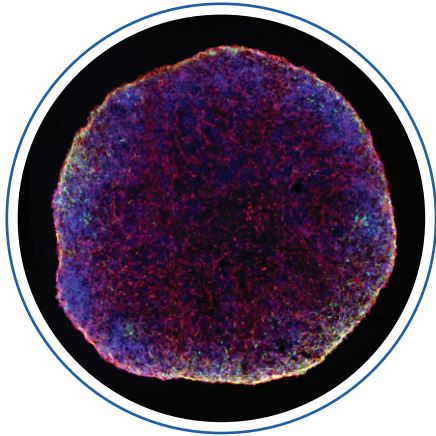
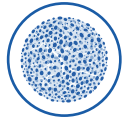


Brain Organoids



MaxTwo Mainframe
Data Acquisition Hardware
Built-in Incubator

MaxTwo Wellplate
Multiwell HD-MEA
6- & 24-Wellplates



Brain organoids are artificially grown 3D aggregates that resemble the embryonic human brain, usually generated from human induced pluripotent stem cells (h-iPSCs).

MaxTwo, our multi-well high resolution microelectrode array (MEA) system, is best suited for long-term and label-free analysis of brain organoids.

MaxTwo's large sensor array at high-resolution enables recording of every active cell across multiple areas of biological samples.

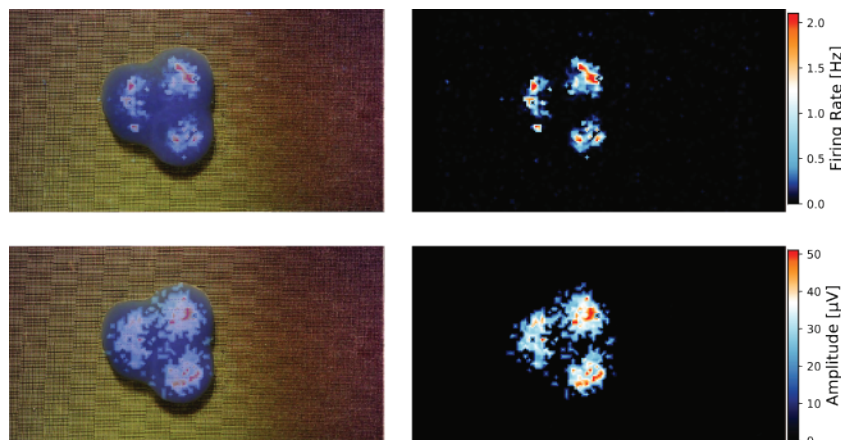
Readouts at different scales

- ⚡ Network level (population spike times, bursts)
- ⚡ Cell level (individual spike times, waveforms)
- ⚡ Sub-cellular level (spatially resolved waveforms)

Capture high quality activity maps from organoids

MaxTwo records the neuronal activity of organoids at high spatio-temporal resolution and generates label-free electrical imaging.

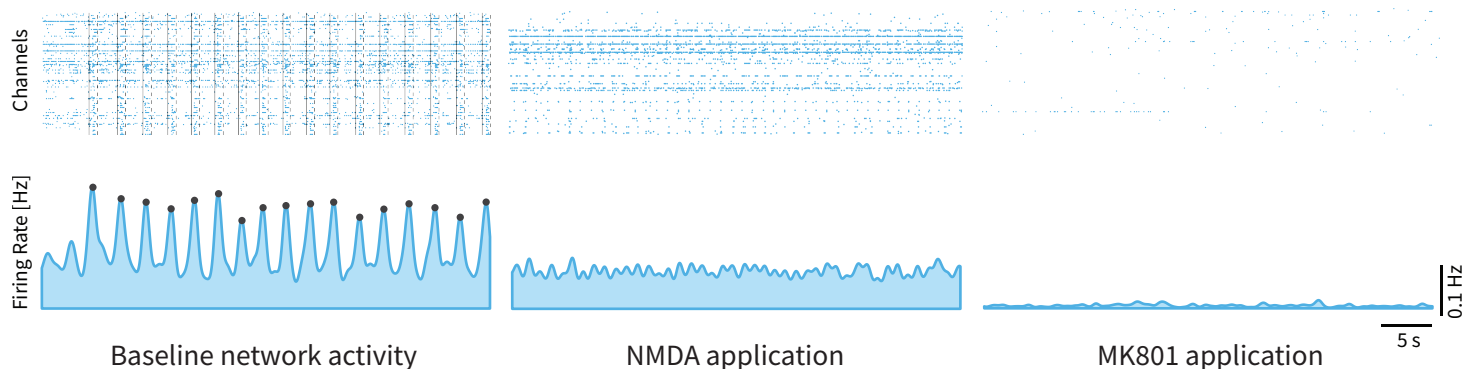
- ⚡ “See” all active cells on top of the array and identify its activity.
- ⚡ Detect small spikes from developing neurons and from cell compartments, such as axons.
- ⚡ Analyze full organoids and determine initiation as well as propagation of network activity.



