BioCAM X

Label-free imaging with high-resolution electrophysiology

APPLICATIONS: Dissociated neuronal cultures / Cardiomyocyte cultures / Human stem cell-derived neurons / Acute brain tissue and explanted retina / Organoids / Disease modelling / Drug discovery / Safety studies, long-term and acute toxicology / LTP & LTD protocols / Plasticity & homeostatic studies / Spontaneous & evoked activities (spikes, fEPSP) / Optogenetics-combined studies / Functional and structural connectivity.

3·Brain

4096 x 18kHz

Originating from 3Brain's expertise gained in the manufacture of the first CMOS high-resolution multielectrode arrays, BioCAM X will boost your research capabilities by enabling simultaneous recordings from a total of 4096 electrodes sampled at 18 kHz per electrode.

You can either choose to store the entire raw signals captured by the BioCAM X or to take advantage of the several available degrees of compression, which will allow you to save space on your hard disk and thus decrease the computational resources required for further data processing.

All-in-one

BioCAM X incorporates further optional functionalities in a compact and solid design, which for most MEA systems come shipped as separate modules, such as a temperature control system and an electrical programmable current-driven stimulator.

Its compact form factor eases integration with other instrumentation, such as microscopes, perfusion and patch-clamp systems.

Thanks to its improved interface, BioCAM X can be controlled with a laptop for better mobility, allowing you to carry the entire recording system in your hand luggage.

HD-MEA probes

Whatever your experimental needs with multi-electrode arrays are, BioCAM X can satisfy them!

Its high sampling frequency and a user-selectable recording bandwidth make the system suitable for recording any kind of electrophysiological signal, from slow field potentials to single action potentials.

The three HD-MEA (high density microelectrode array) probes provide different spatial resolutions and recording areas, allowing full monitoring of electrophysiological signals in a field of view of up to ~26 mm^2 from a large variety of biological preparations, ranging from cell cultures and organoids to brain slices and explanted retina.

BrainWave

BioCAM X is supplied with the latest version of our BrainWave software, which provides real-time visualisation tools for electrophysiological signals during your experiments and stores all your data in HDF5 format.

This standard (adopted by the International Neuroinformatics Coordination Facility) allows cross-platform compatibility and simplifies access to and from most common analysis environments, such as Matlab® and Python™.

brainwave
BIG NEURAL DATA MADE EASY

INTEGRATED STIMULATOR

4 independently programmable
current stimulator channels

LOCKING SYSTEM

single two-position button
for locking/unlocking

ADVANCED EXTERNAL CASE

crafted from aluminum to make
it robust to electromagnetic
and mechanical noise

TECHNICAL SPECIFICATIONS

AMPLIFIER

bandwidth	0.1 Hz - 20 kHz
noise	11 µVrms (0.1 Hz - 20 kHz)
maximum input-referred signal amplitude	4 mV

MAIN CONTROLLER

data resolution	12 bit
# of simultaneous recording sites	4096
full-array (4096) maximum sampling rate	18 kHz / electrode
region-of-interests	recording 1 up to 4 independent subsets of electrodes up to 64 kHz
temperature control	active heating and cooling between 34°C and 40°C
inputs	two analog inputs (-3.3 V to 3.3 V) or triggers (LV-TTL)
control and data interface	Camera Link (mini SDR)

MAGNETIC PLATE

to attach magnetic
perfusion holders

he case

ANTI-SPILL BARRIER

to prevent circuitry damage
due to liquid overflow

TEMPERATURE CONTROL

integrated heating
and cooling system

STIMULATION MODULE (optional)

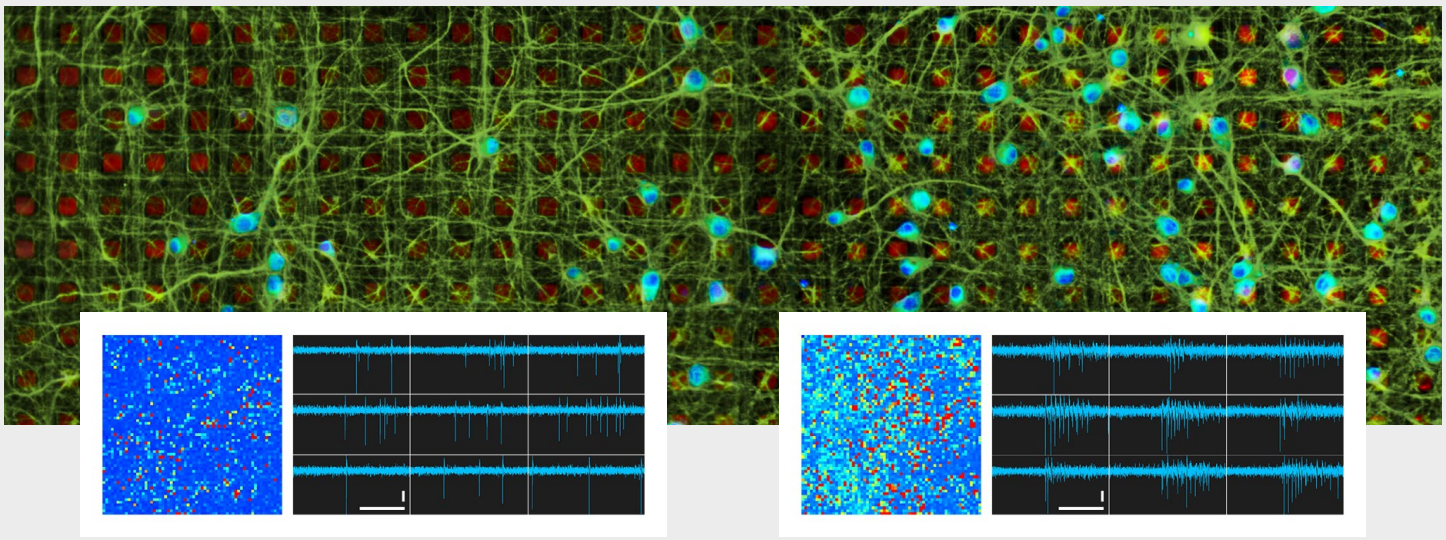
stimulation mode	constant current
internal stimulation sites	16 on-chip (only for HD-MEA Stimulo)
external stimulation sites	4 differential channels accessible on the rear connector
maximum current	+/- 1 mA
stimulation patterns	up to 4 independent stimulation patterns
stimulus generator	programmable patterns (mono/ biphasic, burst, jittering, ...)
time resolution	10 µs
amplitude resolution	10 µA
maximum pulse rate	50 kHz
extended inputs	three LV-TTL GPIOs

