3rd annual Meeting of the GDR 2904 "Multi-electrode systems and signal processing to study neuronal networks"

Abstract Book

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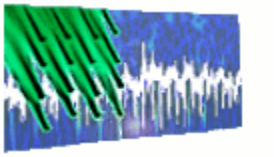

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Program

25/10/2012

08:45 - 09:15 Welcome & Introduction

Session 1- Neural coding and information

09:15 - 10:00 keynote speaker: **Nachum Ulanovsky** (Weizmann Institute, Rehovot, Israel) *Neural codes for 2-D and 3-D space in the hippocampal formation of bats*

10:00 - 10:30 invited speaker: **Vincent Hok** (LNC, Marseille, France) *Place cell firing variability and the space mapping process*

10:30 - 11:00 coffee break & Posters & Industriels

11:00 - 11:15 open talk: **Bruno Cessac**, Rodrigo Coffre, Hassan Nasser (INRIA Sophia Antipolis, France) *On the ubiquity of Gibbs distributions in spike train statistics*

11:15 - 11:30 open talk: **Brandon Farley**, Arnaud Noreña (NIA, Marseille, France) *Spatiotemporal coordination of slow-wave ongoing activity across auditory cortical areas*

11:30 - 12:30 special guest: **Jos Eggermont** (University of Calgary, Calgary, Alberta, Canada) *Sharpness of frequency tuning, cross-correlation distances, and noise-induced plasticity in auditory cortex. A comparison between LFPs and spikes recorded with multi-electrode arrays*

12:30 - 14:30 lunch & Posters & Industriels

Session 2- Sensory and sensorimotor systems and cognition

14:30 - 15:15 keynote speaker: **Daniel Shulz**, Pierre-Jean Arduin, Yves Frégnac, Valérie Ego-Stengel (UNIC, Gif-sur-Yvette, France) *"Master" neurons induced by operant conditioning in rat motor cortex during a brain-machine interface task*

15:15 - 15:45 invited speaker: **Mehdi Khamassi** (ISIR, Paris, France)***:****Reinforcement learning models and dopamine signalling in the basal ganglia*

15:45 - 16:00 open talk: **Joachim Confais**, Bjørg Kilavik, Adrián Ponce-Alvrez, Alexa Riehle (INT, Marseille, France) *Cue anticipation in motor cortex*

16:00 - 16:30 coffee break & Posters & Industriels

16:30 - 16:45 open talk: **Frédéric Stoll**, Charlie Wilson, Julien Vezoli, Maïlys Faraut, Emmanuel Procyk (SBRI, Bron, France) *Time-on-task modulations of beta oscillations during a cognitive task*

16:45 - 17:00 open talk: **Thomas Brochier**, Manuel Zaepffel, Alexa Riehle (INT, Marseille, France) *Spatio-temporal structure of LFP beta band oscillations in monkey motor cortex during reaching and grasping*

17:00 - 18:30 Presentation of multi-electrode products (10 minutes talks)

* Kian Torab (Blackrock Microsystems)
* Daryl Kipke (NeuroNexus)
* Sherman Wiebe (Plexon)
* Dirk Höhl (ThomasRecording)
* Mirko Schanz (MultiChannel Systems)
* Yousef Bsoul (AlphaOmega)
* Victor Rush (Tucker Davis Technologies)
* Georg Malliaras (BEL)

20:00 dinner in the restaurant "Arcenaulx" at the Vieux Port sponsored by *Plexon & NeuroNexus*

26/10/2012

Session 3 - Development and methodology

09:00 - 09:45 keynote speaker: **Bruno Torrésani** (LATP/CMI, Marseille, France) *Combining time-frequency and wavelet methods with multichannel models*

09:45 - 10:15 invited speaker: **Hanna Becker** (I3S, Sophia Antipolis, France) *Blind methods for EEG/MEG data analysis*

10:15 - 10:30 open talk: **Andrea Brovelli** (INT, Marseille, France) *Statistical analysis of single-trial Granger Causality spectra*

10:30 - 11:00 coffee break & Posters & Industriels

11:00 - 11:15 open talk: **Thomas Doublet**, Dion Khodagholy, Esma Ismailova, Pascale Quilichini, Pierre Leleux, Antoine Ghestem (INS, Marseille, France) *New flexible neuronal probes for in vivo experiments*

11:15 - 11:30 open talk: **Sébastien Joucla**, Blaise Yvert (INCIA, Bordeaux, France) *Optimizing electrical microstimulation and MEA devices for the development of neural prosthesis*

11:30 - 12:30 Plenary meeting GDR

12:30 - 14:30 lunch & Posters & Industriels

Session 4 - Functional role of network dynamics

14:30 - 15:15 keynote speaker: **Sonja Grün** (INM6, Jülich, Germany) *Data driven analysis of spatio-temporal cortical interaction*

15:15 - 15:45 invited speaker: **Henrik Lindén** (KTH, Stockholm, Sweden) *Modeling the spatial reach of the LFP signal in laminar cortical networks*

15:45 - 16:00 open talk: **Xavier Leinekugel** (IMN, Bordeaux, France) *Altered segregation of brain states and epileptic phenotype in a mouse model of Huntington's disease*

16:00 - 16:30 coffee break & Posters & Industriels

16:30 - 16:45 open talk: **Huifang Wang**, Christophe Bernard, Viktor Jirsa (INS, Marseille, France) *Finding connectivity by integration of various connectivity analysis methods*

16:45 - 17:00 open talk: **Diego Fasoli**, Olivier Fougeras (INRIA, Sophia Antipolis, France) *Finite size effects in a network of rate neurons*

17:00 - 18:00 Final discussion

18:00 Apéritif

Special Guest

Sharpness of frequency tuning, cross-correlation distances, and noise-induced plasticity in auditory cortex. A comparison between LFPs and spikes recorded with multi-electrode arrays

Jos J. Eggermont

Department of Physiology and Pharmacology, Department of Psychology,University of Calgary, Calgary, Alberta, Canada

Multi-electrode array recordings of spike and local field potential (LFP) activity were made from primary auditory cortex of normal hearing, ketamine-anesthetized cats. We evaluated 259 spectro-temporal receptive fields (STRFs) and 492 frequency-tuning curves (FTCs) based on LFPs and spikes simultaneously recorded on the same electrode. We compared their characteristic frequency (CF) gradients and their cross-correlation distances. The CF gradient for spike-based FTCs was about twice that for 2–40 Hz-filtered LFP-based FTCs, indicating greatly reduced frequency selectivity for LFPs. For spontaneous LFP and spike activity we evaluated 1373 pair correlations for pairs with >200 spikes in 900 s per electrode. Peak correlation-coefficient space constants for the LFP were on average 6.4 mm, whereas for spike-pair correlations it was half of that, at 3.2 mm. This larger correlation distance combined with the reduced CF gradient and much broader frequency selectivity suggests that LFPs are not a substitute for spike activity in primary auditory cortex.

Passive long-term exposure of adult normal-hearing cats to moderate levels (~70 dB SPL) of band-pass-filtered noise, or to band-limited ensembles of dense, random tone pips, can over the course of two weeks lead to a profound decrease of neural activity in the auditory cortex roughly in the exposure frequency range, and to an increase of activity outside that range. This occurs in the absence of damage to the auditory periphery (as reflected in normal distortion product otoacoustic emissions and auditory brainstem responses). During subsequent time in quiet surroundings this recovers over a six-week period back to normal, but retains an apparent reorganization of the cortical tonotopic maps. The use of dense recordings with multi-electrode arrays to reduce bias in assessing tonotopic maps will be highlighted.

