Active Pixel Sensor Micro Electrode Array (APS-MEA): analysis of the network dynamics from hippocampal neuronal populations recorded at high spatio-temporal resolution

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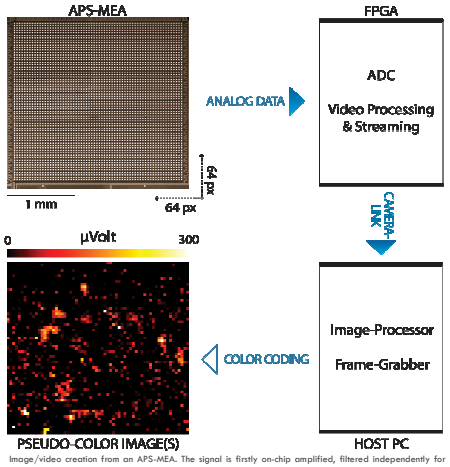
Abstract

High-density microelectrode arrays based on the active pixel sensor technology (APS-MEAs), have been recently developed and successfully coupled with different types of neuronal preparations [1]. The main advantage of this innovative technology relies in the possibility to perform acquisitions on large neuronal ensembles with a high spatial and temporal resolution. The new system allows electrophysiological studies ranging from single cell to large scale populations at the same time.

In this work, we took advantage of this technology to explore either low-density and high-density networks of hippocampal neuronal cultures during spontaneous activity the generation of color coded functional electrophysiological images, offers a time-lapse based approach to the analysis of extracellular neuronal signals.

Methods (Cf POSTER 390.19)

A. High Density APS-MEA Platform



Image/video creation from an APS-MEA. The signal is firstly on-chip amplified, filtered independently for each electrode and multiplexed to an FPGA. This provides an AD converter, real time pre-processing and a serializer for sending the data to the host PC through a high-speed CameraLink interface. Finally pseudo-color images/videos are generated by coding incoming electrophysiological voltages.

The APS-Mea platform (A) we used in our experiments is oriented to the image/video concepts [1]. A full frame acquisition consists of 4096 electrodes (21 µm per side, 42 µm of pitch) sampled at 7,7 KHz and tightly packed in order to approach the cellular dimension and to ensure an electrode density capable of describing network propagations.

Moreover, the spatiotemporal resolution together with the generation of color coded functional electrophysiological images, offers a time-lapse based approach to the analysis of extracellular neuronal signals.

Results: high density cultures

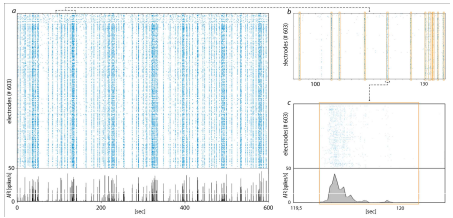
We investigated the activity flow in high density hippocampal cultures (final densities of ~ 2500-3000 cells/mm^2) during spontaneous activity. The spacial activity distribution during identified network bursts (B) was depicted by means of the Center of Activity Trajectory (CAT) (C) [2] defined as:

$$\vec{CA}(t)=[CA_1,CA_2]=\frac{\sum_k A_{TW}(k)\cdot[Col(k)-32.5,Row(k)-32.5]}{\sum_k A_{TW}(k)}$$

$$\vec{CAT}(t_0,t_1)=[\vec{CA}(t_0),\vec{CA}(t_0+\Delta t),\ldots,\vec{CA}(t_1)]$$

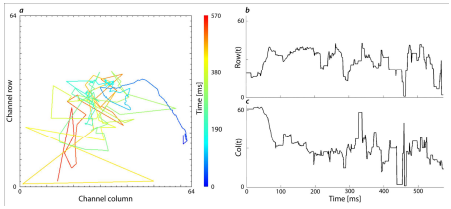
Definition of a CA point and the trajectory between two time positions t_0 and t_1 with a time step Δt. $Col(k)$ and $Row(k)$ represents the column and row number of channel k respectively and $A_{TW}(k)$ a measure of the activity at channel k within a small time window TW.