PHYSICAL SPECS

body material	anodized aluminum and stainless steel
dimensions (WxDxH)	160 x 205 x 38 mm 6.3 x 8.07 x 1.5 inches
weight	approx. 1350 g / 2.98 lb

Dissociated neuronal networks

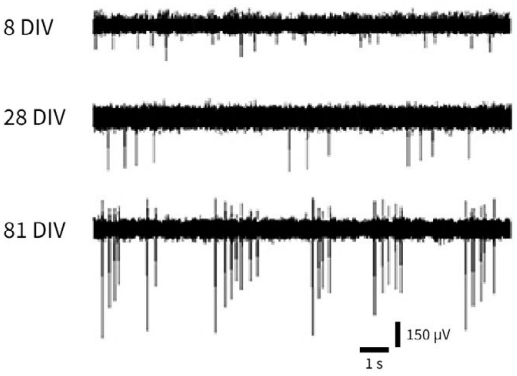
Neuronal cultures grown on HD-MEA are used to investigate fundamental properties of brain processing, to study the physiological and pathological functional activity of cultured models on primary or derived cell-lines and for developing drug-screening or toxicological applications.

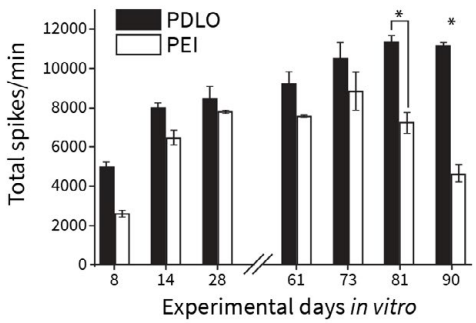


Activity maps and representative signal shapes (bars: 100 ms, 100 µV) of network events occurring in two different dissociated culture models. Left: hippocampal neurons from P0 rats at 14 DIVs *(courtesy of Ms. Sinem M. Sertel, University Medical Center, Göttingen)*. Right: embryonic cortex at 24 DIVs *(courtesy of Ahmad Allouche, SynAging SAS)*. Activity maps are images and videos visualising the level of activity occurring on all 4096 electrodes of the BioCAM X system using a false-colour map (red: >0.3 mV; blue: 0 mV).

Human-derived stem cells

Human stem cell-derived neuronal networks are particularly promising tools for improving our understanding of brain pathologies by in vitro disease modelling. Human neuronal cultures on the BioCAM X system have been validated over several months with spontaneous and electrically evoked recordings.

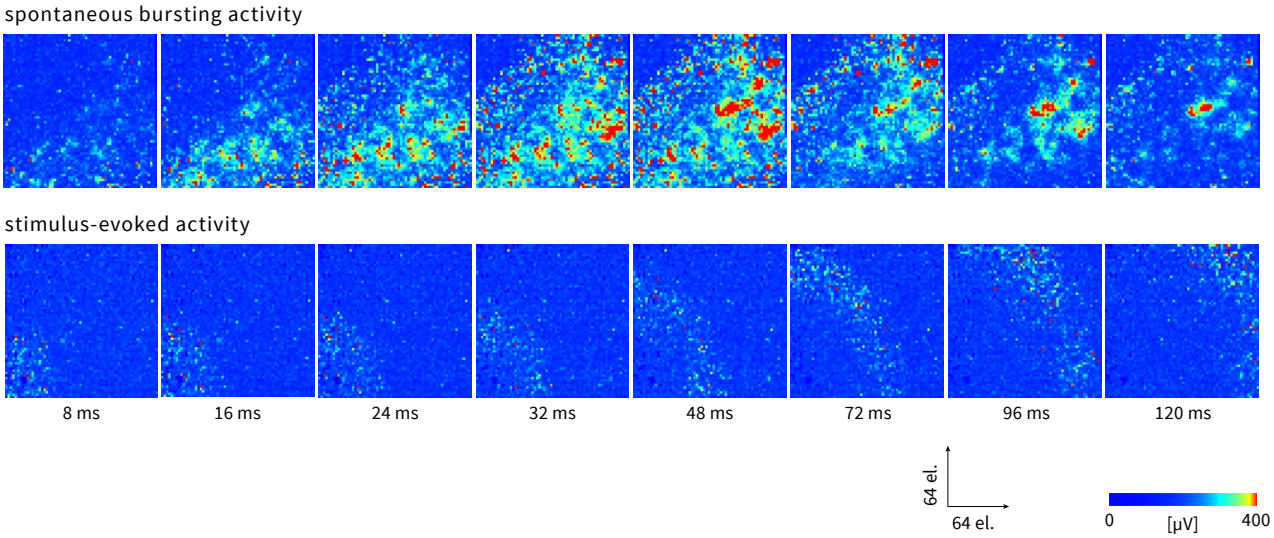




Top: development and maturation of a human-derived neuronal network. Signals increase in amplitude and synchronicity over time. Bottom: trend in the overall network spiking activity on using different adhesion factors to culture the cells on the HD-MEAs *(adapted from Amin et al., Front. Neurosci. 2016).*