Session 1: Keynote Speaker

Neural codes for 2-D and 3-D space in the hippocampal formation of bats

Nachum Ulanovsky

Department of Neurobiology, Weizmann Institute of Science, Israel

The work in our lab focuses on understanding the neural basis of behavior and cognition in freely-moving, freely behaving mammals – employing the echolocating bat as a novel animal model. I will describe our recent studies, including: (i) recordings of 3-D head-direction cells in the presubiculum of crawling bats, as well as recordings from hippocampal 3-D place cells in freely-flying bats, using a custom neural telemetry system – which revealed an elaborate 3-D spatial representation in the mammalian brain; and (ii) recordings of 'grid cells' in the bat's medial entorhinal cortex, in the absence of theta oscillations – which strongly argues against the prevailing computational model of grid formation. I will also describe our recent studies of spatial memory and navigation of fruit bats in the wild, using micro-GPS devices, which revealed outstanding navigational abilities and provided the first evidence for a large-scale 'cognitive map' in a mammal.

Session 1: Invited Speaker

Place cell firing variability and the space mapping process

Vincent Hok

LNC-UMR 7291, CNRS - Aix-Marseille Université, Marseille, France

Place cells are pyramidal neurons in the hippocampus selectively activated while the animal's head is in a particular location in a particular environment. Place cells are therefore characterized by location-specific firing ("place fields"), and their activity is subject to, among other variables, environmental manipulations. In normal conditions, environments are reliably encoded by groups of neurons displaying place fields that can be stable for up to several months. Contrasting with this strong spatial reliability, it has been shown previously that a striking discharge variability exists from one pass to another as the rat goes through a firing field. This variability, termed "overdispersion," correlates with the cognitive load of the behavioral task and may constitute a neurophysiological marker for individual cognitive ability. In a first study, we examined overdispersion characteristics of CA1 place cells in old rats and their individual performance in a delayed non-matching-to-position task. These recordings revealed a positive correlation between the degree of firing variability of place cells and performance during the long delays in the operant task. In order to identify putative sources of modulation of this hippocampal firing variability, we also investigated the effects of prefrontal inactivation on hippocampal place cells activity while the animals solved a goal-oriented navigation task. We found a profound modification of place cell firing variability after suppression of the prefrontal input, suggesting a possible mechanism underlying behavioral flexibility. In a last study, we identified functional subclasses of hippocampal place cells based on their firing variability properties. In conclusion, we suggest that hippocampal overdispersion might be a key component in signal processing, supporting various features such as cognitive inter-individual variability and encoding of the environment's identity.

Session 1: Open Talk

On the ubiquity of Gibbs distributions in spike train statistics

Bruno Cessac, Rodrigo Cofre, Hassan Nasser

NeuroMathComp team (INRIA), Sophia Antipolis, France

In this talk we shall argue that Gibbs distributions, considered in more general setting than the initial concept coming from statistical physics and thermodynamics, are canonical models for spike train statistics analysis. This statement is based on the three following facts, developed in the talk.

1. The so-called *Maximum Entropy Principle* allows one to propose models for spike statistics based on empirical observations, providing constraints for the model. Although this approach has been initially devoted to show the role of weak instantaneous pairwise correlations in the retina [7], it has been recently applied to investigating the role of more complex events such as instantaneous triplets [4] or spatio-temporal events [8]. Probability distributions arising from the Maximum Entropy Principle are Gibbs distributions. The main strength of this method is to be able to include any type of spatio-temporal correlations as constraints for statistical estimations. Its mean weaknesses are (i) It assumes stationarity; (ii) It does not tell how to select constraints among the huge set of possibilities.

2. Other approaches such as the Linear-Non Linear (LN) or Generalized Linear Models (GLM) propose an ad hoc form for the conditional probability that a neuron fires given the past network activity and given the stimulus. Those models have been proven quite effcient for retina spike trains analysis [6]. They are not limited by the constraint of stationarity, but they are based on a questionable assumption of *conditional independence between neurons*. As we show, the probability distributions coming out from those models are also Gibbs distributions, although in a more general sense than 1.

3. Recent investigations on neural network models (conductance based IF with chemical and electric synapses) show that statistics of spike trains generated by these models are Gibbs distributions reducing to 1 when dynamics is stationary, and reducing to 2 in specific cases [1, 2, 3]. In the general case, the spike trains produced by these models have Gibbs distributions *which neither match 1 nor 2.* Additionally, spike correlations are not only produced by a shared stimulus: they have a strong dynamical component due to neurons' interactions.

We shall also briefly discuss a software implementation, designed at INRIA, for MEA spike train analysis using Gibbs distributions [5].

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[3] Cofré R, Cessac B. Dynamics and spike trains statistics in conductance-based integrate-and-_re neural networks with chemical and electric synapses. *Chaos, Solitons and Fractals*, 2012. submitted.

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[5] Nasser H, Marre O, Cessac B. Spatio-temporal spike trains analysis for large scale networks using maximum entropy principle and monte-carlo method. *J Statist Mech*, submitted, 2012.

[6] Pillow JW, Ahmadian Y, Paninski L. Model-based decoding, information estimation, and change-point detection techniques for multineuron spike trains. *Neural Comput.*, 23:1-45, 2011.

[7] Schneidman E, Berry MJ, Segev R, Bialek W. Weak pairwise correlations imply strongly correlated network states in a neural population. *Nature*, 440:1007-1012, 2006.

[8] Vasquez JC, Marre O, Palacios AG, Berry MJ, Cessac B. Gibbs distribution analysis of temporal correlation structure on multicell spike trains from retina ganglion cells. *J. Physiol. Paris*, 2012. in press.

Session 1: Open Talk

Spatiotemporal coordination of slow-wave ongoing activity across auditory cortical areas

Brandon J Farley, Arnaud J Noreña

NIA, UMR 7260, CNRS - AMU, Marseille, France

Natural acoustic stimuli contain important slow (~ 1-10 Hz) temporal modulations, and ongoing neural activity in this temporal range (i.e. slow-wave activity) plays essential roles in auditory cortical processing. However, the spatiotemporal structure of intrinsic slow-wave activity across the auditory cortex is unknown. In particular, can slow-wave ongoing activity be modulated in a spatially-specific (or tuning-dependent) manner, and in congruent regions of multiple cortical fields? We used *in vivo* voltage-sensitive dye imaging in anesthetized rodents to define the functional organization (i.e. best-frequency tuning) across multiple core and belt areas of the auditory cortex, and then recorded spontaneous activity across this defined network. We found that phase-coherence in ongoing slow-wave (4 Hz) activity between core and belt regions was high when they shared similar best-frequency tuning, even if they were distant from each other. While core and belt regions with high phase-coherence were phase-shifted, the phase-shifts matched evoked-activity latency differences measured between the same regions. Thus, during periods of high slow-wave energy, evoked activity is expected to arrive at similar slow-wave phases across areas. Our findings suggest that intrinsic slow-wave ongoing activity patterns support coordinated changes in excitability between functionally-matched but distributed regions of the auditory cortical network. Such a source of activity may be recruited by intrinsic factors to modulate acoustic processing.

Session 2: Keynote Speaker

"Master" neurons induced by operant conditioning in rat motor cortex during a brain-machine interface task

Daniel Shulz, Pierre-Jean Arduin, Yves Frégnac, Valérie Ego-Stengel

Unité de Neurosciences Intégratives et Computationnelles (UNIC), CNRS, Gif-sur-Yvette, France

Brain Machine Interfaces (BMI) often rely on recording the activity of large populations of neurons in monkeys, and implementing complex decoding algorithms to drive a robotic prosthesis. A few experiments, notably by Fetz and collaborators, have challenged this approach by showing that the activity of a single cortical neuron could be used to control operantly an actuator. Moreover, it has been shown that it is not necessary to adapt the control algorithm to the functional properties of the neuron, but rather that the neuronal circuit itself can be trained through operant conditioning to generate the specific patterns of activity that will drive the prosthesis. In these pioneer experiments, it remains unknown whether the long-term modifications underlying the functional changes mostly concern the conditioned neuron chosen to control the prosthesis, or if a larger reorganization of the local circuit takes place.

