Multiwell optical stimulation for control of complex in vitro systems

Optical stimulation to control complex biology

- Optical stimulation techniques enable non-invasive control over cultured cells, tissues, and small organisms with specificity and precision.
- For example, optogenetics techniques enable:
  - Activation or inhibition of cell activity
  - Genetic targeting for cell type specificity
  - Control of gene expression and intracellular signaling
  - Influenza virus infection or cellular processes such as protein localization
  - Optical stimulation also enables control through a range of other techniques, including release of optically-caged compounds, photobiomodulation, phototoxicity assays, and small organism assays.

The Lumos system for multwell optical delivery

Optical stimulation via integrated light-activated ion channels (opto-genetic stimulation) is a powerful and emerging technique that enables simultaneous on-demand, optogenetic control of neuronal and muscle systems in vitro. The Lumos device is an integrated platform that enables optogenetic control over multiwell microplates for enhanced throughput experimentation. The device provides a stable benchtop environment for short- and long-term toxicity studies, enabling the simultaneous stimulation of multiple cell lines, organelles, and molecules in culture.

Multiwell MEA Technology

Why use microelectrode arrays?

Microelectrode arrays (MEAs) provide a high-throughput, benchtop method for evaluating the activity of cultured neurons. MEAs collect data simultaneously from many discrete locations in a cultured neural population, delivering information on both activity and connectivity. MEAs provide a powerful approach for modeling in vivo neural activity in a controlled environment, enabling the study of stem cell characterization and phenotyping, neuroactivity, and synapses.

Why use the Maestro Pro™?

- Label-free, non-invasive recording of extracellular voltage from cultured electrophysiologically 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 resolution delivers results in striking extracellular action potential events
- Industry-leading array density provides high quality data from across the entire culture
- Scalable format (12-, 24-, 48-, and 76-well plates) makes all-throughput reads on a single system
- State-of-the-art extracellular processing chip (BioCer v9) offers low noise, ultra-high frequency content, and enhanced flexibility

Multiwell MEA recording with simultaneous optogenetic stimulation

System design and validation

Optogenetic stimulation provides an optogenetic, targeted, and precise means of perturbing cell and network behavior during electrical activity recording.

Multiwell Optogenetics + MEA example application: Cell-type specific stimulation in a neuromuscular co-culture

Background/Methods:
Understanding of the pathogenesis in neuromuscular disease that leads to the collapse of the neuromuscular junction (NMJ) is poor. A human iPSC-derived neuromuscular system comprised of skeletal muscle and sympathetic neurons was developed for high throughput experimentation as part of this work. The system recapitulates the physiology of the NMJ and disease-like AChR mutants.

Conclusions

- Optical stimulation provides a powerful and precise means of influencing cellular systems.
- The Lumos system enables highly controllable and flexible optical stimulation at the multwell level for advanced and high-throughput experimentation.
- The top-side light delivery format of the Lumos enables simultaneous pairing with other technologies, such as bottom-side imaging or electrophysiology.
- Optogenetic stimulation supplements MEA assays by enabling cell-type specific modulation of activity, real-time tuning of network state, and reduction in well-to-well variability, for enhanced disease modeling and dissection of neural circuitry.

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Enhanced light delivery to multwell microplates for high-throughput optical control of activity and cellular processes

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