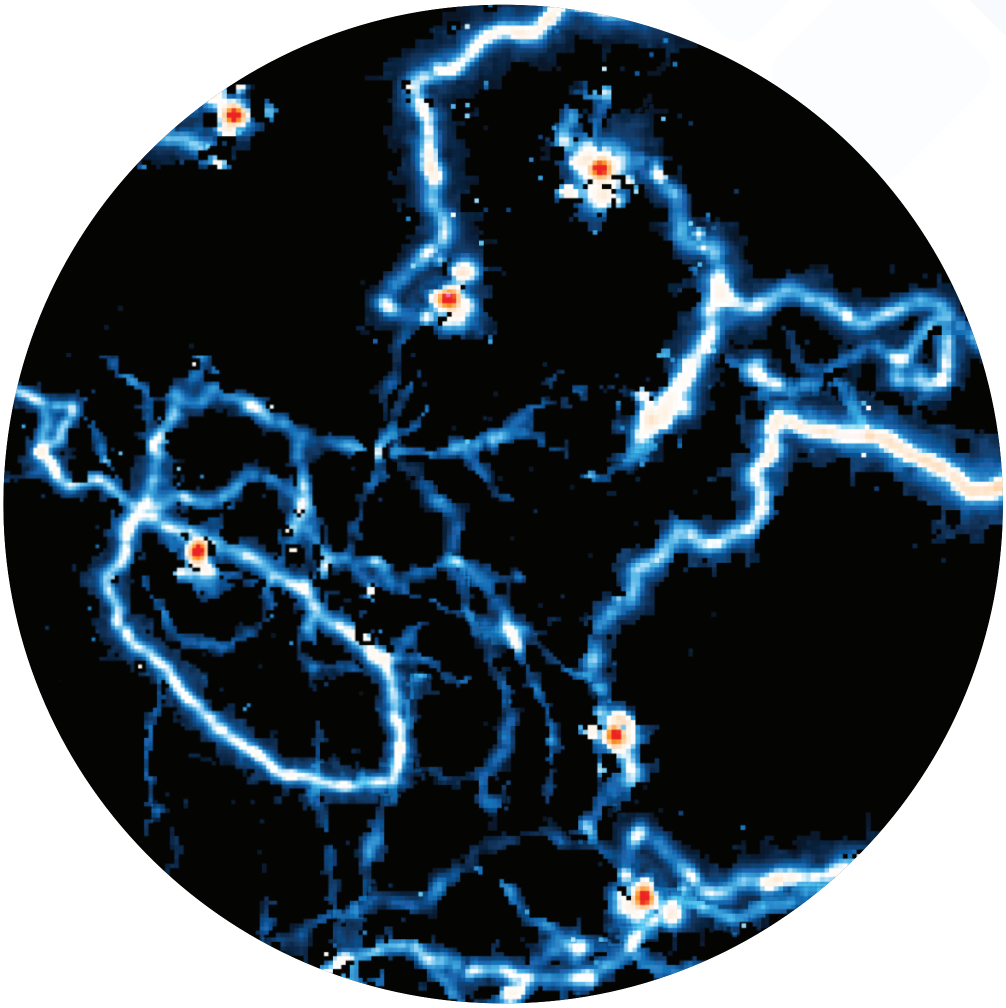
MaxLab Live

AxonTracking Assay



Capture your **Cell's** Activity

Recording Axonal Signals with High-Density Microelectrode Array (HD-MEA) measurements at unprecented resolution and high quality signal, using MaxOne and MaxTwo

