A Miniaturized Transcranial Focused Ultrasound Device for Neuromodulation Research

From Cellular Mechanisms to Proof-of-Concept Applications

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INTRODUCTION

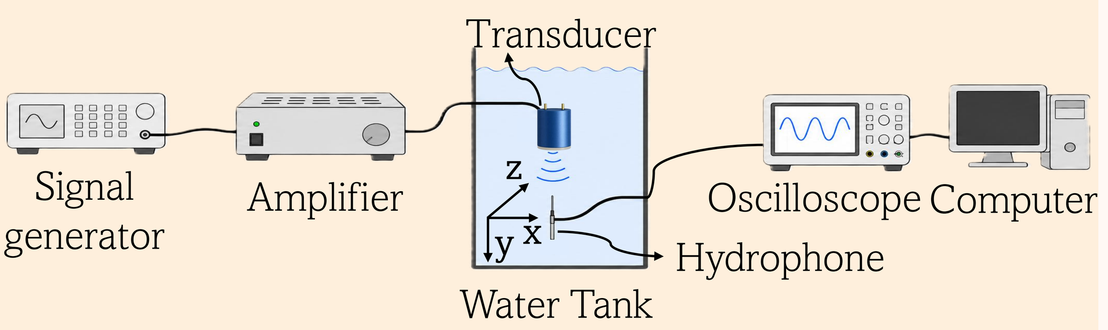
Transcranial focused ultrasound stimulation (tFUS) is an emerging non-invasive neuromodulation technology. In contrast to other non-invasive methods, it can stimulate both cortical and deeper brain structures with unprecedented spatial precision. However, the mechanism underlying its neuromodulatory effects is yet to be understood. In this study, we used a miniaturized ultrasound device to investigate tFUS in both *in vitro* and *in vivo* experimental settings. This poster presents the characterization of the ultrasound transducer, *in vitro* results supported by modelling, and preliminary evoked-potential recordings from small-animal experiments.

CONCLUSIONS

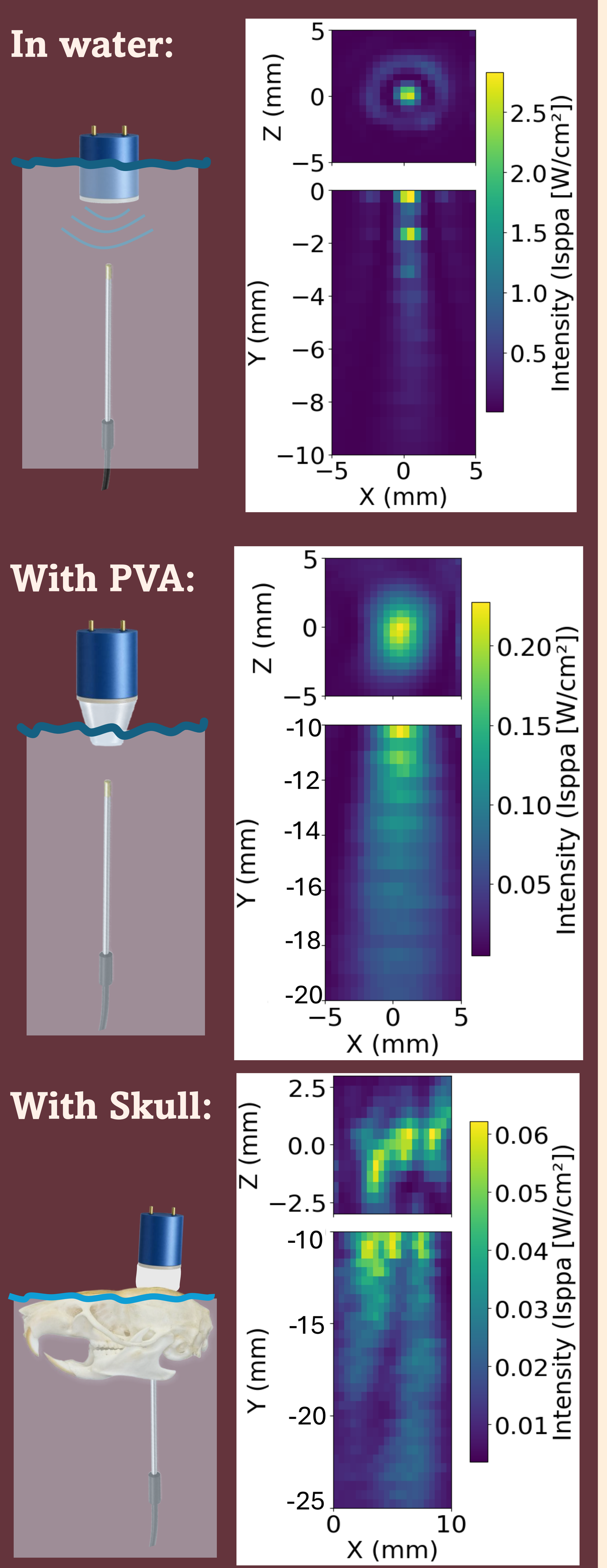
1. A miniature, **custom-made tranducer was manufactured and characterized** by modeling and hydrophone measurements.
2. *In vitro* **ultrasound stimulation induced long-term cellular effects**, including depolarization of their resting membrane potential and increased baseline membrane-potential noise.
3. In the model fitted to the *in vitro* data, **membrane capacitance decreased**, while the **leak-current reversal potential increased**.
4. *In vivo* **transcranial ultrasound stimulation evoked motor responses**, although these were highly variable.
5. *In vivo* **transcranial ultrasound stimulation evoked electrical potentials**, which were robust through multiple subjects

