Analyzing Desynchronizing Effects of Waveforms on Beta-Gamma Coupled Oscillations in Closed Loop Deep Brain Stimulation for Parkinson's Disease

Ayushi Chadha[1,6], Shreya Malge[2,6], Riya Raina[3,6], Ryan Wolk[4,6], Elizabeth Zastavnyuk[5,6]

BOSTON UNIVERSITY

West Windsor-Plainsboro High School North, 90 Grovers Mill Rd, Plainsboro Township, NJ 08536[1]; Columbia High School, 962 Luther Rd, East Greenbush, NY 12061[2]; Briarcliff High School, 444 Pleasantville Rd, Briarcliff Manor, NY 10510[3]; San Francisco University High School, 3065 Jackson St, San Francisco, CA 94115[4]; Newport High School, 4333 Factoria Blvd SE, Bellevue, WA 98006[5]; Boston University, Boston, MA 02215[6]

Introduction

- **Parkinson's Disease (PD)**
  - Progressive neurodegenerative disorder
  - Often characterized by impaired motor movement such as tremors
  - Current evidence suggests that certain aspects of sensory processing is reflected in frequency-specific neural oscillations that communicate over neural networks (Alavash et al., 2017)
  - Excessive Beta-Gamma Phase-Amplitude Coupling indicates PD as it interferes with brain communication (Hodnik et al., 2024)

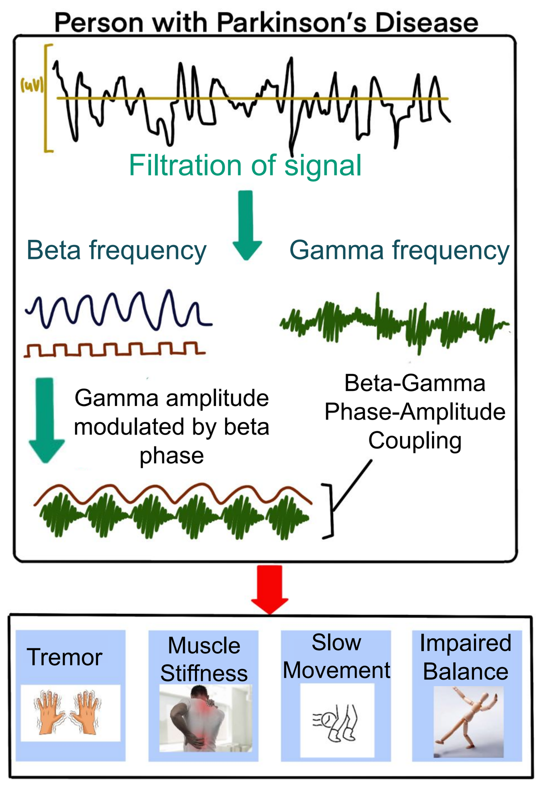

Figure 1. Schematic of brain wave synchronization in Parkinson's patients and symptoms

- **Deep Brain Stimulation (DBS)**
  - An emerging treatment using electrodes in the subthalamic nucleus (STN) to desynchronize beta-gamma brain wave coupling
  - DBS traditionally uses rectangular pulses for stimulation

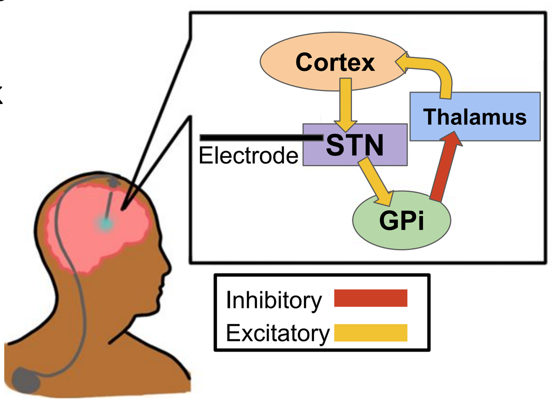

Figure 2. Role of DBS in the brain and motor pathway

Objective: Investigate if alternative waveforms can more effectively desynchronize neural populations

