Final Project

Introduction to computational neuroscience I

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1 Summary of Kumar et al 2011 [KCRA11]

Abstract

This article investigates the neural dynamics underlying Parkinson's disease (PD), focusing on oscillations in the basal ganglia. The study highlights the role of inhibitory inputs from the striatum to the globus pallidus external (GPe) as an important parameter controlling these oscillations, which are linked to motor dysfunctions in PD.

Introduction

Parkinson's disease is characterized by motor and cognitive impairments due to dopamine depletion in the basal ganglia. A distinctive feature of PD is the presence of oscillations within the subthalamic nucleus (STN) and GPe network. These oscillations are associated with deficits in movement initiation and execution, as well as resting tremors. Despite the effectiveness of deep brain stimulation (DBS) in alleviating symptoms, the mechanisms behind its efficacy remain poorly understood.

Methodology

The authors utilized a large-scale spiking neural network model consisting of 3,000 neurons - 1000 excitatory STN neurons and 2,000 inhibitory GPe neurons. The model aimed to explore how varying levels of inhibitory input influence oscillatory activity.

Key Findings

The study reveals that:

- The strength of inhibitory inputs from the striatum to GPe neurons is crucial for controlling oscillatory behavior.
- Increased striatal activity can trigger oscillations in the basal ganglia.
- A unified explanation is proposed for:
  - Absence of oscillations in healthy states.
  - Emergence of oscillations under dopamine-depleted conditions.
  - Suppression of oscillations through DBS.
- The model successfully replicates observed behaviors in patients with PD, accounting for both motor impairments and reduced response inhibition seen in DBS-implanted patients.

Discussion

These findings provide insight into how inhibition influences neuronal synchrony and oscillatory behavior in PD. They suggest that modulation of inhibitory inputs could be a key strategy for optimizing DBS protocols, potentially leading to more effective therapeutic interventions.

2 Analysis of my results

I created a down-scaled model of the STN and GPe network model used in Kumar et al 2011 [KCRA11] and simulated 3 different states: Healthy state, Parkinsonian state, and Parkinsonian state with DBS. Then I analyzed the data from the simulation by creating the following Figures:

2.1 Simulation Raster Plot

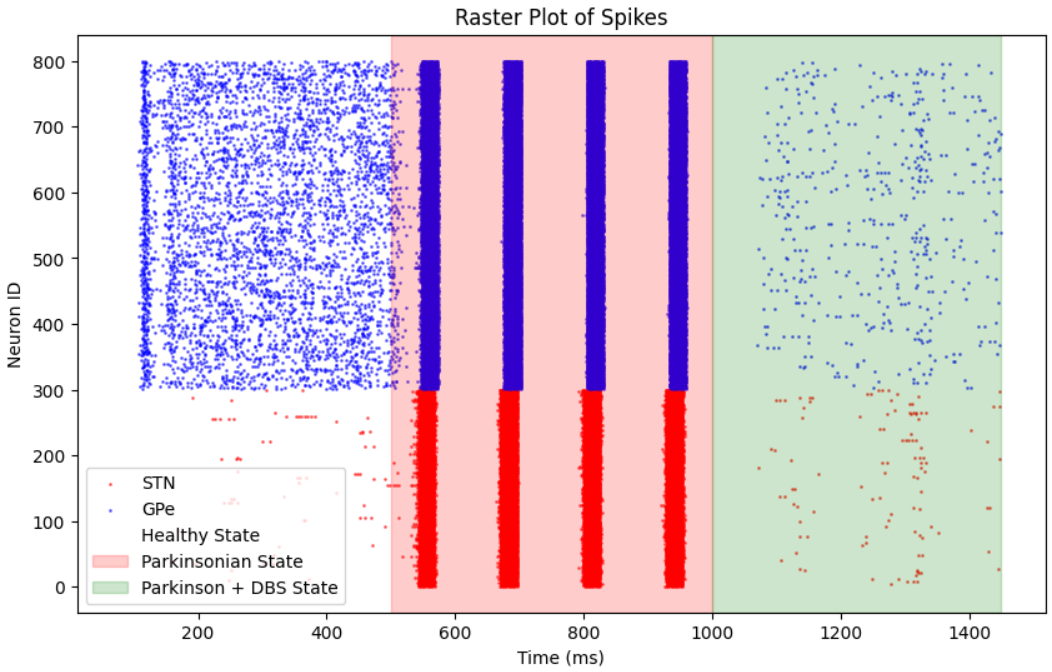

Figure 1: Raster plot of spikes in all 3 conditions

2.2 Firing rate distributions

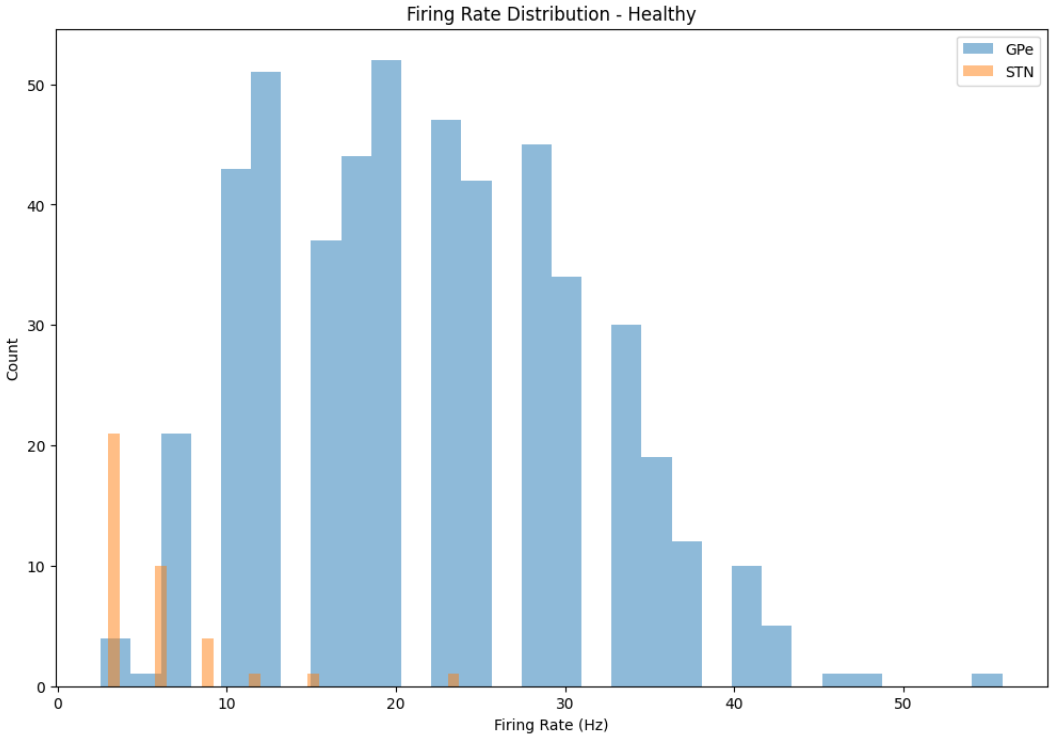

Figure 2: Firing rate distribution in Healthy state

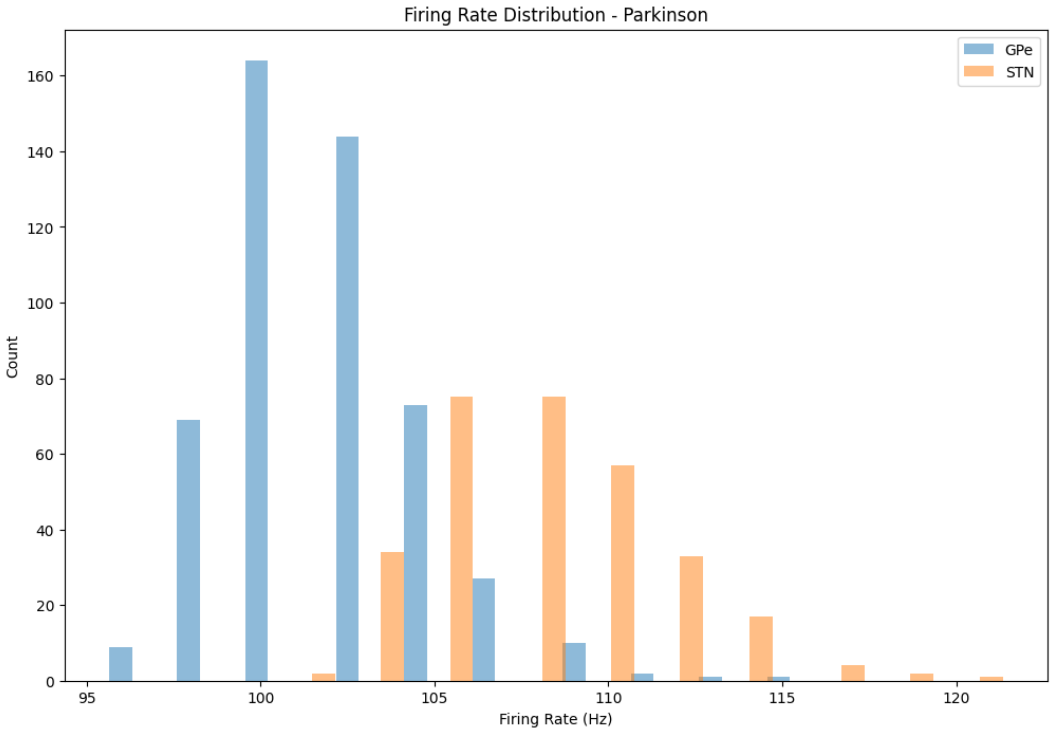

Figure 3: Firing rate distribution in Parkinsonian state

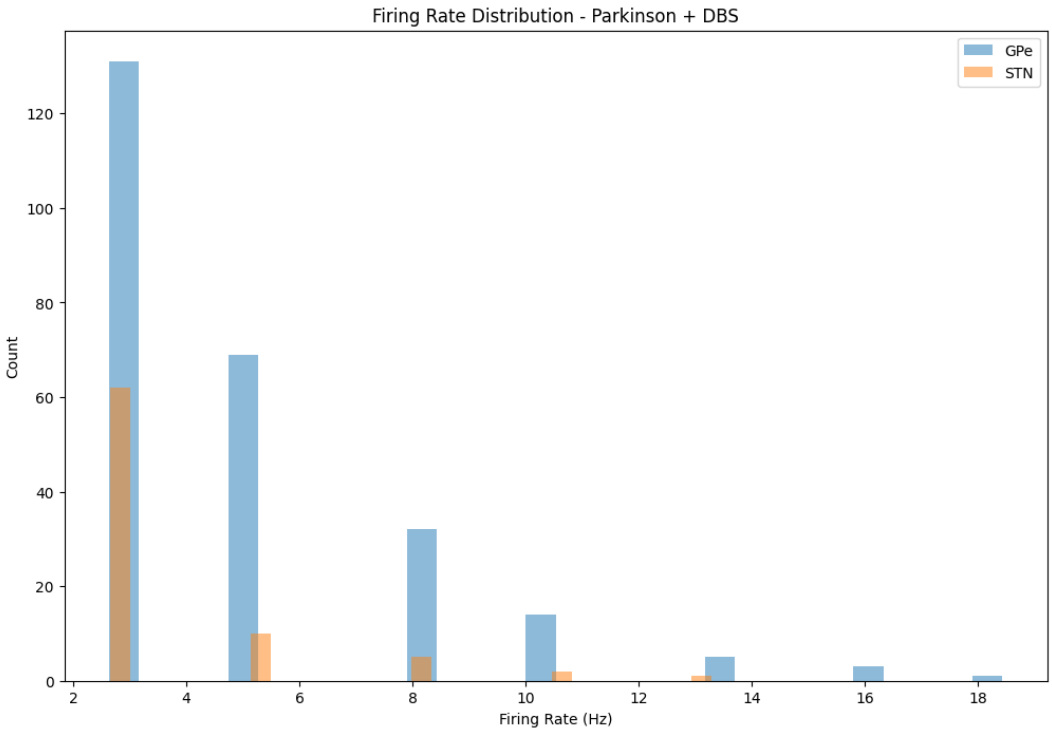

Figure 4: Firing rate distribution in DBS state

2.3 Power Spectra

2.3.1 Comparison of LFP and Simulated STN-GPe network Power Spectra

There are some very distinct characteristics between the Local Field Potential (LFP) and the simulated basal ganglia power spectra. The LFP power spectrum (Figure 5) shows decay, with the power decreasing as the frequency increases. It has sharp periodic dips at approximately 100Hz, 200Hz, and 300Hz. These distinct features of the LFP power spectrum are quite different from the more irregular patterns in the power spectrum from the STN-GPe network simulations. The LFP spectrum has a very broad power range, from 10^3 to 10^{-5}, indicating a high dynamic range in the neural signal.

The simulated basal ganglia (STN-GPe network) data show different patterns in three conditions: healthy brain, Parkinson's disease, and Parkinson's with Deep Brain Stimulation (DBS). In the healthy state (Figure 6), both populations (STN and GPe) have fairly steady activity, with GPe showing a bit more variation than STN. In the Parkinsonian state (Figure 7), we see much stronger activity, especially at lower frequencies (0-100Hz), where both regions show increased oscillations. This matches what we know about Parkinson's disease, where STN and GPe populations synchronize. When DBS is turned on (Figure 8), these excessive oscillations decrease, making the pattern look more like the healthy state.

One big difference we notice is that the simulated data do not show the smooth decrease in power that we see in the real brain recording. This is probably because the simulation only looks at two specific brain regions talking to each other, while the real recording captures the activity of many more neurons and processes. Also, real brain recordings include other biological factors that are not in the simulation, like how signals spread through brain tissue and background brain activity. This shows us what simulations can and cannot tell us about real brain activity.

