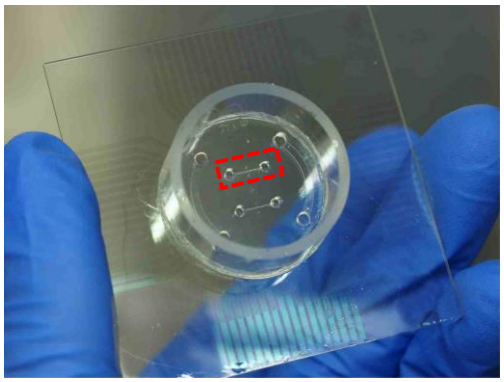
Application Brief

Detection of neural activity in cerebral organoids connected by axon bundles.



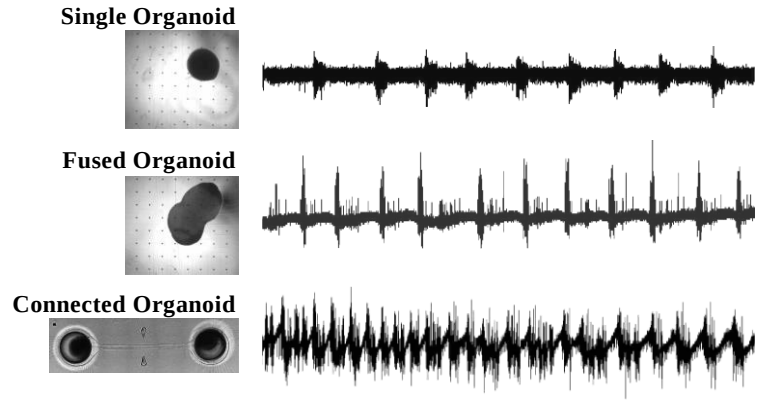
This microfluidic device was mounted on a MED probe with 16 electrodes (4 × 4 array) placed in four areas separated by a short distance. Cerebral organoids were cultured on each electrode area to promote mutual innervation through microfluidic channels, creating connected organoids. This organoid technology has successfully modeled signal transmission between physically distant brain regions.

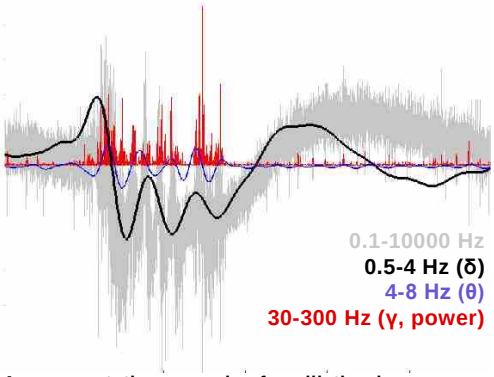
An expanded view of the red frame in the picture on the left. Cerebral organoids were cultured on the left and right electrode areas surrounded by PDMS microfluidic devices. Axonal bundles developed over six weeks to interconnect the cerebral organoids via the micro-channel.

The MEA dedicated to the MED64 system, "MED Probe," features 64 electrodes and their leads to the terminals arranged in the center of a glass substrate. A wide variety of products with different electrode layouts in the center, different electrode materials, with or without chamber rings, and custom production services with your preferred electrode arrangement is available to help with your unique research.

A pattern of 16 electrodes arranged in four areas. To enable surface processing, etc., you can purchase these without the chamber ring attached.

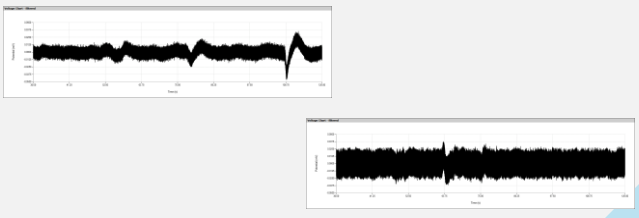
Connected organoids displayed more complex and vigorous neural activity than either single organoids or fused organoids with the same number of cells. These results show that signaling through axonal bundles, which functionally connect physically distant organoids, is important in forming activity patterns. In addition, a low-band activity component called oscillation, which is similar to the EEG of human premature infants, was observed in this activity at a relatively earlier stage (9 weeks) than in single organoids.





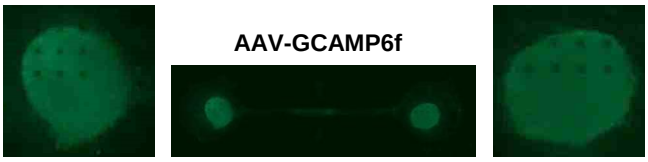
A representative example of oscillation in connected organoids at 9 weeks of culturing. The signals in each frequency band have been extracted from the raw waveform.