Methods

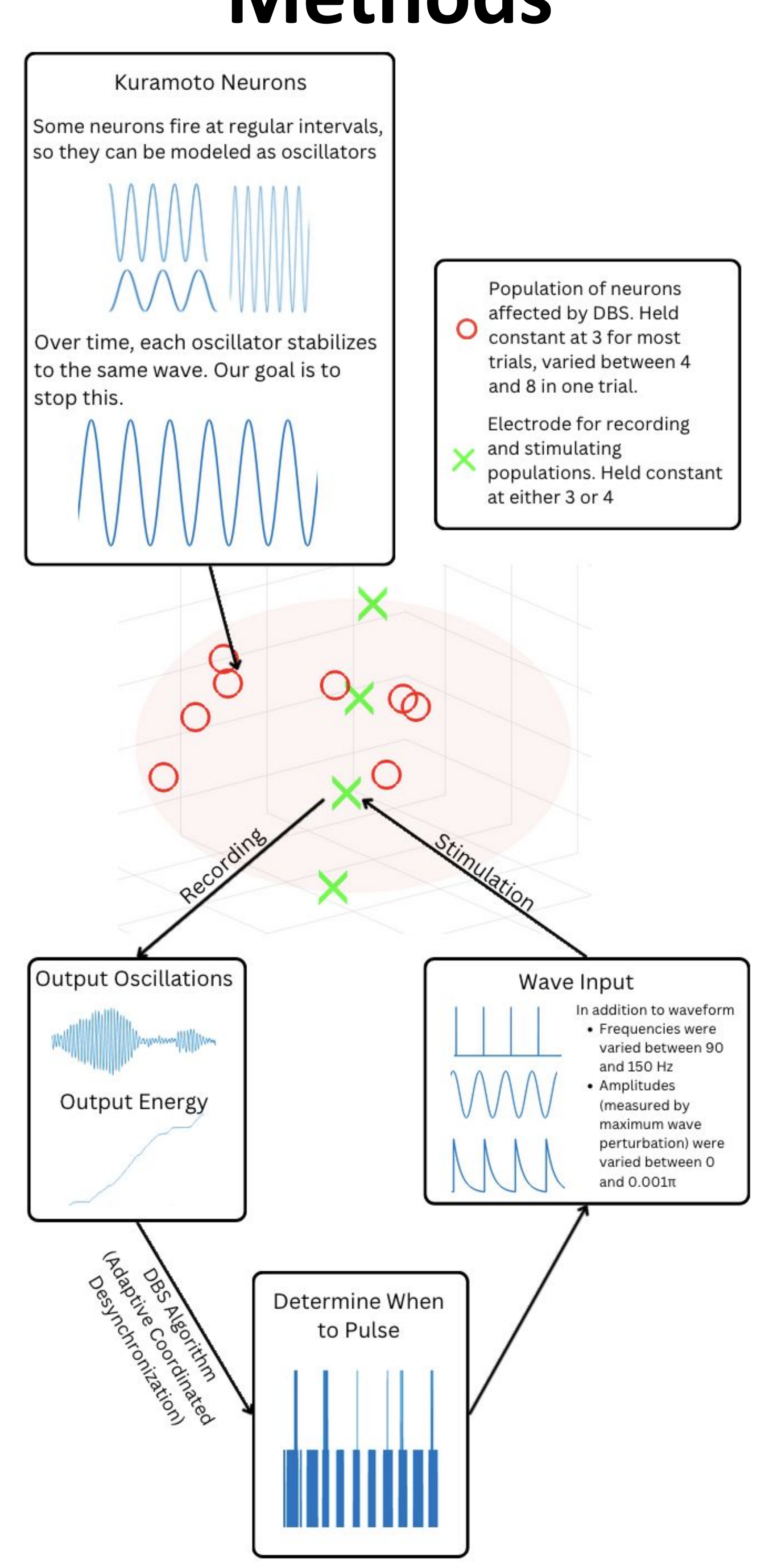

Figure 3: Visual description of our methods

Random number generation is used in the model to mimic random events that can cause beta-gamma coupling. A seed for these random numbers can be set, allowing us to run simulations with identical samples, but different stimulations, allowing us to meet the conditions for a matched pairs t-test with 28 samples in Figure 5. Figure 6 uses an unpaired t-test with 8 samples, and cannot meet the conditions for a paired test due to the differences in random states with different numbers of populations.

