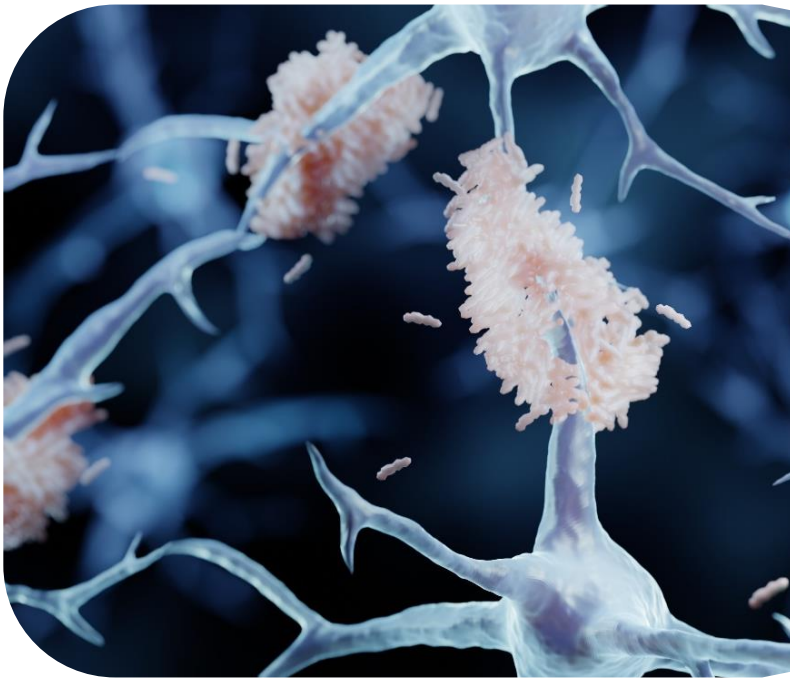
>> Alzheimer's Disease

Alzheimer's disease (AD) is the most common form of dementia worldwide and the prevalence is expected to double by 2050. Despite robust research, current treatments for AD show limited benefit and novel therapeutics are urgently needed. The Maestro microelectrode array (MEA) platform is uniquely suited for neurodegenerative disease research and therapeutic discovery, enabling scientists to noninvasively measure functional activity in 2D and 3D cell models *in vitro* over days or months while preserving the complex structure and communication of neuronal networks.



Learn how the Maestro can enhance Alzheimer's research with **these selected publications:**

Elevated ganglioside GM2 activator (GM2A) in human brain tissue reduces neurite integrity and spontaneous neuronal activity

Yi-Chen Hsieh, Joseph Negri, et al. Molecular Neurodegeneration. (2022)

Alzheimer's disease cases are increasing globally, but therapeutic development remains elusive—in part due to suboptimal disease models. Here, researchers employ multielectrode arrays (MEAs) and imaging to model AD *in vitro* and assess potential pathogenic mechanisms.

Highlights:

- Primary rat cortical neurons treated with brain tissue extracts from AD patients exhibit decreased neural activity.
- Specific amyloid beta ratios and tau levels correlate with dysfunction on MEA and in the neurite integrity assay.
- Proteomics revealed elevated levels of GM2A in AD brain tissue extracts that correlate with dysfunction, and overexpression of GM2A in cultured neurons was sufficient to reproduce this effect.

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Lipid accumulation induced by APOE4 impairs microglial surveillance of neuronal-network activity

Matheus B. Victor, Noelle Leary, et al. Cell Stem Cell. (2022)

Apolipoprotein E4 (APOE4) is a common genetic risk factor implicated in Alzheimer's disease, but it remains unclear how APOE4 may affect neuron-microglia interactions. Using APOE4-expressing iPSC-derived microglia, the authors evaluate deficits in bidirectional communication between neurons and microglia.

Highlights:

- iPSC-derived APOE4 microglia exhibit reduced calcium transients in response to neural activity.
- APOE4 microglia decrease coordinated neural network activity when co-cultured with dissociated neural spheroids.
- Lipid accumulation in APOE4 microglia impairs normal function, and pharmacological treatment to restore lipid homeostasis rescues deficits in neural activity.

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Increased post-mitotic senescence in aged human neurons is a pathological feature of Alzheimer's disease

Joseph R. Herdy, Larissa Traxler, et al. Cell Stem Cell. (2023)

With recent understanding that post-mitotic cells, including neurons, display markers and characteristics of senescence, it has been hypothesized that senescent neurons may contribute to Alzheimer's disease pathology. Researchers use AD patient-derived induced neurons to model neuronal senescence and present senotherapeutics as a potential treatment.

Highlights:

- Post-mortem brains of AD patients contain more senescent neurons than healthy brains.
- Transcriptomics demonstrate that induced neurons from AD patients exhibit senescent patterns compared to healthy, age-matched induced neurons.
- Senescent induced neurons display decreased neural activity and secrete pro-inflammatory factors with the capacity to induce astrogliosis.

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Mechanisms of hyperexcitability in Alzheimer's disease hiPSC-derived neurons and cerebral organoids vs isogenic controls

Swagata Ghatak, Nima Dolatabadi, et al. eLife. (2019)

Human Alzheimer's disease brains and rodent AD models exhibit hyperexcitability, but the underlying mechanisms are not completely understood. Researchers use patient hiPSC-derived cerebral organoids to model AD *in vitro*.

Highlights:

- Patient hiPSC-derived neurons with PS1 or APP mutations are hyperexcitable compared to isogenic controls.
- AD neurons display shorter neurites and disrupted excitatory-inhibitory balance, contributing to increased activity.
- Patient hiPSC-derived neural organoids exhibit similar hyperexcitability, suggesting feasibility as a model to study AD.

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