TITLE: **Controllability and Observability of Rat Brain Activity.**

ABSTRACT:

In a recent work [1], we have shown that there are warning and caveats in the theoretical framework proposed by Gu et al. [2] to characterize brain networks controllability. Drawing on concepts and methods of control theory they quantified the controllability of brain regions starting from anatomical diffusion imaging. In particular, we have shown that one of the main problems in this case is working using undirected brain networks and asking to control the network with one single node. From an experimental point of view, Yang and collaborators [3] have successfully applied a target control approach to the connectome of the nematode *Caenorhabditis elegans*, allowing to predict the involvement of each *C. elegans* neuron in locomotor behaviours.

The scope of this project is two folds. From a theoretical point of view, it will develop the framework of target control [4], specifically for linearized whole brain models around resting states. Then it will investigate the role of the topological structure of directed networks in target control, using whole brain models based on high density directed anatomical DTI of mice. Finally, we will study the "observability" problem associated with the previous controllability framework.

From an experimental point of view, the project will assess the feasibility and design of control experiments in rodents. In particular, specific cortical neurons in-vitro (dissociated cultures) and in-vivo (in the somatosensory barrel cortex) will be stimulated by electrical or optogenetic means and resulting network responses compared to those triggered by physiological stimuli (rat whiskers movement). Finally, using the control framework developed theoretically, we will attempt to predict the activation patterns of a whole network induced by single (or a few) neuron stimulation in quasi-realistic physiological conditions.

REFERENCES (Max 5):

[1] Tu, Chengyi, et al. "Warnings and Caveats in Brain Controllability."

NeuroImage (in press).

[2] Gu, Shi, et al. "Controllability of structural brain networks." *Nature communications* 6 (2015): 8414.

[3] Yan, Gang, et al. "Network control principles predict neuron function in the Caenorhabditis elegans connectome." *Nature* 550.7677 (2017): 519.

[4] Gao, J., Liu, Y. Y., D'souza, R. M., & Barabási, A. L. (2014). Target control of complex networks. *Nature communications*, *5*, 5415.

PARTICIPANTS (PI and co-PIs):

PI: S. Vassanelli

Co-PI. S. Suweis

Other collaborators: M. Corbetta, S. Zampieri, M. Zorzi, (Dal Maschio)

EXPERIMENTAL DATA:

To be acquired	X
Already acquired (ready to be used)	X

Experimentally, we aim at assessing the effect of target control on two systems: a network of dissociated neurons from the mouse hippocampus in culture, and the network of the mouse somatosensory cortex in-vivo. On the first system, we will be able to stimulate targeted single neurons and observe the response at a network level by multi electrode arrays (MEAs) integrated at high density (up to 20,000 microelectrodes/mm^2). We may also combine MEA electrophysiology with Ca^{2+} optical imaging to minimize risk. Similarly, we will take advantage of implantable MEAs for stimulating and recording the barrel cortex neuronal network in vivo. Considering that electrical stimulation is suitable, at present, only for non selective stimulation of subpopulations of neurons in the proximity of a microelectrode, we will combine optogenetic stimulation with MEA recording to increase resolution.

Instrumentation is basically already available in the NeuroChip lab. of SV. New MEAs will have to be purchased as consumables.

ETHICS COMMITTEE:

Obtained	
Conditioned submission*	Expected time response (in months):
Not required	

* request will be submitted only if a PhD student will be associated to the project