Impedance Measurements and Electrophysiological Recordings of Mouse Retinae on a Multifunctional HD-MEA Platform

Author(s):
Ulusan, Hasan; Diggelmann, Roland; Magnan, Chloé; Znidaric, Matej; Viswam, Vijay; Franke, Felix; Hierlemann, Andreas

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Impedance Measurements and Electrophysiological Recordings of Mouse Retinae on a Multifunctional HD-MEA Platform

Hasan Ulusan[a], Roland Diggelmann[a], Chloe Magnan[a], Matej Znidaric[a], Vijay Viswam[a,b], Felix Franke[a,c], and Andreas Hierlemann[a]

[a]ETH Zürich, Department of Biosystems Science and Engineering, Switzerland
[b]MaxWell Biosystems, Switzerland
[c]Institute of Molecular and Clinical Ophthalmology Basel, Switzerland

hasan.ulusan@bsse.ethz.ch

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Impedance measurements on high-density microelectrode arrays (HD-MEAs) can be used to study the morphology of neuronal cells and to image biological tissue, such as the retina. Impedance imaging is a non-invasive method to visualize the position and attachment of the retina on the HD-MEA and can be used in conjunction with electrophysiological recordings of live tissue. It allows for studying the correlation between tissue-to-electrode adhesion, tissue properties and the measured spiking activity of retinal ganglion cells on the HD-MEA.

Material and Methods

The multi-functional HD-MEA chip, developed by our group, features 59,760 electrodes at a pitch of 13.5µm [1]. The electrodes can be arbitrarily connected to several different functional units on-chip, including 2048 units for voltage recordings, 32 units for impedance measurements, 28 units for neurotransmitter detection and 16 units for extracellular voltage- or current stimulation (Figure 1A). We used a dedicated experimental setup (Figure 1B) to project light stimuli onto the photoreceptor layer of mouse retinae while simultaneously recording ganglion-cell activity. Impedance imaging was performed by applying a sinusoidal voltage signal of 50 kHz and 0.1 V_{peak} to the reference electrode and measuring the magnitude and phase shifts of the resultant currents at the individual electrodes. We built an impedance image using 32,000 randomly distributed electrodes on the array by scanning through 1000 different electrode configurations; the image was then completed with spatial interpolation.

Results

Figures 2A-D show the electrophysiological voltage recordings obtained from a high-density recording area, which contained 2025 electrodes arranged in a square of 600µm x 600µm. We extracted the single-cell activity of individual retinal ganglion cells (RGCs) through automatic spike-sorting [2]. Light responses of the RGCs were evoked with a chirp light stimulus. We assessed the tissue location and attachment to the HD-MEA by optical microscopy (Figure 2E) and impedance imaging (Figure 2F) . The retinal tissue caused changes in the impedance magnitude on the electrodes over which it extended; better attachment of the tissue led to higher impedance magnitudes. The impedance image shows that the edges of the retina piece were pressed more strongly onto the array, which led to more electrical activity in these regions as could be seen in the spiking activity (Figure 2G). Moreover, the optic disc of the retina could be identified with both, light and impedance imaging.

Discussion and Conclusion

The orientation and location of the retinal tissue on the HD-MEA chip could be visualized through impedance imaging and could be used to guide electrophysiological recordings. Moreover, smaller structures, like the optical disc of retina, could be identified with light- and impedance imaging. With further improvements of the HD-MEA platform, we will be able to perform impedance imaging of full HD-MEA within less than 30 min and to also measure impedance values at different frequencies to perform impedance spectroscopy of the cells. We then expect to see additional retinal features, such as blood vessels, and to accurately locate those on the chip.

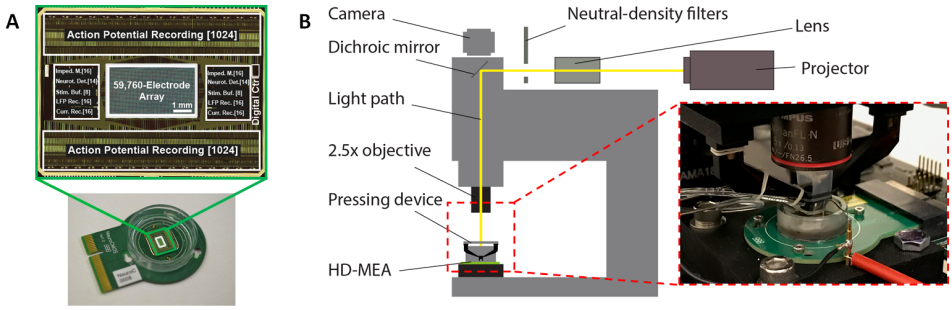

Figure 1: (A) Multi-functional HD-MEA chip micrograph. (B) Experimental setup to apply light stimuli to retina.