Microscopy image (left) of three h-iPSC-derived cortical organoids (DIV 60) overlaid with firing rate and amplitude activity maps (right).¹

Pharmacological manipulation of network bursts in organoids

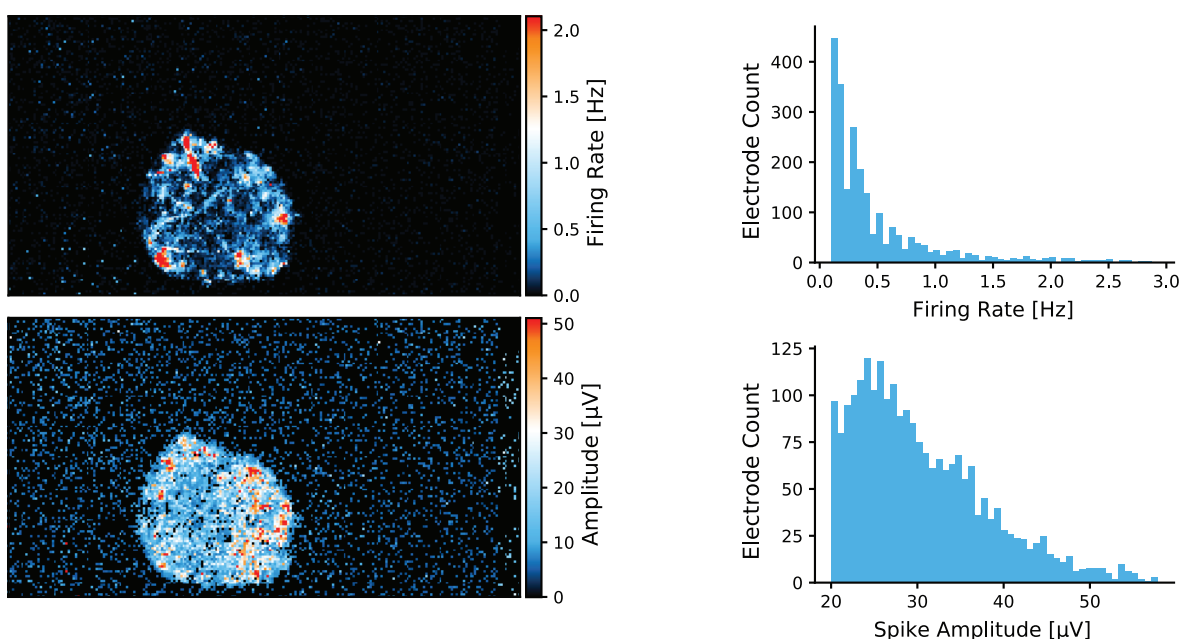
The network bursting activity of h-iPSC-derived cortical organoids (DIV 60) was modulated using N-methyl-D-aspartate (NMDA) and a noncompetitive NMDA receptor antagonist (MK801). A large dose of NMDA decreased the network burst activity, but increased the mean spike firing rate and mean spike amplitude. MK801 decreased both the network burst activity and the mean spike firing rate, but did not affect the mean spike amplitude.¹



