Quantification of seizurogenic activity with the Maestro Pro microelectrode array platform for proconvulsant risk assessment

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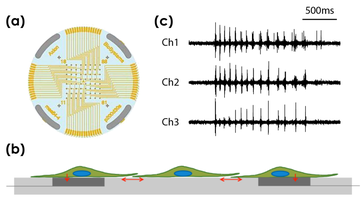
Multiwell MEA Technology

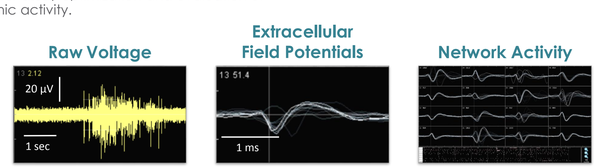
Microelectrode array technology

Thorough characterization of primary and human induced pluripotent stem cell (iPSC)-derived neurons requires analysis of both single-cell and network function. Electrophysiological measurements from multiple individual neurons across a network provide a comprehensive view of neural activity, including functionality, connectivity, and excitability.

Axion BioSystems' Maestro™ multiwell microelectrode array (MEA) platforms provide high-throughput, non-invasive, benchtop systems that simply and accurately record activity from neural networks cultured on dense arrays of extracellular electrodes in each well. They offer a unique *in vitro* approach to modeling *in vivo* neural behavior for applications in neurotoxicity, disease modeling and safety. Here, we describe the benefits of using the Maestro™ MEA platforms for assay optimization and evaluation of seizuregenic activity.

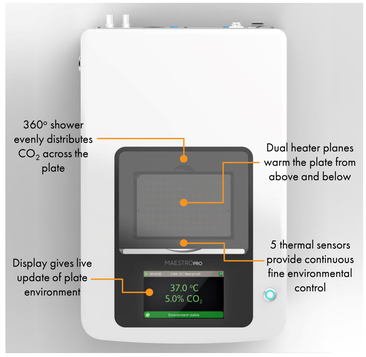


A planar grid of microelectrodes **(a)** interfaces with cultured neurons **(b)**, to model complex, human systems. Electrodes detect changes in raw voltage **(c)** and record extracellular field potentials.



Raw voltage signals are processed in real-time to obtain extracellular field potentials from across the network, providing a valuable electrophysiological phenotype for applications in drug discovery, toxicological and safety screening, disease modeling, and stem cell characterization.

Introducing the Maestro Pro™ and Maestro Edge™



- **Label-free, non-invasive recording** of extracellular voltage from cultured electro-active cells
- **Integrated environmental control** provides a stable benchtop environment for short- and long-term toxicity studies
- **Fast data collection rate (12.5 KHz)** accurately quantifies the depolarization waveform
- **Sensitive voltage resolution** detects subtle extracellular action potential events
- **Industry-leading array density** provides high quality data from across the entire culture
- **Scalable format (12-, 24-, 48- and 96-well plates)** meets all throughput needs on a single system
- **State-of-the-art electrode processing chip (BioCore v4)** offers stronger signals, ultra-low frequency content, and enhanced flexibility

The Maestro Pro™ (left) and Maestro Edge™ (right) offer the latest MEA technology for optimal data.

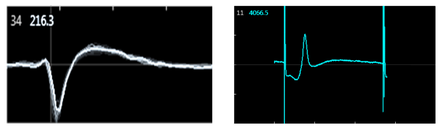
Feature	Maestro Edge	Maestro Pro
Recording Electrodes	384	768
BioCore Chip	6 Chips (v4)	12 Chips (v4)
MEA Plates	24-Well	12-, 24-, 48-, 96-Well
Integrated Hard Drive	0.5 TB	1.0 TB
Touchscreen	No	Yes
Optical Stimulation	No	Yes

Advanced MEA Platforms

Superior signal integrity

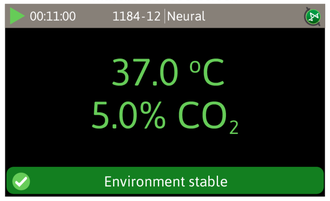
The Maestro Pro and Edge incorporate several advanced features to provide the best signal quality.

The BioCore v4 is the latest, most powerful electrode processing chip from Axion. The chip provides stronger signals, low noise, and ultra low frequency content for the best neural and cardiac signals.

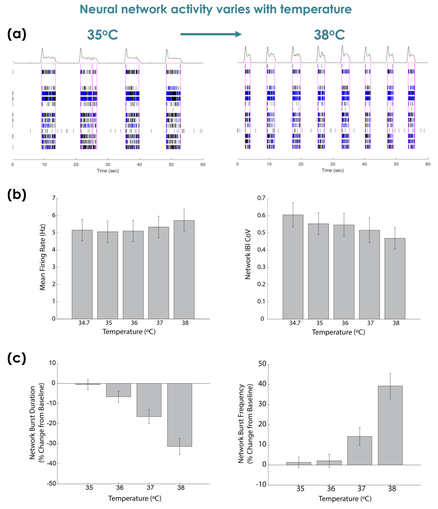


New processing modes provide enhanced neural (left) and cardiac (right) shapes with higher biological fidelity for improved detection of drug effects and stem cell characterization (Asakura et al 2015). Lower noise yields high signal-to-noise for the cleanest signals. Subsequent digital processing keeps channel-to-channel variability low for maximum reliability and reproducibility.