Simulation Code: https://github.com/fourth-bit/RISE_project

Results

Result 1: ***Small Qualitative Differences between Rectangular and Sinusoidal Pulses***

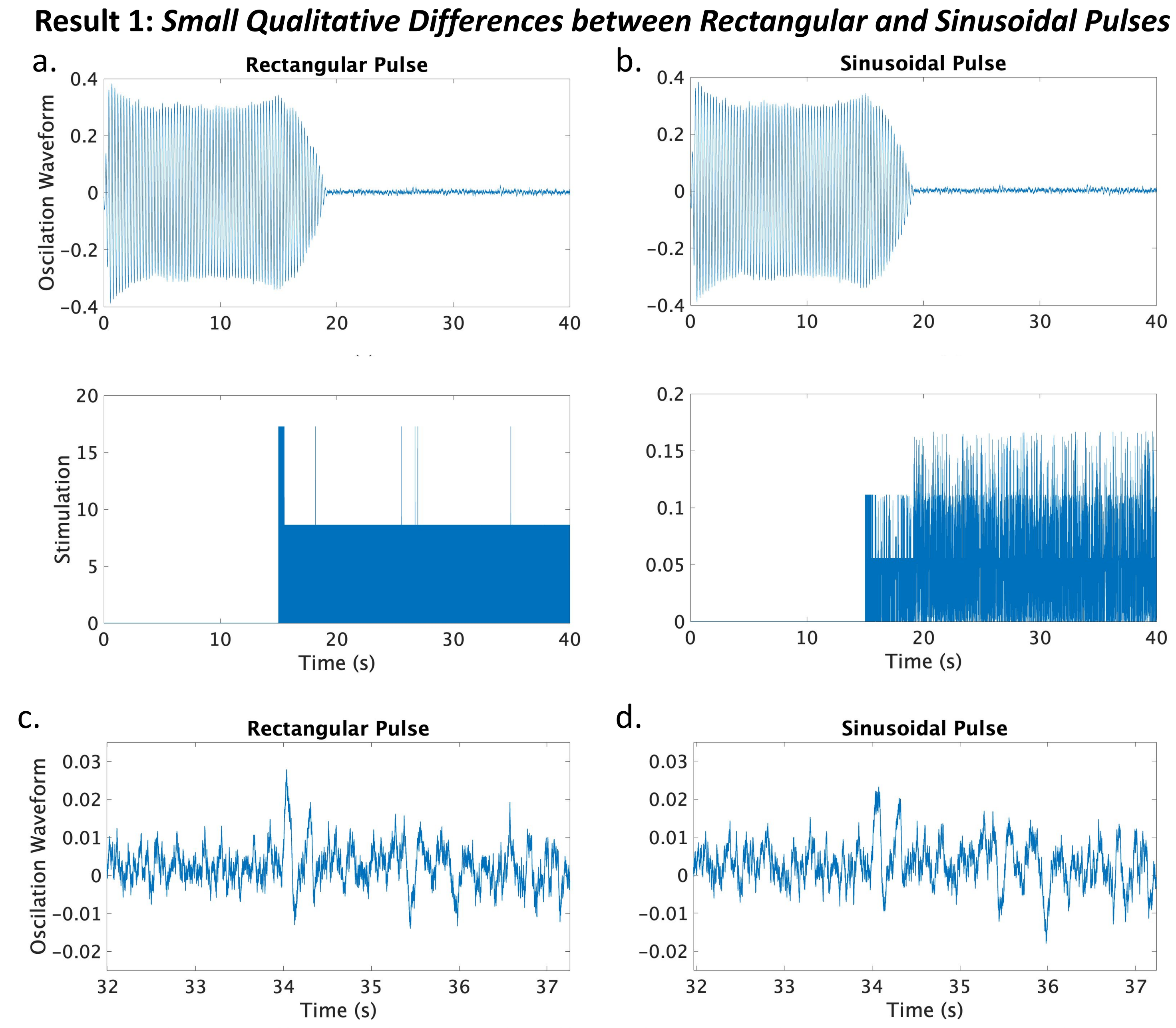

Figure 4. Qualitative differences between the effects of a rectangular wave and a sinusoidal wave run at 40000 samples per second. a-b) From a broad perspective, the overall oscillations are the same, but the stimulation waveforms are different. c-d) There is a small difference in the oscillations due to the change in waveform. This is especially apparent in the peaks and troughs of the oscillation.

