FDV Workshop on Neuro and Cognitive Sciences
Wednesday, May 25th at CRI 9:30am-6pm

"From single neurons to complex pathways: a multi-scale approach of cognition"

Detailed Program

All students slots are composed by 30' of presentation followed by 15' of discussion.

9h30-10h15: Anne-Lise Gaffuri

Laboratoire de Neurobiologie, CNRS-UMR 7637, ESPCI-ParisTech.
Zsolt Lenke

Drosophila melanogaster: a model system to study neuronal GPCRs?

The neuronal receptor for Δ9-tetrahydrocannabinol (Δ9THC), the major psychoactive substance of marijuana, is the type-1 cannabinoid receptor (CB1R), one of the most7 abundant G-protein coupled receptors (GPCR) in the mammalian nervous system. It is commonly known that the activation of endogenous CB1R in the hippocampus causes memory defect. Interestingly, recent reports show dynamic regulation of CB1Rs in projection neurons during development of the rat brain. *In vitro* results obtained by studying morphological changes of CB1R-transfected neurons show that CB1Rs is a negative regulator of axonal and dendrite growth.

However, specific mechanisms involved in neuronal remodeling remain poorly described. This work proposes to validate the drosophila model to study these mechanisms. First, we optimized the drosophila neurons culture protocol to obtain well-differentiated neurons. Then, we validate this *in vitro* model by showing that the CB1R-activity-dependant structural plasticity of neurons is conserved.

In addition, by expression of CB1R in a structure of the fly brain involved in memory process (the mushroom body), we show that hyper-activation of CB1R leads to a specific long-term memory defect, reminiscent of the major cannabinoid effect in the mammalian brain.

These results validate the drosophila model as a model system to study CB1R, a mammalian GPCR. Moreover, we are now able to use the powerful genetic tools of drosophila to characterize the effectors involved in the role of CB1R on neuronal remodeling and on memory process.

10h15-11h00: **Delphine Ladarré**

Laboratoire de Neurobiologie, CNRS-UMR 7637, ESPCI-ParisTech.
Zsolt Lenke

Live imaging of type-1 cannabinoid receptor signaling at single neuron scale

The type-1 cannabinoid receptor (CB1R), one of the most abundant G-coupled protein receptors (GPCRs) in the central nervous system, is localized predominantly on the axonal plasma membrane. Previous study of the host laboratory has demonstrated that its axonal targeting mechanism consists in an initial addressing to somatodendritic membrane, then in a constitutive and activation-dependent endocytosis in this compartment and, finally, in a transport and accumulation on the axonal membrane. However, it is not known how these different activation-dependent targeting steps mobilize intraneuronal signaling pathways. Using a videomicroscope with high spatio-temporal resolution, we imaged the activation of major signaling pathways downstream of CB1R, cyclic AMP/protein kinase A (PKA). We show that the constitutive activation of CB1R requires paracrine and autocrine secretion of endocannabinoids but also involves intracellular endocannabinoids and/or genuine constitutive GPCR activity. Next, we demonstrate that the constitutive somatodendritic activation of CB1R, necessary for constitutive endocytosis, efficiently recruits PKA signaling pathways in this compartment. These results explain how CB1Rs, despite of their predominantly axonal localisation, are able to play a role in dendritic development, as it was previously shown in the laboratory.

11h-11h15**: **Coffee Break

11h15-12h00: **Romain Cazé**

LNC INSERM 960, Boris Gutkin

Intrinsic plasticity in non-linear dendrites gates pyramidal computation.

Dendritic non-linearities (Gasparini et al 2004, Migliore et al 2008), in concert with non-linear somatic spike generation enrich single neuron computation. Two stages of non-linearities, dendritic then somatic, have been proposed to increase the number of possible functions a single neuron can implement (Mculloch & Pitts 1943, Poirazi et al 2001). However how specifics of the dendritic non-linearity define this input/output mapping is still poorly understood.
To address this issue we follow a reduced approach to modelling of pyramidal neurons, based on the analogy with the two-layer perceptron. We then employ boolean algebra to identify the input/output mappings of such a model and find that any real-valued two layer perceptron has a discrete equivalent. This allows us to exhaustively sweep through the classes of parameters key for computation: synaptic placement, synaptic weights, dendritic threshold, somato-dendritic coupling and somatic threshold.
Our results show that variation of only two classes of parameters, the dendritic threshold and the synaptic placement, are sufficient to access the full range of possible input/output mappings. We extend these results to biophysical models of hippocampal and cortical pyramidal neurons. Our study shows that activity dependent modification of dendritic excitability is crucial for regulating pyramidal neuron computation. We futher provide with this study a theoretical basis for recent experimental demonstrations of dendritic plasticity in CA1 pyramidal cells (Losonczy et al. 2008).