maxwell BIOSYSTEMS

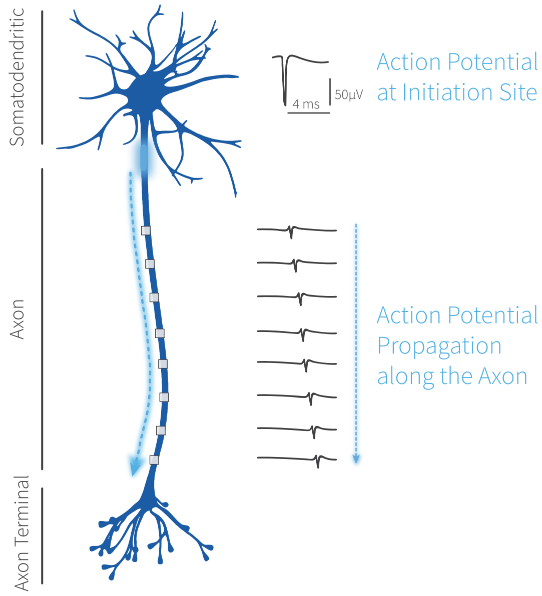
MaxLab Live

AxonTracking Assay

A Novel Approach

Neurons communicate within a network via **action potentials (APs)** propagating along axons. The capability to access axonal physiology is crucial for studying information processing among neurons in healthy and diseased states. However, axonal signals are difficult to measure at a large-scale. Therefore, the combination of reliability, ease of use, throughput, long-term and non-invasive measurement are necessary to monitor and understand neuronal function at a scale that was previously not possible.

High-density microelectrode array (HD-MEA) measurements at unprecedented resolution and high signal quality, using **MaxOne** and **MaxTwo** systems, allow to detect the AP propagation from the initiation site down to distal axonal branches. With the AxonTracking Assay, the identification of the axonal paths is fully automated at the micrometer scale. This live-cell recording and analysis provides novel functional and structural readouts applicable for phenotypic characterization, disease modeling, and drug screening studies.



Automated

The fully automated platform is easy to use and allows for simultaneous recordings of multiple neurons and axonal branches in multiple wells.

Long-Term

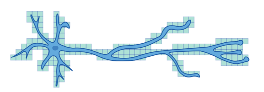
Characterize neuronal maturation, development or treatment effects by recording from your culture over multiple days and weeks.

Label-Free

The electrical recordings are non-invasive and label-free, which avoids introducing side effects from dyes etc.

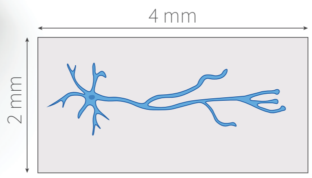
HD-MEA Technology for Recording Axonal Signals

Powered by MaxOne and MaxTwo. Key advantages:



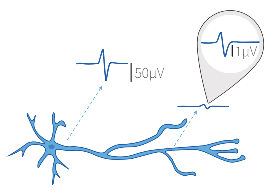
High Spatio-Temporal Resolution

Reconstruct axonal paths by tracking Action Potential propagation at thousands of sites, thanks to the densely packed microelectrode array.



Large Sensor Area

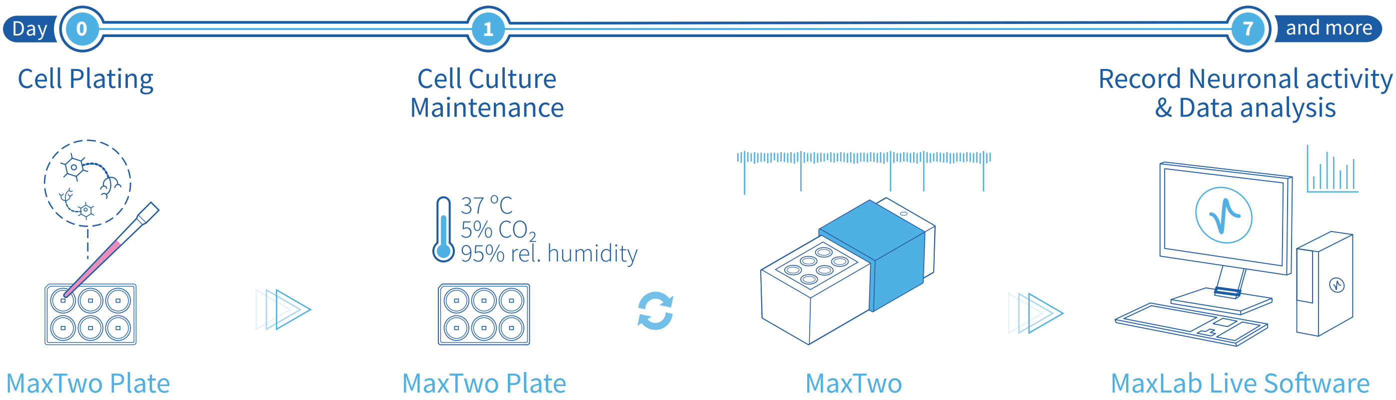
Detect long axonal branches of multiple neurons at the same time with a large sensor area, applicable for 2D and 3D samples.



