Maestro™ multwell MEA

Abstract

The need for simple, reliable and predictive pre-clinical assays for cardiac safety has motivated initiatives worldwide including the Comprehensive in vitro Proarrhythmia Assay (CiPA) and Japan’s Cardiac Safety Assessment (CiPA). Towards this end, the Maestro APEX platform enables assessment of functional in vitro cardiac activity with an easy-to-use benchtop system. The Maestro platform and Maestro cards report electrophysiological signals from cells cultured directly onto an array of planar electrodes in each well of the MEA plate. Functional cardiac cultures developed in 8-9 h. The electrodes detect changes in raw voltage (c) caused by the electrical activity of cardiomyocytes, analogous to the ECG in vivo.

Why use microelectrode arrays?

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

A planar grid of microelectrodes (a) interface with electro-active cultured cells (b) to model complex, human-species in a dish. This enables analysis of changes in raw voltage (c) caused by the electrical activity of cardiomyocytes, analogous to the ECG in vivo.

Raw Voltage

Extracellular Action Potentials

Network Activity

Why use the Maestro? 

• Establishes a non-invasive recording of extracellular voltage from cultured cells in an Axion MEA plate.
• 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 dephosphorylation events.
• Sensitive voltage resolution detects subtle extracellular action potential waveform variations.
• Industry-leading array density provides high quality data through high-integrity information from multiple locations in the culture.
• Scalable format (12, 48- and 96-well plates) meets all throughput needs in a single system.

Key Features

- Lab-free and non-invasive recording of extracellular voltage from cultured cells in Axion MEA plates
- Environmental control as a stable benchtop environment for short- and long-term studies
- Fast data collection rate at 12.5 kHz, accurately quantify magnitude of dephosphorylation events
- Sensitive voltage resolution detects subtle extracellular action potential waveform variations
- Industry-leading array density ensures high quality data through high-integrity information from multiple locations in the culture
- Scalable format from 12-well to 96-well plates, meets all throughput needs in a single system

Maestro APEX™

Why incorporate automation?

• Automated cell-culture improve consistency and reliability of cultures.
• Significant walk-away time frees user for other tasks, increasing efficiency.
• Precalibrated routines for cell spotting, media change, and dosing carry the user through the entire experiment.
• Redesigned environmental control provides continuous delivery of CO2 at all times.
• Incorporate incubator with 44 plate capacity supports many simultaneous studies.
• Integrated HEPA filter and UV illumination ensures sterile operation.

Biological Stability

It is commonly known that small perturbations to cardiomyocyte function can result in variable assay performance. APEX minimizes changes to the local MEA environment, such as: 1) a sterile plate deck that enables dosing directly on the Maestro, and 2) an on-board gas mixer that provides CO2 concentration compensation during dosing to facilitate a rapid return to stable baseline patterns (left).

Efficiency and Throughput

APEX offers significant efficiency gains, as user time is minimal for preparing important baselines. As an example, to support CiPA, Axion software provides a convenient, pre-built dosing environment enabled consistent throughput cardiac safety screening simple from start to finish.

Conclusions

Although the compounds remain blinded, the phenotypic response allows for prediction of low, intermediate, and high risk compounds. The presumed low risk compound (left) caused no change in repolarization, whereas the presumed high risk compound (right) induced significant FPDc prolongation and numerous EAs. By comparison, the presumed intermediate risk compound (middle) failed to prolong FPDc and had few EAs. Axion (right) indicates the proportion of wells that showed an incidence of early afterdepolarizations (EADs).

Example Dose Response

In the above example, the presumed low risk compound (left) caused no change in repolarization, whereas the presumed high risk compound (right) induced significant FPDc prolongation and numerous EAs. Axion software (right) indicates the proportion of wells that showed an incidence of early afterdepolarizations (EADs).

Example Dose Response

Conclusions

Maestro APEX, the first automated MEA workstation, provides significant advancements in research productivity and assay reliability.

- More plates, more data, more discoveries – automated protocols take care of every aspect of MEA plate preparation, maintenance, and assay execution.
- More time – with minimal user interaction, APEX does all the work. For example, the recent completion of the CiPA Phase II study involved less than 6 hours of user time.
- High-quality results – automated plate preparation and advancements in local environmental control ensures quality cell cultures and robust data.