AXION BIOSYSTEMS

NEURAL ACTIVITY ASSAY

COMPREHENSIVE NETWORK ACTIVITY MADE SIMPLE WITH MAESTRO MEA

Why measure neural activity?

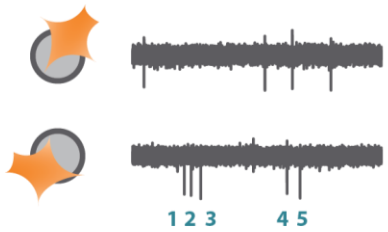
In vitro neural models are a proven powerful strategy for the study of neural function and complex disorders of the human nervous system. The study of neurons has been historically complex, hindering advancements in human biology and treating disease. Maestro microelectrode array (MEA) technology makes it easy to measure electrical network behavior in live cells at high throughput, providing simple functional endpoints that capture biological complexity.

Neural network recordings

Axion BioSystems' Maestro Pro and Maestro Edge provide a flexible, yet intuitive, assay of functional electrophysiology for neural applications. Axion's MEA plates have a grid of tightly spaced electrodes embedded in the culture surface of each well. Neurons (orange) can be cultured over the electrodes (grey), and over time, as the cultures become established, neurons can form cohesive networks with an electrophysiological profile. The resulting electrical activity is captured from each electrode on a microsecond timescale providing both temporally and spatially precise data. The Maestro detects key parameters of neural network function, including activity, synchrony, and oscillation. All three endpoints are required for a complete understanding of functional neural networks.

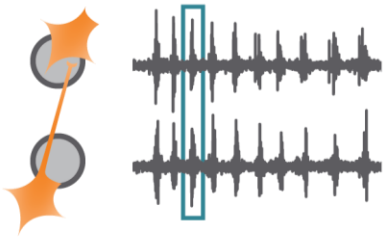
THE MAESTRO ADVANTAGE

- It's easy! Culture cells in each well, load the plate in the Maestro, and press record.
- Industry-leading electrode counts provide access to network-level information at scale.
- Multiwell MEA plates provide throughput flexibility to scale up functional assays.
- Noninvasive, label-free measurements monitor acute responses or long term development.
- Functional endpoints compliment existing assays used in drug screening, developmental biology, and disease modeling.



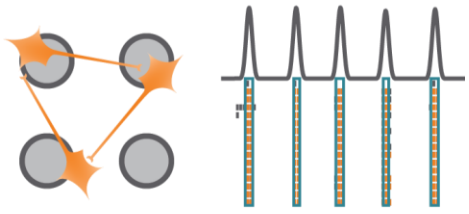
Activity

Action potentials are the defining feature of neuron function. High values indicate frequent action potential firing and low values indicate the neurons may have impaired function.



Synchrony

Synapses are functional connections between neurons. Synchrony reflects the prevalence and strength of synaptic connections, and thus how likely neurons are to generate action potentials simultaneously on millisecond time scales.

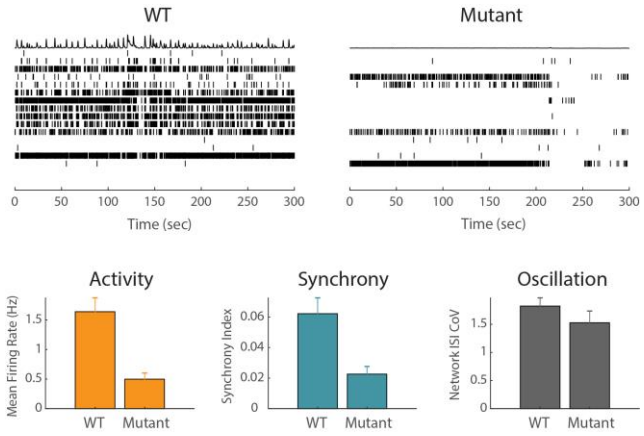


Oscillation

Neural oscillations, defined by alternating periods of high and low activity, are a hallmark of functional networks with excitatory and inhibitory neurons. Oscillation is a measure of how the spikes from all of the neurons are organized in time.