We have tackled this question by using multiple single-unit recordings in the motor cortex of the awake behaving rat. First, we demonstrate that operant conditioning of single unit activity can be successfully achieved in the rat. This is important, since all previous protocols of the same type have been realized in monkeys only, whereas BMI research can undoubtedly benefit from the use of rodent experimental models.

Second, the single units that were successfully conditioned exhibited reproducible increases in activity and fast reaction times after trial onset, indicating that a reliable swift control can be achieved with this protocol.

Third, our results provide evidence for a reconfiguration of the local network generally led in time by the conditioned neuron. Neighboring non-conditioned neurons displayed either no change or smaller increases in firing rate.

Fourth, we describe an anticipatory increase in the firing rate variability of the conditioned neuron before trial onset. This occurred during the early stages of the learning phase only, and disappeared once asymptotic training was completed. This observation suggests a possible role of firing rate variability of a neuron for exploring various timing relationships and stabilizing the most appropriate activity patterns.

Our study demonstrates that conditioning single neurons is a suitable approach to control a prosthesis in real-time, and that learning is accompanied by a network reorganization in which the conditioned neuron occupies a lead position.

Session 2: Invited Speaker

Reinforcement learning models and dopamine signalling in the basal ganglia

Mehdi Khamassi

Institut des Systèmes Intelligents et de Robotique (ISIR), CNRS - UPMC, Paris, France

The phasic activity of dopaminergic (DA) neurons has been hypothesized to encode a reward prediction error (RPE) which corresponds to the error signal in Reinforcement Learning (RL) algorithms. This hypothesis has been reinforced by numerous studies showing the relevance of RL algorithms to describe the role of basal ganglia in classical conditioning. In the first part of the talk, I will give an introduction to RL models, their underlying computational principles, some of their limits and the main properties that established them as good models of dopamine-dependent learning and action selection in the basal ganglia.

In a second part, I will present recent recordings of DA neurons phasic activity during multi-choice tasks which raised contradictory interpretations on whether DA phasic RPE signal contains information about the action the animal has decided to perform or not. I will present our simulations and comparison of different RL algorithms (i.e. Actor-Critic, Q-learning or SARSA) to quantify the amount of information about action conveyed by DA phasic signals. Moreover, we found that DA activity previously reported in such task is best fitted by an RPE which has not fully converged, and which converged slower than observed behavioral adaptation. This suggests that DA activity might only partly be related to the learning mechanisms underlying the observed behavior.

In the last part of the talk, I will present our recent hypothesis that dopamine tonic release in the striatum could participate in regulating the "exploration-exploitation" trade-off. Such trade-off describes the dilemma animals face of choosing between actions that gather new information or actions that exploit existing knowledge. Here we set out to reconcile recent evidence for dopamine's involvement in the exploration-exploitation trade-off with the existing evidence for basal ganglia control of action selection. We first advance the idea of interpreting the basal ganglia output as a probability distribution function for action selection. Using computational models of the full basal ganglia circuit, we showed that, under this interpretation, the actions of dopamine within the striatum change the basal ganglia's output to favor the level of exploration or exploitation encoded in the probability distribution. Finally, by integrating the basal ganglia within a reinforcement learning model, we showed how dopamine's effect on the exploration-exploitation trade-off could be measurable in a probabilistic forced two-choice task previously employed to assess learning (dis-)abilities in Parkinsonian patients ON or OFF medication. Our simulations showed how tonic dopamine can appear to affect learning while only directly altering the trade-off. Thus, our models support the hypothesis that changes in tonic dopamine within the striatum can alter the exploration-exploitation trade-off by modulating the output of the basal ganglia.

Session 2: Open Talk

Cue anticipation in motor cortex

Joachim Confais[1], Bjørg E Kilavik[1], Adrián Ponce-Alvarez[2], Alexa Riehle[1]

[1] *Institut de Neurosciences de la Timone, UMR 7289, AMU - CNRS, Marseille, France*
[2] *Deparment of Technology, Universitat Pompeu-Fabra, Barcelona, Spain*

It has been shown that neurons from the motor areas (primary motor cortex (M1), and dorsal premotor cortex (PMd) display a systematic modulation in firing rate before the onset of the spatial cue, when its timing is known in advance. The purpose of our study is to better understand the function that this anticipatory pre-cue activity may have in motor preparation. We recorded single unit activity in M1 and PMd of two macaques while they performed an arm reaching task. The task involved two consecutive delays of equal duration, cued at trial start. At the end of the first delay (D1), a brief visual spatial cue (SC) provided information about the direction of the forthcoming movement. At the end of the second delay (D2), the monkey had to reach to the indicated target. We defined neurons as “anticipatory” if their activity modulated significantly during D1. About 40% of the 1270 neurons recorded in the two monkeys showed such an anticipatory activity, which either increased (D1up, 59%), or decreased (D1down, 41%) towards SC onset. It appears that by classifying the neurons according to the firing rate profiles during D1, their activity modulation during D2 differed in a systematic way. The D1up neurons were more likely to discharge phasically shortly after the spatial cue and were less active during movement execution, while the D1down neurons showed the opposite pattern. But, regardless of these different profiles of activity, the two categories seemed equally involved in motor preparation, as reflected in their directional selectivity. This pre-cue anticipatory activity may be involved in a "presetting" mechanism of the motor areas when the timing of a relevant information is known in advance. It could participate to a preparatory state of the cortex, in order to efficiently process the spatial cue.

Confais J, Kilavik BE, Ponce-Alvarez A, Riehle A (2012 in press) On the anticipatory pre-cue activity in motor cortex. *J Neurosci*

Session 2: Open Talk

Time-on-task modulations of beta oscillations during a cognitive task

Frédéric Stoll , Charlie RE Wilson, Julien Vezoli, Maïlys Faraut, Emmanuel Procyk

Stem Cell & Brain Research Institute (SBRI), Inserm U846, Bron, France

Neurophysiological investigations of frontal regions of the monkey brain have linked them to cognitive control and performance monitoring. Such functions are critical in order to adapt behaviour both between different demands, such as exploration and exploitation, and also over time. Here we investigate the network of frontal regions involved using macaque monkeys with multiple chronically implanted electrocorticographic (ECoG) electrodes, and performing a test of cognitive control.

Two rhesus monkeys learned the Problem Solving Task (PST; Procyk & Goldman-Rakic 2006), a test of cognitive control in which they had to search amongst several targets for a rewarded target (the search phase, SEA), and then repeat the correct response a number of times (the repetition phase, REP). Monkeys were chronically implanted with at least 22 electrodes resting on the dura mater, covering prefrontal (PFC) and sensorimotor (SM) cortex, to provide ECoG recordings. We analyzed in the time-frequency domain to reveal induced oscillatory signals throughout the task.

We characterized a number of longitudinal markers, including specific patterns in the beta band over PFC and SM cortex, in relation to movements and in the delay period prior to each trial. We showed that these stable markers are modulated by the different cognitive control demands in the SEA and REP phases of the task. In addition, we demonstrated a significant within-session modulation of both the power and frequency of the beta oscillations in the delay period of the task. This within-session modulation was selective to the delay phase of the task. We relate this modulation to ongoing behavioural adaptation throughout a session, and measures such as time-on-task.

