



ABCDE



Scientific Report

First name / Family name

MAURIZIO DE PITTÀ

Nationality

ITALIAN

Name of the *Host Organisation*

INRIA RHÔNE-ALPES

First Name / family name
of the *Scientific Coordinator*

HUGUES BERRY

Period of the fellowship

10/06/2013 to 09/06/2014



I – SCIENTIFIC ACTIVITY DURING YOUR FELLOWSHIP

Scientific activity during the fellowship involved working on several projects as following detailed.

Main Project: Modelling of calcium signalling and propagation in astrocyte processes.

Collaborators: Nicolas Liaudet and Andrea Volterra (University of Lausanne, Lausanne, Switzerland).

Deliverables: 1 poster to be presented at the forthcoming FENS meeting (July 5th-9th, 2014; Milan, Italy); 1 paper in preparation.

Compartmental modelling was deployed to realistically reproduce experimentally recorded spatiotemporal calcium dynamics in astrocytic processes. With this aim, each compartment was modelled by the ChI model for astrocyte calcium dynamics (De Pittà et al., J. Biol. Phys. 2009), and spatiotemporal dynamics was described by the ensemble dynamics of calcium signals in individual compartments coupled by intracellular propagation of inositol 1,4,5-trisphosphate signals. The model predicts that, in addition to the geometry of the processes, multiple biochemical and cell parameters, such as the distribution of the input signals along the processes, are critical factors for calcium propagation. Geometrical aspects of astrocytic processes, such as their length, diameter and cytosolic volume, could control shape, frequency and spatial extent of calcium pulses. Compartmentalization of calcium signals in astrocytic processes also seems crucially dependent on the distribution of calcium stores and channels in the process. Subcellular organization of astrocytic processes could ultimately account for spatiotemporal specificity of calcium signals, entailing different modes of integration of synaptic stimuli by the astrocyte.

Complimentary Project 1: Modelling of intercellular calcium wave propagation in three-dimensional astrocyte networks.

Deliverables: 1 paper published in Frontiers Computational Neuroscience; 1 poster to be presented at the 23rd Annual Meeting of the Organization for Computational Neurosciences (July 26th-31st, 2014; Québec City, Canada).

Biophysical modelling of three-dimensional astrocyte networks of different topologies was deployed while keeping constant intracellular properties and spatial distribution and density of cells in the network. Computer simulations suggest that changing network topology is sufficient to reproduce the distinct ranges of intercellular calcium wave propagation reported in experiments. Unexpectedly, our simulations predict that sparse connectivity should favor propagation. Altogether, these results provide support to recent experimental findings that suggest a functional role for the organization of cell-to-cell couplings in proper astrocyte networks. Dynamic control of this topology by neurons and signalling molecules could ultimately represent a new type of regulation of neuron-astrocyte and astrocyte-astrocyte interactions.

Complimentary Project 2: Characterization of the I/O response function of an astrocyte.

Collaborators: Gilad Wallach, Eshel Ben-Jacob, Yael Hanein (Tel Aviv University,



Israel) and Nitzan Herzog (University of Nottingham, Nottingham, UK).

Deliverables: 1 paper submitted to PLoS Computational Biology.

Biophysical modelling of glutamate-based intracellular calcium signals in astrocytes was deployed to characterize the I/O calcium characteristics of astrocytes in response to glutamatergic synaptic stimulation recorded experimentally by microelectrode arrays. Computer simulations of the model hint that the sigmoid-shaped I/O astrocyte response is due to the combined effect of supralinear integration of synaptic stimuli by the calcium-mobilizing signal inositol 1,4,5-trisphosphate, and the heterogeneity of astrocyte-to-astrocyte couplings. With this regard, astrocytes may be regarded as nonlinear integrators of synaptic signals.

Other Scientific Activities.

- Invited speaker at the weekly computational neuroscience seminar at the Bernstein Center in Freiburg (Germany) (February 26th, 2014).
- Invited speaker at the weekly seminar on neuroscience at the FORTH in Heraklion, Crete (Greece) (May 8th, 2014).
- Co-organizer (with prof. Hugues Berry) of the workshop on “Computational Methods and Modeling of Astrocyte Physiology and Neuron-Glia Interactions”. July 30th-31st, Quebec City, Canada.

II – PUBLICATION(S) DURING YOUR FELLOWSHIP

Papers:

Lallouette J., **De Pittà M.**, Ben-Jacob E. and Berry H. Sparse short-distance connections enhance calcium wave propagation in a 3D model of astrocyte networks. *Frontiers Comput. Neurosci.* (2014). DOI: 10.3389/fncom.2014.00045

Wallach G., Lallouette J., Herzog N., **De Pittà M.**, Ben-Jacob E., Berry H. and Hanein Y. Glutamate-mediated astrocytic filtering of neuronal activity. *PLoS Comput. Biol.* *Under review.*

De Pittà M., Lallouette J., Ben-Jacob E. and Liaudet N., Volterra A. and Berry H. Calcium computation in astrocyte processes (running title). *In preparation.*

Poster abstract to conferences:

De Pittà M., Ben-Jacob E. and Berry H. Mechanism for astrocyte-mediated persistent activity. 2014 Neuroscience Meeting Planner. Washington, DC. Society for Neuroscience. Online.

De Pittà M., Ben-Jacob E. and Berry H. Astrocytic Theory of Working Memory. 23rd Annual Meeting of the Organization for Computational Neurosciences. July 26th-31st, 2014; Québec City, Canada.

Lallouette J., **De Pittà M.**, Ben-Jacob E. and Berry H. The topology of astrocyte



networks controls the propagation of intercellular calcium waves. 23rd Annual Meeting of the Organization for Computational Neurosciences. July 26th-31st, 2014; Québec City, Canada.

De Pittà M., Lallouette J., Liaudet N., Volterra A., Ben-Jacob E. and Berry H. Modelling of Ca^{2+} dynamics in astrocytic processes. 9th FENS Forum for Neuroscience. July 5th-9th, 2014; Milan, Italy.

III – ATTENDED SEMINARS, WORKHOPS, CONFERENCES

- American Psychanalytic Association Conferences, Chicago, IL, USA. June 6th-10th, 2014.
- Annual Meeting of the Organization for Computational Neurosciences, Paris, France. July 13th-18th, 2013.

IV – RESEARCH EXCHANGE PROGRAMME (REP)

IDIBAPS, Barcelona, Spain.

Local coordinator: Albert Compte.

Period: 10/03/2014-15/03/2014.

Introduced to research of all members of Compte's group on computational modelling of working memory. Presented own modelling work on astrocyte-regulation of persistent activity. Also visited the groups of Jaime de la Rocha (role of noise in synchronization of neuronal ensembles) and Maria V. Sanchez-Vives (sleep and cortical oscillations), as well as Jordi Soriano's lab at University of Barcelona (neural networks and characterization of their connectivity).

FORTH, Heraklion, Crete, Greece.

Local coordinator: Yiota Poirazi.

Period: 05/05/2014-10/05/2014.

Introduced to research on dendritic computation by Poirazi's group. Individual discussions with all members of the group. Presented own work on astrocyte modelling to the Institute. Discussed possible future collaborations. Started collaboration with Dr. Benjamin Auffarth (FORTH and Freie Universitat Berlin) on modelling of olfactory bulb that includes glia.