Result 2: ***Pulse Shape has a Small Effect on Synchrony, Large Effect on Electric Energy Usage***

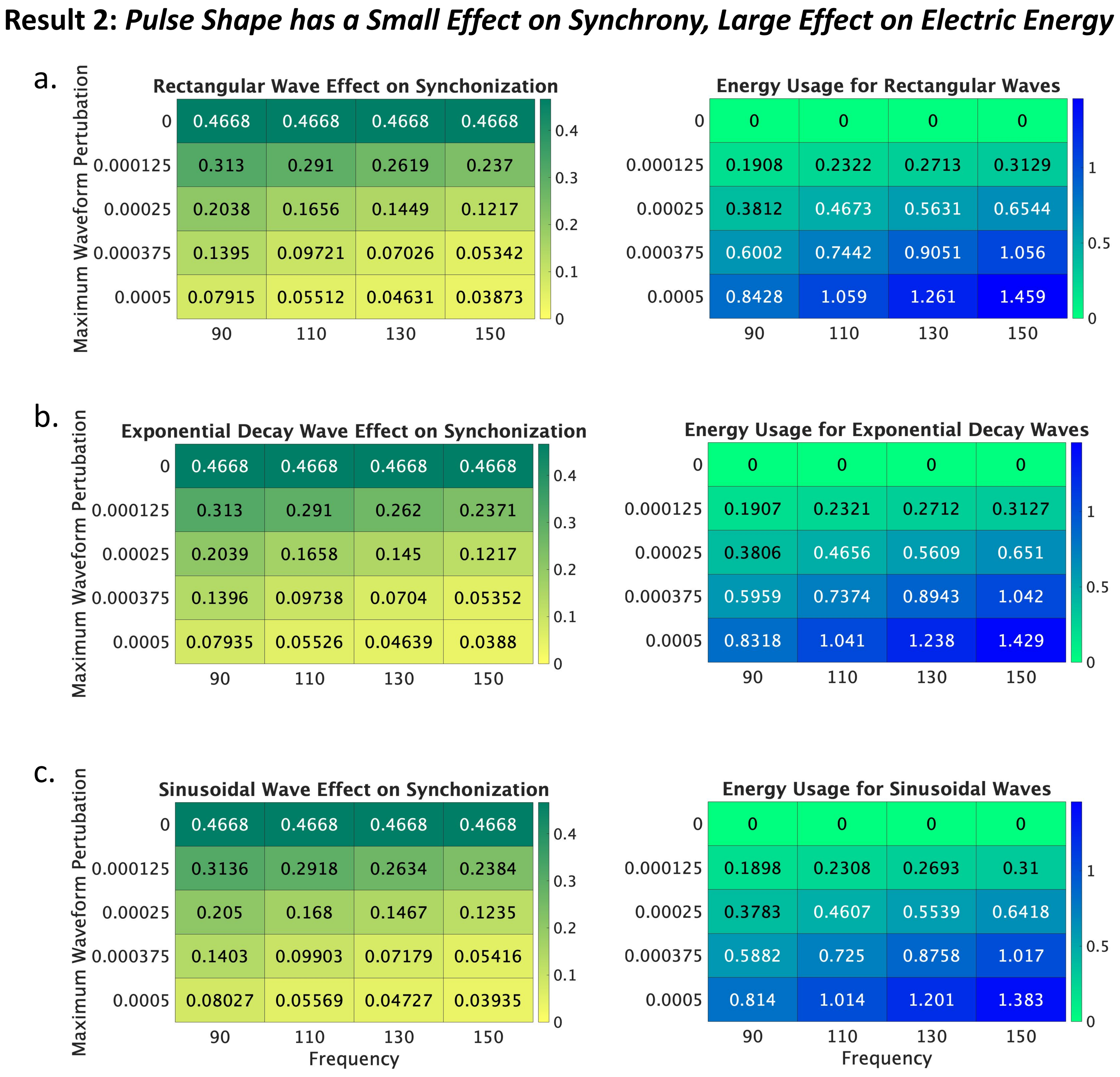

Figure 5: Effect of different types of waves on synchrony and energy usage. a-c) Between the sinusoid wave and both of the others, there is a small, but statistically significant change in synchronization for frequencies greater than or equal to 130 and amplitudes greater than or equal to 0.00025. The same trend holds for energies with frequencies greater than or equal to 110 and amplitudes greater than or equal to 0.00025. The relationship between the exponential decay and rectangular wave is significant for the same set of energies, but there is no statistically significant change in the synchronization.