Session 2: Open Talk

Spatio-temporal structure of LFP beta band oscillations in monkey motor cortex during reaching and grasping

Thomas Brochier, Manuel Zaepffel, Alexa Riehle

Institut de Neurosciences de la Timone (INT), UMR 7289, CNRS - AMU, Marseille, France

Electroencephalogram (EEG) and local field potentials (LFPs) show that brain oscillatory activity recorded across the sensorimotor cortex is modulated in the beta range (15-30Hz) in relation to the planning and execution of voluntary movements. In particular, beta oscillations have been studied in instructed delayed motor tasks in which a cue provides advance information about a movement that has to be performed at the end of preparation delay. In such tasks, it has been classically observed that the power of beta oscillations increases in relation to the cue presentation, decreases gradually during movement preparation and execution and “rebounds” at movement offset. Subtle changes in the experimental protocol can selectively alter these increase or decrease in beta power, suggesting that these modulations originate from several sources. However, the exact location of these sources in the cortical motor network and their functional significance remain debated. To address this issue, we use high-density intra-cortical recordings to study the temporal and spatial modulations of beta oscillations in monkeys performing a forewarned delayed reach to grasp task.

We trained two monkeys to grasp and pull an object using either a *Side Grip* or a *Precision Grip.* The object is either *heavy* or *light*. The trial starts by the monkey pressing a switch. A first cue provides the instruction about the grip. After a delay of 1s, a second cue provides additional information about the object load and also serves as GO signal. The monkey has then to release the switch, grasp the object, pull it and hold it in a narrow position window for 500ms to receive a food reward. Neuronal activity was recorded by using a 100 electrode "Utah" array, chronically implanted at the MI/PMd border. All LFPs were band pass filtered from 0.3-250 Hz and recorded digitally with a 1 kHz sampling rate. We computed beta power by applying a 15-25 Hz band pass filter to the raw LFP signal, before squaring and averaging across trials for each movement type.

Beta oscillations on all electrodes were characterized by a typical synchronization/ desynchronization pattern during movement preparation and execution. Strikingly, the power of beta oscillation in the different task epochs was modulated in space across the array. On overall, the cue-related power increase was larger on the most posterior electrodes toward M1 whereas the movement-related power decrease and the rebound were larger on the anterior electrodes toward PMd. These results demonstrate that beta rhythms are differentially modulated at a very fine spatial scale and confirm the composite nature of beta oscillations in the motor cortex.

***Funding**: Collaborative Research Agreement Riken-CNRS, CNRS (PEPS, Neuro_IC2010), ANR GRASP*

Session 3: Keynote Speaker

Combining time-frequency and wavelet methods with multichannel models

Bruno Torrésani

Laboratoire d'Analyse, Topologie, Probabilités (LATP), CNRS - AMU, Marseille, France

In the first part of this talk, we will briefly review the current trends in time-frequency/time scale analysis, sparse models and corresponding algorithms. We will then consider multi-channel extensions of these methods, focusing on the fusion of informations originating from different channels. A few examples will be discussed in some details, and results on EEG data will be presented.

Session 3: Invited Speaker

Blind methods for EEG/MEG data analysis

Hanna Becker

Laboratoire I3S, Bat. Algorithmes/Euclide-B, Sophia Antipolis, France

EEG/MEG measurements are generally subject to low signal-to-noise ratios and contain multiple artifacts originating, for instance, from eye blinks and muscle movements. Therefore, to extract the signals of interest, the data needs to be preprocessed to reduce the noise and remove artifacts. Furthermore, in the presence of several simultaneously active sources of interest, it is desirable to separate these sources in order to facilitate the analysis of the data. This can be achieved by blind signal processing methods which act on the data without relying on prior knowledge about source positions or source time signals. This presentation gives an introduction to Independent Component Analysis (ICA) and deterministic tensor methods based on the Canonical Polyadic (CP) decomposition with a focus on Space-Time-Frequency (STF) and Space-Time-Wave-Vector (STWV) analysis.

Session 3: Open Talk

Statistical analysis of single-trial Granger causality spectra

Andrea Brovelli

Institut de Neurosciences de la Timone (INT), UMR 7289, CNRS - AMU, Marseille, France

Granger causality analysis is becoming central for the analysis of interactions between neural populations and oscillatory networks. However, it is currently unclear whether single-trial estimates of Granger causality spectra can be used reliably to assess directional influence. We addressed this issue by combining single-trial Granger causality spectra with statistical inference based on general linear models. The approach was assessed on synthetic and neurophysiological data. Synthetic bivariate data was generated using two autoregressive processes with unidirectional coupling. We simulated two hypothetical experimental conditions: the first mimicked a constant and unidirectional coupling, whereas the second modelled a linear increase in coupling across trials. The statistical analysis of single-trial Granger causality spectra, based on *t*-tests and linear regression, successfully recovered the underlying pattern of directional influence. In addition, we characterised the minimum number of trials and coupling strengths required for significant detection of directionality. Finally, we demonstrated the relevance for neurophysiology by analysing two local field potentials (LFPs) simultaneously recorded from the prefrontal and premotor cortices of a macaque monkey performing a conditional visuomotor task. Our results suggest that the combination of single-trial Granger causality spectra and statistical inference provides a valuable tool for the analysis of large-scale cortical networks and brain connectivity.

Session 3: Open Talk

New flexible neuronal probes for in vivo experiments

Thomas Doublet[1, 2, 3], Dion Khodagholy[2], Esma Ismailova[2], Pascale Quilichini[1], Pierre Leleux[1, 2, 3], Antoine Ghestem[1]

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[3] *Microvitae, Ecole Nationale Supérieure des Mines de Saint-Etienne, Gardanne, France*

Recording single cell activity *in vivo* has allowed considerable progress in our understanding of information processing in the brain. Silicon probe based electrodes, enable the recording of neuronal activities in freely moving animals. However, they are not biocompatible and their rigid nature does not allow them to follow the natural movements of the brain, leading to a loss of signal. Which make those probes not suited for long-term recordings.

We developed new flexible organic microelectrodes to minimize the lesions and maximize the recording interface with the tissue. Those conducting polymers and insulator layers provide good biocompatibility and a high mechanical flexibility.

Importantly, the conducting polymer used for the recording site is also organic and provides superior signal to noise ratio as compared to classical recordings sites made of gold. We also developed a new generation of electrodes where the recording site is an organic transistor (OECT), which provides a local pre-amplification of the signal and a gain by more than 30 dB of the signal-to-noise ratio.

These new probes increase the quality and duration of neuronal signals for long-term experiments.

Session 3: Open Talk

Optimizing electrical microstimulation and MEA devices for the development of neural prosthesis

Sébastien Joucla, Blaise Yvert

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Nowadays, multielectrode-based systems offer new possibilities for CNS microstimulation and treatment of neurodegenerative diseases or restoration of functions of injured networks. Yet, MEA systems remain to be optimized to achieve controlled microstimulation of the neural tissue in real-time and on the long term, which requires improving the electronics, electrode materials and microstimulation strategies. Here, we first conducted a modelling study to design penetrating probes that are optimized for focal neural stimulation. Combining a finite element model of the spinal cord and compartmentalized models of both simple and complex neuron morphologies, we evaluated the use of the "ground surface" configuration for penetrating probes, which consists in the integration of a conductive layer on the front side of each shank, for the return of the stimulation current. We showed that this strategy resulted in a focalization of the stimulation extent of neural tissue, compared to the classical monopolar and bipolar configurations. Next, in collaboration with electronicians and material scientists, we developed the new real-time MEA system NeuroPXI, as well as nanostructured conductive diamond electrode arrays showing high biocompatibility, low noise and high safe charge injection limit for small electrode diameters. Currently, these developments aim at being integrated to build neuroprosthetic device for the injured spinal cord.

