Maestro APEX™: introducing the first automated system for microelectrode array (MEA) experiments

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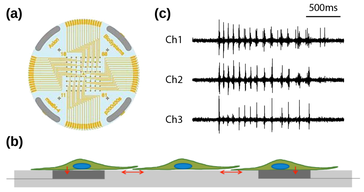
Multiwell MEA Technology

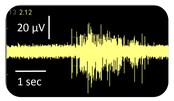
Why use microelectrode arrays?

Microelectrode array technology offers a platform for directly connecting key biological variables, such as gene expression or ion channels, to measures of cellular and network function.

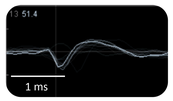
A planar grid of microelectrodes (a) interfaces with electro-active cultured cells (b), modeling complex, human systems in a dish. The electrodes detect changes in raw voltage (c) caused by the electrical activity of nearby neurons or cardiomyocytes.



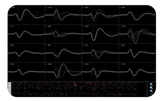
Raw Voltage



Extracellular Action Potentials



Network Activity



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

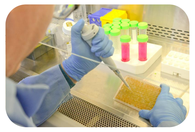
Why use the Maestro?

Axion's Maestro multiwell microelectrode array (MEA) platform enables high throughput evaluation of neural and cardiac activity on the benchtop, with an industry leading 768 electrodes across all plate formats.

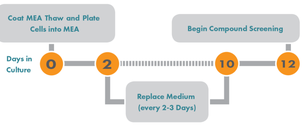
- **Label-free and non-invasive recording** of extracellular voltage from cultured neurons on Axion MEA plates
- **Environmental control** provides a stable benchtop environment for short- and long-term toxicity studies
- **Fast data collection rate (12.5 KHz)** accurately quantifies the magnitude of depolarization events
- **Sensitive voltage resolution** detects subtle extracellular action potential events
- **Industry-leading array density** provides high quality data through the integration of information from multiple locations in the culture
- **Scalable format (12-, 48- and 96-well plates)** meets all throughput needs on a single system

Typical Workflow

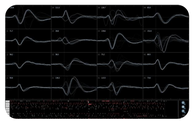
Plate Preparation



Maintenance and Experiments



Data Analysis

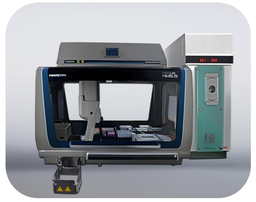


- High throughput MEA applications involve manual plate preparation, regular media exchange for culture maintenance, and sophisticated data analysis.
- Furthermore, plate preparation requires fine precision to position the cell suspension directly over the MEA embedded within each well.
- The Maestro and AxIS have successfully scaled throughput for MEA measurement technology and quantitative analysis, but no solution currently exists to increase throughput at the front-end of the workflow.
- Thus, the throughput of MEA screening applications is currently limited by the reliability and speed of the plate preparation and maintenance pipeline.

Maestro APEX

Why incorporate automation?

Automation affords high precision for reliable plate preparation, coupled with significant walk-away time for cell spotting, maintenance, and dosing experiments.

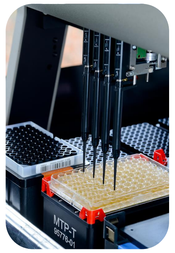


The Maestro APEX features a 4-channel robotic liquid handler, an integrated incubator and gas mixer, and the Maestro multiwell MEA platform.

The feature-packed deck layout has been customized for Maestro users specifically.

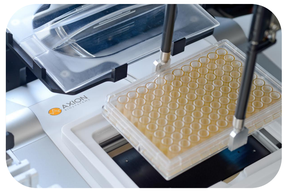
- **Automated cell culture improves consistency and reliability of cultures.**
- **Significant walk-away time frees the user for other tasks, increasing efficiency.**
- **Direct communication with AxIS enables the user to add detailed notes, push configurations, and turn on/off recording.**
- **Motorized operation of the Maestro allows the robot to deposit and remove plates, facilitating experimental flexibility.**
- **Re-designed environmental control provides continuous delivery of CO2, even when the device enclosure is opened for automated dosing.**
- **Integrated incubator with 44 plate capacity facilitates large workflows.**
- **Established routines for cell spotting, media change, and dosing carry the user through the entire experimental workflow.**
- **Integrated HEPA filter and UV illumination ensures sterile operation.**

Comprehensive Functionality



The 4-channel pipet head supplies flexibility for 48- and 96-well MEA plates, and the requisite precision for critical steps in plate preparation.