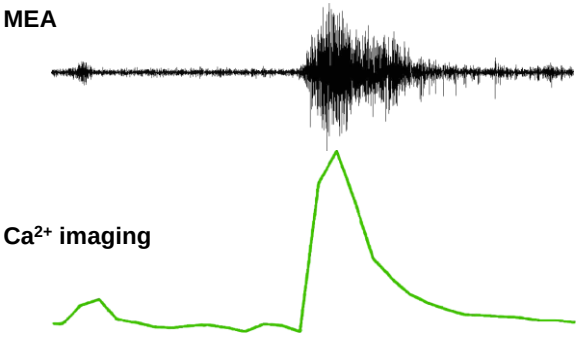
One of the MED64 system's key advantages is its ability to acquire clear, noiseless extracellular potentials due to the performance of its superior electrodes, which are playing the role of a sensor. The neural activity that a mature neural network generates includes not only the high-frequency band signal with spikes, but also the low-frequency band signal with local field potentials or oscillation. Acquiring this broad band of neural activity clearly is important in comprehensively understanding the information processing mechanisms. The MED64 system can capture signals in the low-frequency range, often blocked due to noise elimination, in a state closer to the original waveform without distortion.



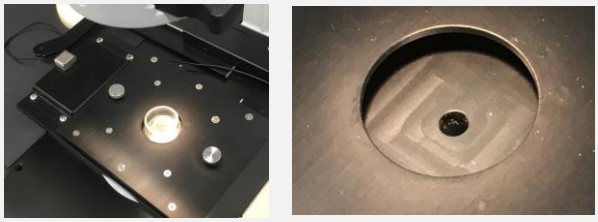
Comparison of unfiltered raw signal waveforms acquired with MED probe electrodes (left), and poorly performing electrodes (right) in the same MEA system. The MED probe features lower baseline noise and can accurately detect biological signals in the low-frequency band.

Simultaneous measurement of Ca^{2+} imaging and MEA. The Ca^{2+} transient (transient increase in intracellular Ca^{2+}) co-occurred the electrical burst activity acquired by MEA in a synchronized burst.



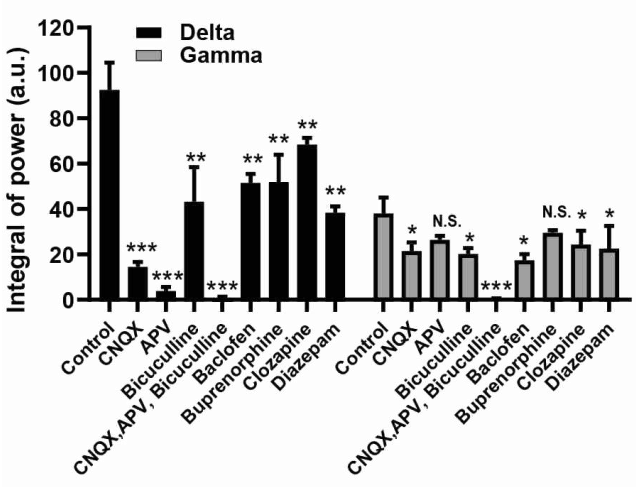


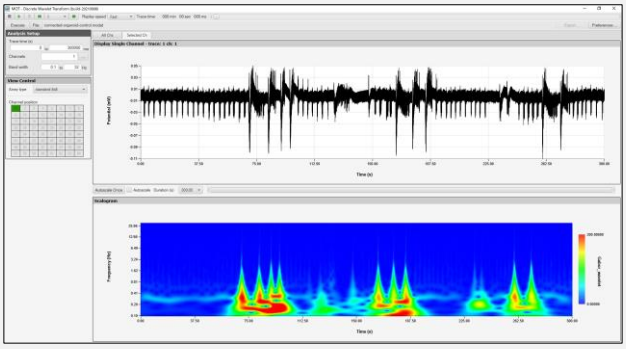
Confirming the positional relationship between each electrode and the sample requires observation under an inverted microscope. The glass substrate and the MED probe's indium tin oxide (ITO) lead make this possible. In addition, the headstage for installing the MED probe is independent of the amplifier itself and can be connected via a 2-m cable, making it easy to mount on a microscope stage and simultaneously acquire data by MEA and functional imaging.



MED connector on the microscope. On the base plate, there is a small hole for inverted observation in the area where the electrodes area of the MED probe is placed.

Neural activities of connected organoid were quantitatively evaluated by the number of spike detections, frequency of synchronized bursts, and power in the delta (0.5-4 Hz) and gamma (30-300 Hz) bands by wavelet transform etc. These indices were consistently affected by various ligand treatments for glutamate and GABA receptors, indicating the possibility of using connected organoids for drug evaluation.





A wavelet transform using MED64 Offline Toolkit. Figure reproduced from the original paper.

In addition to the "Mobius" operation software, programs specialized for offline detailed data analysis are available for the MED64 system. We keep updating programs to improve the system's usability and the functionality, and can also customize it to meet your needs depending the situation (consultation required).

The data in this document was provided by Dr. Yoshiho Ikeuchi and Dr. Tatsuya Osaki of the Institute of Industrial Science, University of Tokyo. The complete contents are available on bioRxiv (https://www.biorxiv.org/content/10.1101/2021.02.16.431387v2). They applied microfluid technology and various analysis methods to their study using MEA in unprecedented ways, and the quoted data here is excerpted to explain features of the MED64 system.

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