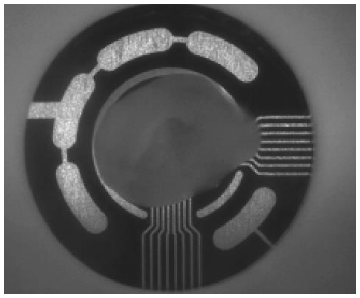
AXION BIOSYSTEMS

NEURAL ORGANOIDS

LEARN MORE FROM *IN VITRO* TISSUE MODELS

The promise of organoids

Three-dimensional induced pluripotent stem cell (iPSC)-derived *in vitro* cell models, commonly referred to as spheroids, organoids, or "mini-brains", more accurately recapitulate the multicellular organization and structure of *in vivo* tissues when compared to traditional monolayer cell cultures. Recent trends in developmental biology and disease-in-a-dish modeling highlight the value of re-creating *in vivo* micro-environments. Assessing the function of 3D models is vital for understanding disease models, drug discovery, and drug safety.

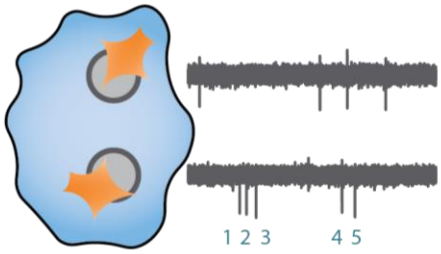


THE MAESTRO ADVANTAGE

- Industry-leading electrode counts provide access to network-level information.
- 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.
- It's easy! Place organoids in each well, load the plate in the Maestro, and press record.

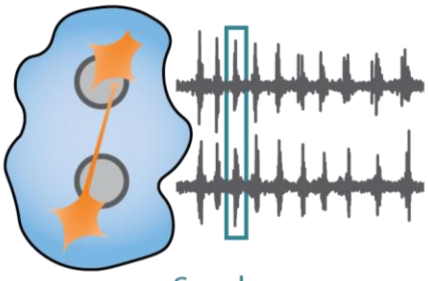
3D tissue model electrophysiology

Axion BioSystems' Maestro Pro and Maestro Edge provide a flexible, yet intuitive, assay of functional electrophysiology for neural 3D constructs. The Maestro platforms allow for easy capture of electrical activity from one or more individual organoids, providing functional neural endpoints that compliment other standard assays for organoids. Electrical activity is captured from neurons (orange) in organoids cultured over electrodes (gray circle). The Maestro MEA system detects key parameters of neural network function, including activity, synchrony, and oscillation.



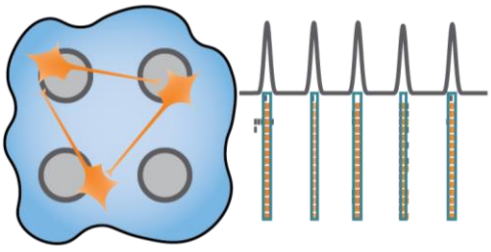
Activity

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.

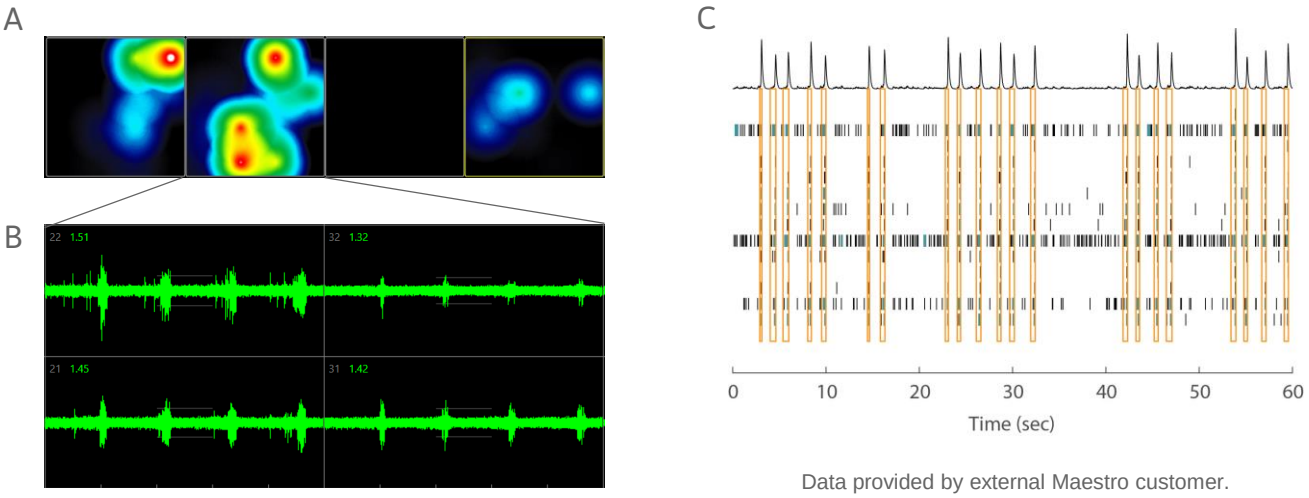


Oscillation

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.

