MICROELECTRODE ARRAY–BASED PLATFORM TO STUDY NEURAL RESPONSES EVOKED BY FOCUSED ULTRASOUND IN *EX VIVO* MOUSE BRAIN MODEL

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Background, Motivation and Objective

The objective of this project was to combine a Focused Ultrasound (FUS) system and a MicroElectrode Array (MEA) System to study the activities and the underlying electrophysiological mechanisms involved in neurostimulation by FUS in an *ex vivo* mouse brain model.

Statement of Contribution/Methods

A mixed FUS/MEA platform was developed for spatial-temporal recording of neural responses induced by FUS exposures in *ex-vivo* hippocampal brain slices from a mouse model. Hippocampal slices were maintained functional by being placed in a MEA chip and perfused with artificial cerebrospinal fluid. The FUS system consisted of a 1.78-MHz transducer ($Ø$: 15 mm, R_c: 15 mm). Low-energy FUS (1.1 MPa, 284 − 6200 cycles) was applied before and after perfusion with sodium channel blocker TTX to confirm the nature of the recorded signals.

Results/Discussion

MEA recordings repeatedly exhibited a characteristic signal composed of a fast negative deflection associated to FUS-induced artifacts followed by one (or multiple) slow deflections occurring several milliseconds after the end of the US-induced artifact and attributed to neural responses. Parametric studies showed that US-evoked neural response magnitudes increased 6-fold (amplitude: 20 − 130 µV, duration: 1.6 − 5.5 ms) when increasing the number of FUS cycles (800 to 6200). After adding TTX, the magnitude of the responses progressively decreased, by 86% after 12 min, confirming the effective blocking of the sodium-dependent neural responses. Multiple electrodes in the MEA matrix exhibited responses of this nature as we believe that they all fell within the focal area of the FUS transducer (focal spot *Ø ≈ 15 mm @ -3dB*). This project was supported by the French National Research Agency (ANR-16-TERC-0017), LabEx DevWeCan, and the Focused Ultrasound Foundation.

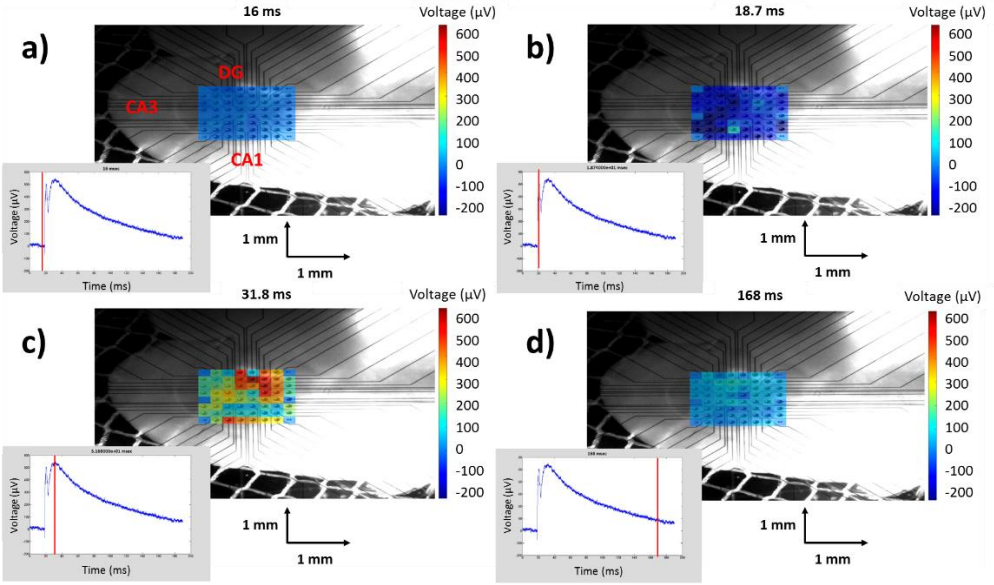

Figure 1 – Voltage amplitude of recorded FUS-evoked signals for all 60 electrodes within the MEA chip at four different time points a) 16.0 ms (before FUS stimulation), b) 18.7 ms (FUS artifact – negative deflection), c) 31.9 ms (Positive deflection attributed to a neural response) and d) 168 ms (slow return to baseline), along with a characteristic electrical signal recorded in electrode 63 of the matrix (time point of the subfigure represented by vertical red line in 2D plot). The slice was placed towards the CA1 or Dentate Gyrus (DG) regions of the hippocampal slice.