Session 4: Keynote Speaker

Data driven analysis of spatio-temporal cortical interaction

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The developments in electrophysiological recording techniques nowadays enable the simultaneous observation of a large number of individual neurons. However, a meaningful interpretation of the resulting high-dimensional data presents a serious challenge. We follow the hypothesis that cortical processing is organized in cell assemblies, i.e. groups of neurons that interact by coordination of their spiking activities. In order to detect such interactions between neurons and thus the activities of neuronal groups, the simultaneous spike trains need to be analyzed for significant spike correlation. For doing that we developed the Unitary Events (UE) analysis method (Grün et al. 1999; 2002a,b) and found dynamically occuring excess synchrony that was clearly related to the behavior of the animals (Riehle et al. 1997; 2001; 2003) and their state of practice of the task (Kilavik et al. 2009). These results were retrieved from mostly pairwise analyses of a few simultaneously recorded neurons. A straightforward extension of the UE method to massively parallel spike train (MPST) recordings, however, is due to the combinatorial explosion not possible. Therefore we developed new methods that are applicable to MPST and which enable to infer higher-order correlations (HOC) between the neuronal activities, which are interpreted as expressions of active assemblies. In this presentation I will discuss such methods (Grün et al. 2008; Schrader et al. 2008; Louis et al. 2010; Staude et al. 2010; Gerstein et al. 2012) and surrogate based approaches to derive the significance of the detected spike patterns (Grün 2009).

Session 4: Invited Speaker

Modeling the spatial reach of the LFP signal in laminar cortical networks

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To build a proper understanding of the dynamics of local cortical circuits it is necessary to monitor the activity of many neurons at the same time. A popular measure in this respect is the local field potential (LFP), the low-frequency part of an extracellularly recorded voltage signal, as it represents the summed electrical activity in populations of neurons in vicinity of the recording electrode. Much of the nature of the LFP signal is, however, still unknown. There are, for instance, contradicting experimental reports on the spatial extent of the region generating the LFP, or in other words, how many neurons contribute to the signal. Here, we present a detailed biophysical modeling approach to investigate the size of the contributing region by simulating the LFP from a large number of neurons around the electrode, in combination with a simplified analytical model. We find that the size of the generating region depends on a combination of factors in the underlying neural activity such as the neuron morphology, the synapse distribution, and the correlation in synaptic activity. For uncorrelated activity, the LFP represents cells within a radius of a few hundred micrometers. If, on the other hand, the LFP contributions from different cells are correlated, the size of the generating region is determined by the spatial extent of the correlated activity. These results suggest that the spatial reach of the LFP signals is not a fixed quantity, instead it varies with the cortical state.

Session 4: Open Talk

Altered segregation of brain states and epileptic phenotype in a mouse model of Huntington's disease

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In addition to several changes in cellular and synaptic properties previously reported in Huntington's disease (HD), attention was recently driven towards the potential relationships between cognitive deficits and sleep disturbances in patients and animal models of HD. In the present study, we have investigated whether the population-activity patterns normally expressed by the hippocampal and neocortical circuits during active and slow-wave states are affected in R6/1 mice, a model of Huntington's disease.

By performing multi-site electrophysiological recordings from the hippocampus and neocortex of R6/1 mice that were either freely moving, head restrained or anesthetized, we observed an altered segregation of active and slow wave brain states, in relation with an epileptic phenotype. Slow-wave state (SWS) in R6/1 was characterised by the intrusion of active-state features (increased 6-10 Hz theta power and depressed 2-3 Hz delta power) and transient, temporally misplaced ("ectopic") theta oscillations. The epileptic phenotype, in addition to previously reported occasional ictal seizures, was characterized by the systematic presence of interictal activity, confined to SWS. Ectopic theta episodes, that could be reversed by the cholinergic antagonist atropine, concentrated interictal spikes and phase-locked hippocampal sharp-wave-ripples. These results point to major alterations of neuronal activity during rest in R6/1 mice, potentially involving anomalous activation of the cholinergic system, which may contribute to the cognitive deficits observed in Huntington's disease.

Session 4: Open Talk

Finding connectivity by integration of various connectivity analysis methods

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This paper studies, in a general way, how to find connectivity among the neural signals by integration of the different results from different connectivity analysis methods, first comparing them to get their advantages and drawbacks, and finally combining these different methods to obtain the accurate connectivity map. It is composed of two parts: induction and deduction. For the induction part, we applied these connectivity analysis methods to simulated data from linear and nonlinear systems with linear/nonlinear coupling with different connectivity structures and with different noise levels and time delays. Our first contribution is to obtain the rules about the corresponding relations between the data's systemic property with structural characters and the performance of these methods. We demonstrtate which set of methods is suited for which type of data and why. For the deduction part, we applied these connectivity analysis methods first to the blind simulated data then to the real LFP data from 13 regions of a rat brain during REM sleep. According to the similarity and difference among the results from the various connectivity analysis methods and rules, we explained the principles to get the correct connectivity of our blind data. In the same way, we can deduce that our LFP data is a nonlinear system with linear coupling without obvious time delay. Then we can find the connectivity by combining the results from four families: correlation, coherence, h2 and mutual information.

Session 4: Open Talk

Finite size effects in a network of rate neurons

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In a first approximation, neurons can be described by rate equations that quantify the frequency of the spiking activity exchanged among them. Another important feature of the brain is noise, that is able to reduce the reliability of the spike train making it a probabilistic process. In our work, we have developed a perturbative analysis in terms of the three sources of randomness of this kind of network: the noise intensity, the uncertainty in the initial conditions and the uncertainty in the distribution of the synaptic weights. This analysis can be performed for many topologies of the connectivity matrix and for an arbitrary finite number of neurons, and reveals three important results. The first is the formation of a stochastic synchronization, and therefore of strong correlations, between the neurons: this is uniquely related to the spectrum of the connectivity matrix, and therefore makes a mean-field description of the network impossible. The second result is the reduction of correlation by an increasing of the network's input, while the third result is that correlation decreases also when we increase the number of connections between the neurons. Since this analysis allows to find the full correlation structure of the network, we think it could help to shed light on the relation between the structural and functional connectivities of the system, a problem which is currently intensively investigated.

Role of the subthalamic nucleus in the coding of informations about an appetitive or aversive reinforcing agent in rats

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Subthalamic nucleus (STN) is a core of the basal ganglia, a set of subcortical structures traditionally considered for their role in the control of movement, but also involved in cognitive and motivational processes. Recent electrophysiological studies have showed that neurons in the STN responded differently to predictive indices and to the obtaining of various rewards (water, sugar and cocaine). However, these studies focused on reinforcing agents having only a positive expected value. It was therefore important to continue these studies by testing the responses of STN on the presentation of aversive reinforcing agents. We therefore investigated the activity of STN during the presentation of quinine, a bitter compound whose consumption is avoided by rats.

To do this, we conditioned 10 rats to perform a reaction time task subscripted for two different rewards. The rats were first conditioned to work for two concentrations of sucrose (4% and 32%). We recorded the activity of single neurons in the STN depending on the concentration of sucrose in the presentation of the light cue, of the obtaining reward and in incorrect trials. The recordings were made while the sucrose solution (4%) was then replaced by quinine. To test the ability of neurons of the STN to intervene in the reward prediction error, we also recorded STN neurons while the announced reward was not delivered in 20% of cases.

Our results showed that the activity of STN neurons could be redistributed depending on the nature of the reinforcing agents available. They also showed that the STN is able of encoding information on quinine. And finally, they suggest that the STN shares, in part, the encoding function of the reward prediction error of dopaminergic neurons. These results consolidate the role of STN in motivation, and provide additional insight on how it treats motivational information.