The Device

Sound is a pressure wave produced when an object oscillates at a given frequency. Ultrasound (US) refers to sound waves with frequency above 20 kHz. We studied the intensity profile of our US transducer by modeling and measurements with a hydrophone.

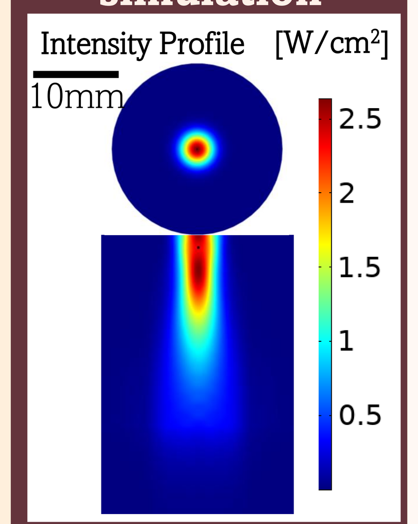


Measurements

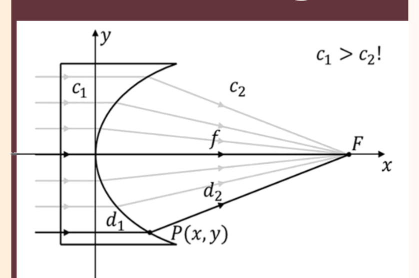


Modeling

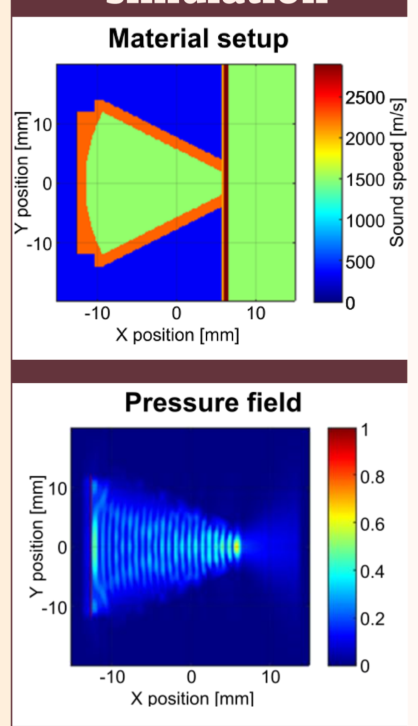
COMSOL simulation



Lens Design



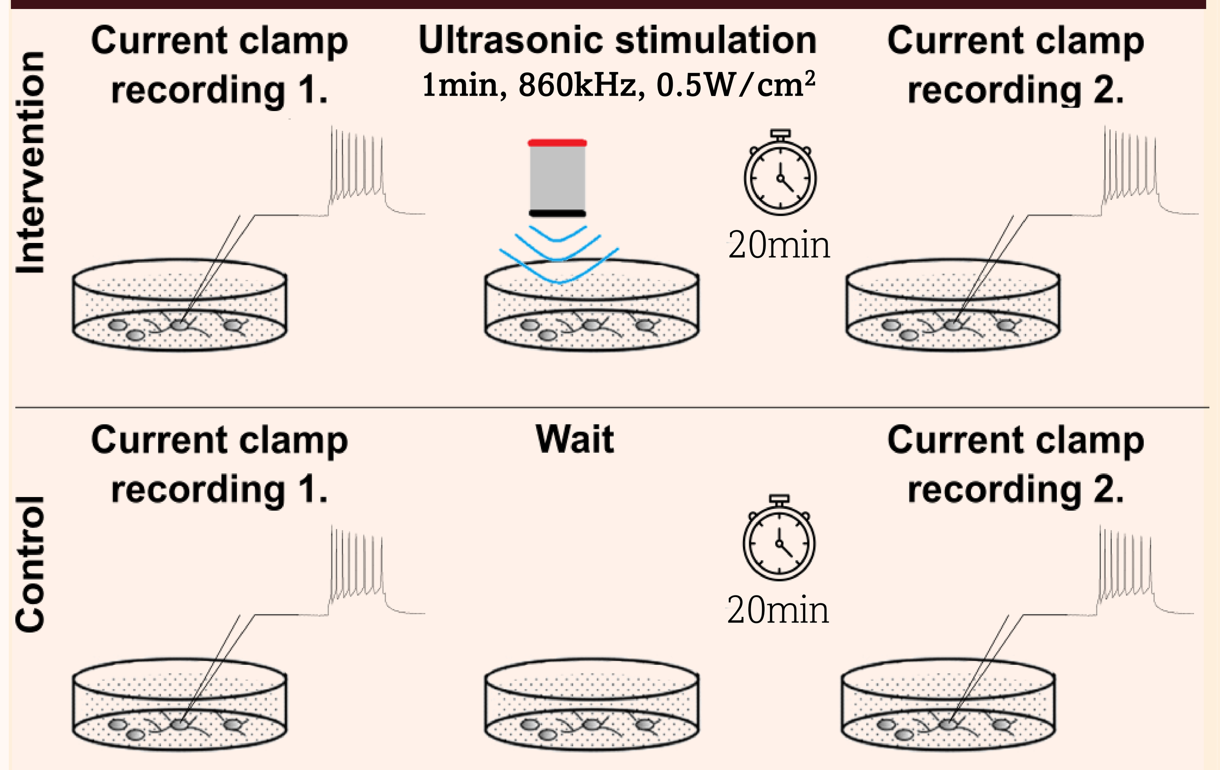
K-Wave simulation



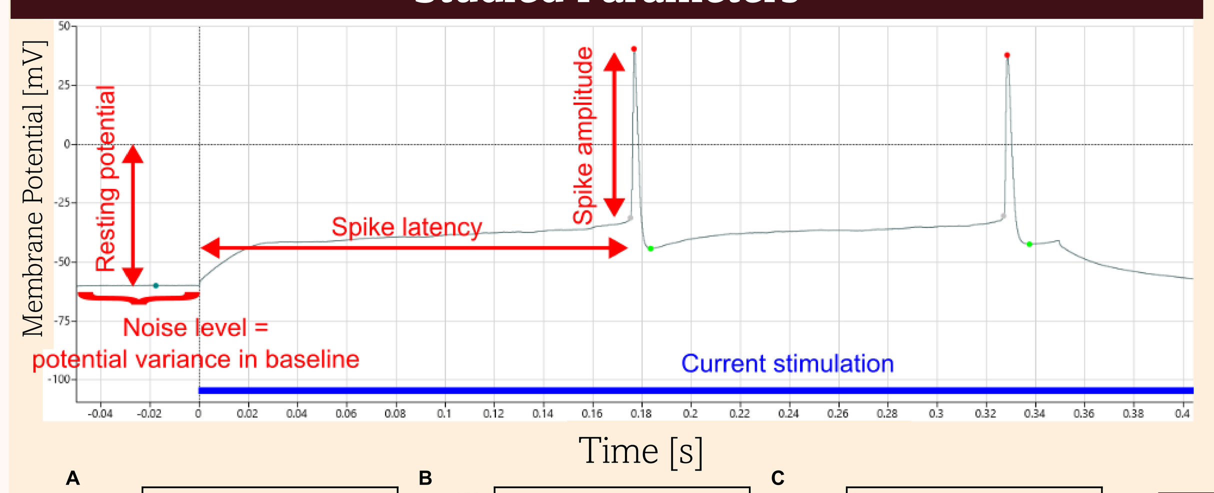
In Vitro Experiments for Long-Term Effects

