Optimization of optogenetic transduction of stem cell derived cardiomyocytes with adeno-associated virus for optically-paced cardiac electrophysiology assays

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Multiwell MEA Technology

The feasibility and accessibility of neural and cardiac in vitro models, particularly induced pluripotent stem cell (iPSC) technology, has allowed complex human biology to be reproduced in vitro at unimaginable scales. Accurate characterization of neurons and cardiomyocytes requires an assay that provides a functional phenotype that closely resembles the in vivo environment. Measuring extracellular action potentials (APs) across a networked population offers a comprehensive characterization beyond standard genomic and biochemical profiling.

Axion BioSystems’ Maestro™-multiwell microelectrode array (MEA) platform provides this comprehensive functional characterization. The Maestro is a non-invasive benchtop system that simply, rapidly, and accurately records functional activity from cellular networks cultured on a dense array of extracellular electrodes in each well.

Introducing the Maestro Pro™ and Maestro Edge™

Multiwell MEA Technology

- Label-free, non-invasive recording of extracellular voltage from cultured electrosensitive cells
- Integrated environmental control provides a stable benchtop environment for absorb and long-term toxicity studies
- Fast data collection rate (12.5 KHz) accurately quantifies the depolarization waveform
- Sensitive voltage resolution detects subtle extracellular action potential events
- Industry-leading array density provides high quality data from across the entire culture
- Scalable format (12-, 24-, 48- and 96-well plates) meets all throughput needs in a single system
- State-of-the-art electronic processing chip (BioCore v4) offers stronger signals, ultra-low frequency content, and enhanced flexibility

The Maestro Pro™ (left) and Maestro Edge™ (right) offer the latest MEA technology for optimal data.

Optimization of Optogenetic Pacing

The Lumos Multwell Optical Stimulator Enables Cardiac Pacing

With optogenetics, light can be used to control and pace cardiomyocytes without artifact. Pacing cardiomyocytes offers many advantages:

- Specify beat rate at 1 Hz for enhanced physiological relevance
- Establish well-to-well and plate-to-plate consistency with matched beat rates in all wells
- Detect user-dependent drug effects for superior safety screening

Capture Threshold Assay to Evaluate Pacing Efficacy

For low light intensity, or ineffective optogenetic transduction, none of the light pulses will elicit or “capture” a cardiac beat (left). For higher levels of light, some beats will “capture”, whereas other stimuli will fail to elicit a beat, resulting in partial capture (middle). With sufficient light intensity, full capture can be achieved at a variety of pacing rates (right). With efficient optogenetic transduction, full capture is typically achieved at ~20-50% light intensity across all wells (bottom).

Optogenetic Pacing with LEAP

With the new BioCorex, the Maestro Pro can now induce and record long-lasting, stable, extracellular action potential like signal shapes, known as local extracellular action potentials (LEAP), on MEAs. Optogenetic pacing and LEAP were used to confirm previous results regarding the drug-drug interaction between Amiodarone and Sofosbuvir. Pacing at 2Hz across all conditions revealed that the combination of Amiodarone and Sofosbuvir causes a significant shortening of the cardiac action potential that is independent of changes in beating rate.

Conclusions

Optogenetics is a powerful tool. When combined with MEA assays, optogenetics can enhance your neural or cardiac assays by reducing well-to-well variability, detecting rate and activity-dependent drug effects, and systematically controlling cell activity for better sensitivity and specificity.