Poster - Session 1

Post-stimulus firing and the corresponding olfactory search strategy

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The mating race of moths is hampered by a discontinuous distribution of pheromone patches. A male moth searching for a mate relies on an optimized search strategy. Upon sensing a pheromone patch, the moth surges upwind whereas loosing the pheromone leads to an extended casting until the pheromone plume is reacquired. Pheromone-sensitive neurons in the antennal lobe of Agrotis ipsilon moths can guide such an action selection. These neurons typically exhibit multiphasic responses: (1) A burst of spikes after stimulus onset (the On) followed by an inhibitory period. The On is assumed to induce surging, i.e. a straight upwind movement. (2) A tonic rebound excitation after stimulus offset (the Off) which is assumed to signal the loss of the stimulus and therefore initiates casting. We here suggest an extended behavioural model that includes two different (but not necessarily discrete) casting strategies based on a separation between Off and baseline activities. The Off indicates a recent loss of the pheromone and induces crosswind zigzagging (assuming that the moth is still inside the plume). Baseline activity, however, indicates the final loss of the stimulus and initiates spiral casting (moth outside the plume). Analyzing the corresponding neurophysiological recordings, we develop a computational model that reproduces the experimental data. In particular, we aim to investigate whether the transition from Off to baseline activity is a discrete or rather a continuous process. The resulting neuron model is then used to control a robot with insect antennae as pheromone sensors.

Categorization between Rising vs. Falling sweeps: Does it affect similarly the functional properties and temporal precision of auditory cortex neurons after an aversive and an appetitive task?

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Over the last 20 years, many studies have described the receptive field reorganizations of auditory cortex neurons occurring when a particular sound frequency became significant. Recently, it has been claimed that the aversive or appetitive nature of the reward influences the type of changes that can be detected in auditory cortex during a learning task (David et al., PNAS, 2011). These data were obtained in awake, behaving, animals during tasks where the animals' attention and strategies could be quite different in the aversive and appetitive conditions. To clarify this problem, we decided here to train animals in a similar categorization task between ascending and descending stimuli in an aversive and an appetitive version using exactly the same stimuli and to analyze the consequences of this training in anesthetized conditions, i.e., when no difference in term of attention and strategies can be suspected.

Experiment 1: Rats were trained in a shuttle box to discriminate between rising sweeps (the CS+, predicting a footshock used as unconditioned stimulus) and falling sweeps (the CS-) in an aversive task (15 CS+ and 15 CS-/session). After achieving the discrimination up to 90% of correct responses, they were trained to generalize to 3 different sets of rising and falling sweeps. Their performance decreased when a new pair of CS+/CS- was introduced but returned to 90% of correct responses for each pair of CS+/CS- in 2 sessions.

Experiment 2: Water-deprived guinea pigs were first trained to lick a spout in an operant chamber then were trained to discriminate between a CS+ (ascending or descending FM sweep) and a CS- (ascending or descending FM sweep). Water was available during the CS+ but not during the CS-. Once the animals have learned the initial discrimination, 3 other sets of rising and falling sweeps were introduced (these stimuli were the same as for the trained rats). Both in rat and in guinea pig, spectro-temporal receptive fields (STRFs) of auditory cortex neurons were tested under urethane anesthesia 24-48h after completion of behavioral training.

Results: In rats (aversive task), the STRFs of the trained animals were larger both in terms of bandwidth (2.75 vs. 1.95 octaves) and of duration (20.23 vs.11.04ms) than in control animals. The response strength within the STRFs was also higher (50.9 vs. 28.6 spikes/sec). In guinea pigs (appetitive task), the STRFs of the trained animals were larger in terms of response duration (34.21 vs.28.62ms) but not in terms of bandwidth (2.09 vs. 2.01 octaves) than in control animals. The response strength within the STRFs was also higher (43 vs. 36 spikes/sec) in trained vs. untrained animals.

Conclusions: These results suggest that when tested under anesthesia (without attentional effects) the consequences of a discrimination/categorization task are not fundamentally different in an aversive and an appetitive version of such task. Thus, the differences previously reported could be the consequences of different animal's strategies or different attentional load.

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Chronic neurophysiological markers of a test of cognitive control

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Neurophysiological investigations of frontal regions of the monkey brain, such as lateral prefrontal cortex (PFC) and anterior cingulate cortex, have linked them to cognitive control and performance monitoring respectively. Yet the ways in which these regions dynamically interact with each other and with motor output throughout a cognitive control task are less understood. Here we investigate the network of brain regions involved using macaque monkeys with multiple chronically implanted electrocorticographic (ECoG) electrodes, and performing a test of cognitive control.

Two rhesus monkeys learned the Problem Solving Task (PST), a test of cognitive control in which they had to search amongst several targets for a rewarded target (SEA), and then repeat the correct response a number of times (REP). After this a change signal instructed them to begin a new problem by searching again. Monkeys were chronically implanted with at least 22 electrodes resting on the dura mater, covering PFC and sensorimotor cortex, to provide ECoG recordings referenced to a post-frontal electrode. We analyzed recordings in the time-frequency domain to reveal induced oscillatory signals throughout the task.

We used ECoG recordings to characterize a number of longitudinal markers, including the desynchronization and synchronization pattern in the beta oscillations over sensorimotor cortex related to movements in the task, further oscillations in the same frequency band in the delay period prior to each trial. We showed that these markers are modulated by the different cognitive control demands in the SEA and REP phases of the task.

In addition, we demonstrated a significant within session modulation of both the power and frequency of the beta oscillations in the delay period of the task, that was both selective to this phase of the task and reliably produced on the majority of days of work. We relate this modulation to ongoing behavioural adaptation throughout a session.

Poster - Session 2

How short can a vowel be and still be recognized? A comparison between cortical neurons and human listeners

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We investigated the neural coding of timbre by recording neural responses in the primary auditory cortex of urethane anaesthetized guinea-pigs to a set of 5 vowels (*/a/, /e/, /i/, /o/, /u /,* pitch G#4) with different durations (2 to 128ms).

By recording responses to very short snippets of vowels, we aimed to investigate whether the coding abilities of cortical neurons would be robust even in situations where potentially less spikes over time were available, as well as for sounds with a spectrum lacking sharply-defined harmonics. This set of stimuli was also used for a psychophysical experiment with human listeners. The task for listeners was to identify the vowel type (5AFC). Confusion matrices were obtained from the behavioral results. From perfect at 128ms, the listeners' performance decreased as duration shortened but stayed above chance down to snippets of 4-ms duration.

The ability to discriminate the vowels of each cortical site, as well as of all the 16 simultaneously recorded sites, was also quantified from confusion matrices computed from a naïve Bayes quadratic classifier. The main results were: 1) in general, the discrimination ability of each cortical site was poor, lower than 2 vowels, even for the longest durations. Therefore, it was never possible to reach performance similar to the psychoacoustics based **on the activity of a single cortical site**; 2) taking account of all simultaneously recorded cortical sites led to much better discrimination and outperformed psychoacoustics for short vowel duration; 2) high frequency neurons were better than low frequency ones at discriminating vowels. This could be accounted for by the difference in sound energy between vowels, which was larger for higher harmonics than lower ones. These results suggest that, down to very short duration, both cortical neurons and listeners still have access to a reasonable representation **of the stimulus acoustics.**

Poster - Session2

Cue anticipation and processing in monkey motor cortex

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Motor cortex holds an established role in movement preparation and execution. Interestingly, it also exhibits short-latency (~100ms) phasic responses to sensory cues, particularly evident in delay tasks that separate in time the presentation of sensory information from the movement execution itself. Furthermore, pre-cue anticipatory modulations are observed when the cue timing is predictable. We studied how motor cortical activity associated with visual cue anticipation and processing is related to behavioral performance and the activity during movement execution. We recorded neuronal discharges and local field potentials (LFPs) in two macaques performing a visuomotor delay task, in which the timing of the spatial cue (SC) and the GO signal was indicated at each trial-start.

About 40% of neurons showed increasing or decreasing activity before SC. Many of the neurons that increased their pre-cue firing rate also had a short-latency phasic response to SC, while those that decreased their pre-cue firing rate were more active during movement execution. However, both subsets were similarly directionally selective during the preparatory delay.

