Ultrasonic Stimulation of Neurons

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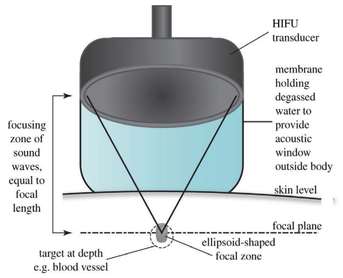
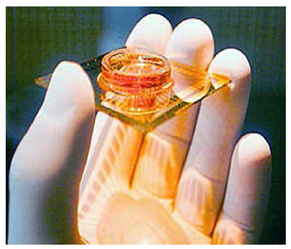
Introduction

- **Neurostimulation** uses external stimuli such as electrical signals delivered using electrodes or light pulses
- **Problem:** Current light methods are not conducive for in vivo translation
- **Solution:** Stimulate neurons acoustically
- **Idea:** Noninvasive ultrasound stimulation on a particular region of the brain
- **Image:** The bottom image displays the manner in which the ultrasound transducer is focused to achieve optimal imaging results



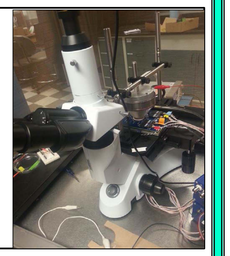
Materials

- Custom Sonic Concepts High Intensity Focused Ultrasound (HIFU) transducer
  - 1.1 MHz center frequency
  - 51.74 mm focal depth
- 64-channel micro-electrode array (MEA)
- Broad bandwidth transducer
  - 1-20 MHz bandwidth
- Mice cortical neurons



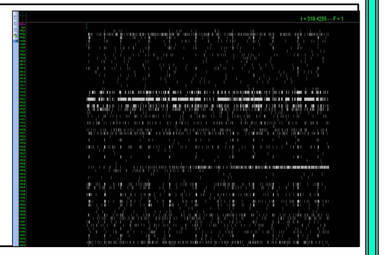
Methods

SETTINGS:
- HIFU settings included a frequency of 3.3 MHz at a 0.04% duty cycle
- Broadband settings of 100mV at 2 or 5 kHz repetition rates were used
- An image of the setup can be seen in the attached image
  - This includes the HIFU transducer and MEA

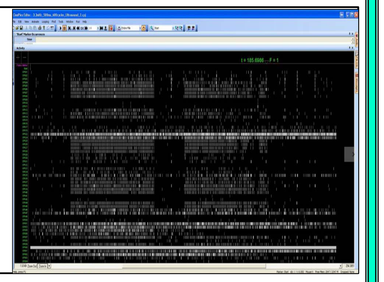


ALIGN TRANSDUCER
- Mice cortical neurons were placed on the MEA and the transducer was moved such that the cells were in the focal range of the transducer
- The image shows the transducer being focused on the dish below it prior to neural stimulation

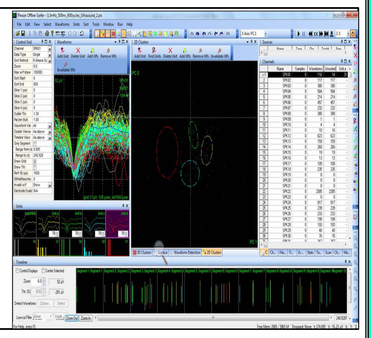
BASELINE
- Baseline recordings acquired with a dish containing only saline (no cells)
- A sample baseline recording can be seen to the right
  - Consistency and patterns should be noted
- White lines are indicative of neuronal activity where each mark is specific to one of the 64 channels



RECORDING OF DATA
- The signal was recorded from cell cultures in media
- Two minutes of sonication was recorded followed by one minute of transducer inactivity
- The image represents a segment of data in which the transducer was alternating between the on and off settings
  - Darker areas indicate the inactive periods

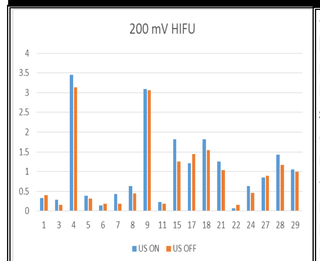


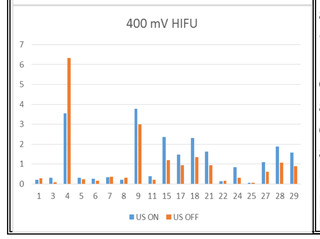
ANALYSIS
- Offline peak sorter was used for separation of noise from neuronal activity
  - A representation of this program is shown
  - This allows visualization of spike and noise trains, as well as activity in each channel per unit time
- "Spike trains" were analyzed for possible neuronal activity in Matlab
  - Spike trains are any activity segments that are not caused by noise



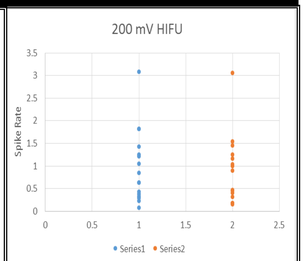
Results

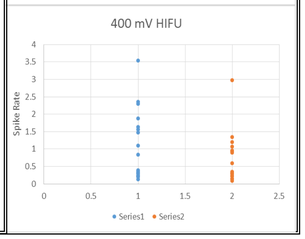
HIFU Results



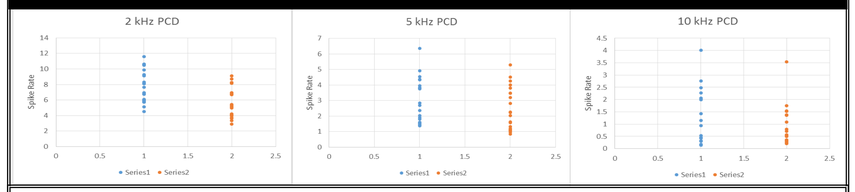


- The bar graphs to the left represent the spike rates over time during both periods of ultrasonic sonication and inactivity (separated by channel number)
- The scatter plots to the right are indicative of results found as spike rates versus transducer activity
- Results seemed to indicate that the 3.3 MHz excitation did not induce a statistically significant change in neuronal activity as quantified using rate of action-potential spikes detected by the MEA

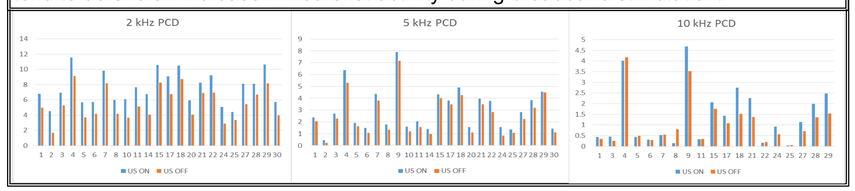




Broadband Results



Correlation may be noted between the broadband stimulation and neuronal activity. Transducer activity points to greater neuronal activity as compared to activity during ultrasound absence. The bar graphs below once again show spike rate over time by channel. The above scatter plots represent this data once again as spike rates during transducer activity and inactivity time periods, respectively. Both representations of data tend to defend an increase in neuronal activity during broadband stimulation.



Conclusions

- **Result:** Ultrasound stimulation could prove to be a promising method for neurostimulation
  - **Significance:** This method is much less invasive than current practices
- **Result:** Broadband ultrasound produced an observable increase in neuronal activity
  - **Significance:** Unable to be applied for trans-cranial neurostimulation as the ultrasound penetration is limited at high frequencies
- **Future Study:** Attempt to achieve the same results as produced by the broadband transducer with a HIFU transducer in the low MHz range.