High Signal Quality

Catch the smallest signals propagating along axons, down to single micro-volts-range, with low-noise recording channels.

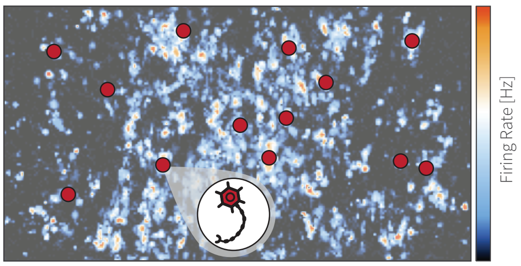
Experimental Workflow



Assay Workflow

Record

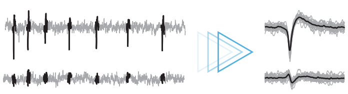
Record the active neurons identified with the ActivityScan Assay.



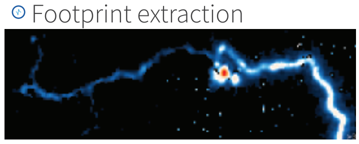
Process

Reveal the axonal morphologies through a series of processing steps

- Spike sorting
- Spike-triggered averaging

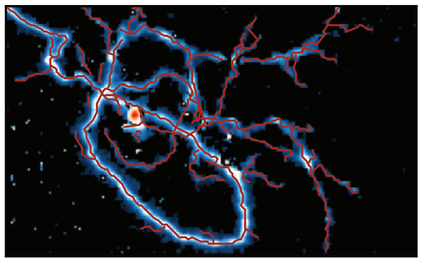


- Footprint extraction



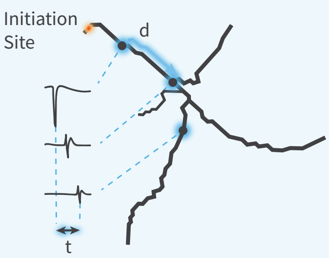
Analyze

Identify individual axonal branches and reconstruct the morphology of the neurite outgrowth using an unsupervised object-tracking algorithm.