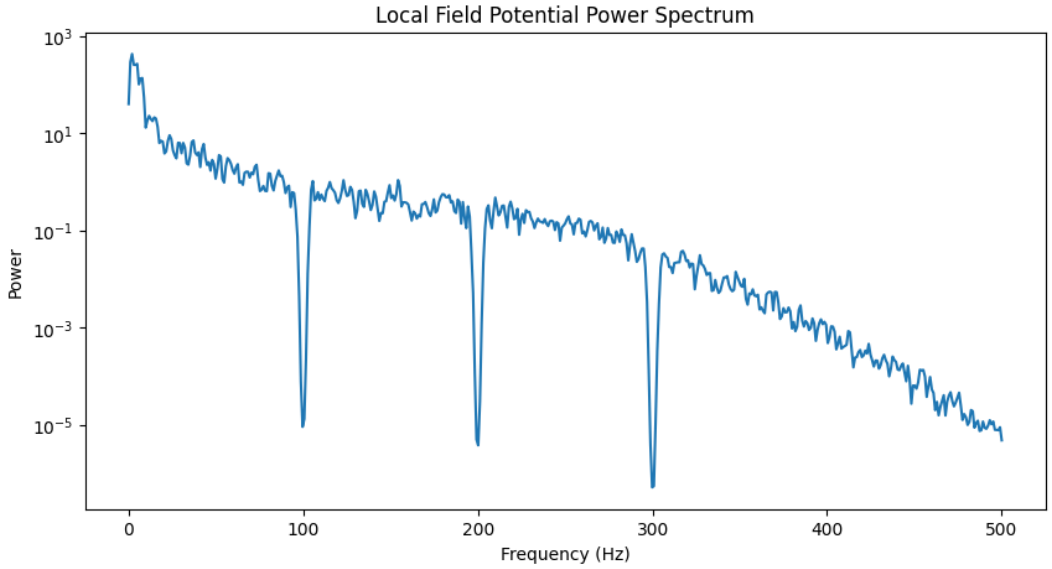

Figure 5: Power Spectrum of Local Field Potential from Macaque monkey's brain

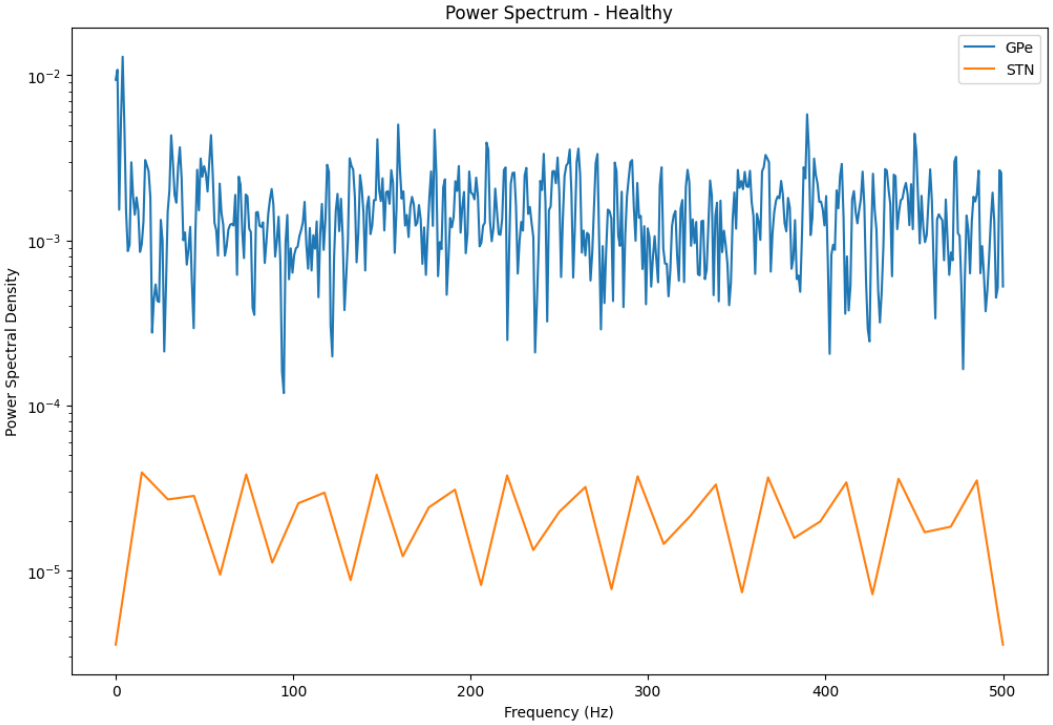

Figure 6: Power Spectrum of simulated Healthy state of STN and GPe

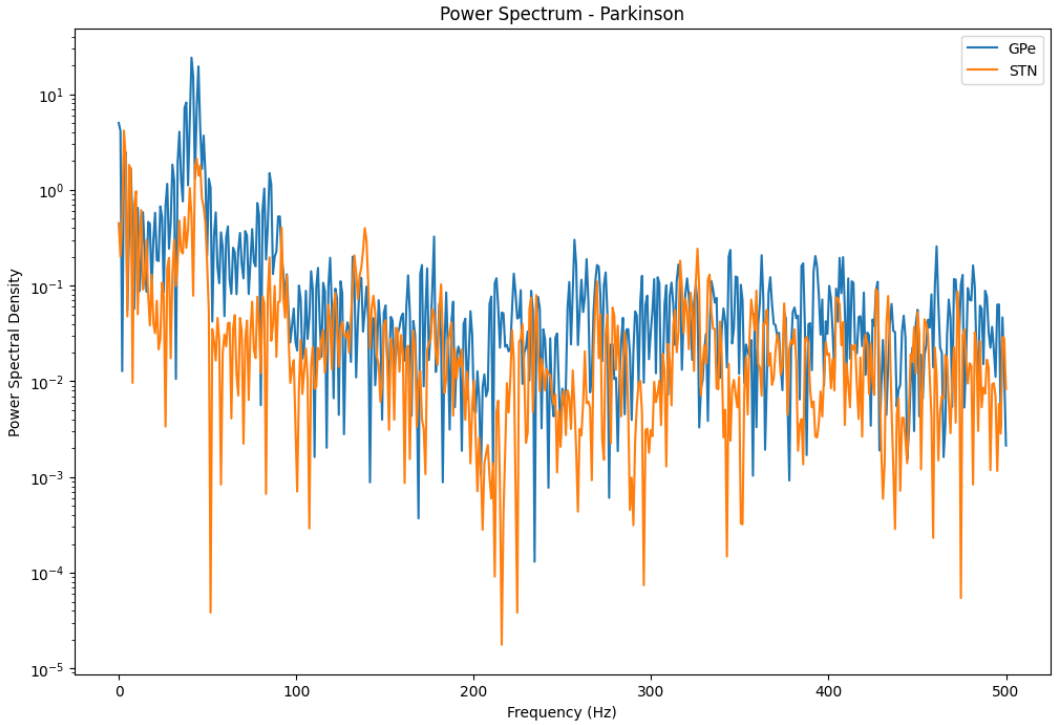

Figure 7: Power Spectrum of simulated Parkinsonian state of STN and GPe

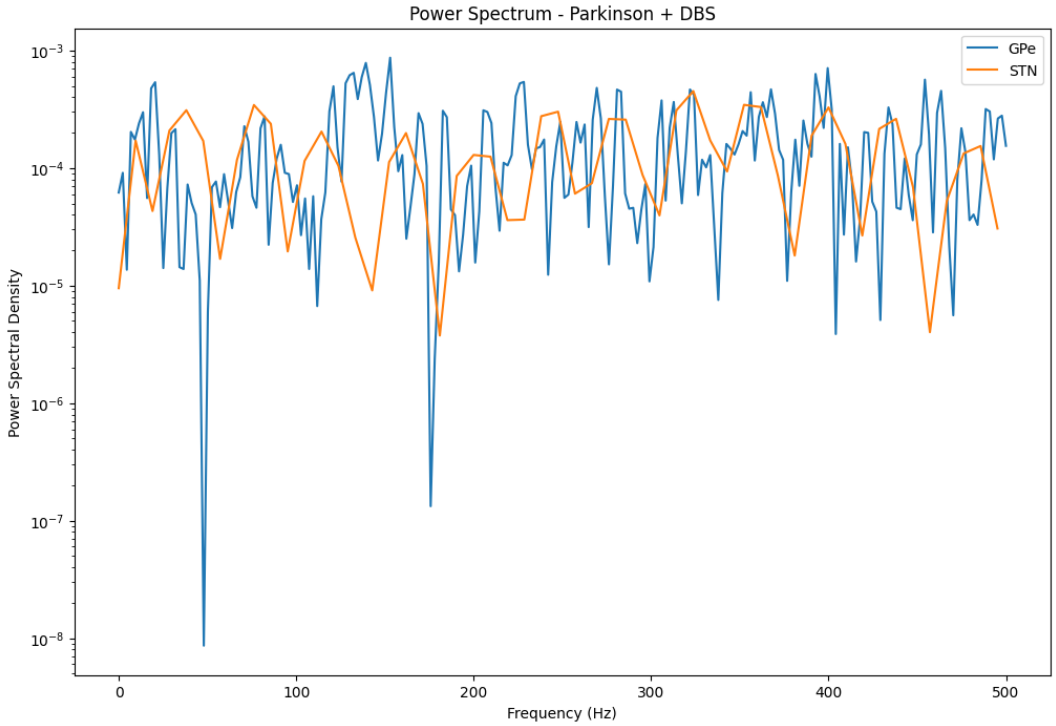

Figure 8: Power Spectrum of simulated Parkinson + DBS state of STN and GPe

2.4 Auto-correlation functions

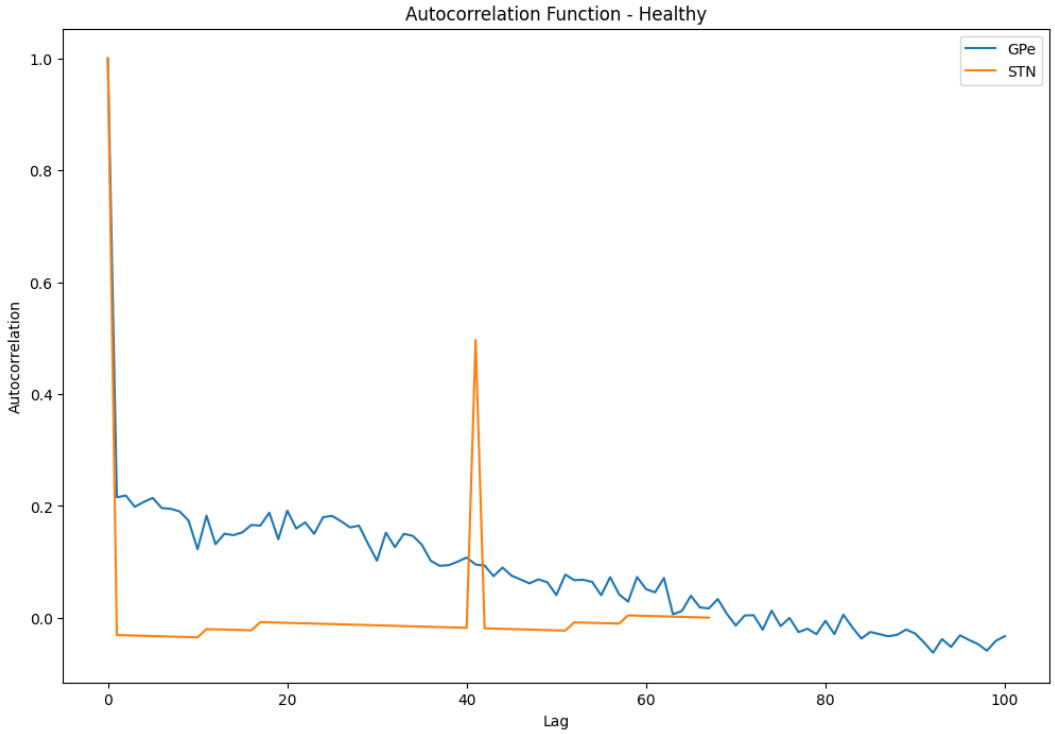

Figure 9: Autocorrelation functions of STN and GPe in Healthy state

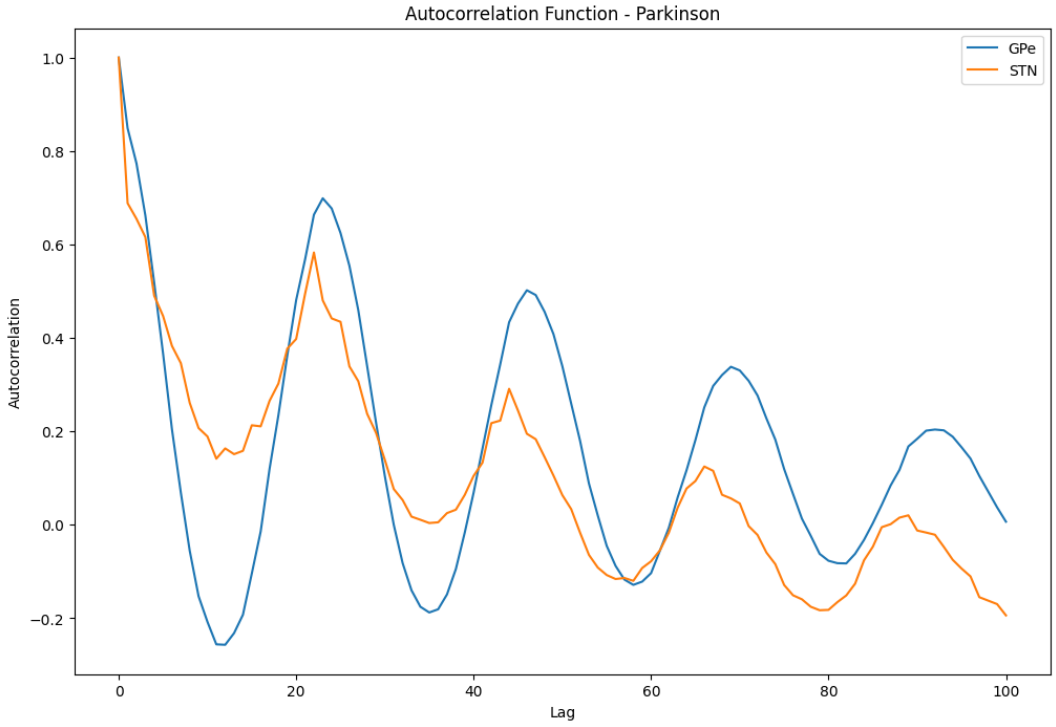

Figure 10: Autocorrelation functions of STN and GPe in Parkinsonian state

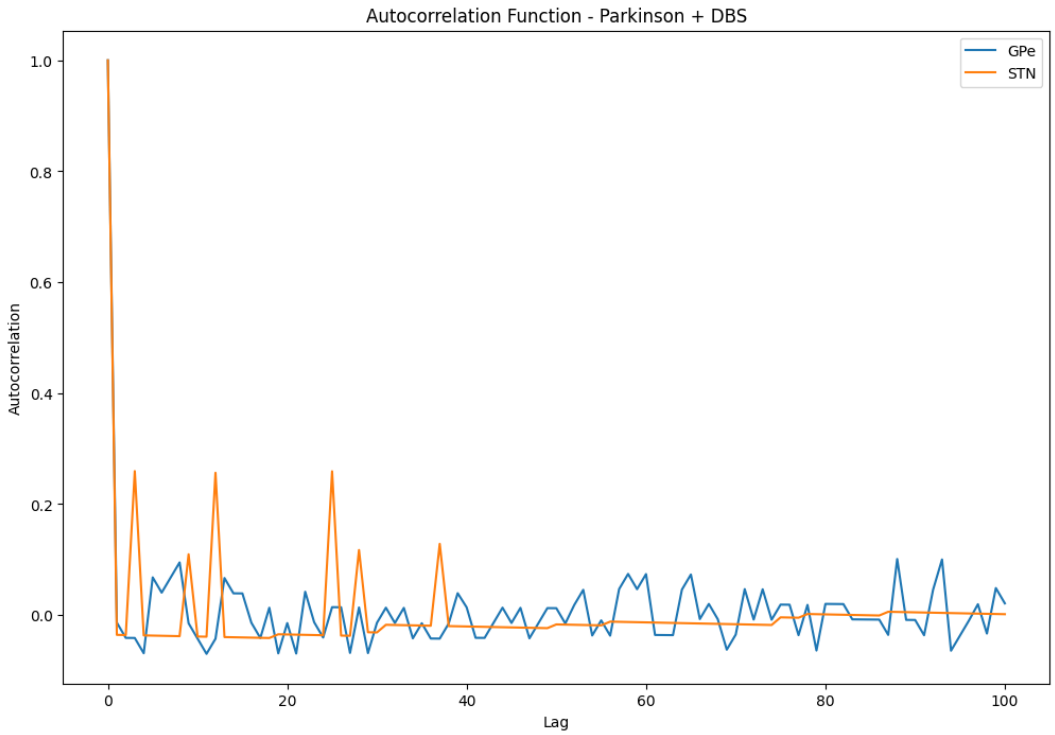

Figure 11: Autocorrelation functions of STN and GPe in Parkinson + DBS state

2.5 Sensitivity of DBS effects to amplitude changes

2.5.1 Effect of DBS Amplitude Variation on Neural Activity