Track spontaneous and electrically evoked activity patterns

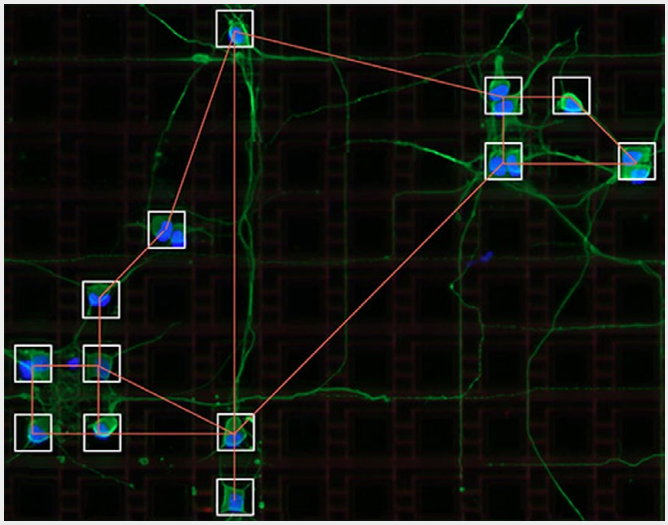
Investigate network activity and connectivity at a micrometre spatial scale with millisecond time resolution, which resembles a standard imaging technique, but is completely label-free.



Two examples of spatio-temporal propagating patterns in hippocampal cultures.
Top: spontaneous synchronous bursting activity. Bottom: evoked response to a biphasic electrical stimulus delivered to the bottom-left corner of the array *(courtesy of L. Berdondini NetS³Lab, Fondazione Istituto Italiano di Tecnologia, Italy).*

Connectivity Study

Investigate functional connectivity at a cellular scale with the BioCAM X system. Combined with optical imaging, it provides a powerful tool to unravel structure-function relationships in cultures.

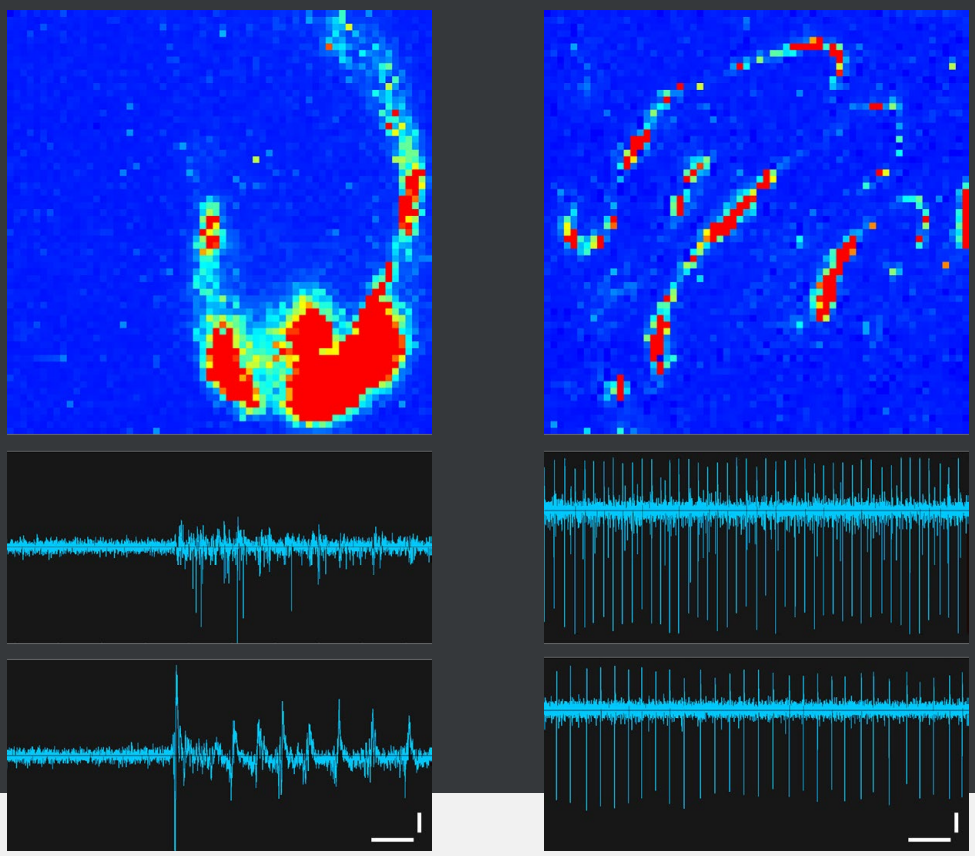


Reconstruction of the structural links (red lines) of a neuronal culture grown on an HD-MEA *(courtesy of L. Berdondini NetS³Lab, Fondazione Istituto Italiano di Tecnologia, Italy).*

Brain slices

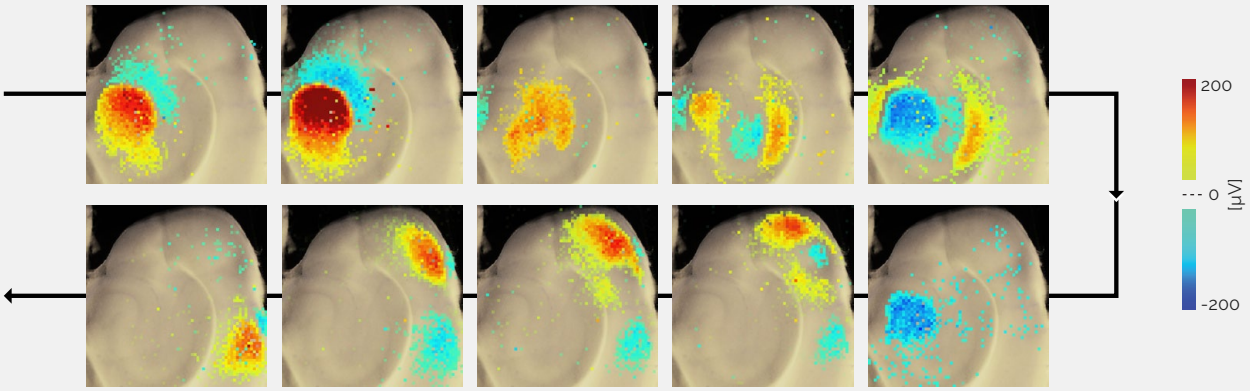
BioCAM X and its HD-MEAs with 4096 electrodes allow the researcher to visualise both spiking activity and field potential propagation over large brain circuits (up to 26mm^2).