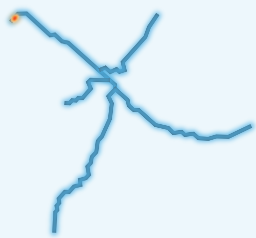


Metrics

Neuron Conduction Velocity

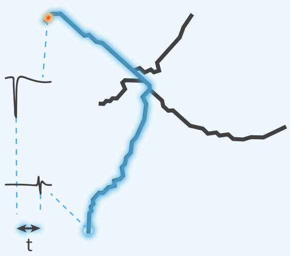


Total Detected Axon Length

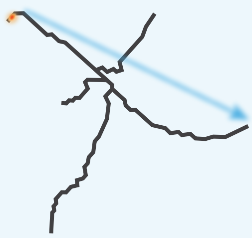


Longest Branch Length

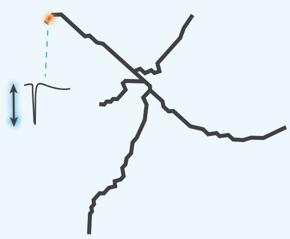
Longest Latency



Longest Distance from Initiation Site



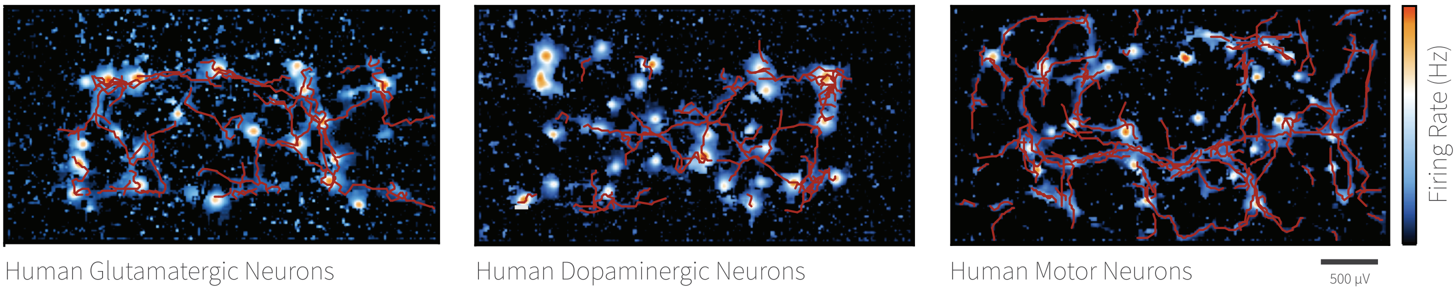
Amplitude at Initiation Site



Results

AxonTracking Assay in Human Neurons

Propagating APs along axonal processes recorded from different human induced pluripotent stem cells-derived (iPSC-derived) neuronal cell lines (FujiFilm Cellular Dynamics, Inc., USA).

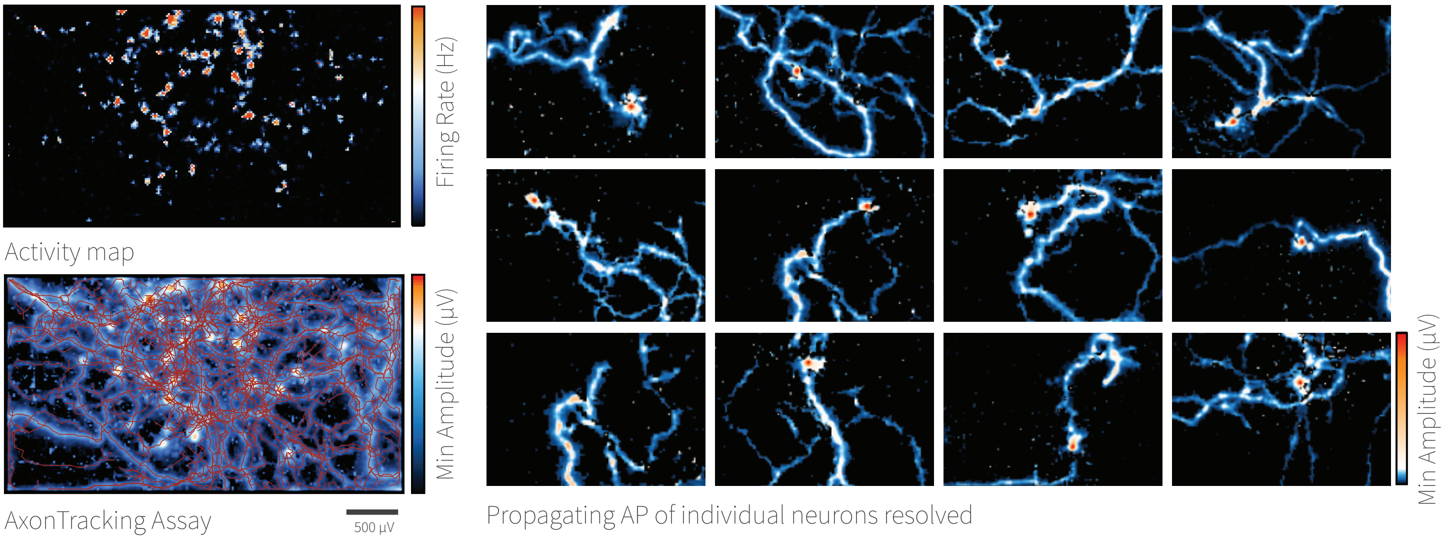


Human Glutamatergic Neurons Human Dopaminergic Neurons Human Motor Neurons

Data courtesy: Bio Engineering Laboratory of ETH Zurich in Basel, Switzerland.

