MASTER 2 Sciences du Vivant - IMaLiS
Interdisciplinary Master in Life Sciences

Proposition of laboratory internship

Academic Year 2018-2019

Pathway (please select one or more):

- Neurosciences
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Receiving team:

- Name of the internship supervisor:David Hansel
- Position of the internship supervisor: DR CNRS
- Email: david.hansel@parisdescartes.fr
- Tel: 0607508403
- Team name: Cerebral Dynamics, Plasticity and Learning
- Name of the team co-leader: David Hansel
- Lab name:, Integrated Neuroscience and Cognition Center
- CNRS / INSERM Unit number: 8002
- Lab location:Université Paris Descartes
- PhD School (ED): ED3C

Selected publications of the team (maximum 5, during the last four years)

T. Arakaki, A. Leblois, S. Charpier & D. Hansel, *The role of striatal feedforward inhibition is the maintenance for absence seizures*, J Neurosci. 36:9618-32, 2016.

D. Darshan, W.E. Wood, S. Peters, A. Leblois, D. Hansel, *A canonical neural mechanism for behavioral variability,* Nature Comm. 8:15415. doi: 10.1038/ncomms15415, 2017.

JJ Pattadkal, G Mato, C van Vreeswijk, NJ Priebe, D Hansel. *Emergent Orientation Selectivity from Random Networks in Mouse Visual Cortex*. Cell Rep. 2018 Aug 21;24(8):2042-2050.e6. doi: 10.1016/j.celrep.2018.07.054.

R Darshan, C van Vreeswijk, and D Hansel *Strength of Correlations in Strongly Recurrent Neuronal Networks* Phys. Rev. X 8, 031072 2018.

L. Lebovich, R Darshan, Y. Lavi, D.Hansel* and Y. Loewenstein*, *Idiosyncratic choice bias in decision tasks naturally emerges from neuronal network dynamics*, bioRxiv 284877; doi: https://doi.org/10.1101/284877 & Nature Human Behavior, in revision.

Research project of Remi Baroux

Title of the proposed project: Recurrent dynamics and competition in basal ganglia

Description of the project: Basal ganglia (BG) are crucial in motor program selection. BG are also involved in movement disorders. In particular, BG neuronal activity in Parkinsonian animals and patients is more oscillatory and more synchronous than in normal individuals.

The cortex-basal ganglia-thalamic network involves many feedback loop of different polarities. In previous work we have developed a minimal computational model of BG network dynamics in non-human primates[1]. Itrelies on the fact that the direct (cortex–striatum–GPi–thalamus– cortex) and the hyperdirect loops (cortex–subthalamic nucleus–GPi–thalamus– cortex) have different polarities. The dynamical competition between these 2 loops can provide the BG–cortex system with the ability to perform motor program selection. Under the assumption that dopamine potentiates corticostriatal synaptic transmission in the model, moderate dopamine depletion leads to a complete loss of this ability whereas high depletion can lead to synchronous oscillations. This model predicts that a loss of selection ability occurs before oscillations appear, suggesting that Parkinson's disease motor impairments are not necessarily related to abnormal oscillatory activity. Leblois et al.[2] tested this prediction in MPTP treated monkeys and reported evidence in line with the behavior of the model that synchronized oscillatory activity appears lately in BG during progressive Parkinsonism.

Our goal is to investigate the hypothesis that in rodents normal and pathological β range oscillations are of subcortical origin. Several feedback loops involving the thalamus and BG nuclei but not the cortex are identified in rodents. We will develop *in-silico* models of the cortex-BG-thalamus network. Its architecture will rely on published data groups[3]. It will have rate-based neuronal dynamics[1] for which numerical simulations can be guided by analytical calculations. It will simulate motor behaviors. To this end, the recurrent as well as feedforward connectivities will be functionally organized[1]. The network will perform action selection and movement generation in response to sensory cues represented as an external input to the cortex and/or striatum. The direction of the generated movement will be the direction of the population vector[4] of the cortical neuron activities. We will use this computational platform to test the role in the generation of pathological β rhythms of the different pathways embedded in the circuit. In particular, we will study the putative roles of the striato-pallidal loops (which include several striatal and pallidal sub- populations) as well the striato-pallido-thalamo-striatal loops. We will characterize in our model how the phase relationships between the activity of the different populations during sustained pathological β oscillations depend on the model parameters. We will also model "optogenetic" manipulations at different network locations and study their suppressing or enhancing effects on β activity. Comparison with experiments will shed light on putative mechanisms of pathological β activity.

This project will be conducted in tight interaction with our collaborators T. Boraud, A. Leblois and N. Mallet, experimentalists at the Institute of Neurodegenerative Diseases (IMN, UMR 5293, Bordeaux).

R. Baroux will primarily work on the development of the computational platform and on a first batch of tests to investigate its non-linear dynamics. Depending on the progress the other questions will be addressed.

References:

1- Leblois, A., Boraud, T., Meissner, W., Bergman, H. & Hansel, D. Competition between feedback loops underlies normal and pathological dynamics in the basal ganglia. *J. Neurosci.* 26, 3567–83 (2006).

2 -Leblois, A. *et al.* Late emergence of synchronized oscillatory activity in the pallidum during progressive Parkinsonism. *Eur. J. Neurosci.* 26, 1701–13 (2007).

3- Corbit, V. L. *et al.* Pallidostriatal Projections Promote Beta Oscillations in a Dopamine-Depleted Biophysical

4- Georgopoulos, A., Lurito, J., Petrides, M., Schwartz, A. & Massey, J. Mental rotation of the neuronal population vector. *Science (80-.).* **243,** 234–236 (1989). Network Model. *J. Neurosci.* **36,** 5556–5571 (2016).

Why INC should support this project and Remi Baroux: Remi Baroux is an excellent student. This is testified by is achievements at PACES and at the admission exam at ENS. He impressed all the members of our team by the remarkable quality of the first presentation he gave at our weekly group meeting, two weeks only after beginning his project. Remi perfectly fit the project he is working on : 1) He joined our team because he wanted to work on a theoretical project with tight connections with pathologies. 2) He is already familiar with the functions and the dysfunctions in which basal ganglia are involved. 3) He wants to improve his knowledge on the theory of non-linear dynamical systems 4) His plan is to continue with a Ph.D in theortical neuroscience on a topic which requires close collaboration with experimentalists: this fits pertfectly with the "philosophy" of our team.

This project is a priority of our team: its outcomes will be included as preliminary results in the ANR application that together with our experimentalists collaborators in Bordeaux will submit next Fall.

Last but not least: the theoreticians of the "Cerebral dynamics, memory and learning " team have never benefitted of INC support for an M2 project.

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