Activity map from the 64 by 64 electrode array and examples of the quality of the signals (bars: 100 ms, 100 µV) acquired from a rat cortico-hippocampal slice (left) and a mouse cerebellum tissue (right).



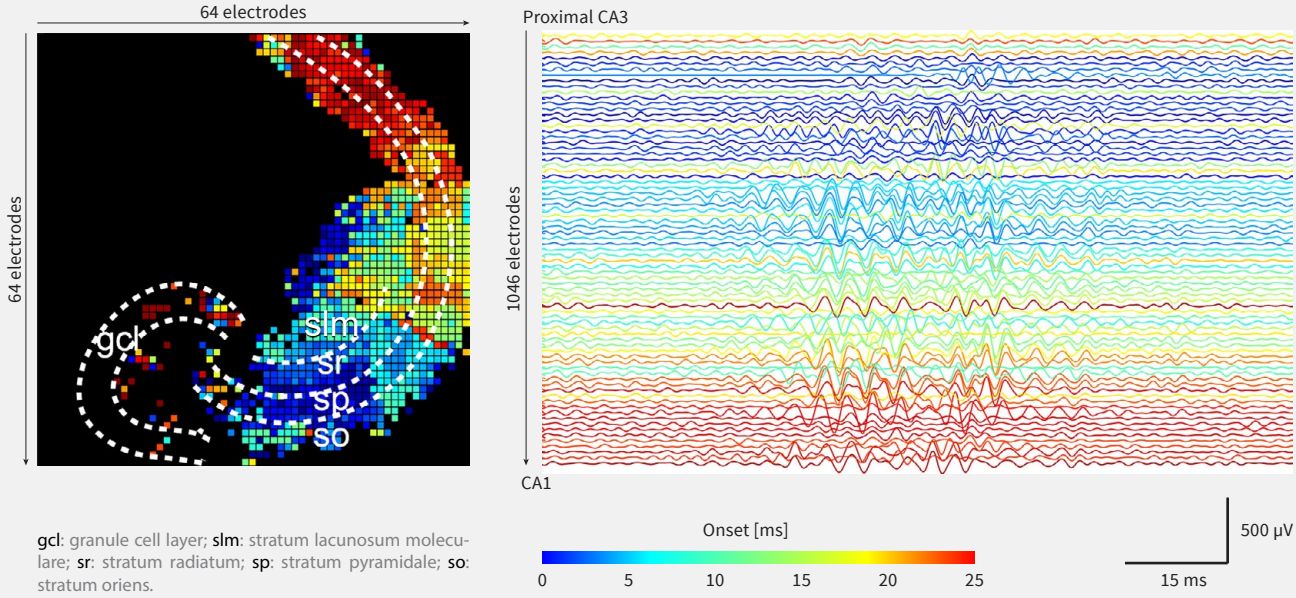
Large brain tissues under control

Monitor spontaneous/evoked activity patterns propagating over different brain regions.



Superimposition of a chemically induced inter-ictal event on the cortico-hippocampal brain circuit *(adapted from Ferrea et al., Front. Neural Circuits 2012).*

BioCAM X enables the simultaneous monitoring of large areas of neuronal tissue over a long period, thus allowing you to explore the spatial heterogeneity and temporal synchronicity of signals within connected brain areas.

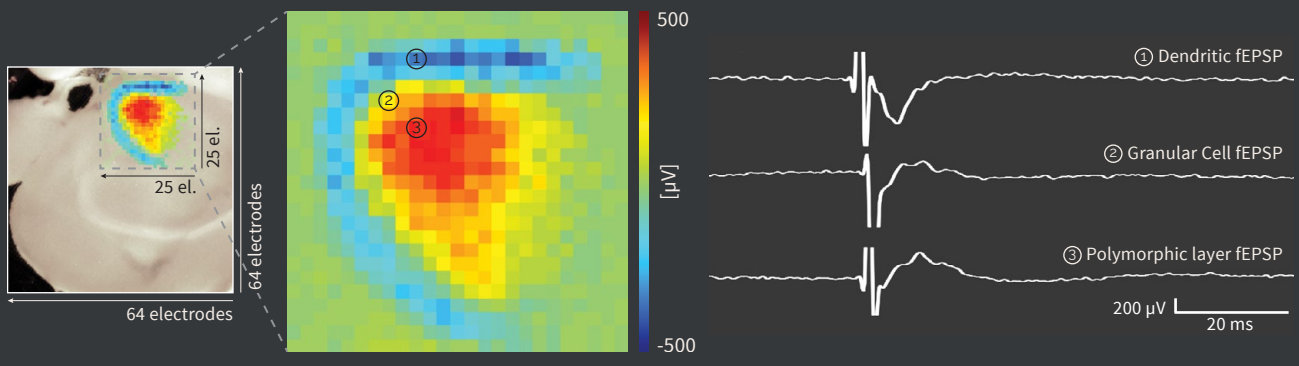


gcl: granule cell layer; **slm**: stratum lacunosum moleculare; **sr**: stratum radiatum; **sp**: stratum pyramidale; **so**: stratum oriens.