An integrated 44-plate incubator provides ample storage for high throughput MEA experimentation.

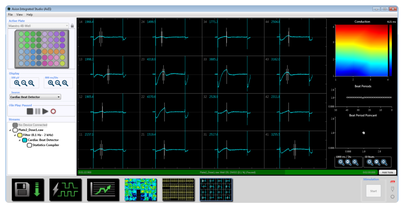


The re-designed ECmini utilizes a patent-pending "shower" concept to maintain CO_2 control at the Maestro during dosing or plate movement.

AxIS Integration

Seamless AxIS integration allows Maestro APEX to load plate maps and configurations, initiate recordings, run stimulation protocols, and add annotation tags during live experiments.

In addition, AxIS continues to serve as the back-end automated software for quantitative data analysis. New features like customized plate maps and data aggregation make it easier and faster than ever to analyze MEA data.

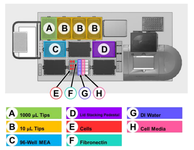


Applications in Screening

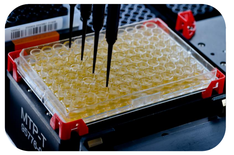
Walk-away Time

Optimization of automated protocols for cell spotting and dosing experiments enable the user to "set it and forget it", as Maestro APEX executes a complex series of tasks. Significant "walk-away time" allows users to focus on the science, rather than the implementation.

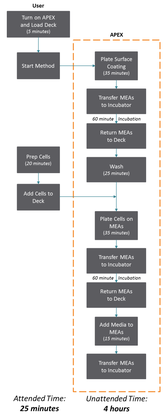
Further, automated culture maintenance ensures that the cells are ready for evaluation when you are, as media exchange can happen afterhours.



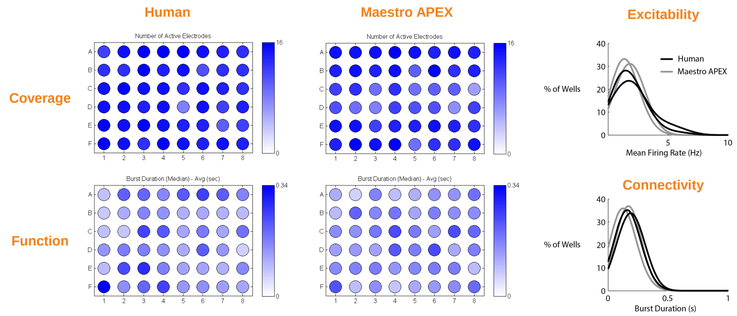
The operator sets up the deck and provides the cells…



…while Maestro APEX does the rest.

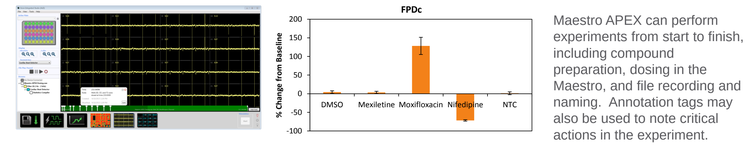


Neural Validation



The quality of neural cultures relies on coverage of the electrodes and functional qualities of the network. The automated precision and custom protocols of the Maestro APEX provide high quality neural cultures by matching the coverage and function exhibited by expert human cell spotting, as indicated by measures of neural excitability and connectivity.

Cardiac Automated Dosing



Maestro APEX can perform experiments from start to finish, including compound preparation, dosing in the Maestro, and file recording and naming. Annotation tags may also be used to note critical actions in the experiment.

Conclusions

- The Maestro multiwell MEA platform connects key biological variables to cellular and network function by extracting information from complex biological systems *in vitro*.
- While the Maestro and AxIS have successfully scaled throughput for MEA measurement technology and quantitative analysis, no solution has been available to increase throughput at the front-end of the workflow.
- The Maestro APEX, the first automated MEA workstation, features a 4-channel robotic liquid handler, an integrated incubator and gas mixer, and the Maestro multiwell MEA platform.
- The precision and custom protocols of the Maestro APEX provide high quality, automated MEA plate preparation, culture maintenance, and dosing experiments to accelerate screening for cardiac and neural applications.