EXAMPLE APPLICATION 1: iPSC DISEASE MODELING

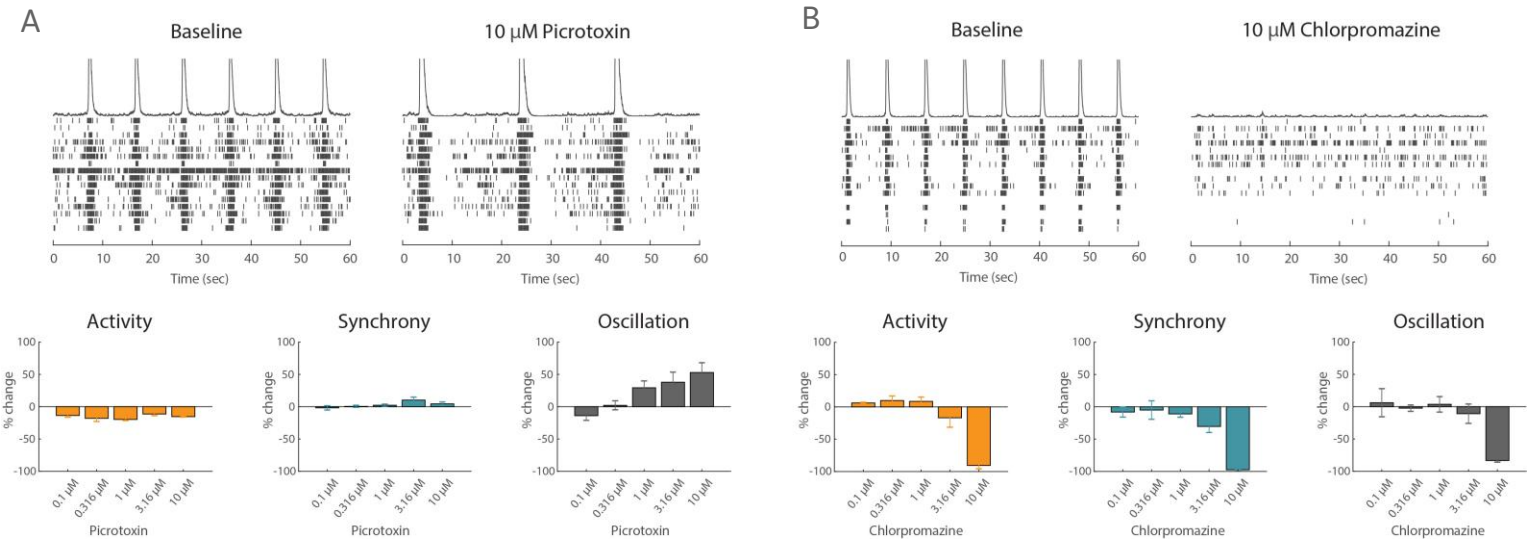
Significant advancements in reprogramming basic human cells (induced pluripotent stem cells, iPSC) from both healthy and diseased donors into any cell type has laid the foundation for exploring human disease *in vitro*. In an iPSC-derived model of schizophrenia, the oscillation measure suggests there is little difference in neural networks in the mutant and wild type (WT) cells. However, the Maestro revealed a decrease in activity and synchrony in the mutant neurons relative to WT, an effect that would have been missed when looking at oscillation alone.



Representative well-wide raster plots showing spikes generated by mutant and WT iPSC-derived neurons (top). The mutant neurons showed decreased activity and synchrony relative to WT, but no change in oscillation (bottom).

EXAMPLE APPLICATION 2: NEUROTOXICOLOGY

Functional assessment is crucial to understanding potentially adverse effects on neuronal networks. The Maestro excels in preclinical studies to screen for unwanted seizurogenic activity. In iPSC-derived neurons, Picrotoxin, a proconvulsant compound, caused an increase in oscillation in a dose-dependent manner, while having no effect on activity and synchrony. The antipsychotic medication, Chlorpromazine, had a very different effect, decreasing activity, synchrony, and oscillation at high concentrations. Biological complexity in neural networks is important, and all three of these measures are required to fully understand it. Maestro MEA makes it easy to capture and describe functional network behavior.



A) Well-wide raster plots showing spikes generated in the same well before and after dosing with Picrotoxin (top). Picrotoxin increased oscillation, but had no effect on activity and synchrony (bottom). B) Well-wide raster plots showing spikes generated in the same well before and after dosing with Chlorpromazine (top). Chlorpromazine decreased activity, synchrony, and oscillation (bottom).