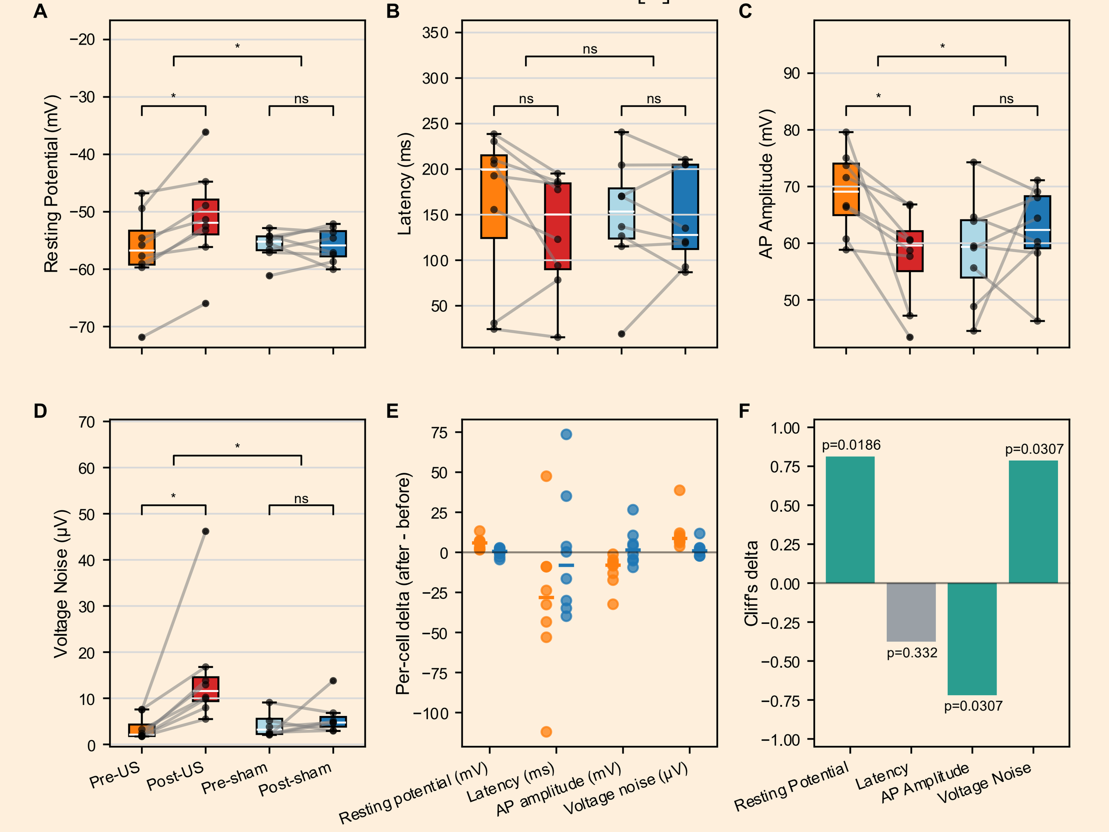
We investigated the long-term (~20mins) cellular effects of ultrasound stimulation. Hippocampal cell cultures were studied by whole-cell current-clamp recordings, before ultrasound stimulation and after. The control group did not received stimulation, but was measured twice with a similar time gap.