The effects of DBS treatment are very sensitive to modulation of the amplitude. I analyzed these effects in both directions: decreasing the amplitude from -180 pA to -188 pA, and increasing the amplitude from -180 pA to -174 pA.

Decreasing Amplitude (-180 to -188 pA) When we decrease the amplitude from -180 pA (Figure 14) through -184 pA (Figure 13) to -188 pA (Figure 12), we observe a gradual but subtle reduction in neuronal activity. The initial state at -180 pA has sparse firing patterns in both STN and GPe populations. As the stimulation amplitude increases negatively to -184 pA and subsequently to -188 pA, there is a further decrease in firing density. However, the firing pattern maintains its characteristics, suggesting that amplitudes beyond -180 pA yield only incremental effects in neural activity suppression.

Increasing Amplitude (-180 to -174 pA) Increasing the amplitude has more pronounced effects on neural behavior. Increasing to -178 pA (Figure 15) results in the emergence of coordinated firing patterns, particularly around 1300 ms, where both the STN and GPe populations display synchronized activity. An additional increase to -174 pA (Figure 16) amplifies this effect, manifesting itself in two distinct periods of highly synchronized firing (approximately at 1150 and 1300 ms). This progression suggests that increasing the DBS amplitude above -180 pA compromises the suppression of pathological synchronized firing patterns in Parkinson's disease.

Conclusion These observations indicate that -180 pA potentially represents a threshold value, where lower amplitudes produce diminishing returns in neural suppression, while higher amplitudes rapidly lead to the reemergence of synchronized firing patterns. The relationship between the amplitude of DBS and the neuronal firing patterns underscores the delicate balance required in the treatment of PD symptoms by DBS.

