Improvements to Multiwell Microelectrode Array Technology for Characterization of Neural and Cardiac Electrophysiology in Vitro

Millard, D.C.; Hayes, H.B.; Chvatal, S.A.; Nicolini, A.M.; Arrowood, C.A.; Clements, M.; Ross, J.D.

[1] Axion BioSystems, Atlanta, GA

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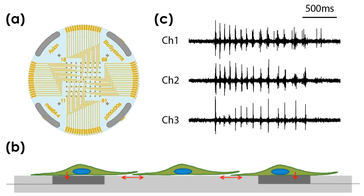
Multiwell MEA Technology

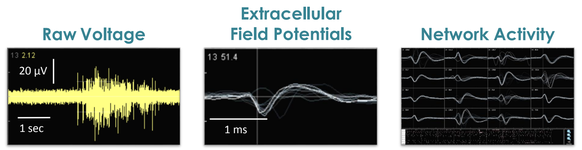
Microelectrode array technology

The flexibility and accessibility of induced pluripotent stem cell (iPSC) technology has allowed complex human biology to be reproduced *in vitro* at previously unimaginable scales. Accurate characterization of stem cell-derived neurons and cardiomyocytes requires an assay that provides a functional phenotype. Measurements of electrophysiological activity across a networked population of cells offer a comprehensive view of function beyond standard characterization through genomic and biochemical profiling.

Axion BioSystems' Maestro™ multiwell microelectrode array (MEA) platforms provide this functional characterization through a non-invasive benchtop system to simply, rapidly, and accurately record functional activity from cellular networks cultured on a dense array of extracellular electrodes in each well.

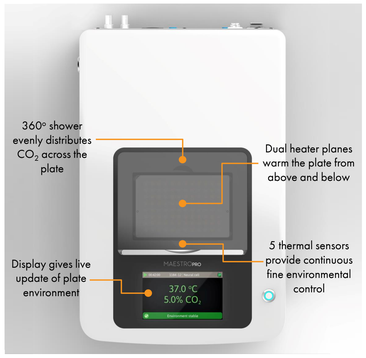


A planar grid of microelectrodes **(a)** interfaces with cultured neurons or cardiomyocytes **(b)**, to model complex, human systems. Electrodes detect changes in raw voltage **(c)** and record extracellular field potentials.



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 amplitude
- **Sensitive voltage resolution** detects subtle extracellular action potential events
- **Industry-leading array density** provides high quality data by integrating across locations in the 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

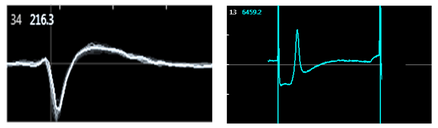
Feature	Maestro Edge	Maestro Pro
Recording Electrodes	384	768
BioCore Chip	6 Chips (v4)	12 Chips (v4)
MEA Plates	24-Well	12-, 24-, 48-, 96-Well
Integrated Hard Drive	0.5 TB	1.0 TB
Touchscreen	No	Yes
Optical Stimulation	No	Yes

Advanced MEA Platforms

Superior signal integrity

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

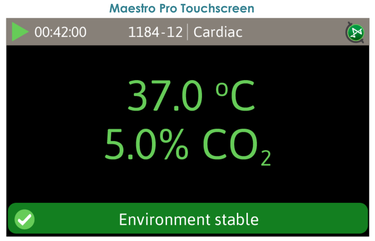
The BioCore v4 is the latest, most powerful electrode processing chip from Axion. The chip provides stronger signals, low noise, and ultra low frequency content for the best neural and cardiac signals.



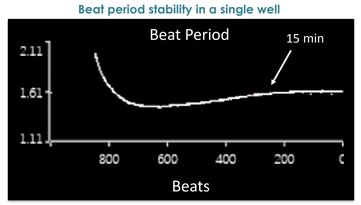
New processing modes provide enhanced neural (left) and cardiac (right) shapes with higher biological fidelity for improved detection of drug effects and stem cell characterization (Asakura et al 2015). Lower noise yields high signal-to-noise for the cleanest signals. Subsequent digital processing keeps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

Integrated environmental controls

Maestro Pro Touchscreen

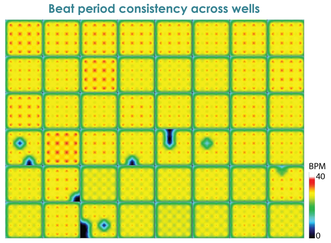


Beat period stability in a single well



Temperature and CO2 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, cardiac beating stabilizes in less than 15 minutes (top, right). The environment is consistently controlled across the whole plate for low well-to-well variability (bottom, right), yielding optimal data quality and reliability every time.