Experimental Design



Studied Parameters

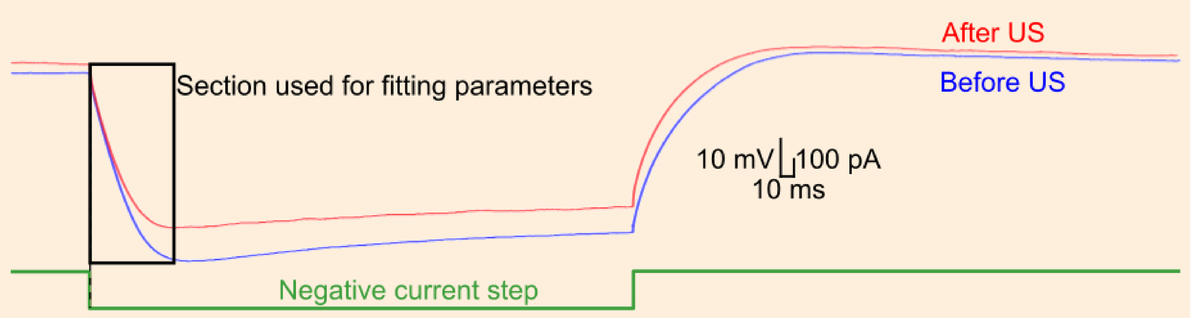


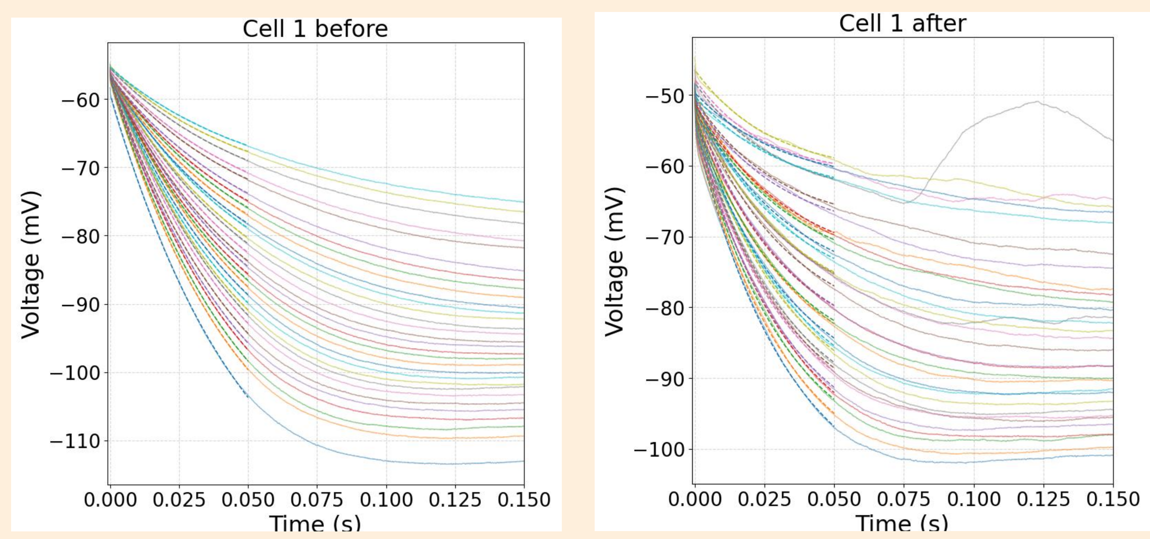


RESULTS

We fitted exponential functions to the membrane potential during the beginning of the current steps. This was done before the stimulation and after the stimulation for both, the active and the control group. The results indicate that the membrane capacitance could be the reason behind the experimentally observed changes.