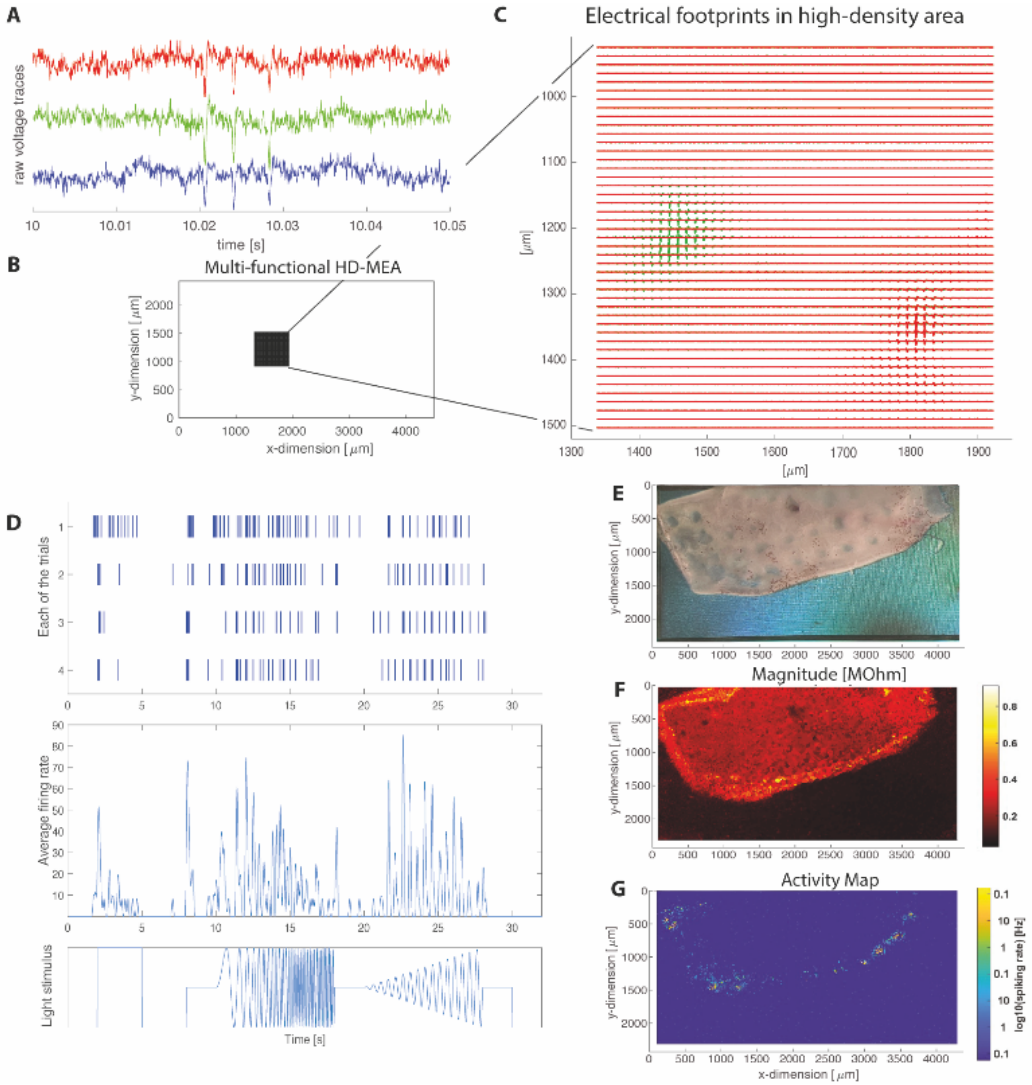

Figure 2: (A) Voltage traces on three example electrodes showing spikes of an RGC. (B) Schematic of the multi-functional HD-MEA depicting the 45x45-electrode high-density recording area. (C) Electrical footprints of two RGCs located in the high-density recording area in (B). (D) Spiking activity of 4 trials of a light stimulus of a single light sensitive neuron where the light stimulus contains a full-contrast flash, a frequency and a contrast modulation chirp. (E) Microscopy image of the mouse retina on the NeuroCMOS HD-MEA chip. (F) Difference in impedance magnitude values measured by the electrodes. (G) Activity map of the RGC neurons.

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