

# Interaction of electrical and ultrasonic neuromodulation

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## Objective

To explore the interaction of ultrasonic and electrical neuromodulation in the Neuronal Intramembrane Cavitation Excitation (NICE) computational model.

## Introduction

**Transcranial focused ultrasound** (tFUS) has gained attention as a technique to modulate neuronal activity reversibly, non-invasively and with high spatial accuracy.

Combining tFUS with existing electrical neurostimulation modalities (tDCS, TMS, DBS...) might help to unravel the underlying biophysical and physiological mechanisms of ultrasonic neuromodulation. E.g., in a recent study of Legon et al. (2018) tFUS is paired with TMS, allowing to assess the effect of ultrasound on TMS metrics (MEP, SIC1, ICF...) [1]. In this computational study, we investigate the interaction of ultrasonic and electrical neuromodulation in the neuronal intramembrane cavitation excitation model (NICE; [2, 3]).

## Methods

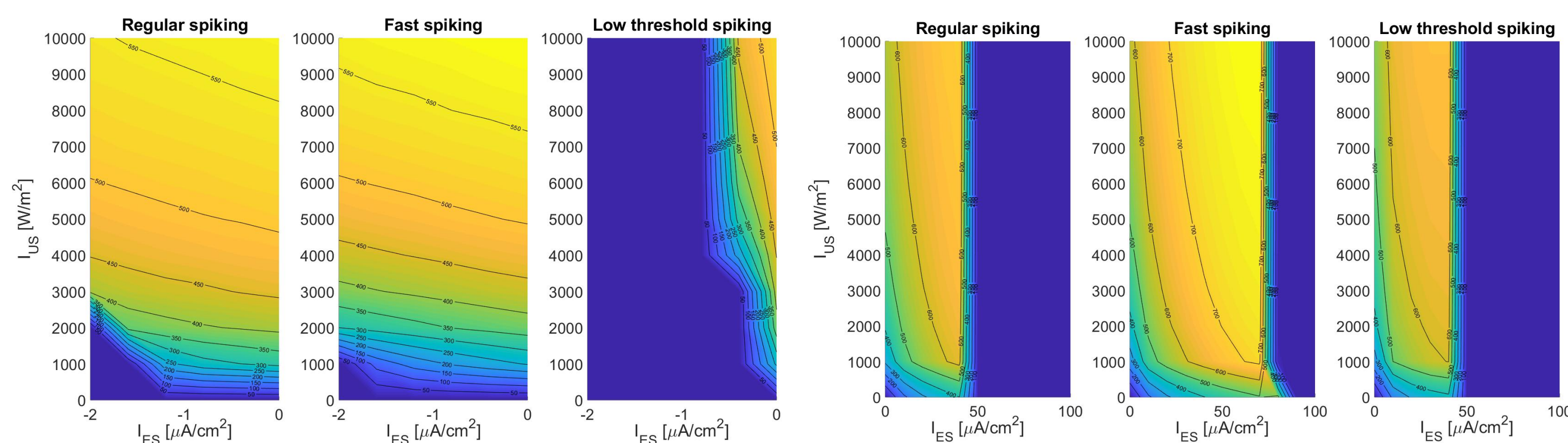


Figure 1: Contour-plot of firing rates for combined electrical and ultrasonic stimulation.

Investigation of interaction of continuous-wave and pulsed, electrical and ultrasonic waveforms.

1. Ultrasound-neuron coupling: bilayer sonophore model (Krasovitski)
2. Neuron models: cortical Pospischil-models (RS, FS, LTS) and subthalamic nucleus Otsuka-model (STN)