Fitting exponentials

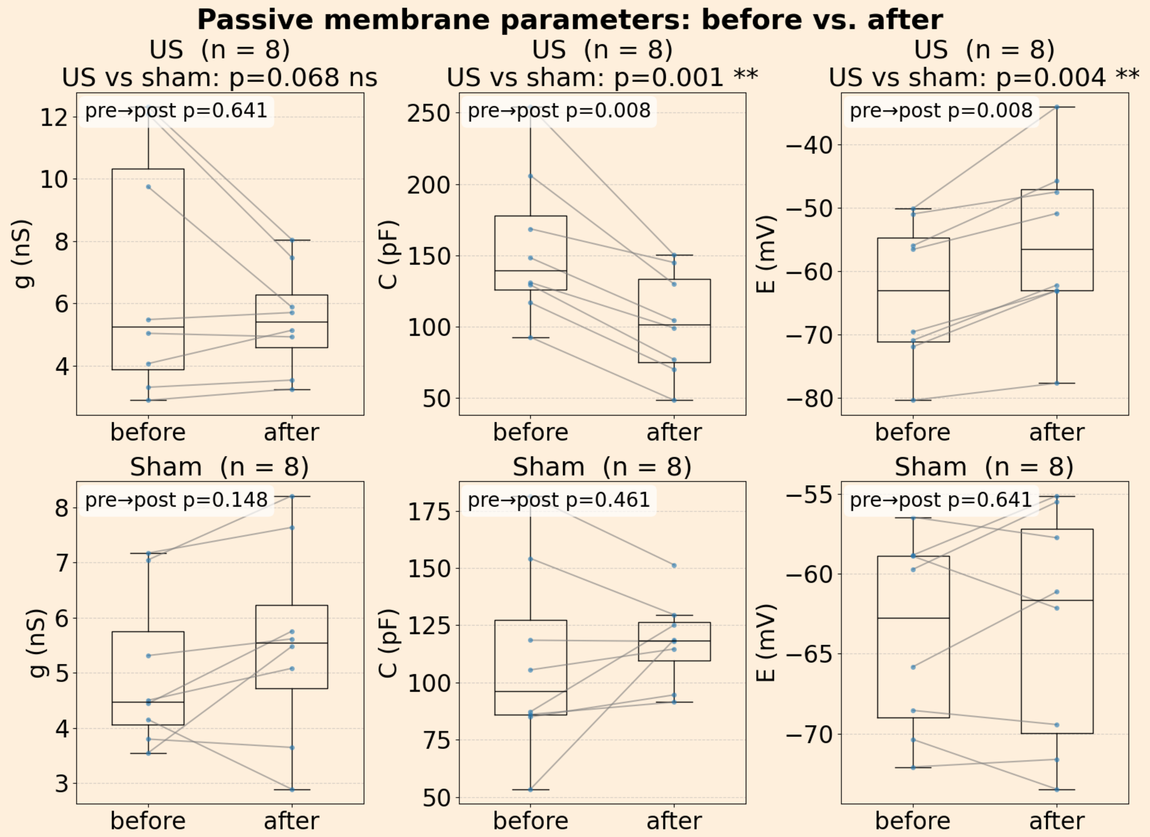




Dynamics: $C \cdot \frac{dV}{dt} = -g_l \cdot (V - E_l) + I$ Excluding Na^+ and K^+ currents

