Laboratory of Cellular Neuropharmacology

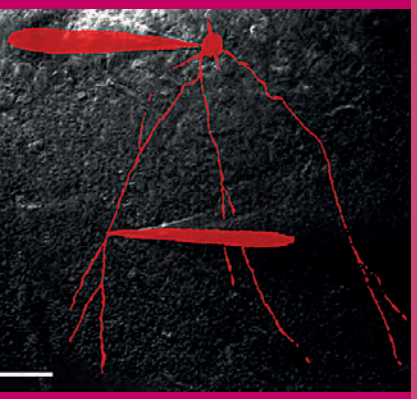
Department of Pharmacology

Head of Momentum-supported Laboratory: János Szabadics, PhD

Mission statement

The primary goal of the laboratory is to better understand the underlying neuronal circuitry of the hippocampus, in particular the cellular interface between the dentate gyrus and CA3 regions. The anatomical structure of the hippocampus is evolutionarily preserved among mammalian species, including human and rodents, and this cortical area plays crucial roles in certain learning and memory functions. The interaction of neuronal activities in the CA3 area of the hippocampus provided by mossy fibres (the axon of dentate gyrus granule cells) and auto-associative networks of local pyramidal cells is essential in the ability to distinguish novel situations from previously acquired memories. The mossy fibres introduce certain novel information about the environment in the CA3 network, and this incoming excitation is correlated with previously acquired memories that are represented by the interconnected synaptic network of local pyramidal cells. The research group focuses on the cellular mechanisms of this interaction using various techniques. The central methodology of the laboratory is *in vitro* patch clamp electrophysiology (including paired recordings of synaptically-coupled neurons, and direct dendritic and axonal recordings), which is combined with correlated anatomy and immunohistochemistry, calcium imaging, computational modelling and virus labelling. Combinations of these methods allow us to investigate how inputs are translated and processed into neuronal output within individual neurons, and what are the fundamental mechanisms of synaptic communications between individual neurons.

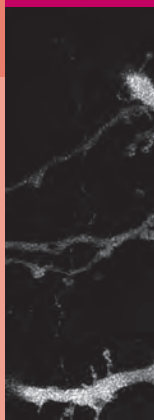
The laboratory started its operation on July 1st 2009 after a new young investigator position was created by the institute with the support of the Network of the European Neuroscience Institutes (ENI-Network). The current projects of the laboratory are funded by the Wellcome Trust, by the "Momentum" Young Investigator Program from the Hungarian Academy of Sciences and by the Hungarian Brain Research Program.



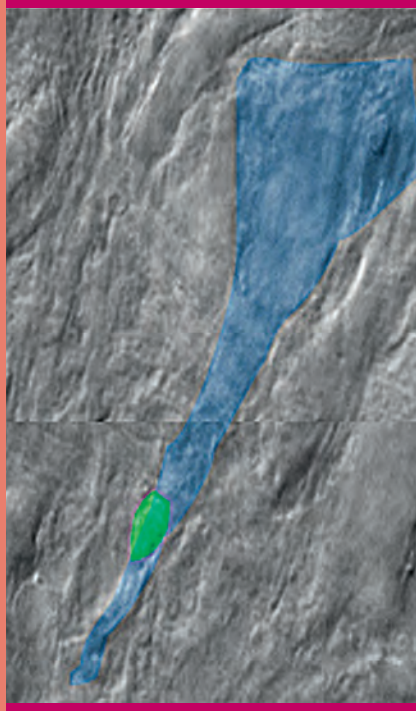
Dual somato-dendritic recording from a dentate gyrus granule cell.

Paired recording from a synaptically coupled mossy fibre axon and CA3 pyramidal cell.