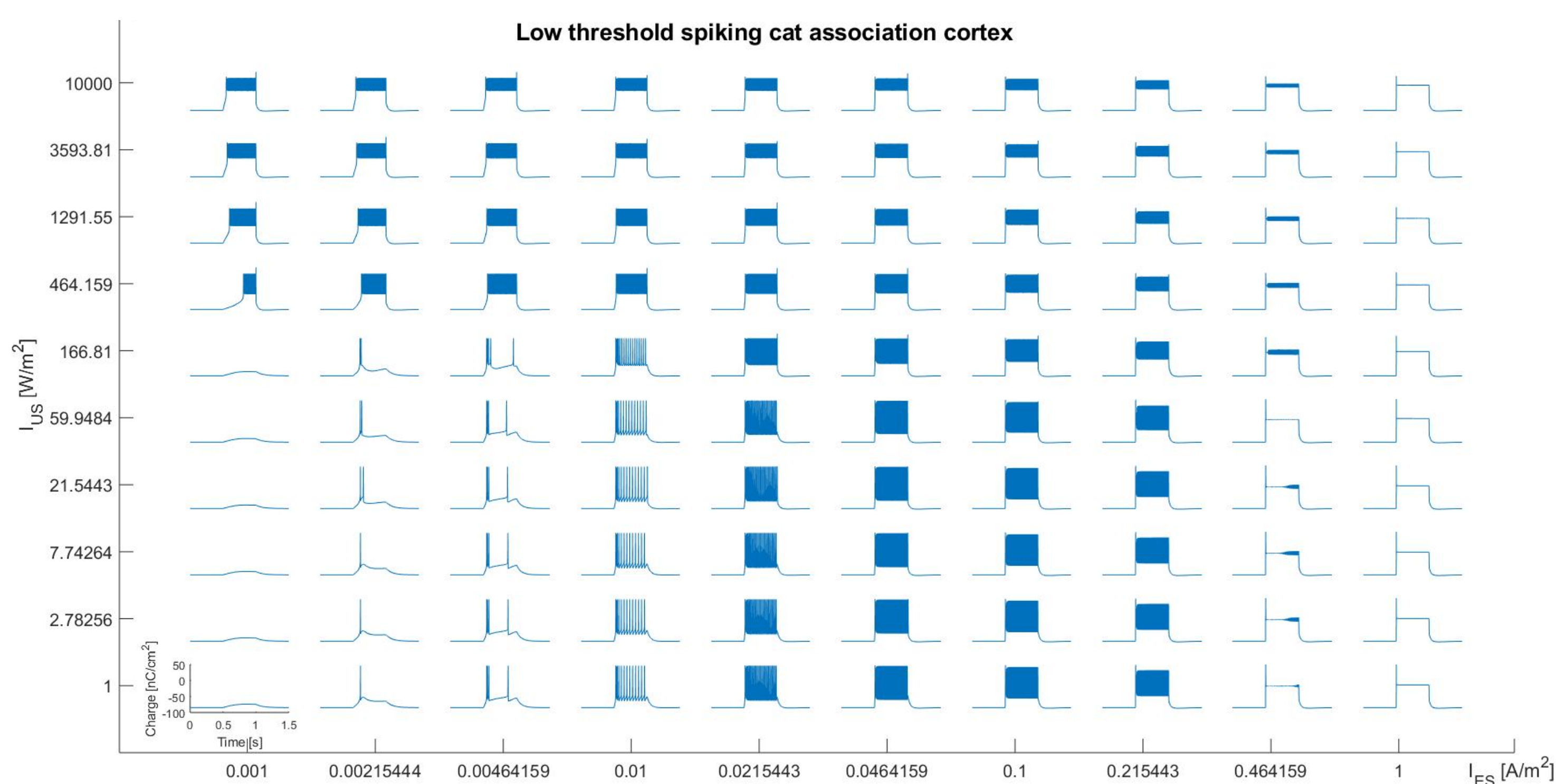


Figure 2: Firing rate in low-threshold spiking model for combined ultrasonic and electrical stimulation

