Focused Ultrasound for Neuromodulation of Crayfish

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Introduction

1. Neuromodulation is the alteration of nerve activity through targeted delivery of a stimulus to specific neurological sites in the body.
2. Neuromodulation can have multiple therapeutic effects including: pain relief, suppressing epileptic seizures and symptoms of psychiatric disorders, and verifying targets in the brain prior to ablative surgery [1].
3. Focused Ultrasound (FUS) has been used for neuromodulation and has shown promising results.
4. This project has two main goals: 1) to gain a better understanding of FUS for neuromodulation through the literature, and 2) gain skill in the crayfish dissection protocol and understand and develop the testbed.

Background – Action Potentials

1. Stimulus initiates release of neurotransmitters.
2. Binding of neurotransmitters causes Na/K movement through voltage gated ion channels to initiate action potential.
3. Action potential travels along axon to presynaptic terminal to release neurotransmitters [6].

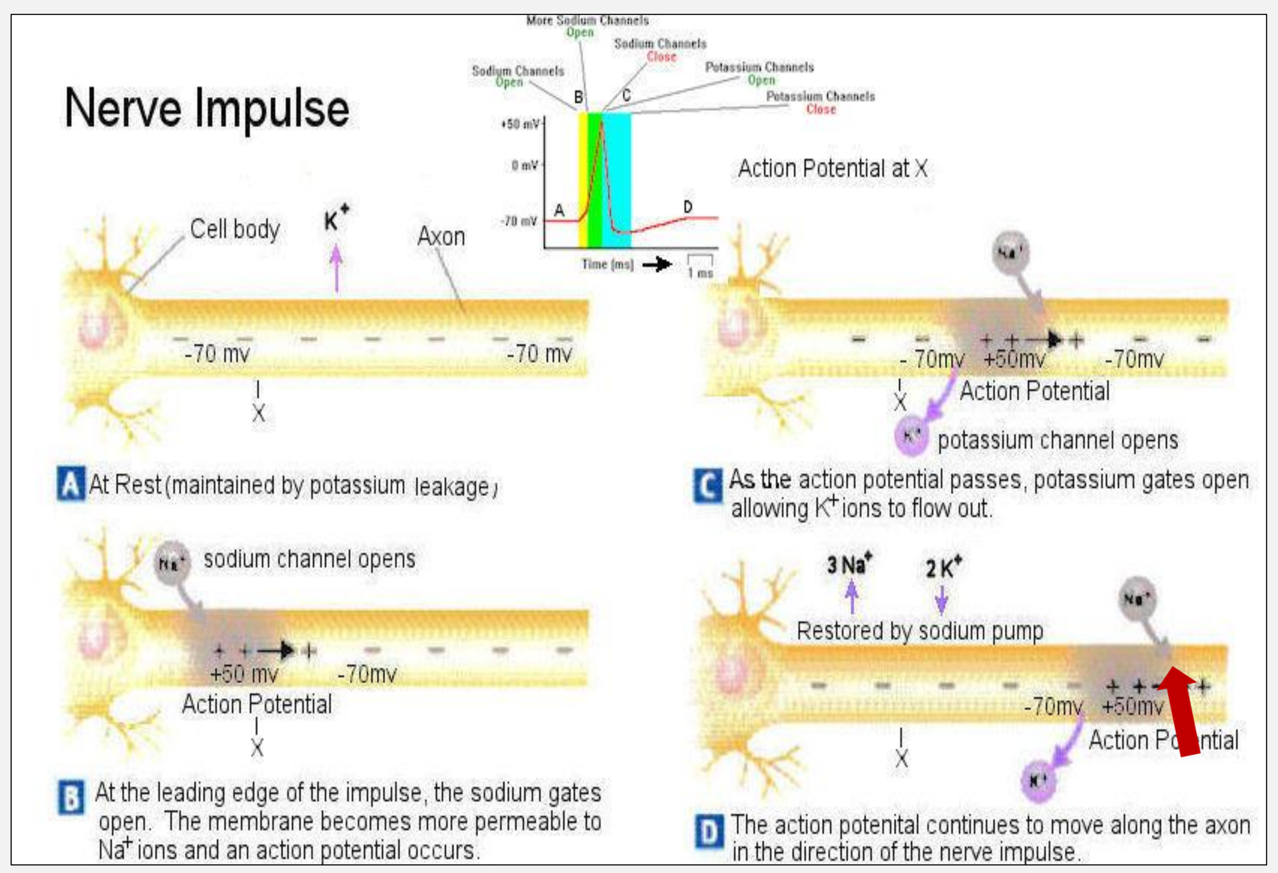

Fig. 1: Action potential process [9].

