward.
Behavioural analysis showed that monkeys expressed (1) different levels of uncertainty reflected in markers of hesitation, and (2) an adaptive checking behaviour modulated by the distance to the bonus reward. Preliminary single-unit recordings in prefrontal cortex revealed also markers of uncertainty and self-initiation of checking.

High-frequency oscillations in human and monkey cortex during sleep

Le Van Quyen Michel [1*], Muller Lyle [,2*], Dehghani Nima [,3], Cash Syd [,4], Halgren Eric [,5], Hatsopoulos Nicho [,6], Destexhe Alain [,2*]

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With 100-electrode Utah arrays (4×4 mm) in human and monkey, we analysed spontaneous high-frequency LFP oscillations (>20 Hz) in the neocortex during wakefulness and the different stages of sleep. In both monkey and humans, in all states, we found spatially coherent beta (20-35 Hz) and gamma range (40-80 Hz). We applied phase-based analysis methods to precisely quantify the propagation of these patterns. We found that beta oscillations are strongly phase-locked with near zero phase lag. In contrast, gamma oscillations formed waves of activity that propagate over the array (~30 cm/s). After separation of units between «regular-spiking» (RS) and «fast spiking » (FS) neurons based on spike waveform, we found a strong increase in FS firing during beta/ gamma patterns. Furthermore, correlated firings of spatially distant neurons (>1 mm) were detected during these high-frequency patterns. We conclude that beta/gamma waves organize and modulate cortical population activity over large-scale patches of cortex

Role of astrocytes connexin in the regulation of sleep oscillatory pattern

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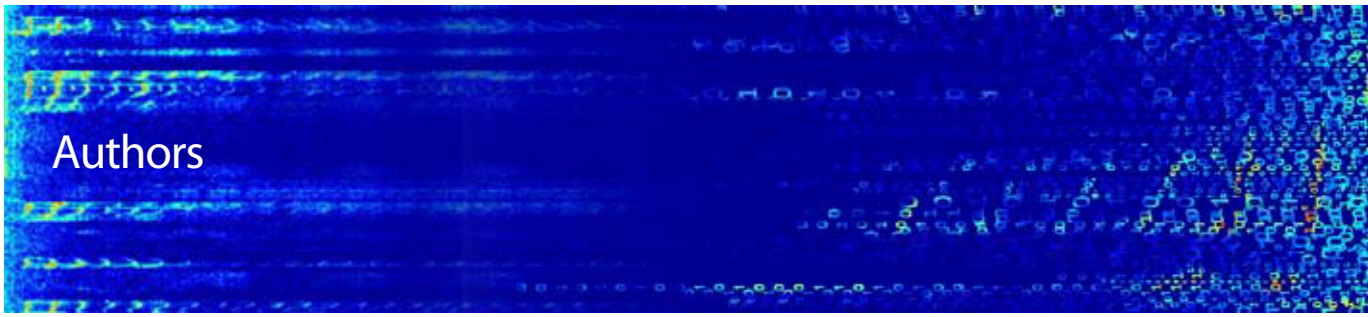
Coordination across brain structures is thought to be crucial for memory consolidation and our project aims at challenging the classic «neurocentric» view of brain rhythms regulation during sleep. Indeed, recent evidences showed that astrocytes can regulate cortical slow oscillations during sleep and are involved in brain processes related to memory deficits induced by sleep deprivation, both mechanisms being mediated by A1 adenosine receptors.
Astrocytes express connexins that form either hemichannels or gap junction, and we therefore investigated their role in the fine regulation and coordination of oscillations during natural sleep, by multi-site recordings in wild-type mice or transgenic mice double knock-out for astrocytic connexins Cx43 and Cx30 (dKO).
Our results shows that there is a massive decrease of slow oscillations during sleep in dKO mice in olfactory bulb, confirming the results obtained in vitro by Lisa Roux, supporting the involvment of astrocytes in regulation of neuronal network functioning and brain oscillatory activity.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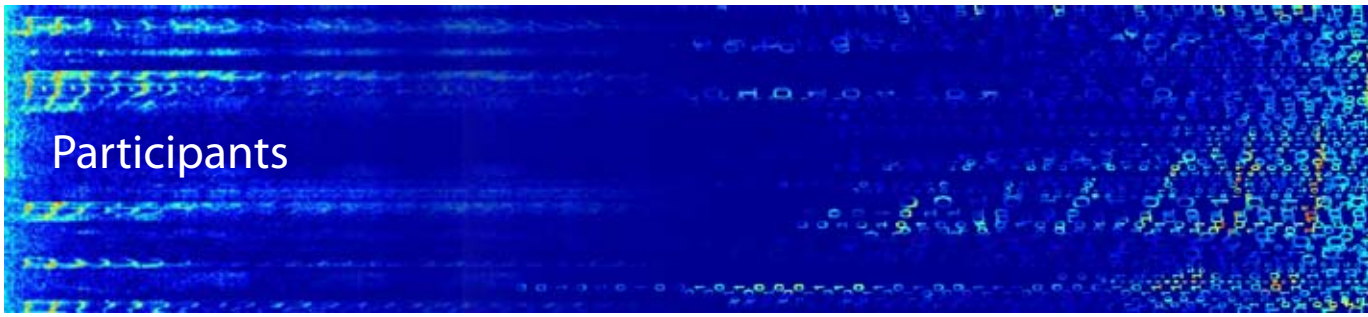
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