Result 3: ***The Number of Populations Near Electrodes Greatly Affects Synchrony***

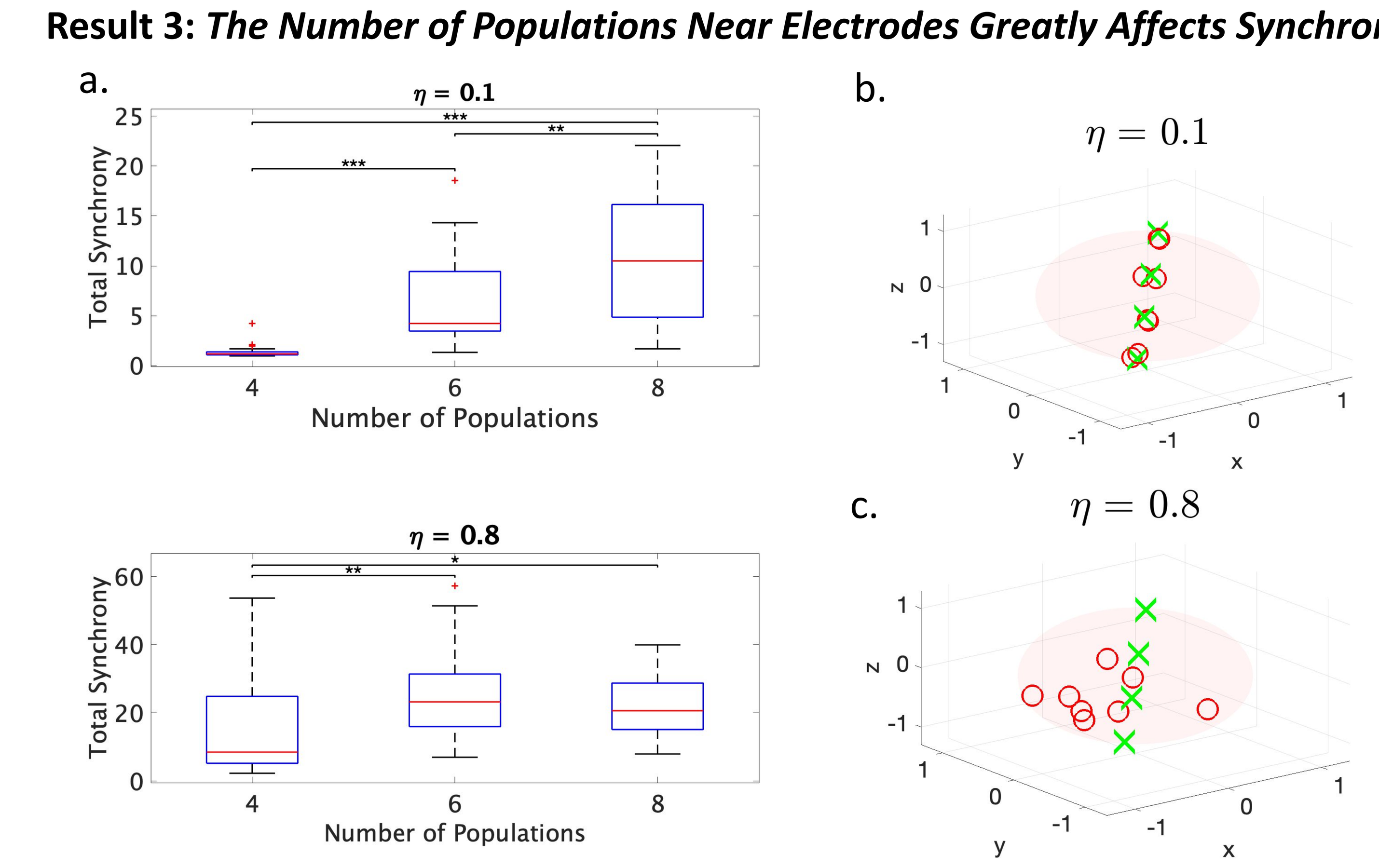

Figure 6. When there are multiple populations near an electrode, its effectiveness and reliability in stopping synchrony decreases. a) When there is a 1:1 ratio, and the dispersal of populations is low, there is low synchronization and high consistency. Both of these effects disappear when the η (configuration parameter) is increased and when the number of populations is increased. b-c) Representations of the simulation's 3D space with 4 electrodes and 8 populations for different η values.