- **Existing Neuromodulation Methods**

1. Existing methods are invasive and lack target specificity.
2. Examples: pharmacological and chemical methods, optogenetic-based methods, electrical methods, magnetic and current stimulation, deep brain stimulation, vagus nerve stimulation, and subdural and epidural cortical stimulation [2,3,4].

Background - Ultrasound

- **Focused Ultrasound (FUS)**

1. FUS is non-invasive and has good spatial resolution.
2. Focused ultrasound is the delivery of sound energy greater than 20kHz through an acoustic lens that focuses the ultrasound to one point [5].
3. Typical FUS parameters: Frequency = 0.25 MHz – 1.0 MHz, Acoustic Intensity = 0.1 – 12.6 W/cm^2, Pulse Repetition Frequency = 0.1 – 3.0 kHz, Duty Cycle = 0.1 - 3.0 % [2,3,4,7].

- **Previous Work**

1. One study found that transcranial FUS stimulated neuronal activity to evoke motor behaviors in mice [3].
2. Another study found that FUS stimulated paw movement in rabbits [2].
3. Another study found that transcranial FUS suppressed epileptic signal bursts in rats [7].

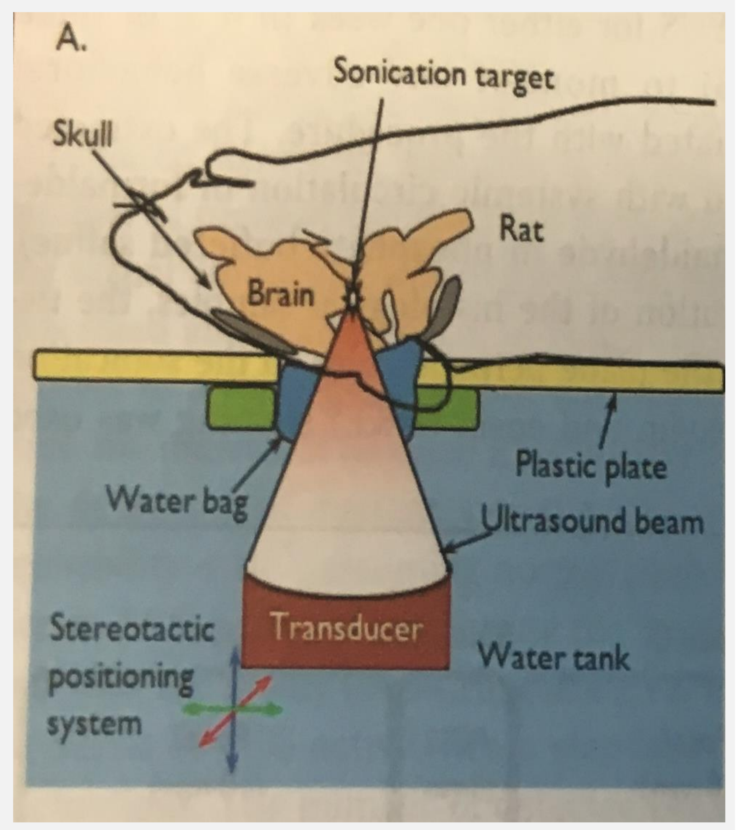

Fig. 1: FUS transducer with lens setup [4].

FUS Neuromodulation Theories

1. One study proposed the continuum mechanics hypothesis of ultrasonic neuromodulation in which ultrasound produces effects on viscoelastic neurons and their surrounding fluid environments to alter membrane conductance [10].
2. Another study proposed that FUS influences membrane fluidity, turbidity, and permeability, and thereby affects the ion channels and concentration gradient [7].

