MASTER 2
Neurosciences Fondamentales et Cliniques
UCB Lyon 1, Lyon, France

Internship proposal 2020-2021
(internship from January to end of May 2021)

Host laboratory: Lyon Neuroscience Research Center, CRNL
CH Le Vinatier, Bât Neurocampus, 95 Bd Pinel, 69675 Bron Cedex, France

Host team:
TIGER (Translational and Integrative Group in Epilepsy Research), BELIV (Bioelectrochimie in vivo) technological Platform

Internship supervisor:
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Project title:
DYNAMIC RECRUITMENT OF BRAIN GLYCOGEN ENERGY STORES BY NEURONAL ACTIVITY

Project summary :
Brain energy stores consist mostly in glycogen present in astrocytes. They are recruited in hypoglycemic or ischemic conditions to fuel brain cells when energy supplies are limited, but also during normal brain functioning. The amount of energy metabolites that can be supplied from glycogen stores, and the time course of this recruitment is still unknown. Our laboratory has developed ultrasmall microelectrode biosensors to monitor the extracellular concentrations of glucose and lactate in the brain (1,2). Using these devices, we will investigate the possibility of glycogen stores recruitment during cortical spreading depolarization (SD), a wave of massive depolarization of neurons and glial cells that represents a major metabolic challenge to the brain. Our laboratory has determined that SDs induce a rapid decrease in extracellular glucose coupled to lactate release in the interstitial fluid, reflecting increased glucose consumption through aerobic and anaerobic glycolysis (3). We hypothesize that glycogen stores are recruited during SDs, and we will block glycogen degradation into glucose by local administration of 1,4-dideoxy-1,4-imino-D-arabinitol (DAB). We will determine the effects of DAB on glucose and lactate extracellular concentrations, as well as on the dynamic glucose and lactate changes evoked by SD. We hypothesize that blocking glycogen recruitment during SDs will decrease the availability of glucose and/or lactate, and increase the time needed to repolarize brain cells. This study will identify a role for glycogen stores during high brain metabolic demand, and improve our understanding of brain metabolism.

References related to the research topic:
(1) Chatard C, Sabac A, Moreno-Velasquez L, Meiller A and **Marinesco S** (2018) Minimally invasive microelectrode biosensors for brain monitoring based on platinized carbon fibers. *ACS Central Science*. 4: 1751-60.
(2) Chatard C, Meiller A and **Marinesco S** (2018) Microelectrode biosensors for in vivo analysis of brain interstitial fluid. Electroanalysis 30: 977-998.

Please send your proposal to emiliano.macaluso@univ-lyon1.fr and marion.richard@univ-lyon1.fr for publication on the website.

(3) Meiller A, Sequeira E and **Marinesco S** (2020) Electrochemical nitric oxide microsensors based on a fluorinated xerogel screening layer for in vivo brain monitoring. *Anal Chem.* 92(2):1804-1810. doi: 10.1021/acs.analchem.9b03621

(4) Balança B, Meiller A, Bezin L, Dreier J, Lieutaud T and **Marinesco S** (2017) Altered hypermetabolic response to cortical spreading depolarizations after traumatic brain injury in rats. *J Cereb Blood Flow Metab.* 37(5):1670-1686.

(5) Le Douce J, Maugard M, Veran J, Matos M, Jego P, Vigneron PA, Faivre E, Toussay X, Vandenberghe M, Balbastre Y, Piquet J, Guiot E, Thuy Tran N, Taverna M, **Marinesco S**, Koyanagi A, Furuya S, Gaudin-Guerif M, Goutal S, Ghettas A, Pruvost A, Bemelmans AP, Gaillard MC, Cambon K, StimmerL, Sazdovitch V, Duyckaerts C, Herard AS, Delzescaux T, Hantraye P, Brouillet E, Cauli B, Oliet S, Panatier A and Bonvento G (2020) Impairment of Glycolysis-Derived L-Serine Production in Astrocytes Contributes to Cognitive Deficits in Alzheimer's Disease. *Cell Metabolism.* 31(3):503-517.e8 doi: 10.1016/j.cmet.2020.02.004.