B. Network bursts identification



(a) Raster plot and average firing rate of 10 min of spiking activity recorded from 603 active electrodes. The synchronization of the patterns and the recruitment of many channels highlight the presence of network bursts. (b, c) Successive zooms show network bursts profile and their identified region (orange rectangles)

C. Center of Activity Trajectory (CAT)



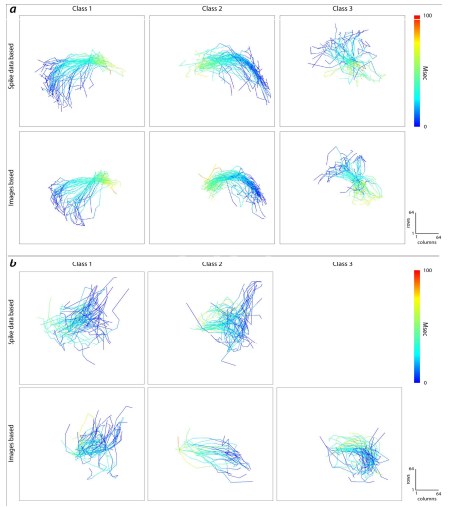
(a) CAT for a network burst lasting 570ms recorded from a 28 DIV hippocampal culture. (b, c) Corresponding time series for row and column increments

CATs showed two distinct phases (C). An initial phase with a more stable and quasi-linear course that corresponds to first tens of milliseconds of the pattern in which activity follows wave-like propagating pathways; A second phase where CAT starts to jump apparently randomly between opposite positions that corresponds to a possible reverbereting phase.

CATs were truncated to the initial phase and then classified using automated k-means algorithm.

CATs were calculated based on spiking activity and on voltage amplitude (D) as obtained by means of the imaging approach offered by the APS-MEA platform.

D. Spike-based & Images-based CATs

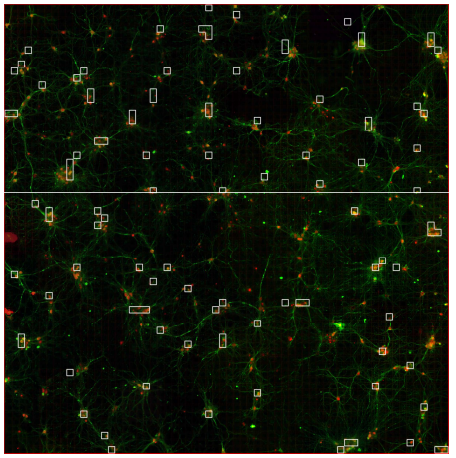


Comparison of CATs constructed over 150 (a) and 126 (b) network bursts identified during 10 min of spontaneous activity either on the base of identified spikes (first rows) or by processing the functional images coming from the APS-MEA platform (second rows).

Results: low density cultures

We explored also the opportunities that the high resolution could offer with low density cultures. To this end, we coupled activity maps highlighting channels that showed consistent spiking rate with morphology derived from fluorescence images, finding a good agreement between them (E). Being cells homogeneously distributed and well separated it is possible to investigate network behaviors at different levels.

E. Activity-morfology coupling



Immuno-fluorescence of low-density (final density of ~90 cells/mm^2) hippocampal culture at 33 DIV with superimposition of detected avtive channels (spike rate > 0.05 spikes/sec)

Conclusions & Perspectives

The unprecedented resolution and number of pixels provided by APS-MEA technology allows to further explore neuronal dynamics and to bridge the gap from single cell to network level studies.

Coupled to high density cultures this tool is capable to finely trace activity propagation by directly processing the recorded functional images; thus opening new perspectives for non-spike-based analysis.

Moreover the use of APS-MEA with low density cultures gives access to different levels in the network, from single cells, to microcircuits up to the entire population.. This could allow to investigate the reciprocal activity dependent effects of such units.

[1] Berdondini, L., et al., Lab on a Chip, 2009. **9**: p. 2644-2651.
[2] Chao, Z.C., et al., Neuroinformatics, 2005. **3**:p.263-280.