Spatial distribution (right) and temporal occurrences (left) of fast ripples detected in the hippocampus and DG *(adapted from F. Ortiz, R. Gutiérrez, SfN 2016).*

Focus on details

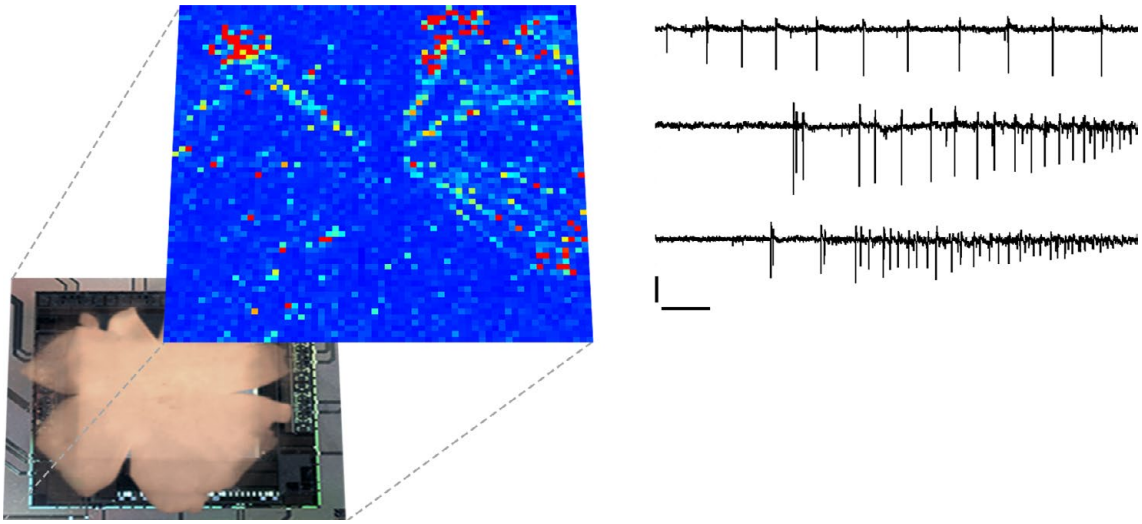
The HD-MEA's spatial resolution finely resolves signals coming from dendritic compartments or somatic layers within sub-areas of the circuitry.



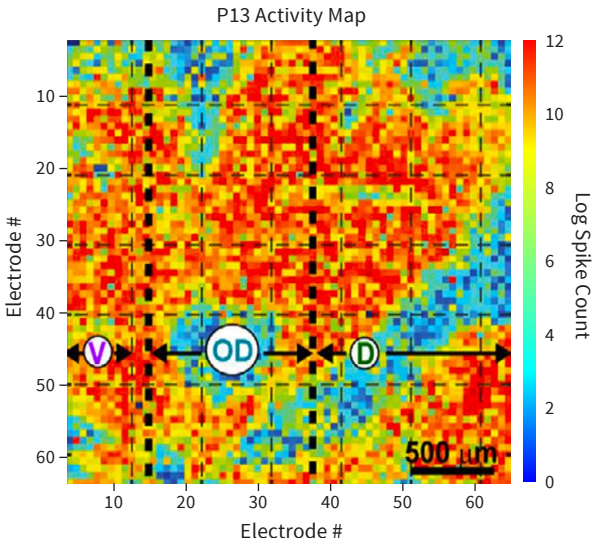
Activation of the DG upon stimulation of the perforant path. The different signal shapes recorded by the HD-MEA match the anatomical organisation of the brain area (*adapted from Ferrea et al., Front. Neural Circuits 2012).*

Retina

Either spontaneous or light-induced activity from the explanted retinas of different animals (e.g. murine, salamander, primates, etc.) can be recorded with the BioCAM X HD-MEA system.



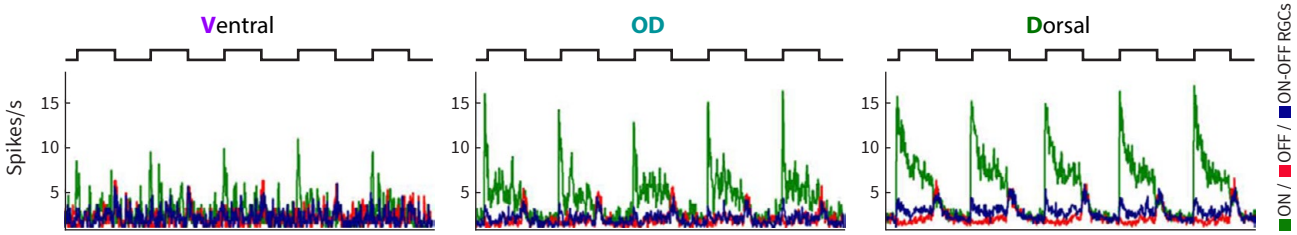
Mouse retina displaced on the HD-MEA. Colour map activity shows ganglion cell activation (on the right signal amplitude examples; bars: 100 ms, 500 µV) and axonal propagation toward the optic disk *(courtesy of E. Sernagor and G. Hilgen, The Institute of Neuroscience, Newcastle, UK).*



Pan-retinal recording

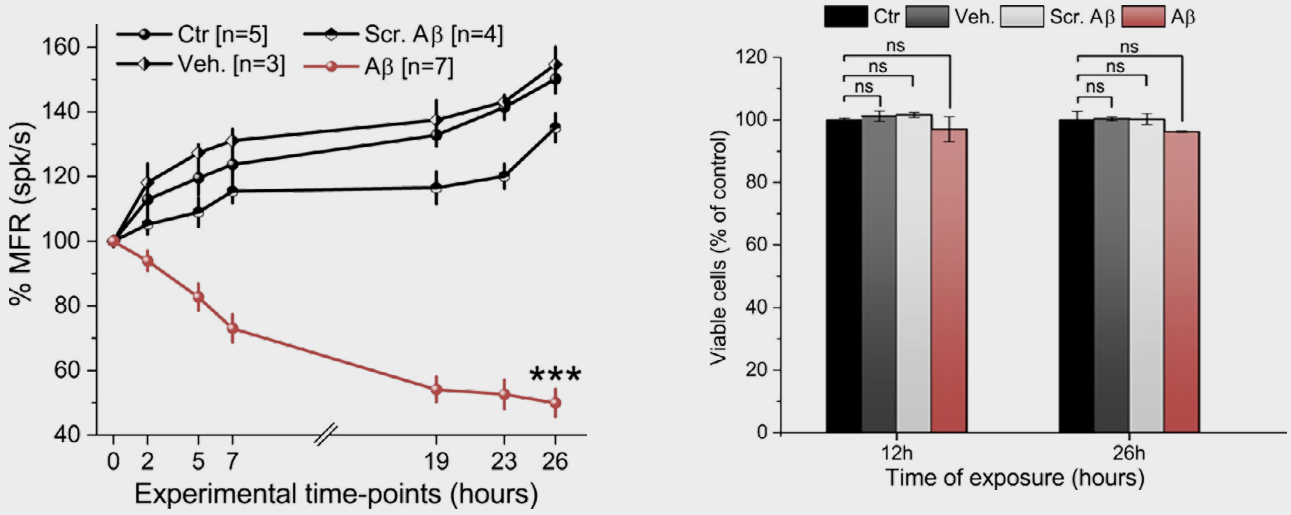
The spatial extent (from 7.1 to 26.2 mm²) of HD-MEAs allows long range interactions and heterogeneous spatial responses to light stimuli to be investigated over large retinal areas.