12h00-12h45: **Jérémie Sibille**
Rouach Nathalie (Collège de France) Holcman David (ENS)

Astrocyte just a supportive cell for neurons or a new scale for neuronal integration?

Astrocytes are in the crossection of the major function of neurons (metabolism, Neuroscular-coupling, morphological support, ionic homeostisis, immun reaction). So let's see at which scale those interactions gets relevant for neurotransmission.....

***12h45-13h45**: Lunch Break*

13h45-14h30: **Maéva Vignes**
Curie's Institute - Jean-Louis Viovy and Bernard Brugg

In vitro reconstruction of neuronal networks and applications to study neurodegenerative diseases.

Experimental models used to study brain development and degeneration range from whole animal models, which preserve the anatomical structures but greatly limit the experimentation at the cellular level, to dissociated cell culture systems, that allow detailed manipulation of cell phenotype but lack the highly ordered and instructive brain environment. Thus new experimental models are needed to facilitate both individual cell manipulation and brain connectivity reconstruction. Thus, I am working on microfluidic cell culture systems that allow to handle neurons and axons in micron size environments and to mimic in vitro the development and/or degeneration of some physiological neuronal pathways.

14h30-15h15: **Alexandre Grémiaux**
INRA, Jean-Pierre Rospars and INRIA Dominique Martinez

Neural encoding of sex-pheromone in moth olfactory brain: from data analysis to modelling

What are the fundamental laws driving olfactory information encoding in the brain? To bring forward this question, we focused on the particular case of sex-pheromone encoding in the moth (*Agrotis ipsilon*) olfactory brain, our approach combining data analysis and neural network modelling.

In moth, the sex pheromone plume emitted by females is detected by specialized olfactory receptor neurons (ORNs) housed in antennal sensilla of conspecific males. A large number of ORNs converge towards a few glomeruli in the olfactory brain (antennal lobe), where they connect synaptically to a smaller number of projection neurons (PNs).

We studied the signal transformation from ORNs to PNs by mixing modelling and statistical analysis of single neuron responses at different concentrations of sex pheromone. In order to understand better the observed transformation, we developed a phenomenological model of ORN population response as an input for a simple glomerulus network model.

The results suggest that the heterogeneity of ORN responses plays an essential role in the signal transformation from ORNs to PNs. Also, this transformation may be seen as an optimal strategy to code for both identity and quantitative aspects (temporal structure, concentration...) of an odour.

***15h15-15h30**: Coffee Break*

15h30-16h15: **Mélanie Strauss**

Sates of consciousness in sleep.

16h15-17h15: **Stella de Bode**
University of California, Los Angeles

Post Cerebral Hemispherectomy: From Equipotentiality to Irreversible Lateralization of Language.

We will report data from 20 individuals who have undergone either Left or Right cerebral hemispherectomy (complete removal or partial removal/complete disconnection of one cerebral hemisphere due to life-threatening seizures). Language abilities (lexicon, syntax and phonological skills) of one isolated hemisphere (right or left) were investigated using standardized tasks. The results suggest that two hemispheres are performing similarly and slightly below age-matched controls if the resected hemisphere has been damaged prenatally. A lesion after even a few postnatal months of normal development results in the familiar from adult aphasics profile when individuals with the isolated right hemisphere perform very poorly on all tasks, especially, syntactic.

17h15-18h00: **Luc Boruta**
ALPAGE (Univ. Paris 7 & INRIA), LSCP (EHESS, ENS & CNRS)

Learning phonemes in parallel universes.

Though the phonemic inventory of a language is typically small, phonetic and phonological processes yield manifold variants for each phoneme. Allophonic rules relate phonemes to their variants, expressing the contexts in which the latter occur. I am interested in describing procedures by which infants, learning their native allophonic grammar, could reduce the variation and recover words. Combining insights from both computational and behavioral studies, I endorse the hypothesis that infants are good distributional learners and that they may `bootstrap' into language tracking statistical regularities in the signal. I present a comprehensive framework to model the acquisition of phonemes, combing acoustic, distributional and lexical cues. In order to combine these indicators without creating artificial numerical interferences, I reformulate the task as a clustering problem and use the so-called "parallel universes" approach.