The LFPs contained directionally selective visual evoked potentials (VEPs) to SC that varied with the delay-duration between SC and GO. Whereas VEPs were larger in short-delay trials, movement related potentials (MRPs) around movement onset were larger in long-delay trials. Moreover, VEPs were negatively and MRPs positively correlated with behavioral reaction times.

Finally, we measured changes in the power of LFP beta (~20Hz) and slower oscillations (5-10Hz; broadly reflecting the VEPs and MRPs), to compare the state transitions in neuronal activity around SC and movement onset. These state transitions consisted in a concurrent decrease in the power of beta oscillations and increase in the power of slower oscillations. The transition from cue anticipation to processing, triggered by SC, was similar in magnitude and rate to the subsequent transition from movement preparation to execution, further demonstrating the importance of early cue processing in motor cortex.

We propose that this motor cortical activity during cue anticipation and processing is embedded in a timing network. It may reflect a presetting mechanism that complements the subsequent processing during movement execution, while prohibiting a premature response.

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Poster - Session 2

Reward size and motor effort are represented in the neuronal activity at different levels of the monkey basal ganglia

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Motivation to perform an action requires convergence and integration of limbic, motor and associative information. The basal ganglia (BG) are known for their implication in processes involving these different types of information. We recorded 308 neurons in the striatum, 149 TANs (Tonically Active Neurons) and 159 PANs (Phasically Active Neurons), and 92 neurons in the external globus pallidus (GPe) of two monkeys performing a visuomotor task with four conditions with different cost (force to develop)/benefit (reward size) ratios for the animal. More than 60% of the TANs were modulated at the visual stimuli or at the reward and 46% responded to both, with no difference among the conditions. PANs showed peaks of activity to the visual stimuli, the force development or the reward. Their activity was modulated by the amount of force at the time of the force development (52/73, 71%) and by the reward size at the reward (29/38, 76%). Interestingly, 45% (33/73) of the PANs also showed an effect of the size of the upcoming reward at the development of the force, and 66% (25/38) an effect of the amount of force exerted at the time of reward. In GPe, neuronal activity was modulated in response to the visual stimuli (54%), the development of the force (85%) and/or the reward (79%). Most of the GPe neurons responded to multiple events of the task (86%) and were usually (71%) modulated by the task conditions. At the reward, neurons were modulated by the force to develop, the size of the reward or the interaction between these 2 variables (20, 13 and 9% respectively). Our results suggest that the motor and motivational information, encoded separately in the striatum (PANs) at different events of the task, converge in GPe where one single neuron can be modulated by these events.

Functional role of the Cerebellum in the gamma-band synchronization of the sensory and motor cortices

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The cerebellum is a structure essential for the control of movement, but its contribution to motor cortex dynamics remains largely unknown. We examined the influence of the cerebellum on cortical activity in rats during haptic exploration. To this end, we recorded the field and cellular activity in the motor cortex, sensory cortex and motor thalamus before and after inactivation of the cerebellum. Our results show that the inactivation of the cerebellum decreases the firing rate of cells in the thalamus and in the motor cortex of the vibrissae during episodes of free whisking in the air. We also found a decreased spectral coherence between the motor cortex and the sensory cortex in the gamma band during whisking. Our results show that the cerebellum is a major determinant of the sensory-motor cortical interactions during motor activation.

Poster - Session 2

Cortical readout of prosthetic vision: a parametrical study.

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Stimulating the retinal network is seriously considered as a tool to restore visual function in a large number of human retinal pathologies (ARMD and RP). To test the functional impact of retinal implants, we made quantitative comparisons between visual and electrical evoked activities at the level of the population in the primary visual cortex. As implants, we used sub-retinal matrices of 1mm diameter supporting 9 to 17 electrodes (CEA-LETI, Grenoble). Using visual stimulation, retinotopic organization, retino-cortical magnification factor, stimulus intensity response function and dependence to stimulus size were characterized. These benchmarks were then used to interpret the electrically-evoked cortical activities induced by the retinal implants in terms of their hypothetic visual counterparts.

By manipulating the size of our electrical stimulation (single electrode vs. whole implant), we generated activations of increasing size in the cortex at the expected retinotopic position. However, these cortical activations were much larger than predicted by the size of the implants, suggesting a non-linear recruitment of the retinal network with potential diffusion of the electrical currents. We observed that manipulation of a single parameter of the electrical patterns, such as intensity, leads to modulations of cortical activation along several dimensions and could affect the size as well as the brightness of the percept as recently shown in human patients. To overcome these pitfalls, new electrical stimulation paradigms were designed and tested that allow focalizing cortical activations to match visual evoked activity.

These observations are important for the development of functional retinal implants and optimal features of electrical patterns. We think that providing embedded functional tests of the implant is a necessary step for the progress in this field.

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Poster - Session 2

Spatial organization of beta-band local field potential oscillations during delayed reach to grasp movements

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The local field potential (LFP) is thought to reflect activity of neurons in the vicinity of the recording electrode [1]. In primary motor (MI) and premotor (PM) cortex, LFP oscillations in the beta band (10-40 Hz) are typically observed during motor preparation [2]. Recent studies suggest that the LFP reflects a dynamic propagation of neuronal activity over several millimeters [3-5]. To further characterize the topographic features of oscillatory LFP activity in motor cortex, we here study the spatio-temporal organization of the LFP during a delayed reach to grasp task. Two monkeys are trained to grasp and pull an object with high or low force using either a side or a precision grip. In recording sessions of the grip-precue condition, after the monkey initiates the trial the grip type is revealed by a visual cue. After a delay period, a second visual cue provides the complementary information on the load force. The latter cue also serves as the GO signal. In force-precue conditions, the order of presenting the grip and force cues is reversed. The LFP is recorded via a 10-by-10 Utah electrode array implanted between MI and dorsal PM. We analyze the power spectra of the LFP for different task periods and cortical positions. Next, we compare these power spectra between task periods and/or conditions based on the amplitude of spectral peaks and shifts of the prominent frequency of the beta oscillation. To investigate whether the spatial organization of the LFP shows wave-like properties, we also determine the coherence of the LFP between pairs of electrodes as well as phase shifts of the LFP over the array. From these observations we calculate a map of averaged phase shifts and directions. To further test the hypothesis of an underlying wave propagation, we determine the corresponding propagation speeds (cf. [3]) as a function of time and cortical position. Finally, we discuss these findings in the context of previous work on relating the LFP to precise spike correlations exhibited in the network [6].

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Poster - Session 3

Simple and versatile fabrication of polymer micro-electrode arrays

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In the last decade, microelectrode arrays (MEAs) have become an invaluable tool to study different properties of neural networks such as network formation, network dynamics and signal processing. The traditional technology is based on micro-sized metallic electrodes produced through photolithographic etching of physical deposited noble metal coatings. As the size of the electrodes decrease, however, both signal quality and stimulation ability drop due to the high impedance of the metal-tissue interface. Moreover, the fabrication of such devices relies on traditional silicon patterning technology, making commercially available MEAs expensive and restricted to rigid substrates. Conducting polymers such as poly(3,4-ethylenedioxythiophene) doped with poly (styrenesulfonate) (PEDOT:PSS), show lower impedance and higher capacitance compared to metals, as well as an augmented biocompatibility. Thanks to their mechanical properties and process ability, conducting polymers can be solution-processed by low cost printing techniques on flexible substrates, leading to a new generation of prosthetic devices with unique conformability and form-factors. Here we present a novel approach to photolithographycally define polymer MEAs, patterning at the same time the polymer active sites as well as the insulating layer. The process is extremely versatile and can be used to pattern onto a large variety of substrates (hard and flexible), any kind of organic material. We validated the MEAs by in vitro recording of electrophysiological signals from mouse hippocampus slices, showing how our platform is capable of monitoring spontaneous single-unit activities as well as evoked responses induced by drug perfusion into the nervous tissue.