On/Off/On-Off ganglion cells show different response profiles in different areas of the same mouse retina *(adapted from G. Hilgen et al., Sci. Rep. 2017).*



Disease-in-a-dish

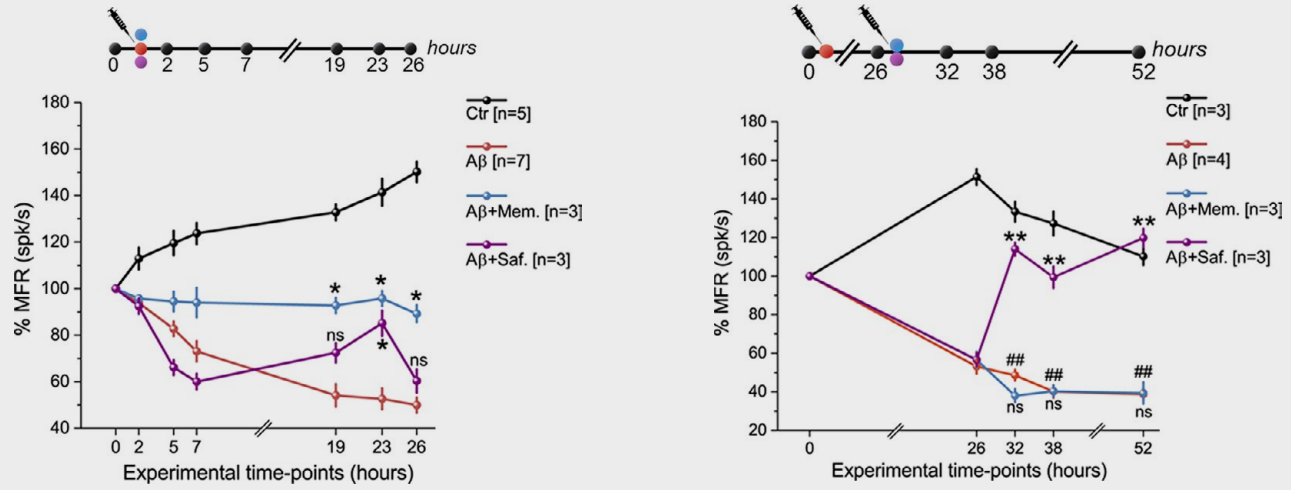
BioCAM X is the ideal tool to develop in vitro models of severe long-term neurodegenerative diseases, such as Alzheimer's and Parkinson's, with increased sensitivity compared to other assays.



Sensitivity of HD-MEA to low dose Aβ-oligomer concentration (100 nM). While the HD-MEAs show strongly impaired functional activity (left, red curve), the MTT assay does not show significant cell death (right) *(adapted from Amin et al., Scientific Reports 2017).*

Drug discovery

The rescue effects of neuroprotective compounds can be evaluated in label-free assays with unprecedented statistical significance and with a superior sensitivity compared to common cell viability assays.