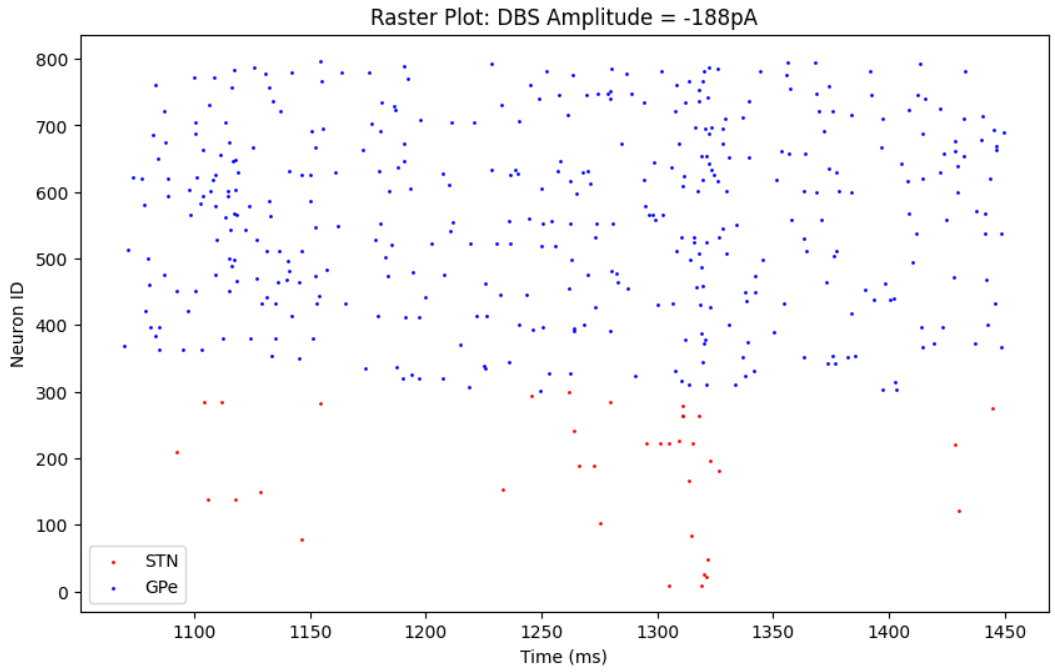

Figure 12: Raster Plot of STN and GPe in Parkinson + DBS state with DBS amplitude of -188pA

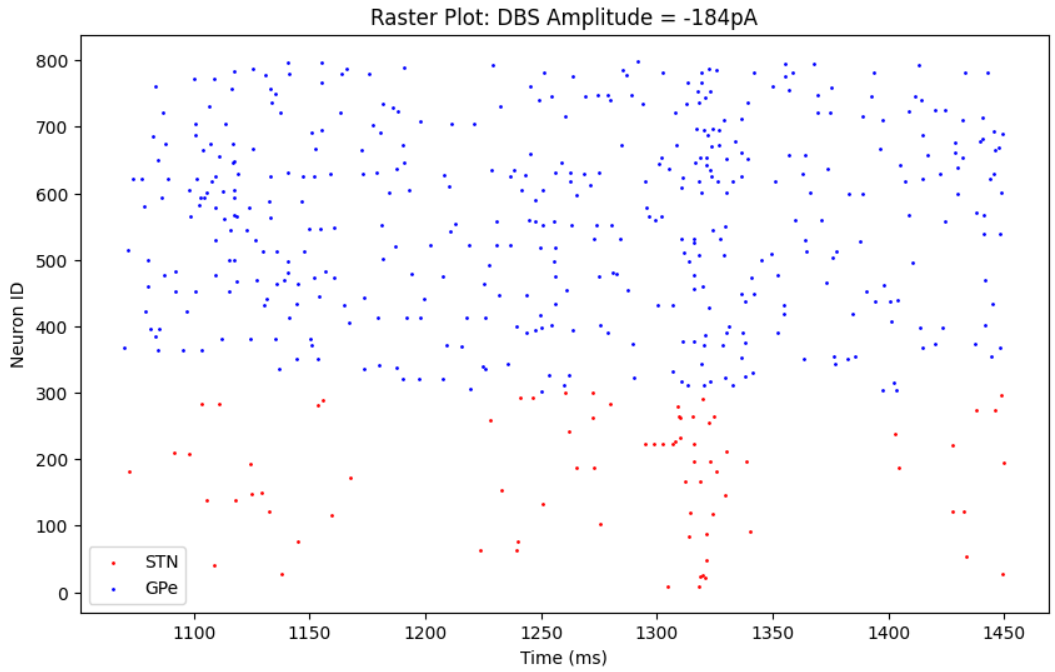

Figure 13: Raster Plot of STN and GPe in Parkinson + DBS state with DBS amplitude of -184pA

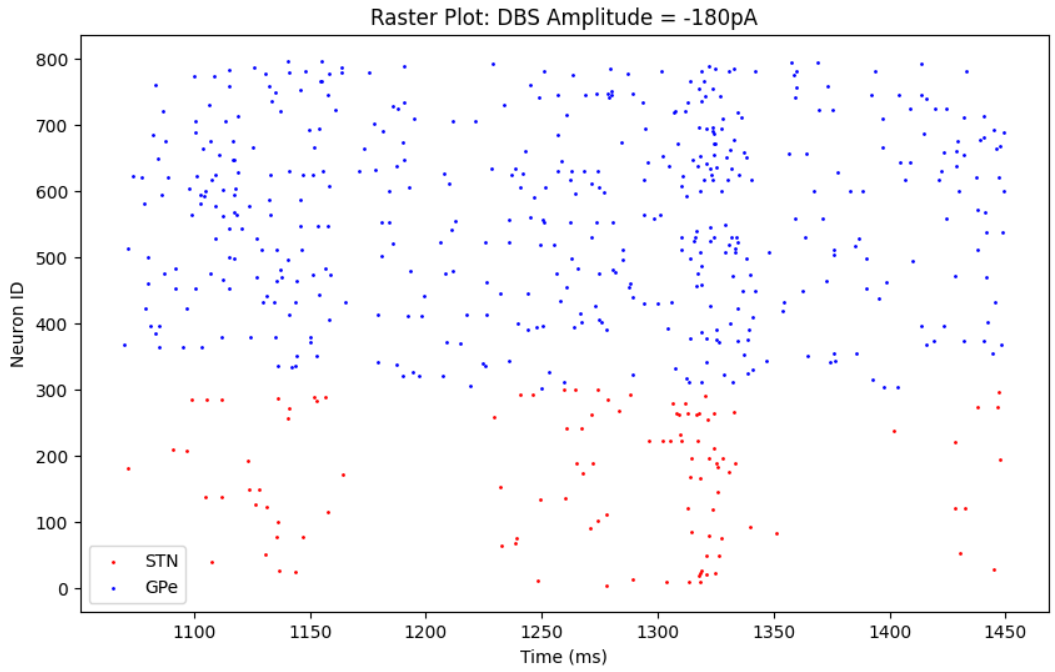

Figure 14: Raster Plot of STN and GPe in Parkinson + DBS state with DBS amplitude of -180pA

