Quantification of functional network electrophysiology from stem cell derived neurons with multiwell microelectrode array technology

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**Multiwell MEA Technology**

**Why use microelectrode arrays?**
- The feasibility and accessibility of induced pluripotent stem cell (iPSC) technology has allowed complex human biology to be reproduced in vitro at a previously unimaginable scale. Accurate characterization of stem cell-derived neurons and cardiomyocytes requires an easy-to-use and high-throughput platform.
- For these electro-active cells, measurements of electrophysiological activity across a networked population of cells provides a comprehensive view of function beyond standard characterization through genetic and biochemical analyses alone.
- The MEA platform offers a solution by providing a label-free, non-invasive bench top system that is simply, rapidly, and accurately record functional activity from a population of cells cultured on an array of extracellular electrodes.

**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.
- Sensitivity voltage resolution detects subtle extracellular activity from electrophysiological phenomena.
- Industry-leading array density provides high quality data from across the entire culture.
- Scalable format (15-, 24-, 36-, and 96-well plates) meets all throughput needs on a single system.
- State-of-the-art electrophysiology processing chip (BioCore™) maximizes data capture, frequency content, and enhanced flexibility.

**MEA Assay with Neurons**

**Neural Electrophysiology Phenotypes**
- **Excitability** - Neurons may fire multiple action potentials within a short time period, called a burst. Established protocols detect and quantify burst behavior.
- **Connectivity** - Synaptic connections between neurons in a population may lead to coincident action potentials. Network burst and synchrony measurements quantify connectivity.

**iPSC-Neuron Maturation**
- The Maestro’s high electrode count and label-free recording provides the perfect platform for long-term evaluation of neural network formation from proliferating iPSC neurons. Maturation of the culture can be confirmed through the evolution of network electrophysiology metrics such as mean firing rate (MFR), bursting, and synchronous network bursts.

**Characterizing hiPSC-derived neurons and compound effects**
- The Maestro Pro is 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 CellGluNeuron culturing and to evaluate the effects of Picrotoxin, a common seizimuic compound. Network burst phenotypes were compared between CellGluNeuron 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.

**Conclusions**
- The Maestro multiwell MEA platform enables functional characterization of neural cell culture activity with a flexible, easy-to-use benchtop system.
- AxIli software makes analysis and reporting of functional data simple and hassle-free with an array of automatically generated metrics and advanced analysis tools.
- By bringing human biology to a dish, hiPSC-derived neurons deliver biologically relevant data to allow for disease-in-a-dish modeling. The Maestro has been used to publish results with the following models of neural disease:
  - Fragile X, Autism, Epilepsy, Huntington’s, Parkinson’s, Williams Syndrome, Dravet Syndrome, Cysticayne Syndrome, Alzheimers, and others.