Beat period consistency across wells



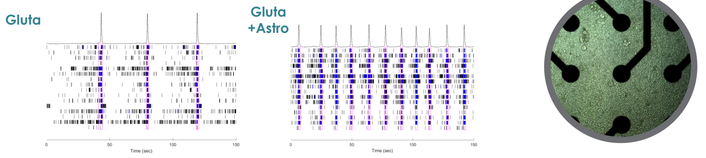
Intuitive "one button" recordings

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 name 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.

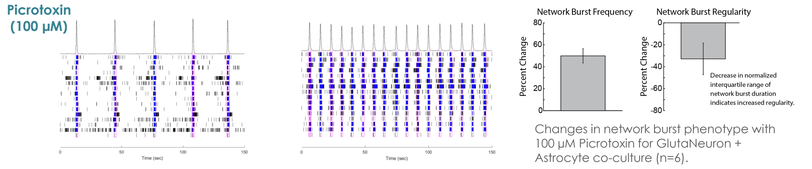
Neural MEA Assays

Characterizing hiPSC-derived neurons and compound effects

The Maestro Pro and Edge are compatible with a wide array 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 optimize iCell® GlutaNeuron culturing and to evaluate the effects of picrotoxin, a common seizurogenic compound. Network burst phenotypes were compared between iCell GlutaNeurons cultured alone or co-cultured with astrocytes on a Classic MEA 48 and CytoView MEA 48. The CytoView MEA 48 plate allowed for cell and network visualization in parallel with electrophysiological measurements.



Astrocytes significantly altered the network burst phenotype of GlutaNeurons. (Data from a CytoView MEA 48.)



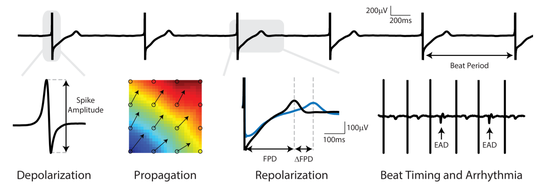
Changes in network burst phenotype with 100 µM Picrotoxin for GlutaNeuron + Astrocyte co-culture (n=6).

Picrotoxin caused an increase in network burst frequency and burst regularity, indicating seizurogenic properties.

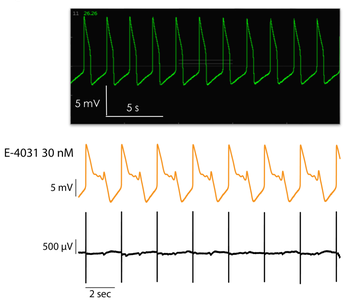
Cardiac MEA Assays

Assessing of whole cell cardiomyocyte behavior

The Maestro MEA platforms enable assessment of functional *in vitro* cardiomyocyte activity. The Maestro detects and records electrical signals from a cardiomyocyte synctium in each well. Multiple electrodes per well provide precise detection of key electrophysiological parameters, such as depolarization, propagation, repolarization, arrhythmias, and early after depolarizations (EADs).



With the new BioCore4, the Maestro Pro can now induce and record long-lasting, stable, extracellular action potential-like signal shapes, known as local extracellular action potentials (**LEAP**), on MEAs. LEAP provides significantly enhanced resolution for confirmation and detection of potential prolongation along with easy EAD detection and classification.



The LEAP Advantage

- **Label free and non-invasive** measurement of action potential-like signal shapes
- **High amplitude potential** (5-15 mV) and high signal-to-noise ratio
- **Long-lasting and stable signals** (> 10 min, up to hours)
- **Easy inspection** of potential prolongation and EADs
- **Simple induction and high throughput**