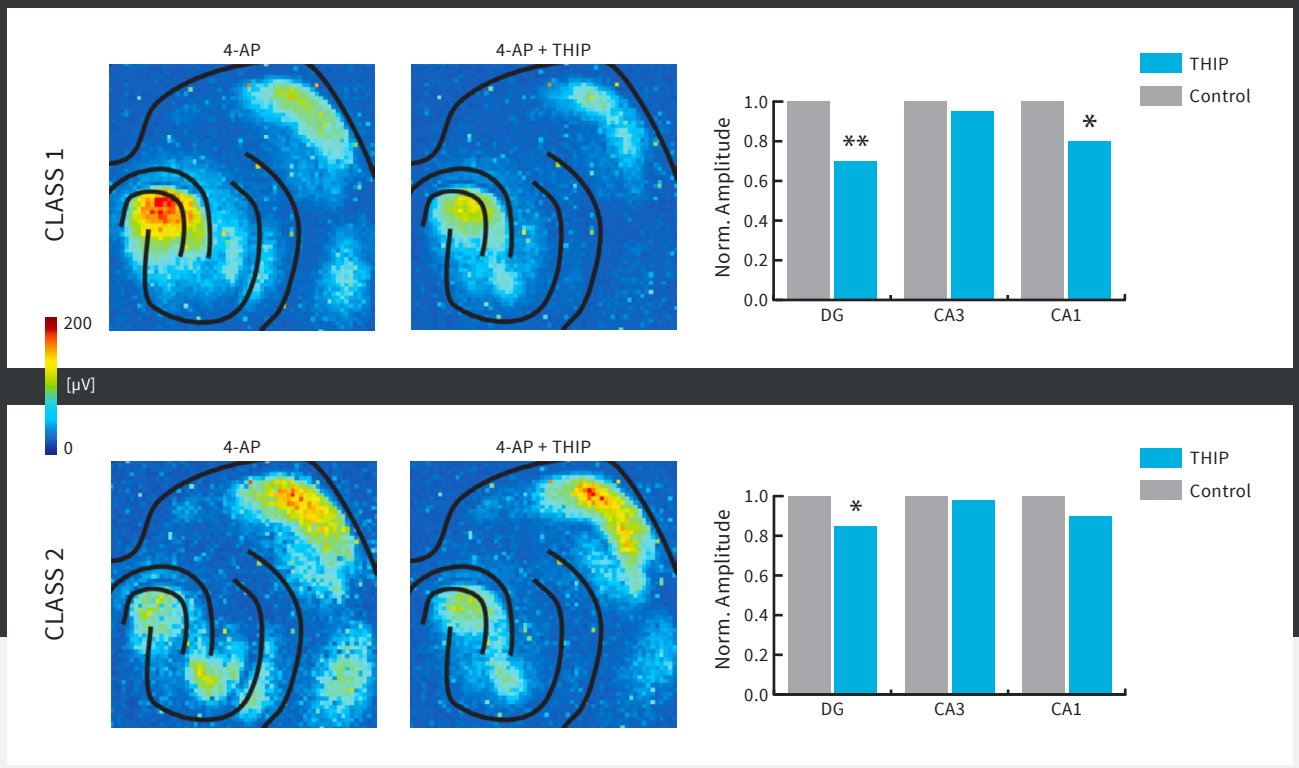


Evaluation of the rescue effects of neuro-protective compounds. Administration of memantine or saffron at different time points (left: co-administered with Aβ-oligomers; right: administered 26 hours later than Aβ-oligomers) leads to completely different results *(adapted from Amin et al., Scientific Reports 2017).*

Safety, toxicology and mechanism of action

Understanding the potential targets of molecules, for example in the field of epilepsy, can be performed by BioCAM X in label-free mode, at a micro-scale level and over large brain regions.

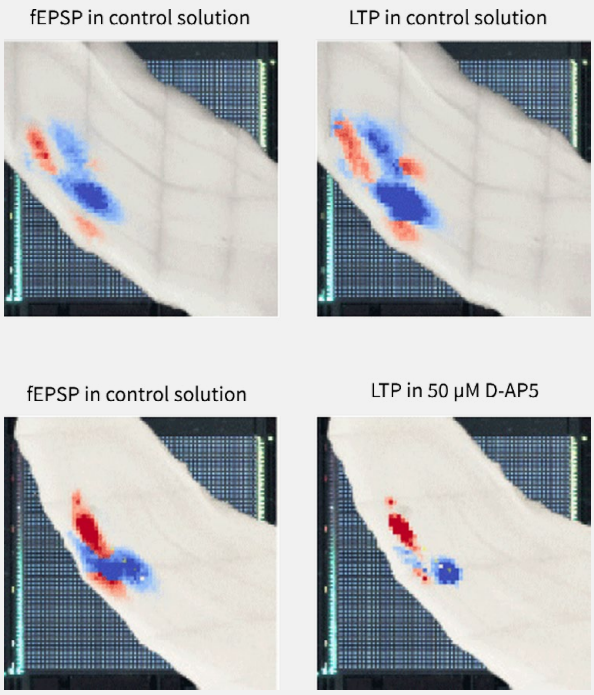
The anticonvulsant drug THIP differentially affecting two distinct classes of epileptic events is detected by the BioCAM X system *(adapted from Ferrea et al., Front. Neural Circuits 2012).*



Long Term Potentiation/Depression

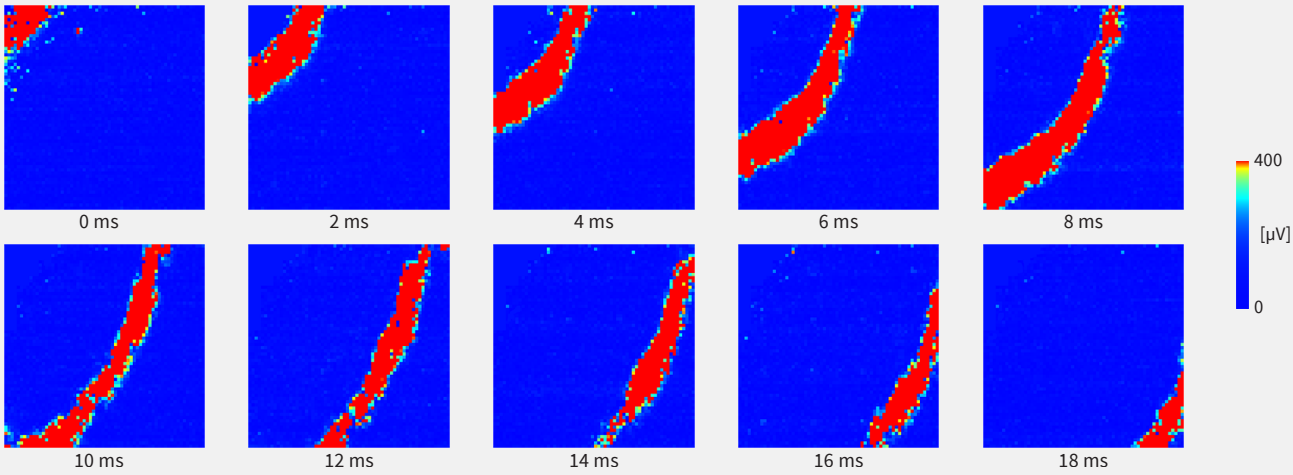
LTP/LTD protocols are routinely used in evaluating memory deficit induced by neurotoxic compounds. BioCAM X allows a large area of interest to be monitored, revealing heterogeneous compound effects with high statistical significance.

Effect of D-AP5 on the LTP of CA1.
Compared to the control (upper panel), D-AP5 spatially inhibits potentiation, affecting both the amplitude and spread of the signals (lower panel) *(courtesy of A. Ugolini, Aptuit Verona).*