AxonTracking Assay in Long-Term Neuronal Cultures

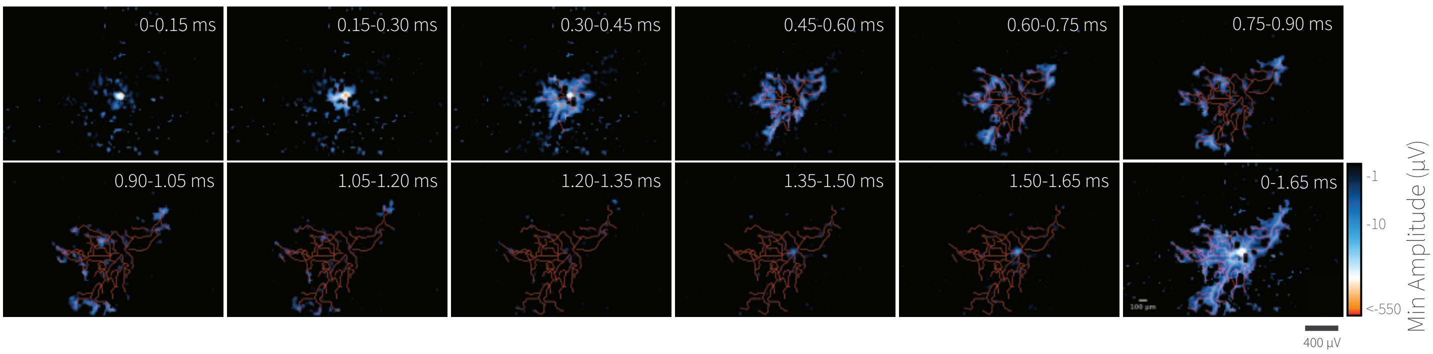
Neurons and propagating APs can be resolved even in cultures with long and dense axonal processes (iPSC-derived glutamatergic neurons, DIV 63, Elixirgen Scientific, USA).



Propagating AP of individual neurons resolved

AP Propagation Along Axons

Propagating APs along the axonal processes of a rat primary cortical neuron shown in a time-series:



References

Bakkum, D. J., Frey, U., Radivojevic, M., Russell, T. L., Müller, J., Fiscella, M., Takahashi, H., & Hierlemann, A. "Tracking axonal action potential propagation on a high-density microelectrode array across hundreds of sites." Nat Commun. 4, 2181 (2013).

Bullmann, T., Radivojevic, M., Huber, S. T., Deligkaris, K., Hierlemann, A., & Frey, U. "Large Scale Mapping of Axonal Arbors Using High-Density Microelectrode Arrays." Front. Cellular Neurosci. 13, 404 (2019).

Case Study

Electrophysiological Characterization of Neurons Modeling Neurological Diseases using High-Density Microelectrode Arrays

ioGlutamatergic Neurons

Wild type ioGlutamatergic Neurons (WT) are human iPSC-derived glutamatergic neurons (bit.bio,UK).

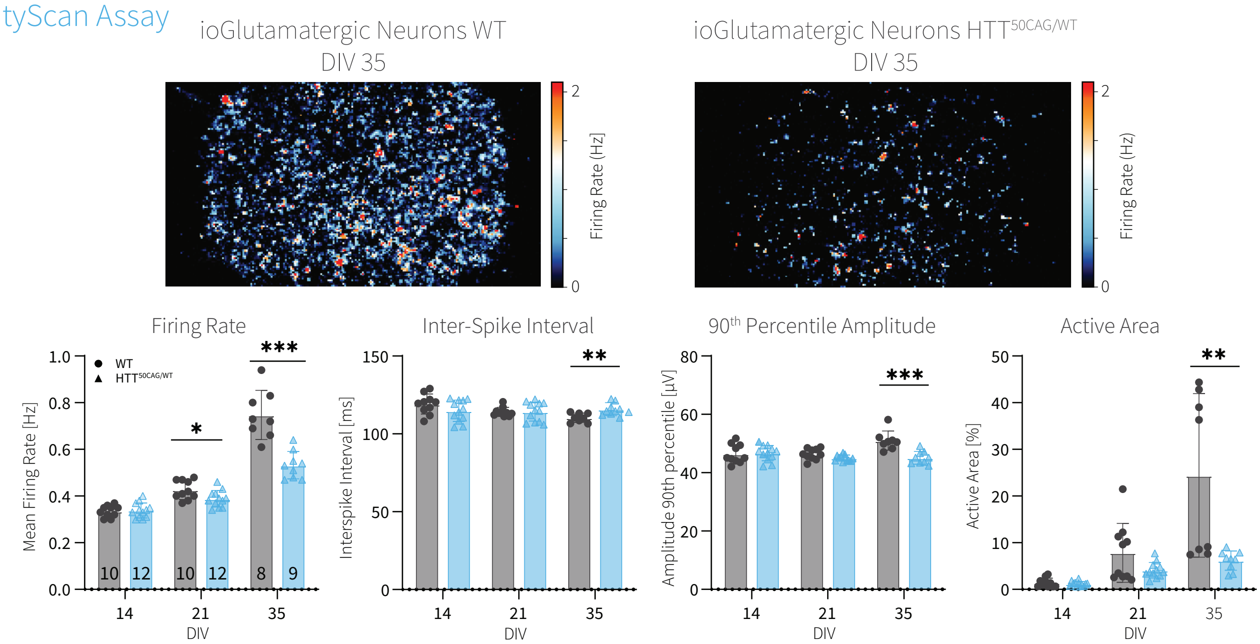
ioGlutamatergic Neurons Modeling Huntington's Disease