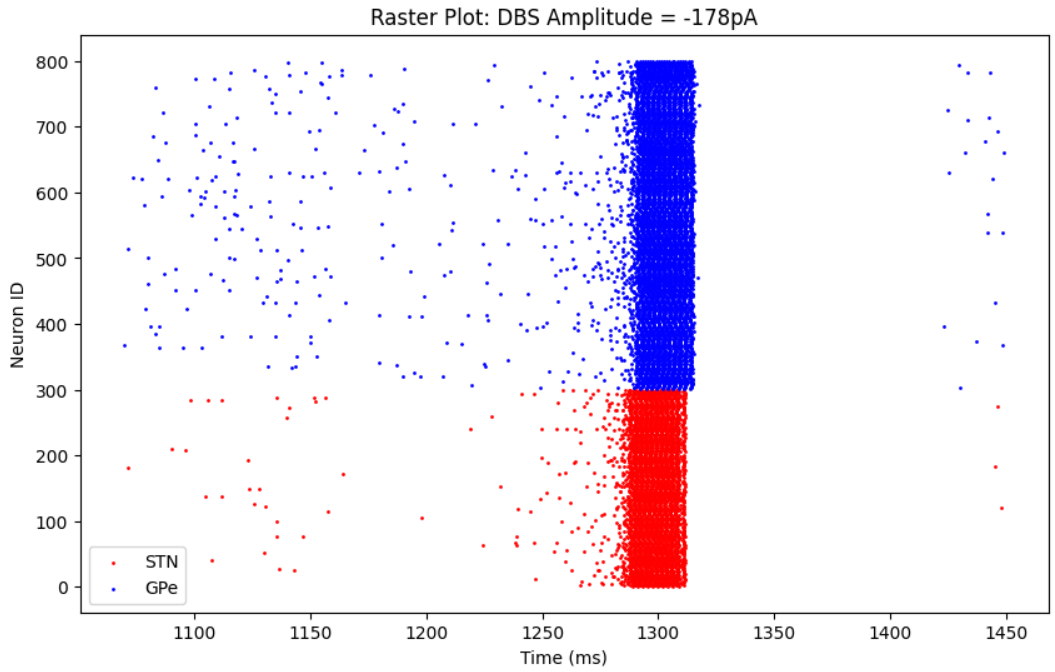

Figure 15: Raster Plot of STN and GPe in Parkinson + DBS state with DBS amplitude of -178pA

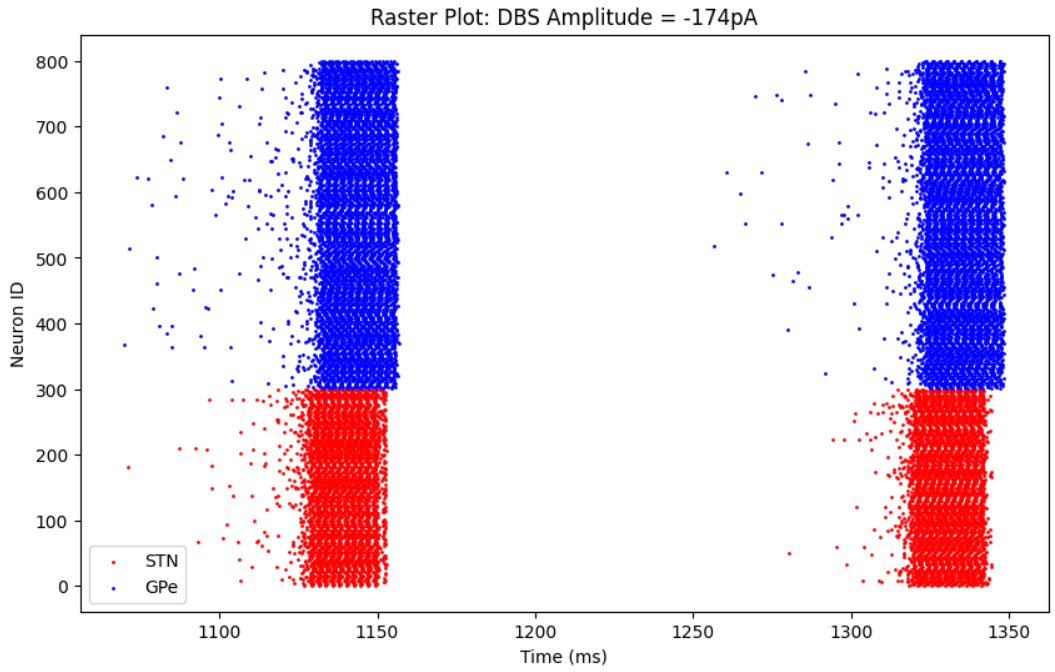

Figure 16: Raster Plot of STN and GPe in Parkinson + DBS state with DBS amplitude of -174pA

References

[KCRA11] Arvind Kumar, Stefano Cardanobile, Stefan Rotter, and Ad Aertsen. The role of inhibition in generating and controlling parkinson's disease oscillations in the basal ganglia. *Frontiers in Systems Neuroscience*, 5, 2011.