Solution: $V(t) = V_{inf}(I) + (V_0 - V_{inf}(I)) \cdot e^{\frac{-t}{\tau}}$,

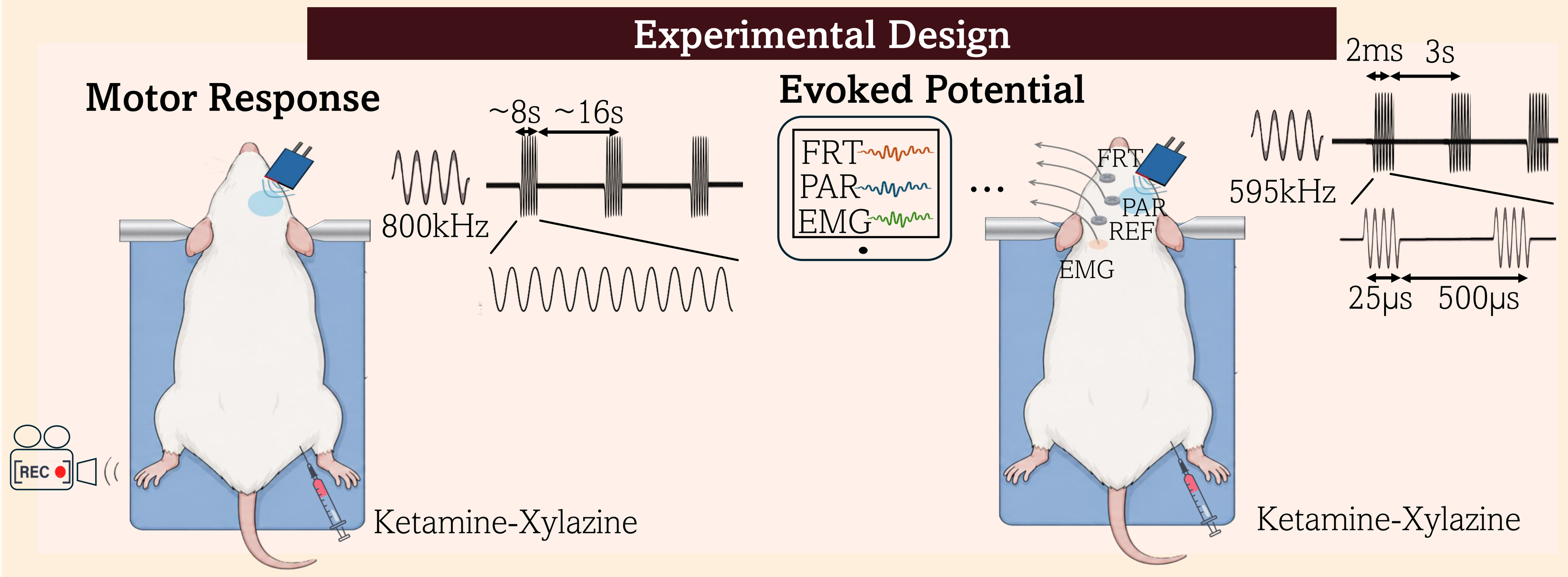
where $V_{inf}(I) = E + \frac{I}{g}$ and $\tau = \frac{C}{g}$ *Free parameters during fitting*



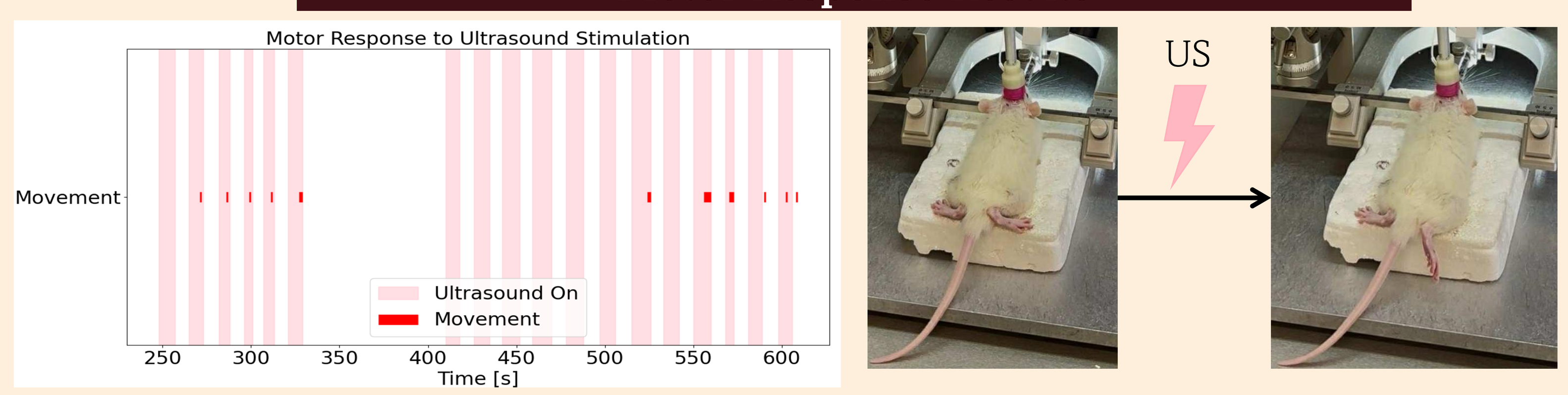
In Vivo Experiments

To validate the device, we carried out simple in vivo experiments. First, we attempted to elicit motor responses by stimulating the motor cortex of anesthetized rats, but the results proved to be highly variable. Therefore, we instead measured ultrasound-evoked potentials using EEG above the frontal and parietal cortex, while also recording EMG activity from the neck muscle.