ioGlutamatergic Neurons $HTT^{50CAG/WT}$ are ioGlutamatergic Neurons carrying the disease-relevant 50 CAG trinucleotide repeat expansion, associated with Huntington's disease. $HTT^{50CAG/WT}$ neurons have been reprogrammed from human iPSCs using the opti-ox™ (optimised inducible overexpression) reprogramming technique[1].

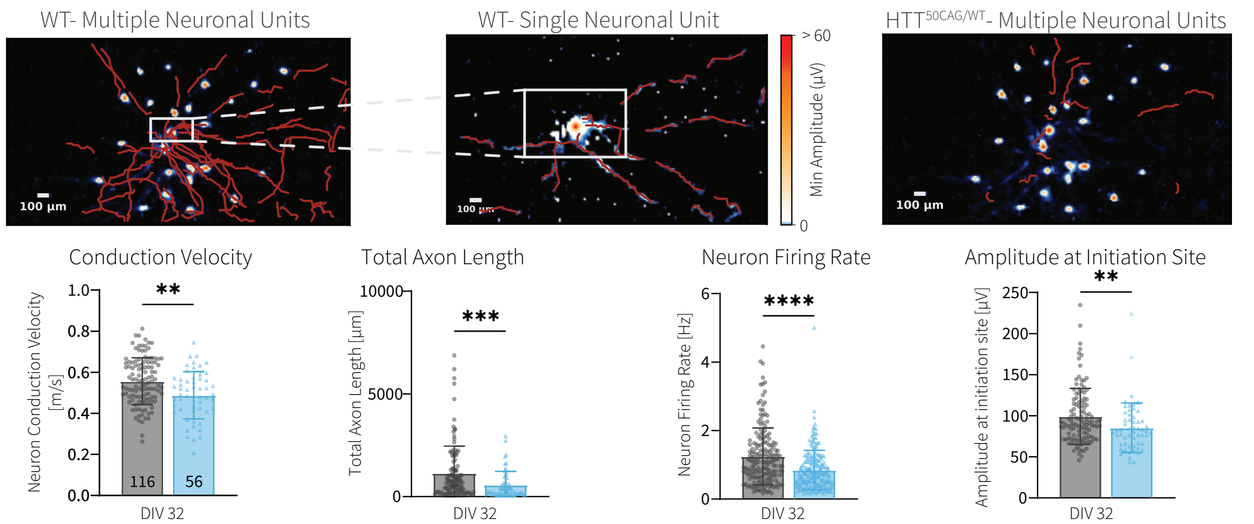
Protocol

200k ioGlutamatergic neurons (bit.bio, UK); 40k iCell Astrocytes (Fujifilm Cellular Dynamics, Inc., USA)

ActivityScan Assay



AxonTracking Assay



Statistics used: Kurskal-Wallis test with Dunn's correction

Conclusions

The disease line $HTT^{50CAG/WT}$ showed slower maturation compared to the WT line. Highly reproducible differences in activity and axonal maturation were obtained comparing the disease line to the control.

References

[1] Pawlowski, M., Ortmann, D., Bertero, A., Tavares, J. M., Pedersen, R. A., Vallier, L., & Kotter, M. R. "Inducible and deterministic forward programming of human pluripotent stem cells into neurons, skeletal myocytes, and oligodendrocytes." Stem cell reports, 8(4), 803-812 (2017).

Data was recorded at Early Discovery at Charles River Laboratories, United Kingdom.

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