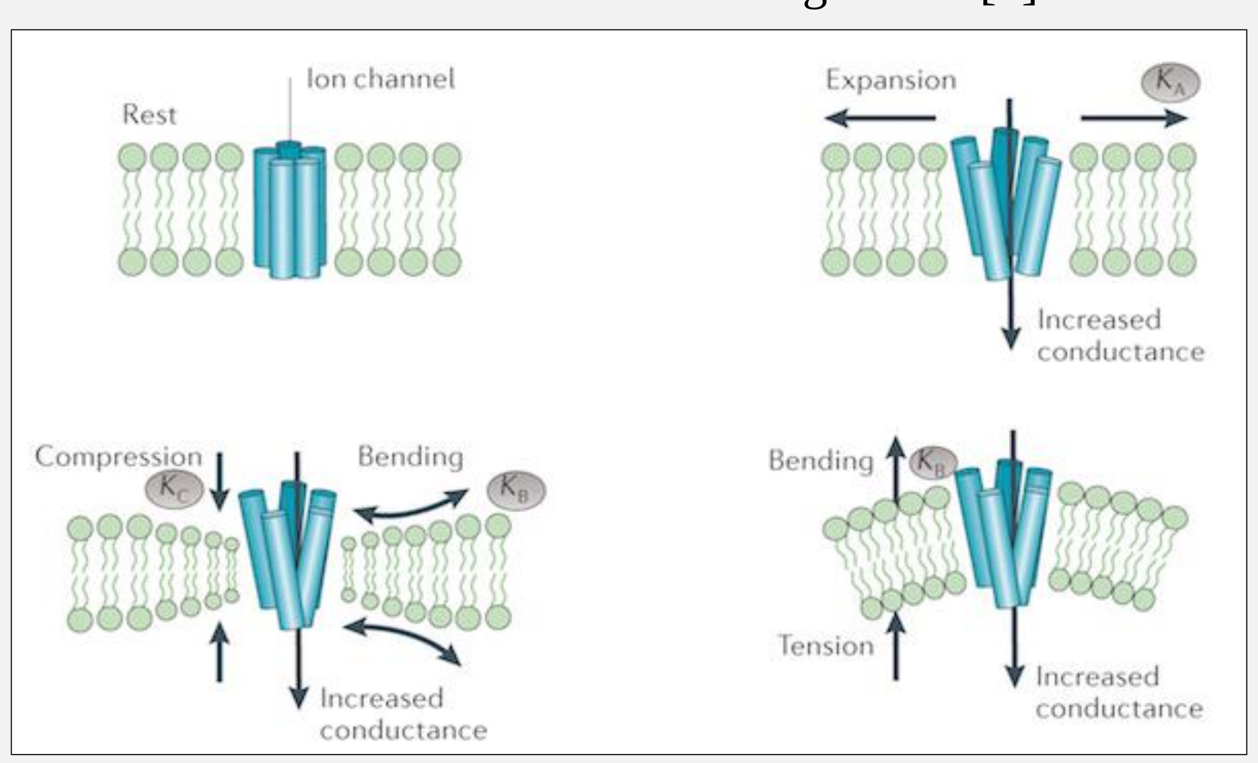

Fig. 3: Continuum mechanics hypothesis of ultrasonic neuromodulation [10].

Experimental Design

- **Why Crayfish?**

1. Crayfish are good test subjects due to their simple nervous system and well-established dissection protocol.
2. The crayfish nervous system is composed of one long axon with ganglions and nerves branching off of the ganglions.
3. The focus of this project is the third nerve.