Integrated environmental controls



Temperature and CO_2 are automatically and precisely controlled by the Maestro. The Maestro Pro's touchscreen **(above)** notifies the user that the environment is stable and ready. As a result of a precisely controlled environment, neural activity is stable. **(a, b)** When temperature increases, mean firing rate as well as network burst regularity both increase. **(c)** Variation in temperature also affects network burst duration and frequency.



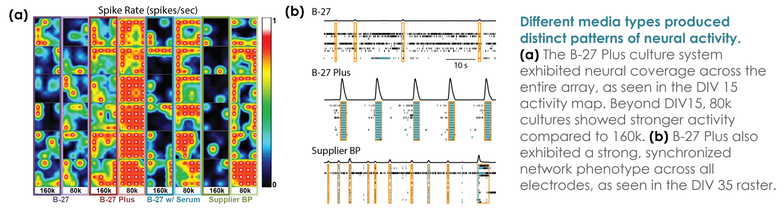
Intuitive "one button" recordings

The Maestro Pro and Maestro Edge offer "one button" setup. With the push of one button, the plate is docked and environmental controls automatically adjust. The integrated barcode scanner recognizes the plate identifier and automatically names files and logs plate usage for convenient experiment tracking. Finally, AxIS Navigator makes execution and analysis of MEA experiments simple and easy. Offline tools provide added data visualization and export as needed.

Neural Proconvulsant MEA Assays

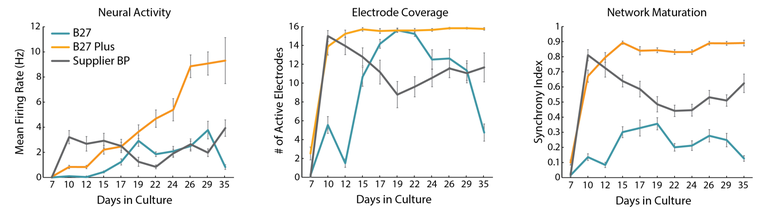
Optimizing culture conditions for MEA assays using Maestro Pro

The Maestro Pro and Maestro Edge are compatible with a range of MEA plate types and throughput scales that are ideal for optimizing stem cell development, plating conditions, and exploring compound effects. Here, we used the Maestro Pro to compare medias for network development and long-term culture with primary rat cortical neurons. CytoView MEA 48-well plates (n=3) were seeded at 80,000 or 160,000 cells per well across 4 media conditions (n=6 per condition per plate).



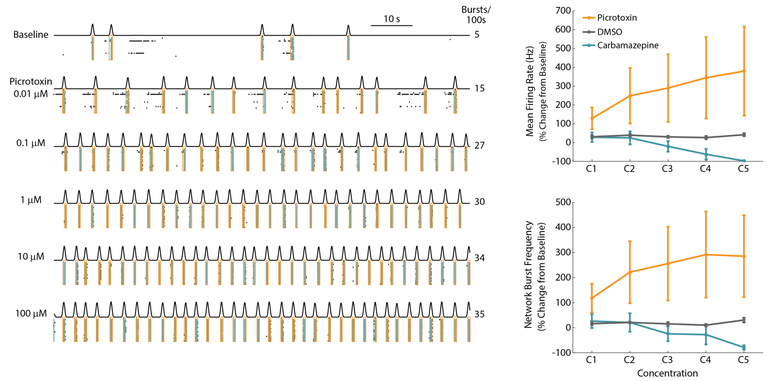
Different media types produced distinct patterns of neural activity. **(a)** The B-27 Plus culture system exhibited neural coverage across the entire array, as seen in the DIV 15 activity map. Beyond DIV15, 80k cultures showed stronger activity compared to 160k. **(b)** B-27 Plus also exhibited a strong, synchronized network phenotype across all electrodes, as seen in the DIV 35 raster.

B-27 Plus facilitated long term culture health with strong activity, electrode coverage, and network maturity



Proconvulsants readily distinguished from other compounds

Primary rat cortical neurons in B-27 Plus media were sequentially dosed with a proconvulsant (Picrotoxin, a $GABA_AR$ antagonist, 0.01 to 100 µM), antiepileptic (Carbamazepine, a sodium channel blocker, 1 to 100µM), or vehicle control (DMSO, 0.1 to 0.5%). Picrotoxin elicited a clear proconvulsant phenotype characterized by increased mean firing rate, network burst frequency, and network burst regularity. In contrast, carbamazepine reduced firing and network bursting.



Conclusions

The Maestro Pro is a comprehensive yet intuitive system for neural assays. The powerful BioCore4 ensures signal fidelity, while the integrated environmental controls are ideal for both acute and chronic assays. High-throughput capacity, barcode organization, and software tools make optimization across many conditions and detection of key neural network phenotypes more advanced and easier than ever.