Grant Agreement number: 284801

Project acronym: ENLIGHTENMENT

Project title: Exploring neural coding by novel optogenetic, high-density microrecordings and computational approaches: Towards cognitive Brain-Computer Interfaces

Funding Scheme: FET OPEN

PUBLISHABLE SUMMARY

Project context and objectives

Brain-Computer Interface (BCI) research has seen an explosive growth in the past decade given the major application potential of these technologies. Despite the many advances, there are still a significant number of problems to be resolved before achieving the complete 'brain-computer symbiosis'. Effective communication between brains and computers can only be achieved through the implementation of highly parallel communication channels to and from the brain and through a better understanding of the brain's actual information coding scheme, the adaptive dynamics of its behavior, and the predictive nature of the its sensorimotor internal models.

The ENLIGHTENMENT project consortium aims to develop a combination of advanced multisite, single unit neural activity monitoring, closed-loop patterned and cell specific activations, and computational techniques that would identify cell ensemble activation in real time. We will create a technological platform for directly **interacting with cell assemblies** in a **two-way dialogue**.

The **technological objectives** addressed in this project are:

- Realization of an ***experimental platform combining cell type specific light-induced neuronal activation with multisite extracellular recordings of ensemble activity*** with a probe combining tetrode electrodes for recording and optic fibers for stimulation in the same site. The platform will be configured as a ***closed-loop approach*** thus being capable of reading instantaneous ensemble activity, detecting "important" activity configurations, and consequently driving an array of independent optical stimulators with specific patterns. This should be obtained within an implant of small size, compatible with freely moving experiments in rats and mice. Selective expression of the ***optogenetic channels*** (Channelrhodopsins (ChR2) and archaerhodopsin-3 (Arch)) in specific cell populations is obtained by viral vector transduction.
- Development of ***methods allowing to infer functional interactions between neurons from the recording of the concerted activity of the neural population, in response to a given stimulation***. We will develop robust and efficient learning algorithms for Boltzmann machines, which deduce interactions from the correlations in the activity, and inverse Integrate-and-Fire (IF) approaches, which infer the interactions of a network of IF neurons from their spiking times. This will allow us to characterize how interactions are modified in response to specific

stimulation patterns. The algorithms must be fast enough that the outcome can be used to periodically update the stimulation protocol during the experimental session.

First year results

During the 1st project year, consortium partners have developed a first **prototype allowing light activation to be combined with multi-site tetrode-based recordings** of neural activity and demonstrated a system capable of delivering light stimulation based on online spike detection. This includes a **32-channel acquisition system** with **online spike-sorting** capabilities as well as a **control system** running **custom developed software** on Labview allowing closed recording/stimulation loops.

The electrical activity readout and optical brain stimulation are achieved by a microdrive capable of hosting independently movable tetrodes that can be lowered to the target area, together with integrated optic fibers. The electrodes and optic fibers are connected to the closed-loop system, which consists of four main components:
(1) a head-mounting board that amplifies, multiplexes and digitally transmits the neural activity data to the digital I/O board, (2) a controllable optic set-up, (3) a data acquisition card providing the digital I/O and analog output pulses, and (4) a custom software that controls the acquisition, visualization, and analysis of the recorded signals. With the current version we can perform spike detection on 32 channels and control the optical stimulation (based on analyzed data) within 8 msec. We are currently working to increase the number of channels, while decreasing the signal processing time.

In order to investigate the network activity in awake rodents, we have developed **viral vectors** allowing efficient and cell-type specific expression of light-activated proteins (e.g. excitatory neurons). Algorithms have been refined in order to infer the neuronal connectivity map from the recorded activity data. The algorithms and some applications have been recently published by S. Cocco and one collaborator (see J. Barton and S. Cocco, *Ising models for neural activity inferred via selective cluster expansion: structural and coding properties*, J. Stat. Mech. P03002 (2013)).

Cellular and network responses to different light induced stimulation patters have been investigated using the previously described experimental platform in both in vitro and in vivo preparation

Expected final results and their potential impact and use

In this project we aim to advance the spatio-temporal resolution of closed-loop stimulation/recording systems, come up with algorithmic approaches for reliable, online, computer-aided neuronal data analysis as well as create computational models allowing to infer connectivity and to predict dynamic processes in neuronal systems.

We believe that the knowledge to be developed in this project has a novel and foundational character for basic neuroscience, neuroengineering and computational technologies, medical device technologies as well as for the society of tomorrow.

Additional information can be found at:
www.enlightenment-fp7.eu