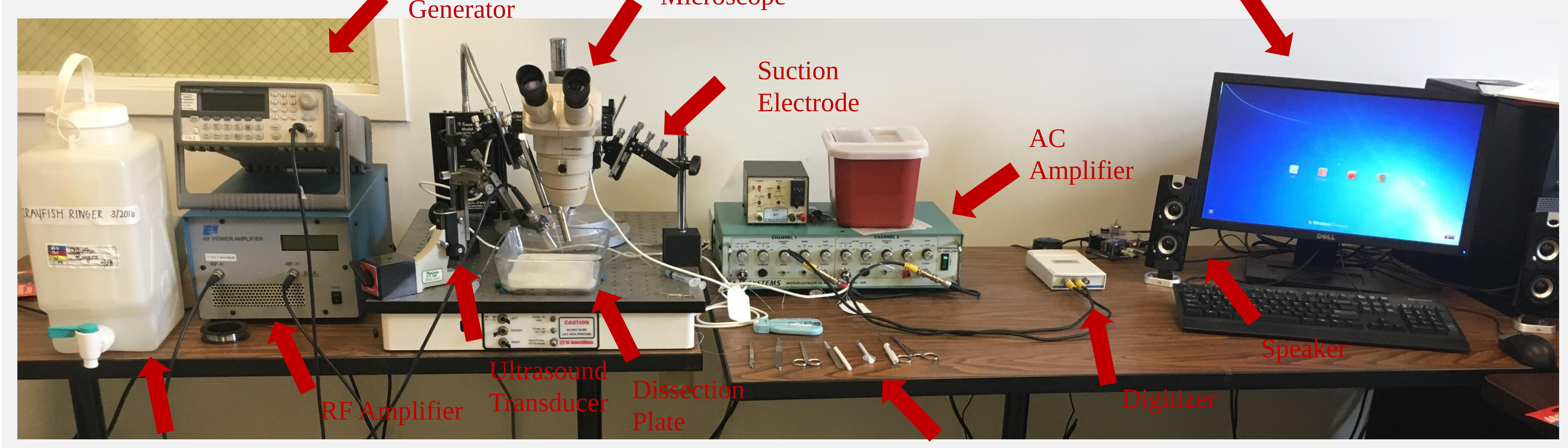

Fig. 5: Experimental setup.

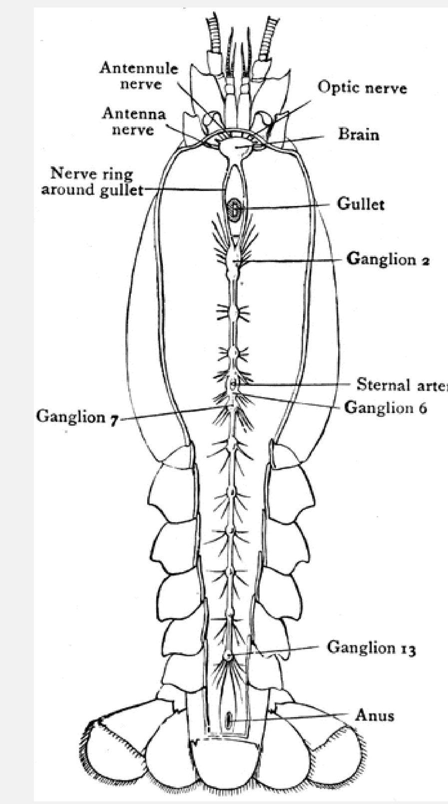

Fig. 4: Diagram of crayfish nervous system [8].

