Poster only

Multi-site electrical stimulation integrated on 4'096 high density micro electrode arrays (MEAs) reveals the effective connectivity of dissociated neuronal cultures

Alessandro Maccione[1,], Thierry Nieus[1], Alessandro Simi[1], Hayder Amin[1] and Luca Berdondini[1]*

1 Istituto Italiano di Tecnologia (IIT), Neuroscience and Brain Technology Department – Genova, Italy

* Corresponding author: alessandro.maccione@iit.it

High density MEAs, providing recording capability from thousand of electrodes, are nowadays a commercial tool (www.3brain.com) used to investigate spontaneous or chemically modulated activity in dissociated cultures as well as *ex vivo* brain tissues. In previous paper we already demonstrated that such as high spatial resolution (4'096 electrodes, 42 um pitch on a 2.7 mm by 2.7 mm active area) allows to infer the functional connectivity of low density cultures both at global network level and at the resolution of microcircuits of few cells, showing that functional connectivity qualitatively maps the topological and morphological spatial distribution of the network (Maccione et al., 2012). As a further step to better understand how information is processed in neuronal networks, here we present preliminary results on effective connectivity obtained by electrically stimulating dissociate cultures using a new generation of high density devices that integrate stimulating capabilities. These innovative MEAs provide 4'096 recording electrodes with a pitch of 81 um (active area of 8 mm by 8 mm) interlaced with stimulating electrodes every 8 recording sites. We applied on dissociated hippocampal networks at 18-21 DIVs a train of biphasic signals (3 Volt peak to peak, duty cycle 500 us) at low frequency (0.2 Hz) for each of the 16 stimulating sites, inducing repetitive and reliable responses.

The analysis of the resulting Post Stimulus Time Histograms (PSTHs) show interesting features. First, the "early response" just after the deliver of the stimulus as observed on conventional MEAs, considered to be a non sinaptically propagated response (Wagenaar et al., 2005), is almost absent. Second, the PSTH center of mass changes according to the distance from the stimulation site. Interestingly, the induced propagating patterns are reliable and situ dependent, showing that the stimulation in different areas is able to elicit specific responses not belonging to the repertoire of spontaneous bursting activity.

As a perspective, these results suggest that the stimulating capability of high density MEA combined with optical imaging might be a valuable tool to reconstruct the effective connectivity, opening thus new perspectives in understanding network signal processing.