Safety studies on cardiac cells

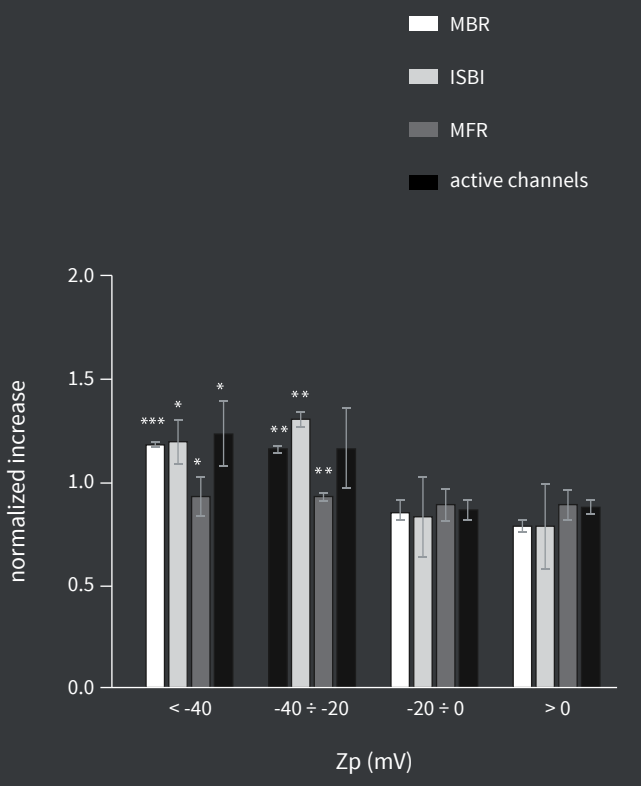
Cardiac drug safety screening is a mandatory step in drug development. BioCAM X and HD-MEAs allow researchers to finely characterise toxic effects, evaluating different parameters such as the contractile period, spike amplitude, duration and propagation velocity.



Cardiac wave lasting 20 ms propagating over an HD-MEA of 5 x 5 mm^2 *(courtesy of L. Berdondini NetS³Lab, Fondazione Istituto Italiano di Tecnologia, Italy).*

Toxicology studies on neuronal networks

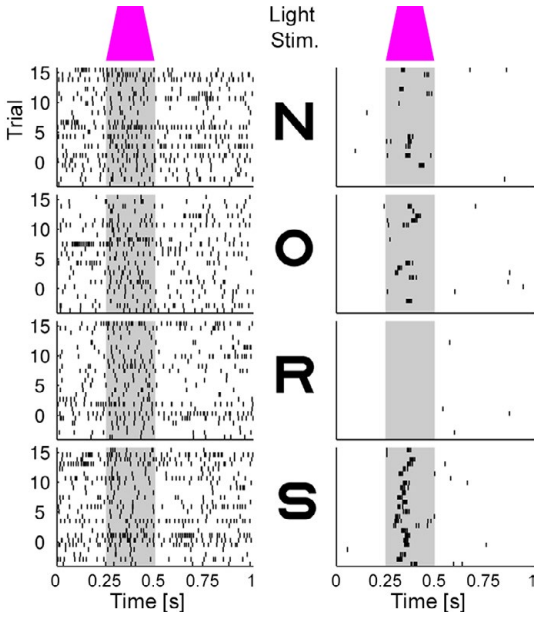
Aberration of neuronal electrical activity is an early marker of neurotoxicity. Parameters such as the firing rate or network synchronicity (burst activity) can be easily quantified in vitro by BioCAM X to evaluate the potential toxic effects of compounds under study.



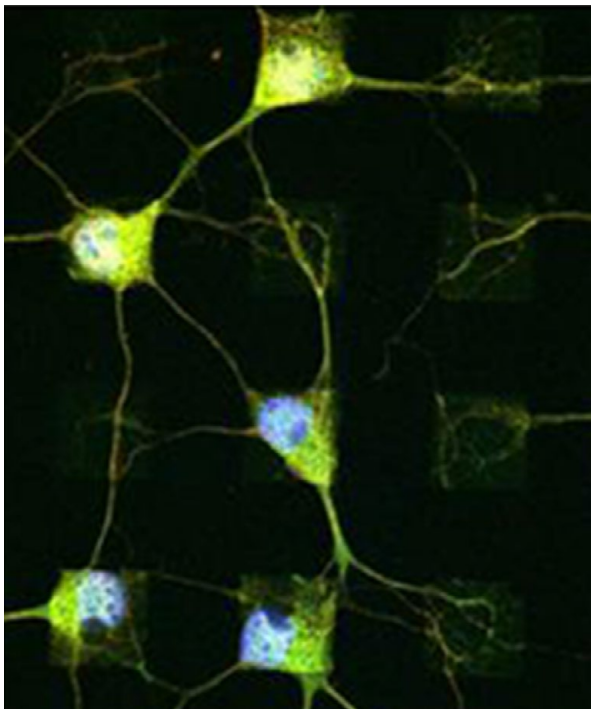
Effect of electrically charged nanoparticles. An increase in the negative charge (x-axis) results in a significant variation of parameters such as mean firing rate (MFR), mean bursting rate (MBR) and interspike burst interval (ISBI). *(adapted with permission from Dante et al. ACSNano 2017, copyright © 2017 American Chemical Society).*

Optogenetics

Combine the precise spatial excitation/inhibition capabilities of optogenetics with the appropriate detection tool: BioCAM X can accurately detect small and local functional changes induced by optogenetic stimulation.



Optogenetic stimulation with different light patterns (“N”, “O”, “R”, “S”) provides reliable responses on a dystrophic retina affected by retinitis pigmentosa after basal activity suppression with meclofenamic acid (MFA). Left: no MFA. Right: with MFA *(adapted from J.M. Barrett et al., Sci. Rep. 2016).*



Further BioCAM X uses

Use BioCAM X in other contexts, such as studying progenitors’ integration in cell cultures, performing real-time closed-loop experiments or characterising specific chemical functionalisation of the electrode-neuron interface.
To discuss further possibilities, contact our team of application specialists on 3brain.com.

Precise neuron placement on functionalised platinum electrodes *(adapted with permission from Mescola et al. 2016, Langmuir. Copyright 2016 American Chemical Society).*

MADE IN SWITZERLAND

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APPLICATIONS

- Dissociated neuronal cultures
- Cardiomyocyte cultures
- Human stem cell-derived neurons
- Acute brain tissue and explanted retina
- Organoids
- Disease modelling
- Drug discovery
- Safety studies, long-term and acute toxicology
- LTP & LTD protocols
- Plasticity & homeostatic studies
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- Optogenetics-combined studies
- Functional and structural connectivity

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