RECORDING RETINAL WAVES WITH A 4,096 ELECTRODES ARRAY
NOVEL ANALYTICAL AND DATA SHARING TOOLS

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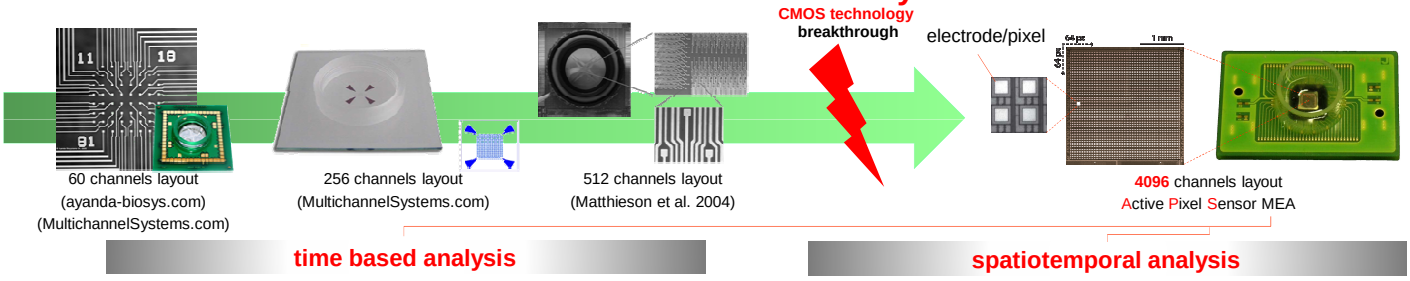
Waves of spontaneous activity sweep across the immature retina. The spatiotemporal information encoded in these waves is believed to play a crucial role in guiding the formation of connections in the visual system. To this day, no experimental approach has provided enough accuracy to analyse wave dynamics in great detail, and mostly, to understand how the spatiotemporal features of this early retinal activity changes with development.

Using the APS MEA with 4,096 electrodes (64x64 array, 21 µm resolution) recording at 7.8kHz [1], we have been able to record pan-retinal waves in the neonatal mouse with unprecedented spatiotemporal accuracy. These recordings will help further understand the role of retinal waves upon the wiring of the visual system.

To enable sharing of the novel retinal data acquired with the APS MEA system between different laboratories (e.g. Genova, Newcastle, Edinburgh, Cambridge), we are using the resources provided by CARMEN (Code Analysis, Repository and Modelling for e-Neuroscience), a new data sharing facility developed in the UK with funding from the Engineering and Physical Sciences Research Council- http://www.carmen.org.uk/. CARMEN allows us to share data and analytical codes over the internet.

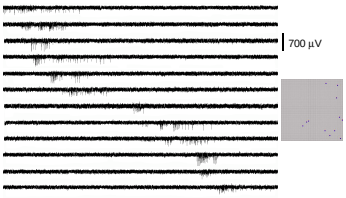
[1] Active pixel sensor array for high spatio-temporal resolution electrophysiological recordings from single cell to large scale neuronal networks. Berdondini L et al. Lab Chip 9, 2644-2651 (2009).

The Active Pixel Sensor MEA system

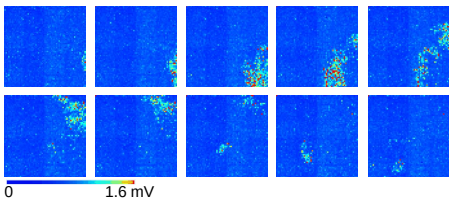


DATA PROCESSING AND ANALYSIS

1. Visualization of raw data



Traces of raw signals generated by retinal ganglion cells recorded from 12 channels selected within the path of an episode of spontaneous bursting activity in a postnatal day (P) 10 retina. Increasing delays in bursting onset reveal propagating activity patterns across the network.



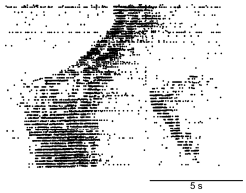
A two dimensional view of the activity is necessary to visualize these patterns. This is shown in time lapse single frames of activity raw data acquired every 0.5 s. The extracellular signals are shown in a false colour map by computing the signal variance.

2. Spike detection

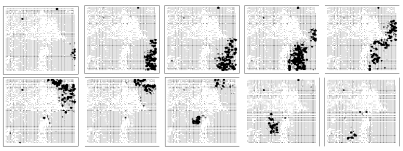
Spike detection is performed off-line using a recently developed Precise Timing Spike Detection (PTSD) algorithm [1], enabling fast and precise identification of the spike events.