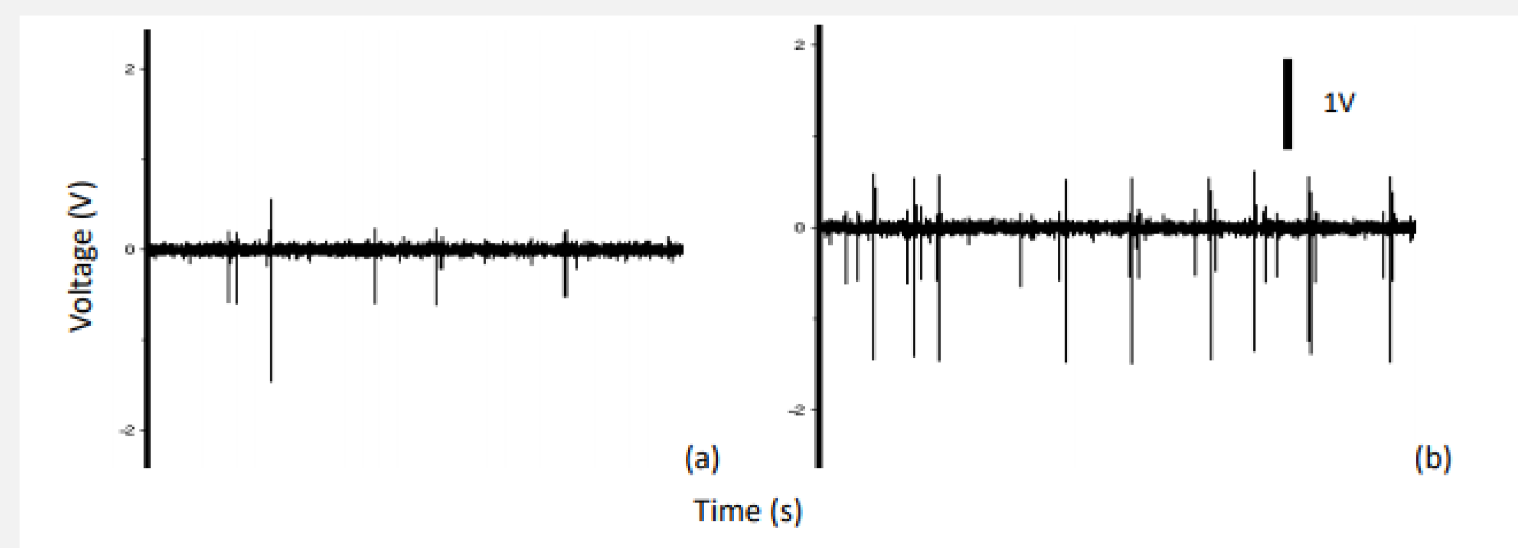

Fig. 6: Spike train trace of the crayfish third nerve with (a) and without (b) stimulation of the telson over a 2 second interval sample. Nerve spike frequency and amplitude notably increases during stimulation. Gain = 10000 [11].

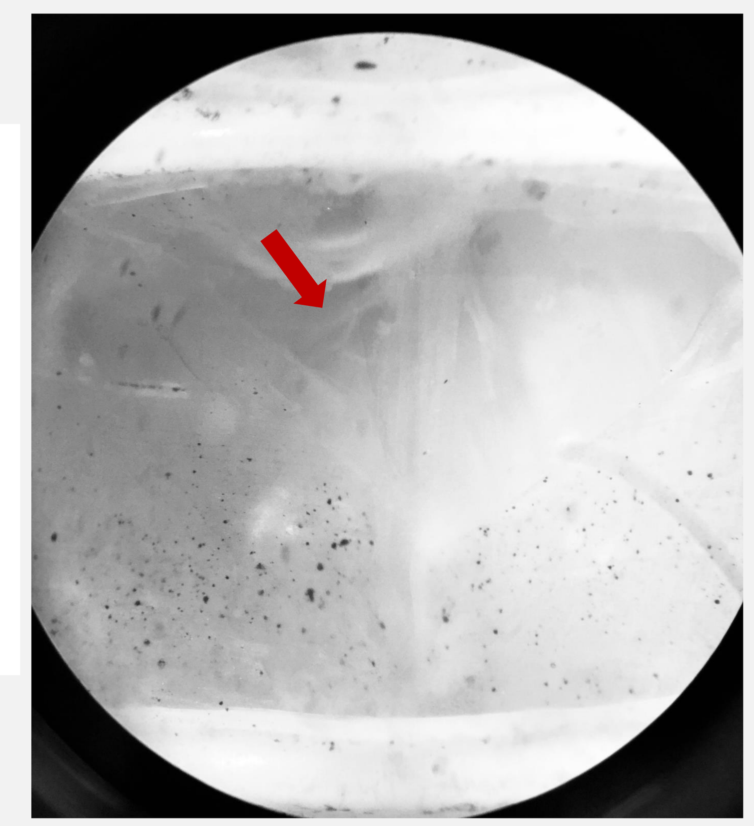

Fig. 7: Microscope image of the crayfish third nerve.

Conclusions

1. The short term significance of this project is the better understanding of FUS for neuromodulation and the crayfish dissection protocol, and the development of an experimental testbed.
2. The long term significance of this research is in developing a method of application of FUS for medical practices.
3. Future goals: To determine the optimum ultrasonic parameters to invoke a neuromodulation response in a crayfish. To identify particular regions in the crayfish nervous system that produce the strongest neuromodulation response in a controlled manner.

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References

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