Discussion

Discussion of Results:

- **Rectangular and sinusoidal waveforms had significantly different effects on desynchronization, with sinusoidal pulses having slightly less desynchronization (~0.001), while rectangular and exponential decay waveforms were not significantly different.**
- **The sinusoidal and exponential decay waveforms decreased energy consumption by 5% and 2% in comparison to the rectangular waveforms.**
- Desynchronization decreased when η (configuration parameter) increased and the number of neural populations at each electrode increased.
- The various waveform stimuli caused slight temporal differences in oscillation amplitude that did not affect overall desynchronization time from onset of stimulus

Limitations:

- The model does not account for the varying conductivity of brain tissue and the dendritic and axonal structures of neurons, both of which change the influence of the electric field on the neural populations.
- Models instantaneous effects, neglects duration of stimulation and the effects of DBS on a larger time scale
- Assumes "small populations" of neurons are all coupled
- The Kuramoto model does not account for neuron level ion induced action potentials
- When changing the configuration and spread of neural populations, the model cannot factor in axons or the fact that distant populations may not be connected

Future Work:

- Changing the k (Coupling constant) and the η (configuration parameter) together in this model to test more complex coupling and configuring systems
- Modeling the effects of waveform stimulation on desynchrony in different conditions, such as in a movement state, as beta power decreases in moving patients (Eisinger et al., 2020).
- Adapting model to simulate separate electrodes to model patients with multiple DBS inputs
- Studying the effect of waveform stimulus for DBS in real organisms or model that is more biologically focused.
- Modeling this project to represent electrode being placed in different areas of the brain, such as the GPi or GPe to simulate alternative neurodegenerative diseases or the effects of DBS in other steps in the motor pathway

References

Alavash, M., Daube, C., Wöstmann, M., Brandmeyer, A., & Obleser, J. (2017). Large-scale network dynamics of beta-band oscillations underlie auditory perceptual decision-making. *Network neuroscience (Cambridge, Mass.)*, *1*(2), 166–191. https://doi.org/10.1162/NETN_a_00009

Eisinger, R. S., Cagle, J. N., Opri, E., Alcantara, J., Cernera, S., Foote, K. D., Okun, M. S., & Gunduz, A. (2020). Parkinsonian Beta Dynamics during Rest and Movement in the Dorsal Pallidum and Subthalamic Nucleus. *The Journal of neuroscience : the official journal of the Society for Neuroscience*, *40*(14), 2859–2867. https://doi.org/10.1523/JNEUROSCI.2113-19.2020

Foutz, T. J., & McIntyre, C. C. (2010). Evaluation of novel stimulus waveforms for deep brain stimulation. *Journal of Neural Engineering*, *7*(6), 066008. https://doi.org/10.1088/1741-2560/7/6/066008

Hodnik, T., Roytman, S., Bohnen, N. I., & Marusic, U. (2024). Beta-Gamma Phase-Amplitude Coupling as a Non-Invasive Biomarker for Parkinson's Disease: Insights from Electroencephalography Studies. *Life (Basel, Switzerland)*, *14*(3), 391. https://doi.org/10.3390/life14030391

Karekal, A., Miocinovic, S. & Swann, N.C. Novel approaches for quantifying beta synchrony in Parkinson's disease. *Exp Brain Res* **240**, 991–1004 (2022). https://doi.org/10.1007/s00221-022-06308-8

Kent, A. R., & Grill, W. M. (2014). Analysis of deep brain stimulation electrode characteristics for neural recording. *Journal of Neural Engineering*, *11*(4), 046010. https://doi.org/10.1088/1741-2560/11/4/046010

Weerasinghe, G., Duchet, B., Bick, C., & Bogacz, R. (2021). Optimal closed-loop deep brain stimulation using multiple independently controlled contacts. *PLOS Computational Biology*, *17*(8), e1009281. https://doi.org/10.1371/journal.pcbi.1009281

Acknowledgements

We would like to thank Karla Montejo and Ryan Senne for their support and for introducing us to the principles of computational neuroscience. We would also like to extend our gratitude to the other Teaching Fellows who were available to help us with our project. Finally, we want to thank our families for their unwavering support and for allowing us to participate in this program.