FUNCTIONAL ACTIVITY FROM CEREBRAL ORGANOIDS

Cerebral organoids generated from human induced pluripotent stem cells (hiPSCs) exhibit spontaneous neural activity, with increasing firing, synchrony, and oscillation as networks mature. The Maestro enables recording of multiple organoids at once (A). By day 30 in culture, organoids exhibits network bursts of activity (B and C), indicative of strong network formation.

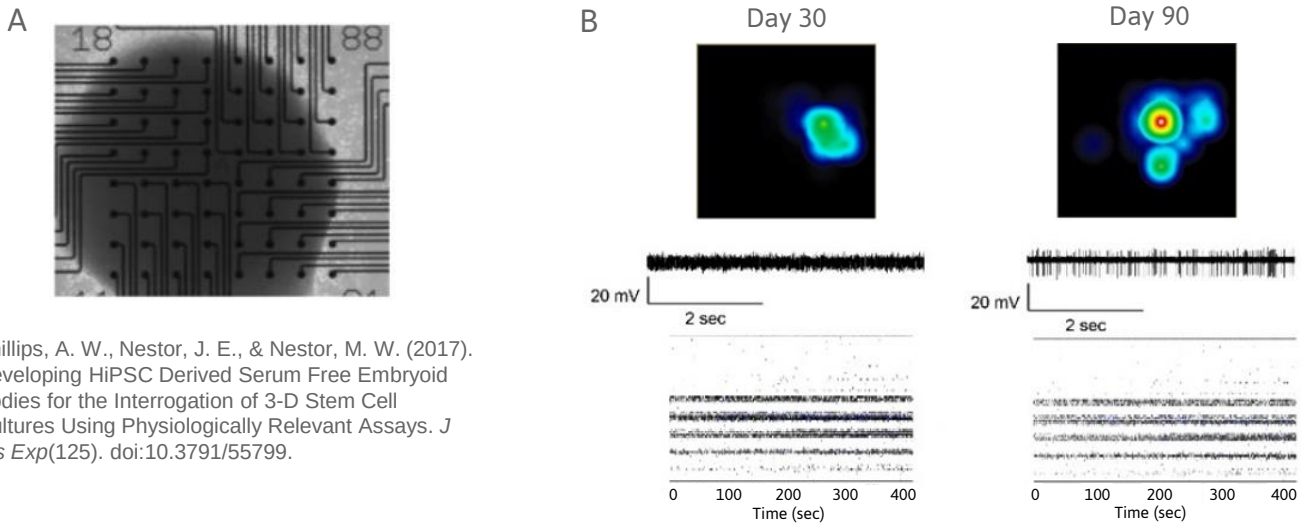


Data provided by external Maestro customer.

A) Activity map displaying firing rate for 4 cerebral organoids. B) Examples of continuous voltage data recorded from different electrodes in one well. Activity is recorded from different sites on the same organoid. C) Well-wide raster plot showing spikes generated by the organoid in B across all 16 electrodes and network connectivity resulting in network bursts. Teal tick marks indicate electrode bursts, and orange boxes indicate network bursts.

3D STRUCTURES PROVIDE MORE COMPLEX MODELS

Serum-free embryoid bodies (SFEBs) are a 3D model system generated from hiPSCs which recapitulate some aspects of cortical network development. SFEBs can be recorded on MEAs over long time periods to monitor development and maturation. Cortical networks in SFEBs show an increase in the number of spikes and bursts between day 30 and 90 as the network develops.



Phillips, A. W., Nestor, J. E., & Nestor, M. W. (2017). Developing HiPSC Derived Serum Free Embryoid Bodies for the Interrogation of 3-D Stem Cell Cultures Using Physiologically Relevant Assays. *J Vis Exp*(125). doi:10.3791/55799.

A) Image of SFEB attached to an MEA plate. B) Activity map shows firing rate across the entire well, illustrating SFEB coverage over the electrodes and magnitude of firing at day 30 and 90. Raw traces and well-wide raster plots show the development of activity over time.