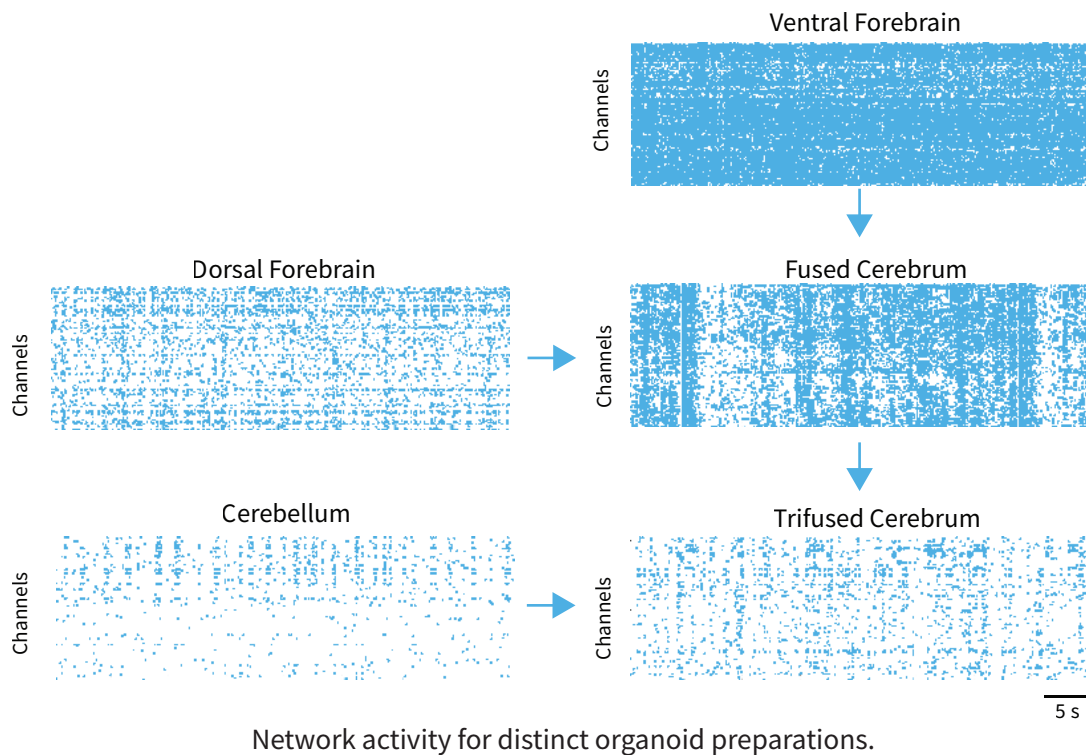
Raster and network burst activity plots of h-iPSC-derived cortical organoids during the baseline and following pharmacological applications of NMDA and MK801.

Functional characterization of organoids modeling different brain regions

The high resolution MaxTwo system allows one to precisely identify and isolate active areas across a wide range of organoids modelling different brain regions. The progressive complexity of the modeled regions correlates with an increased synchrony in the recorded network activity.²



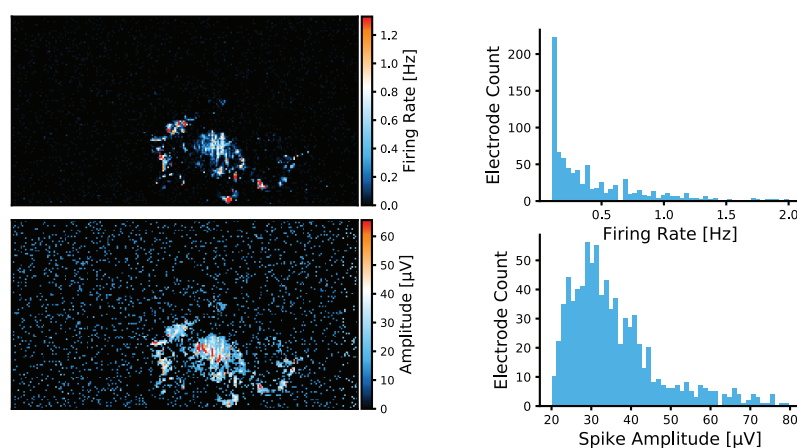
Firing rate and amplitude activity maps (left) together with histograms presenting the distributions of these parameters at the electrode level (right) for a fused h-iPSC-derived (dorsal + ventral) cerebral organoid (DIV56).



