

# Investigating Cellular And Molecular Mechanisms That Determine Thresholds For Damage In Brain Tissue Due To Electrical Stimulation

Camila De Barros Leandro, Biomedical Engineering Major

Mentor: Jitendran Muthuswamy, Principal Investigator

Fulton School of Engineering

QR CODE

## Background:

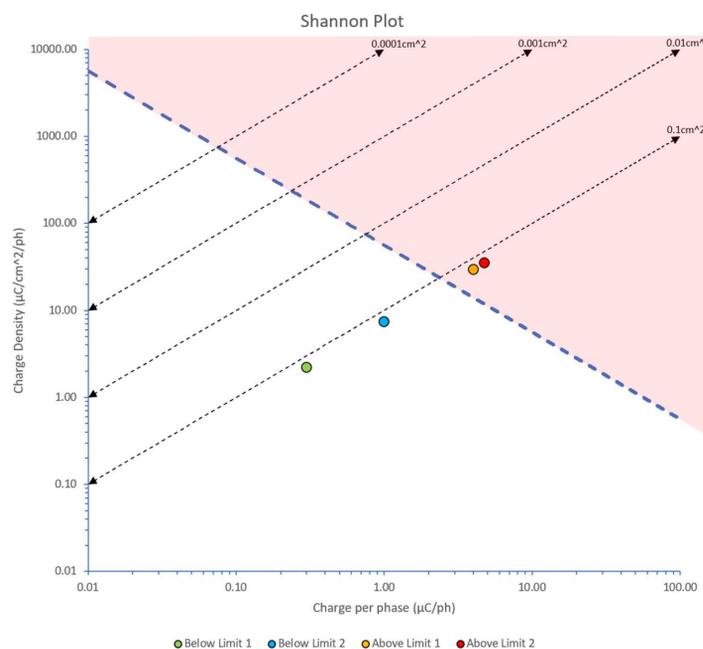
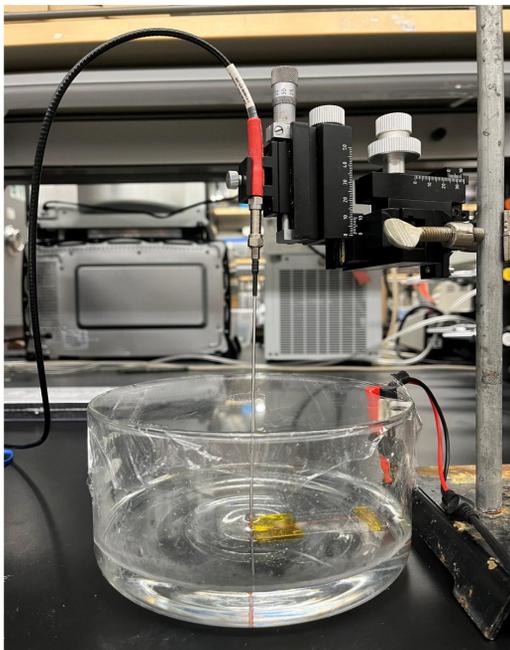
- The threshold between safe and damaging levels of electrical stimulation in brain tissue is often defined by the Shannon limit, which relates charge density to charge per phase of the electrical stimulation waveform.
- Knowing the causal mechanisms to cell deterioration during electrical stimulation will allow for improved designs to existing devices and facilitate the safe implementation novel treatment methods.

## Objective & Research Question:

The goal of this project is to identify the role of oxygenation in injury to neural cells undergoing electrical stimulation, while further exploring oxygenation patterns when stimulation falls below and above the Shannon limit.

## Methods:

- Electrical stimulation was applied to an in-house electrochemical cell
  - 2 platinum-iridium macro-electrodes fixed to a slide are placed in a glass dish
  - Glass dish is filled with phosphate-buffered saline (PBS)
- Partial pressure of oxygen was measured via a fiberoptic probe
- The primary data which was analyzed consisted of the amount of oxygen (%) present within the area of stimulation



### Stimulation Parameters

Pre-train delay	300s
Post-train recovery	600s
Train burst width	300s
Inter-pulse period	7ms