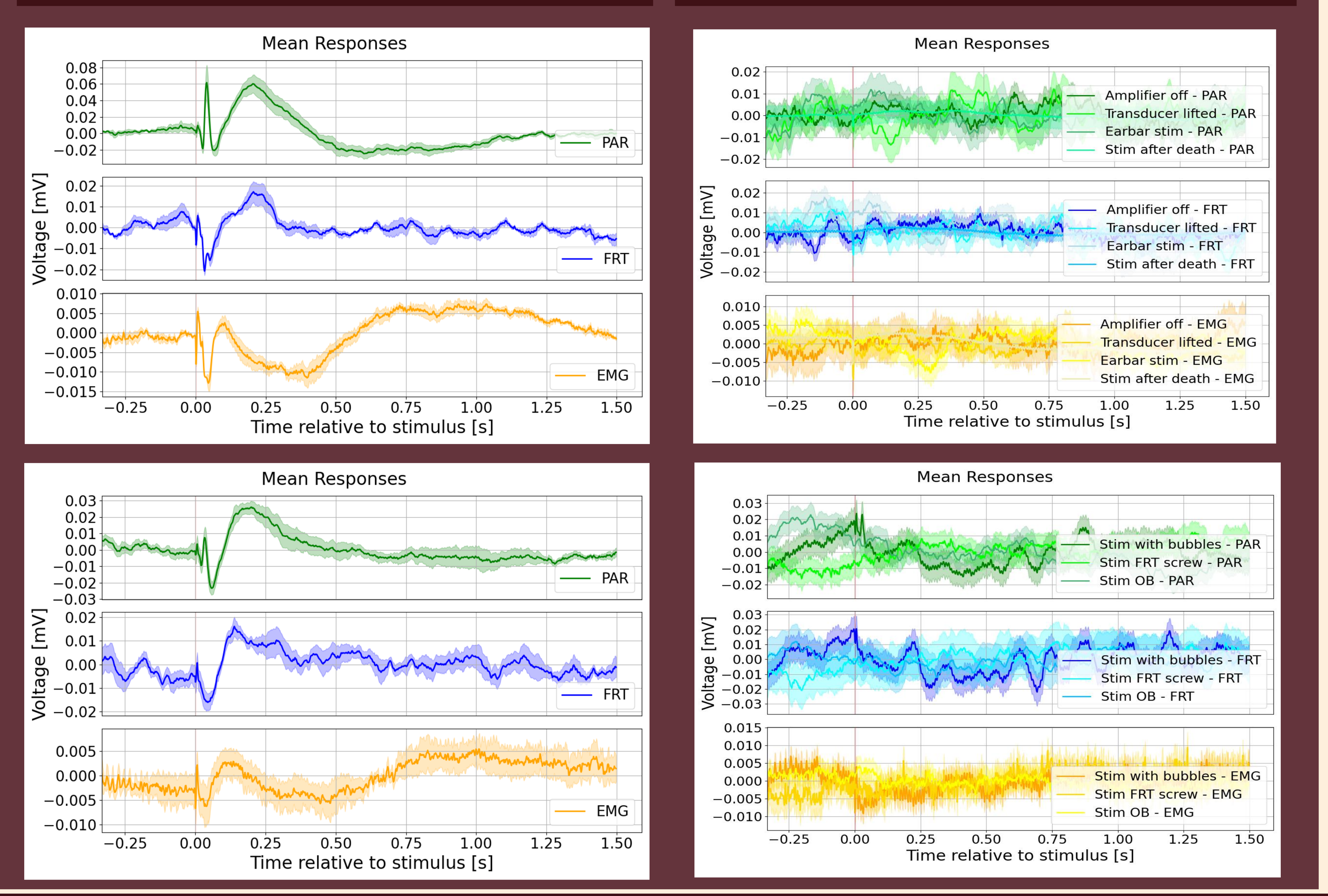
Experimental Design



Motor Response Results



Ultrasound Evoked Potentials Results



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