## Results

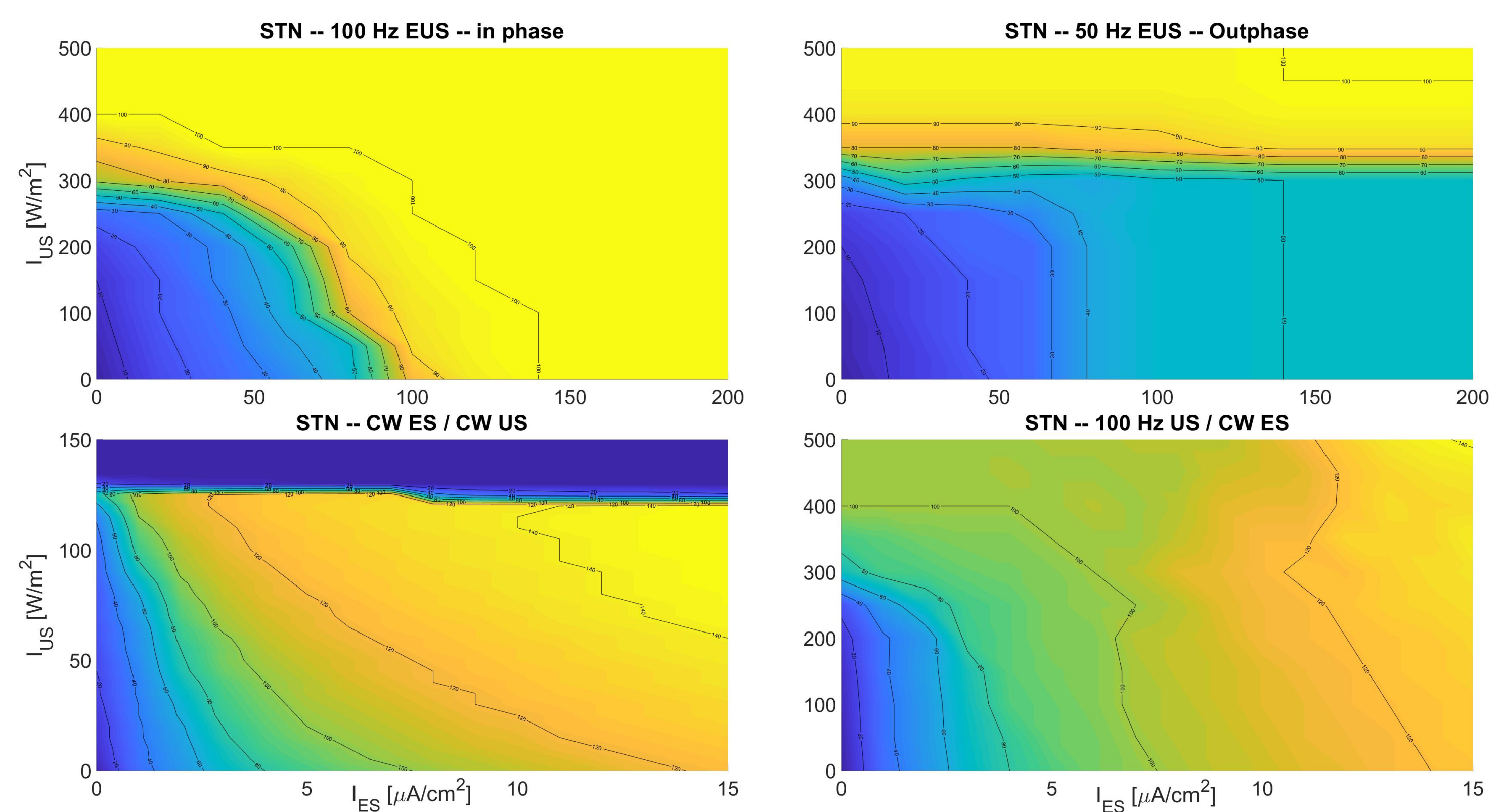


Figure 3: Contour FR-plots for combined US/ES stimulation in the Otsuka-model

Potential of combined ultrasonic and electrical neurostimulation:

- **Lower intensity thresholds**
  - Simultaneous application of subthreshold electrical current and subthreshold ultrasonic intensity capable of eliciting spikes
  - Interaction of ultrasound and electrical current: higher firing rates at lower intensity
- *Expected significance:* improved safety and therapeutic effect
- **Increased cell-type selectivity**
  - Reversed order of excitation by combining negative (hyperpolarizing) current and ultrasound
- **Increased spatial accuracy**

## Conclusion

The interaction of simultaneously applied electrical and ultrasonic waveforms in the NICE-model is investigated. Our results indicate that combining both stimulation modalities might improve safety (lower threshold intensities per modality), spatial accuracy and selectivity (manipulation of the order of excitability).

As future work, we intend to investigate the effects of simultaneous application of ultrasound and electrical neuromodulation on computational network models and spatially-extended (multi-compartmental) neurons.

## References

- [1] W. Legon, P. Bansal, R. Tyshynsky, L. Ai, and J. K. Mueller, "Transcranial focused ultrasound neuromodulation of the human primary motor cortex," *bioRxiv*, 2018.
- [2] M. Plaksin, S. Shoham, and E. Kimmel, "Intramembrane cavitation as a predictive bio-piezoelectric mechanism for ultrasonic brain stimulation," *Physical review X*, vol. 4, no. 1, p. 011004, 2014.
- [3] M. Plaksin, E. Kimmel, and S. Shoham, "Cell-type-selective effects of intramembrane cavitation as a unifying theoretical framework for ultrasonic neuromodulation," *eNeuro*, pp. ENEURO-0136, 2016.