Quantification of Seizurogenic Activity with Multiwell Microelectrode Array Technology for Proconvulsant Risk Assessment and Disease-in-a-Dish Epilepsy Models

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Multiwell MEA Technology

Why use the Maestro?

Axion’s Maestro™ multiwell microelectrode array (MEA) platform enables functional cellular analysis in the benchtop with an industry leading 768 electrodes across all plate formats.

Typical Assay Workflow

- Maestro experiments involve seeding cells onto the MEA plate and allowing the neural network to mature over a period of days to weeks.
- MEA technology is label-free and non-invasive, such that the maturation process can be monitored through repeated recordings over that time frame.
- The network electrophysiology phenotype provides a functional measure in response to perturbations of key biological variables, such as pharmacology or gene expression.

MEA Assay for ProC Risk Assessment

Network Electrophysiology Phenotypes

- Activity: Several compounds from different classes. The ability of the network electrophysiology phenotype to inform proconvulsant safety was assessed with these compounds from each of these four different classes:
  1) Pharmacokinetically active and known ProC (e.g., "Lumos")
  2) Excitatory: compounds that increase activity, but have no known ProC risk
  3) Anti-epileptic Drugs (AEDs) – compounds used to treat epilepsy clinically
  4) Inhibitory: compounds that decrease activity, but are not known AEDs

Proconvulsant Assay – Study Design

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Typical Assay Workflow

- Plate Preparation
- Maintenance and Maturation
- Experiment

Raw Voltage Extracellular Action Potentials Network Activity

Raw voltage signals are processed in real-time to obtain extracellular action potentials from across the network via up to 64 electrodes, providing a valuable electrophysiological phenotype for applications in drug discovery, toxicological and safety screening, disease models, and stem cell characterization.

Advanced Applications

Disease-in-a-Dish Models – Dravet Syndrome

In vitro measurements of network activity may also be used to study valproate-induced disorders of genetic origin, such as Dravet syndrome. In an in vitro model of Dravet syndrome, the culture exhibit an enhanced network phenotype characterized by significantly longer bursts in mature cultures.

Gross Network Bursting Measures Excitability

The magnitude of the network burst phenotype is modulated by neuroactive compounds and single neuron level activity is insufficient to distinguish drugs (1) the whole-cell control from picrotoxin (ProC) and (2) carbamazepine (AED) from strychnine (AED).

Mean Firing Rate Reflects Functionality

The network phenotype can be monitored in real-time and is highly reliable across replicates.

[1] While fMRI did not differentiate the vehicle control and placebo, the network burst magnitude after exposure to proconvulsant activity, as measured by network bursting measures excitability.

Conclusions

- The Maestro™ multiwell MEA platform enables functional characterization of neural cell culture activity and connectivity with a flexible, easy-to-use, benchtop system.
- Axion software and advanced analysis tools make evaluation and reporting of functional data simple and hassle-free with an array of automatically generated metrics.
- Maestro™ MEA delivers accurate and predictive results on functional neural network biology in a convenient benchtop platform furthering safety and toxicology, disease-in-a-dish modeling, and drug discovery research.