Junior scientists: János Brunner, Máté Neubrandt
Undergraduate research assistant: Viktor Oláh
Technician: Dóra Kókay



The diversity of GABAergic neurons is manifested at several functional levels. One of these functionally defining properties is the cell-type specific innervations of GABAergic cells by excitatory pathways which enables pathway specific activation of distinct inhibitory circuits. We obtain simultaneous recordings from presynaptic mossy fibre terminals and synaptically-coupled CA3 neurons, which are identified with *post hoc* immunohistochemistry and morphological analysis to directly study monosynaptic connections between distant dentate gyrus granule cells and CA3 neurons, providing novel opportunities to better understand the neuronal circuitry of the hippocampus. Specifically, we are interested in how physiologically relevant activity patterns influence the neuronal output of individual hippocampal mossy fibres. Other major interests of the group are the mechanisms of the input integration in granule cells. To directly measure the propagation of signals along the dendritic arbors of granule cells we employ dendritic recordings, optical stimulation and calcium imaging, and verification of the obtained data by multicompartmental modelling. Similar research is pursued on the input integration of the CA3 GABAergic cells, which are the major targets of the mossy fibres, where we focus on the cell type-specific modulation of the input integration by potassium conductances. We also investigate the potential cellular consequences of the unique capability of the dentate gyrus to generate new neurons throughout the life of the animals by using a specific retroviral labelling method to birth-date adult-born granule cells. Altogether, these projects will reveal fundamental components of the cellular interface between the dentate gyrus and CA3 regions, and thus provide novel insights into the machinery of higher order neuronal functions.

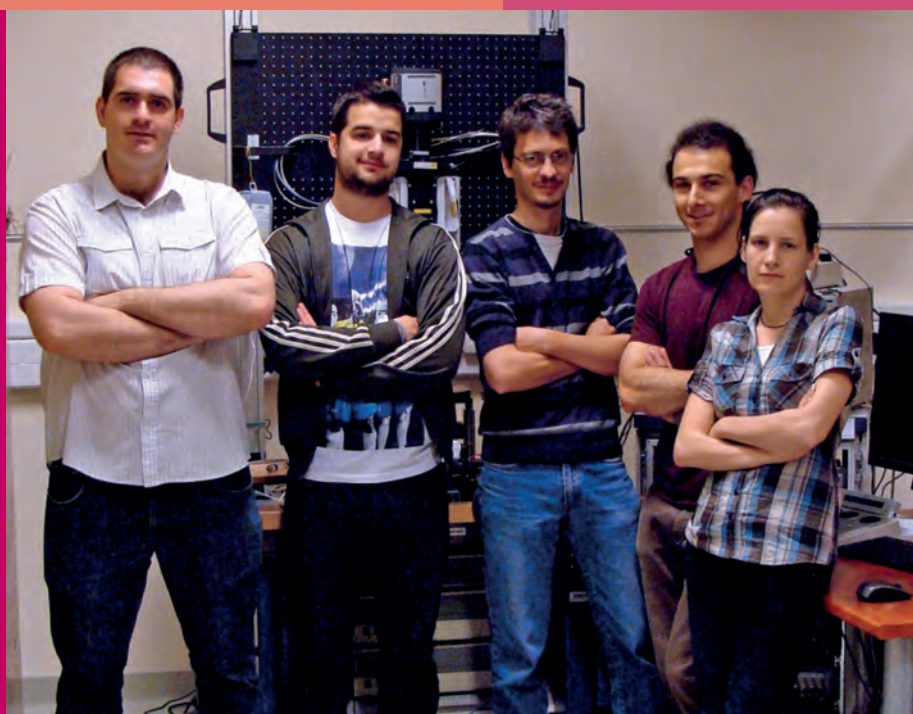


Nomarski image of the apical dendrite of a CA3 pyramidal cell (blue) and a mossy fibre terminal in acute slice.

Selected publications from the last 10 years:

- Brunner J, Ster J, Van-Weert S, Andrási T, Neubrandt M, Corti C, Corsi M, Ferraguti F, Gerber U, Szabadics J. Selective Silencing of Individual Dendritic Branches by an mGlu2-Activated Potassium Conductance in Dentate Gyrus Granule Cells. J NEUROSCI 33: 7285-7298 (2013)
- Brunner J*, Neubrandt M*, Van-Weert S, Andrási T, Kleine Borgmann FB, Jessberger S, Szabadics J. Adult-Born Granule Cells Mature through Two Functionally Distinct States. eLIFE 3: e03104 (2014)

from left: János Brunner, Viktor Oláh, János Szabadics, Máté Neubrandt, Dóra Kókay



Spiny lucidum cell in the CA3 area.