### Below Limit 1

Pulse duration	60 $\mu\text{s}$
Current	5mA

### Below Limit 2

Pulse duration	200 $\mu\text{s}$
Current	5mA

### Above Limit 1

Pulse Duration	400 $\mu\text{s}$
Current	10mA

### Above Limit 2

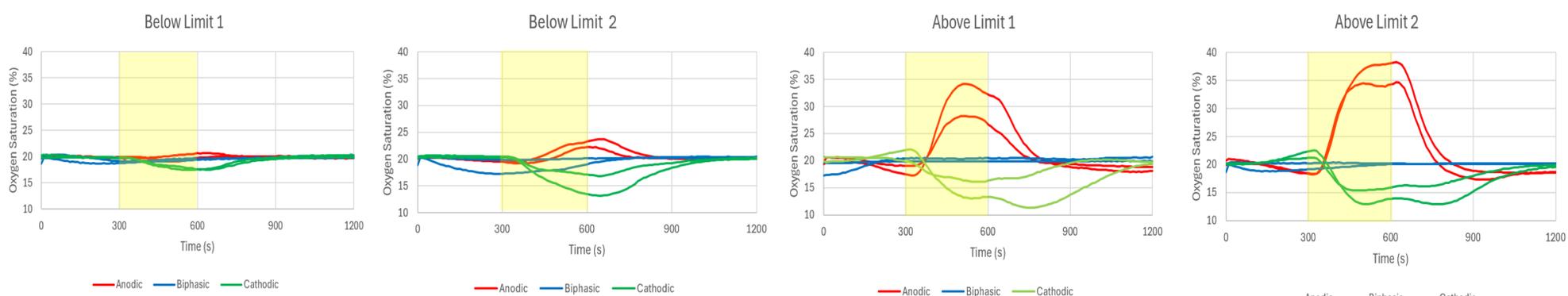
Pulse Duration	475 $\mu\text{s}$
Current	10mA

## Results:

A negative trend in oxygen concentration was found in response to cathodic stimulation through the electrodes, that returned to normal levels after stimulation was no longer being applied.

A small negative trend in oxygen concentration was found, followed by an increase in concentration in response to anodic stimulation through the electrodes. A return to normal levels was observed after stimulation was no longer being applied

No significant alterations in oxygen saturation was found after applying biphasic stimulation through the electrodes.



## Discussion:

These sets of experiments depended on the process of hydrolysis to observe any changes in oxygen saturation around the area of the electrodes, due to the utilization of PBS within an in-vitro experimental set up. Future considerations should address the lack of biological influences within this set up. Doing so by replacing the PBS with artificial cerebral spinal fluid will more accurately represent conditions present inside of the brain while carrying out in vitro-experimentation. Furthermore, in-vivo experiments will be carried out using lab rats, resulting in more representative real-time data outlining how brain cells are affected during and after electrical stimulation. Additional factors such as local changes in temperature as well as carbon dioxide saturation within the tissue should also be considered to gain additional context behind any potential cellular and molecular mechanism(s) behind brain tissue damage due to electrical stimulation.

## Acknowledgements:

Special thank you to Dr. Jitendran Muthuswamy and Michael D'Saachs for their support and guidance throughout this project.

## References:

- Jiří Ehlich et al., "Direct measurement of oxygen reduction reactions at neurostimulation electrodes," *Journal of Neural Engineering*, vol. 19, no. 3, pp. 036045–036045, Jun. 2022, doi: <https://doi.org/10.1088/1741-2552/ac77c0>.
- R. B. Buxton, "Thermodynamic limitations on brain oxygen metabolism: physiological implications\*," *Journal of physiology*, Feb. 2024, doi: <https://doi.org/10.1113/jp284358>.
- I. Ougorets and J. J. Caronna, "Coma - Part IV Chapter 62," in *Critical Care in Medicine*, 3rd ed., J. E. Parrillo and R. P. Dellinger, Eds., Mosby, 2008, pp. 1309–1328.
- R.-M. Deng, Y.-C. Liu, J.-Q. Li, J.-G. Xu, and G. Chen, "The role of carbon dioxide in acute brain injury," *Medical Gas Research*, vol. 10, no. 2, pp. 81–84, Jun. 2020, doi: <https://doi.org/10.4103/2045-9912.285561>
- K. Chung, "Investigating changes in local oxygen profiles at safe and unsafe stimulation intensities to characterize the mechanism of tissue damage." Arizona State University, May 2024. [Online]. Available: <https://docs.google.com/document/d/1OhOQ6wh1w0sUMLYNFZJv3fRIU04TKR/edit?tab=t.0#heading=h.30j0zll>

Stimulation Parameter	Oxygenation Variance
<b>Cathodic Stimulation</b>	
Below Limit 1	12.5%
Below Limit 2	24.97%
Above Limit 1	31.66%
Above Limit 2	29.3%
<b>Anodic Stimulation</b>	
Below Limit 1	2.39%
Below Limit 2	14.84%
Above Limit 1	56.1%
Above Limit 2	82.36%
<b>Biphasic Stimulation</b>	
Below Limit 1	2.23%
Below Limit 2	1.87%
Above Limit 1	0.31%
Above Limit 2	0.11%