[1] A novel algorithm for precise identification of spikes in extracellularly recorded neuronal signals. A. Maccione, M. Gandolfo, P. Massobrio, A. Novellino, S. Martinoia and M. Chiappalone, J Neurosci Meth (2008), DOI 10.1016/j.jneumeth.2008.09.026

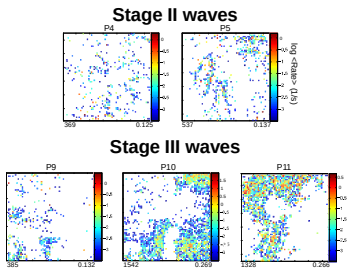
3. Spike train visualization



Raster plot of detected spikes during the same activity episode as in Section 1. Each line represents one active channel. The plot reveals complex spatiotemporal patterns.

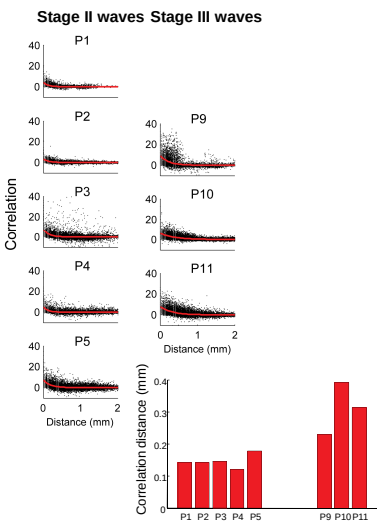


Time-lapse images of the firing rate calculated in 0.5 s bins for all channels. The size of the dots is proportional to the firing rate

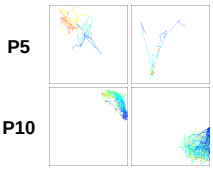


Maps of activity (log firing rate, all active channels) obtained during 10 min of continuous recording. Early waves (Stage II, cholinergic) are random, hence no clear patterns are detected on the maps. Late waves (Stage III, glutamatergic), however, become more repetitive and spatially restricted.

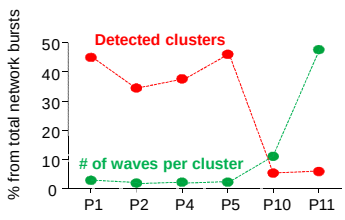
4. Quantification of spatiotemporal activity patterns



Scatter plots of pairwise correlations (covariance of spike count changes) as a function of the distance between the electrode pairs. The column plot illustrates the decay constant of the exponential fit (red line on scatter plots) at different developmental stages. Correlations become stronger with development.



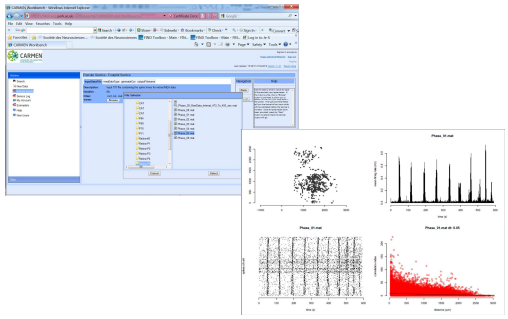
After identifying network bursts, the Center of Activity Trajectory (CAT) is computed on the raw data providing a trajectory that represents the "center of mass" of the electrical activity. Blue – trajectory start. Red – trajectory end.



CATs are classified into clusters [1]. Across development, the number of detected clusters decreases dramatically and the number of waves belonging to each cluster increases, demonstrating that Stage III waves do not propagate in random patterns anymore.

[1] Tracking burst patterns in hippocampal cultures with high-density CMOS-MEAs. Gandolfo M, Maccione A, Tedesco M, Martinoia S and Berdondini L, *J Neural Engineering* (2010) (in Press).

CARMEN FOR DATA AND CODE SHARING



We use CARMEN as a platform to share APS data files (Matlab matrices of spike times). These files are then used to perform further analysis using codes written in R or in Matlab. Currently we have analytical tools that were written in R to analyze neural activity from 60 channels MEAs that have been deployed on the CARMEN portal. These tools have been modified so make them compatible with MEA data acquired using different platforms, including the APS MEA. In the example above, the 4-plot service generated a map of the active electrodes, a plot of the average firing rate, a raster plot of the active channels and a plot of the correlation index between pairs of electrodes [1]. We are in the process of developing many more visualization and quantification tools that will be deployed on the CARMEN portal in the near future.

[1] Transient period of correlated bursting activity during development of the mammalian retina. Wong RO, Meister M, Shatz CJ. Neuron 11, 923-938 (1993).