Project title: Modeling the Metabolic Diversity of the Brain's Glial Cells

Project leader: Prof. Dr. Renaud Jolivet, Dr. Marian Breuer

Function: Professor of Neural Engineering and Computation

Collaborators: Prof. Dr. Ilja Arts

Proposal (250 words):

Introduction: The brain consists of a variety of cell types, and neurons only constitute around half of the brain cell population. The other cell populations, collectively known as glial cells, support and interact with neurons in various ways. Glial cells play a pivotal role in normal brain function as well as neurodegenerative and other disorders, and thus their understanding is of importance in the context of public health. However, while glial cells are known to play an important role in brain metabolism overall, their particular metabolic functions and interactions are far from understood.

Hypothesis and Objectives: This project will study the metabolic functions of different types of glial cells, as well as their metabolic interactions, and how these are affected in aging and different pathological conditions.

Setting and Methods: The project will make use of large publicly available neuroscience transcriptome data sets to build models of the metabolic network of various types of glial cells, and to study how these glial cells interact with each other in the brain. The project will then make use of other transcriptomes to investigate these interactions in aging and in various diseases of the central nervous system.

Impact: The metabolic functions and interactions of glial cells in normal brain function address an important knowledge gap in basic neuroscience; while their perturbations in aging, neurodegenerative diseases and other pathological conditions could help to elucidate disease mechanisms as well as suggest potential intervention strategies – with strong potential impact in healthy aging and disease diagnosis and therapy.

Requirements candidate: Highly motivated student with good English communication skills and proactive and resolute attitude. The project requires good programming skills and an interest for the complexity and diversity of the brain's heterocellular population. The ideal candidate would have a foundation in biochemistry and cellular metabolism on the one hand, and some computational skills on the other hand, preferably in Matlab. Applications with background in only the biochemical or computational side are still welcome, if the applicant can make a case for being able to catch up in the other aspect.

Keywords: Biological Foundations of Human Health and Diseases, Computational Biology, Systems Biology, Metabolic Modeling, Neuroscience, Aging

Top 5 selected publications:

1. Cullen CL, Pepper RE, Clutterbuck MT, Pitman KA, Oorschot V, Auderset L, Tang AD, Ramm G, Emery B, Rodger J, **Jolivet RB** & Young KM **"Periaxonal and nodal plasticities modulate action potential conduction in the adult mouse brain"** *Cell Rep.* (2021), 34:108641. Citations (Web of Science): 15

2. Caruso G, Caraci F & **Jolivet RB "Pivotal role of carnosine in the modulation of brain cells activity: Multimodal mechanism of action and therapeutic potential in neurodegenerative disorders"** *Progress in Neurobiol.* (2019), 175:35. Citations (Web of Science): 42

3. Madry C*, Kyrargyri V*, Arancibia-Cárcamo IL*, **Jolivet RB***, Kohsaka S, Bryan RM & Attwell D **"Microglial Ramification, Surveillance, and Interleukin-1β Release Are Regulated by the Two-Pore Domain K^+ Channel THIK-1"** *Neuron* (2018), 97:299. Citations (Web of Science): 182, top 1% cited in Neuroscience & Behaviour

4. **M. Breuer**, T. M. Earnest, C. Merryman, K. S. Wise, L. Sun, M. R. Lynott, C. A. Hutchison III, H. O. Smith, J. D. Lapek Jr., D. J. Gonzalez, V. de Crécy-Lagard, D. Haas, A. D. Hanson, P. Labhsetwar, J. I. Glass, Z. Luthey-Schulten **"Essential Metabolism for a Minimal Cell"** *eLife* (2019), 8:e36842. Citations (Web of Science): 53

5. D. Haas, A. M. Thamm, J. Sun, L. Huang, L. Sun, G. A. W. Beaudoin, K. S. Wise, C. Lerma-Ortiz, S. D. Bruner**, M. Breuer**, Z. Luthey-Schulten, J. Lin, M. A. Wilson, G. Brown, A. F. Yakunin, I. Kurilyak, J. Folz, O. Fiehn, J. I. Glass, A. D. Hanson, C. S. Henry, V. de Crécy-Lagard. **"Metabolite Damage and Damage Control in a Minimal Genome"** *mBio* (2022), **13**:e01630-22. Citations (Web of Science): 2