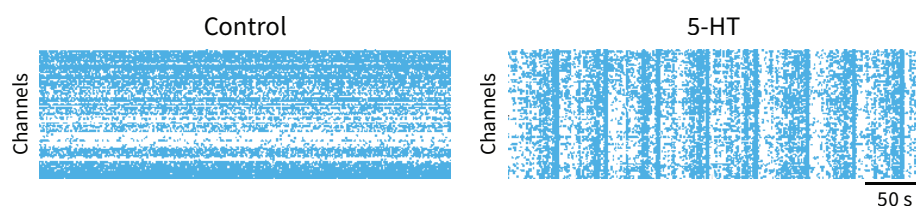
Network activity for distinct organoid preparations.

Effects of serotonin exposure during cerebellar maturation

Cerebellar dysfunction often involves a prominent loss of Purkinje cells (Taroni and DiDonato, 2004). Serotonin (5-hydroxytryptamine, 5-HT) is reported to be involved in the regulation of the morphological maturation of Purkinje cells (Kondoh et al., 2004; Oostland and van Hooft, 2013). 5-HT treatment during the maturation of cerebellar organoids is hypothesized to lead to higher efficiency of morphological and physiological maturation in Purkinje cells. Treated organoids showcase synchronized network bursting activity, as a functional indicator of synaptic maturation.²



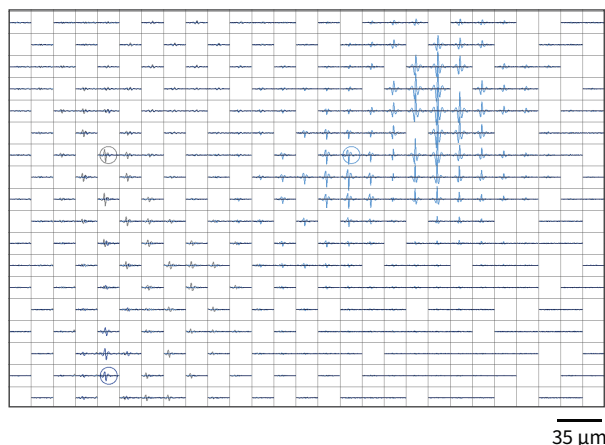
Firing rate and amplitude activity maps (left) together with histograms presenting the distribution of these parameters at the electrode level (right) for a 5-HT treated h-iPSC-derived cerebellar organoid (DIV56).



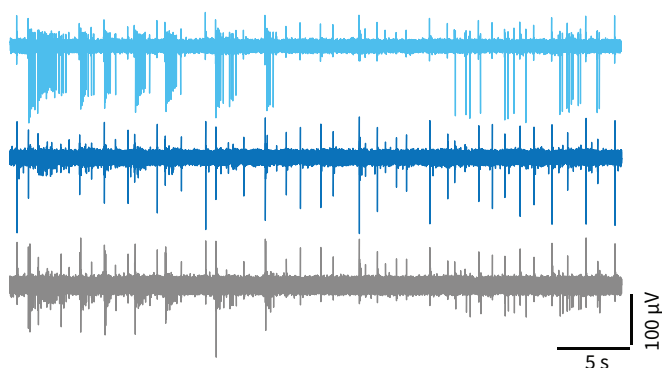
Raster plots illustrating the network activity of control and 5-HT treated h-iPSC-derived cerebellar organoids.

Track single cells in organoids

Neurons up to a depth of 100 μm (Frey et al., 2009; Obien et al., 2019) can be precisely detected and isolated in brain organoids. Electrical footprints and single-cell spiking patterns can be extracted to analyze signal propagation and cell activation dynamics.¹



Three neurons identified from one area of an organoid; circled electrodes indicate the reference used to obtain the electrical footprints for each neuron (right).



Traces of the three identified neurons, each with a different activity pattern.



Electrical footprints of the three identified neurons.

- 1 Data obtained in collaboration with Hopstem Bioengineering Co., Ltd., Hangzhou, Zhejiang, China. Organoid image on the first page, top right is courtesy of Dr. Anxin Wang.
- 2 Data obtained in collaboration with the Stem Cell Engineering Research Group (SCERG) at iBB - Institute for Biosciences and Bioengineering of Instituto Superior Técnico, Universidade de Lisboa, Portugal. Special thanks to Ana Rita Gomes, MSc, for carrying out the experiments.

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