Poster - Session 4

Building a directional anticipatory response along the motion trajectory in V1

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To process motion the visual system need to reduce noise and ambiguities. Such noise and ambiguities can arise when global motion is processed through a local aperture: the so-called “aperture problem”. To disentangle ambiguity, it has been proposed that V1 end-stopped neurons could extract 2D cues and initiate the integration of global motion information (Pack and Born 2001; Pack et al. 2003).

Here we propose that V1 neurons do not only provide a local analysis of contours in their classical receptive field, but may participate into a more complex and dynamical information processing when seen at the population level. In response to a moving object along a trajectory, neurons activated all along the motion pathway could dynamically bias the global population activation through inter- and intra-cortical propagation of activity. To investigate this issue, we first recorded with a single-unit electrode from a population of neurons in V1 of 2 alert fixating monkeys. The spatial profile of the receptive field (RF) and the directional tuning of the cell was first carefully characterized using sparse-noise stimuli and moving bar respectively. Our main protocol consisted of bars moving to a fixed direction but with different orientations and for different path lengths before reaching the RF of the recorded neurons.

Our results show that a bar moving towards a long trajectory generates an anticipatory response that build-up gradually with time before the bar actually enters into the RF of the cell. Importantly, such anticipatory response is mostly untuned for orientation. To confirm that our results across a population of simultaneously recorded neurons with a fine grain distributed receptive field locations, we used a UTAH array implanted in para-foveal V1 with the same stimulation paradigm. Our preliminary results confirm the observations carried out with the single electrode and provide crucial information about the cartographic retinotopic integration by V1 network.

Poster - Session 4

Role of electric synapses in spike train statistics of integrate and fire neural networks

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Communication between neurons involves chemical synapses as well as electric synapses (gap junctions). On theoretical grounds, the role of gap junctions in encoding and shaping collective dynamics as well as spike train statistics is quite less understood than the role of chemical synapses. In this work, we analyse mathematically the collective spike train statistics in conductance-based Integrate and Fire neural networks with chemical and electric synapses. We show that this statistics is characterized by a Gibbs distribution whose potential can be explicitly computed. This provides a firm theoretical ground for recent studies attempting to describe experimental rasters in the retina as well as in the parietal cat cortex by Gibbs distributions and maximum entropy principle. The main observation resulting from our analysis is that spike statistics is *indecomposable*. The probability of spike patterns does notfactorize as a product of marginal, per-neuron, distributions. As a consequence, in that model, *there is absolutely no way to defend that neurons act as independent sources*. Additionally, correlations mainly result from the chemical and electrical interactions between neurons (correlations persist even if there is no external current / stimulus). We also point out that the Gibbs distribution obtained in our model is quite more complex than Ising model or Generalized Linear Models used in retina spike train analysis. Especially, it involves spatio-temporal spike patterns is non stationary, and correlations are induced by dynamics not only by stimulus. Handling spatio-temporal events in Gibbs distributions requires more subtle algorithms than simultaneous events as those considered in the Ising model and its extensions. This work suggest that electric synapses could have a stronginfluence in spike train statistics of biological neural systems, especially theretina where gap junctions connections between several cells-type (e.g. amacrine and ganglion cells or amacrine-bipolar) are ubiquitous.

Rodrigo Cofre, Bruno Cessac. Dynamics and spike trains statistics in conductance-based integrate-and-fire neural networks with chemical and electric synapses . *Chaos, Solitons and Fractals, submitted,* 2012.

Brain state-dependent functional reconfiguration of entorhinal cortex networks in control and epileptic rats

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In order to support the production of different cognitive functions, neuronal networks can support the emergence/expression of different oscillatory activities associated to different brain states. One possible mechanism at the core of such versatile function is that a given network could dynamically change its functional structure, e.g. the expression of connections between neurons, as a function of the brain state.

We investigated whether such a mechanism is present in the temporal lobe, which networks are known to play an important role notably in episodic memory and navigation.

We used in vivo high-density recordings (32-sites silicon probe) in entorhinal cortex to isolate the spike trains of numerous neurons and reconstructed their functional connectivity matrix during theta and slow oscillations in anesthetized rats. We show that entorhinal cortex networks can be dynamically reconfigured in a brain state-dependent fashion.

This is also of particular importance in the context of epilepsy, in which temporal lobe circuits are deeply anatomically reorganized. Using the same approach in epileptic rats (pilocarpine model of temporal lobe epilepsy), we show a functional hyper connectivity in the entorhinal cortex and investigate how such restructured networks are dynamically reconfigured. Such in vivo functional correlate to the structural reorganization of temporal lobe networks could be have a key role in neuronal synchronization and generation of seizures, but also in the emergence of the associated cognitive deficits, like an impairment of episodic memory.

Poster - Session 4

Specific stimulation of septal cholinergic neurons by light-activated channelrhodopsin2 displays brain state-dependent influence on hippocampal rhythms in the mouse in vivo

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Septal neurons are believed to play an important role in the generation of the hippocampal rhythms. However, the functional contributions of the cholinergic, GABAergic and other septal neurons are still debated. We used transgenic mice expressing ChR2 under the control of the cholineacetyltransferase (ChAT) promoter, by transfecting a CRE-driver mouse strain (CRE recombinase under the control of the cholineacetyltransferase promoter, ChAT-CRE) with an AAV vector carrying a double floxed ChR2-YFP construct, or cross-breeding with Ai32 mice (CRE-reporter mouse strain bearing a double floxed ChR2-YFP construct). Local light stimulation in the medial septum was achieved by an optic fiber coupled to a DPSS laser (473 nm), while hippocampal activity was monitored using 16 or 32-channel linear silicon probes spanning over CA1 and dentate gyrus layers, under anesthesia as well as in behaving animals. Under urethane anesthesia, sinusoidal or pulse stimulation (0.1 to 12 Hz, 10 seconds) of septal cholinergic neurons reliably induced an increase in theta-band oscillations in the hippocampus, associated with a strong decrease in ripple incidence and a decreased activity of CA1 pyramidal cells. This effect was independent from the stimulation frequency. In chronically-implanted animals, the theta increase was reliably observed during surgery (isoflurane anesthesia), but was not sustained during freely moving recordings. Nevertheless, the decrease in ripple incidence was still present. Therefore, septal cholinergic neurons strongly influence hippocampal rhythms, differentially according to brain state.

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

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The activity of neuronal networks in the cortex is controlled by a variety of GABAergic neurons. During development, in the hippocampus, early born GABAergic neurons act as hub nodes that function in orchestrating network dynamics through a high degree of functional and structural connectivity (Picardo et al. 2011). These early born GABAergic cells remain into adulthood but whether neuronal hubs exist in adult cortical circuits remains unknown. This issue cannot be addressed in vitro due to the long-range axonal arborizations of adult early born GABAergic neurons. To this aim, we have adapted a previously described chronic window on the brain (Dombeck et al. 2010) to allow large scale calcium imaging from hundreds of hippocampal neurons simultaneously in unanesthetized head restrained adult mice. The mouse is free to run on a treadmill allowing self-paced changing of visual and tactile cues. Intra hippocampal local field potential is simultaneously recorded to identify the state of the hippocampal network, i.e. theta, large irregular activity. To monitor the activity of some oriens GABAergic neurons as well as pyramidal cells, we use a genetically encoded calcium indicator (GCaMP3). This calcium indicator is only sensitive to bursts of action potentials. We are using the onsets of calcium transients to analyze spatial, temporal and oscillatory relationships between neurons. In this way, we will describe the functional connectivity structure of the adult hippocampus.

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