# Closed Loop Deep Brain Stimulation for Parkinson's disease with Frequency Modulation

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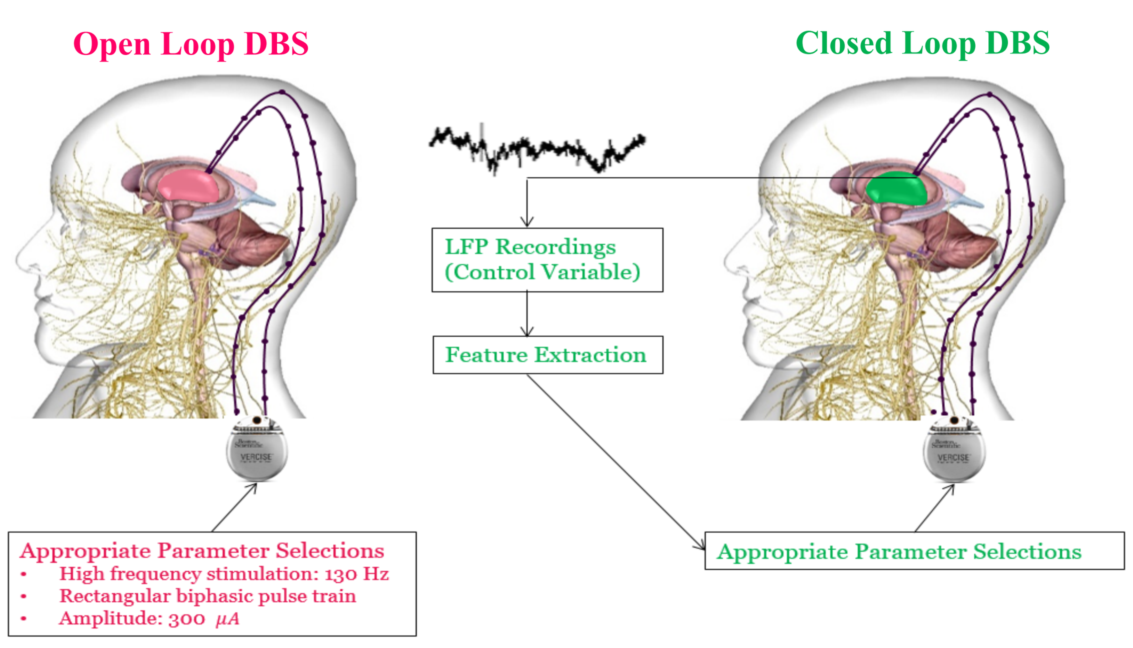
**Abstract**- Neural oscillations within the Basal Ganglia (BG) circuitry are associated with Parkinson's Disease (PD) and are observable through the Local Field Potential (LFP) of the Subthalamic Nucleus (STN) or Globus Pallidus externa (GPe) neurons. LFP amplitude modulation in a delayed feedback protocol for Deep Brain Stimulation (DBS) is shown to destabilize the complex intermittent synchronous states. However, traditional High Frequency Stimulations (HFS) often intensify the synchronization of highly fluctuating neurons, are less efficient in activating all neurons in large scale networks and consume more battery of the DBS device. Here, we investigate the partially synchronous dynamics of a STN-GPe coupling network to examine the effect of frequency adjustment in the stimulation signal. The frequency of the stimulation signal is adjusted according to the nonlinear delayed feedback LFP of the STN population. Frequency adjustment protocol with a fixed stimulation amplitude is shown to increase the desynchronization efficiency and neuronal activation by 25% and 16.2%, respectively, while reducing the energy consumption by 31.5% compared to amplitude modulation methods for stimulation of large networks (1000 neurons).

**DBS Therapy**- DBS has shown to improve various symptoms associated with PD by desynchronizing LFP oscillations of STN neurons. The main approaches to improve the desynchronization process and therapeutic efficiency of DBS are shown below. Developing an efficient stimulation protocol requires simultaneously considering these approaches based on the patient 's symptoms. [1].

**Paradigms of Stimulation:**

- *Open-loop Stimulation* where often a HFS train of stimulation pulses is applied to the target region regardless of its effect on desynchronization.
- *Closed-loop Stimulation* in which the parameters of the stimulation pulse is modulated according to the level of synchronization through a feedback loop.
- *On-demand Stimulation* where the DBS pulse is only applied at some specific predefined time periods.




**Proposed Method**- Here, we used a modified STN-GPe oscillator model to investigate our proposed delayed feedback frequency adjustment protocol. The parameters of the STN-GPe oscillator model are designed to reflect the experimental recordings [2].

**STN-GPe Oscillatory Model**

$$C_m \frac{dV}{dt} = -I_L - I_{Na} - I_{Ca} - I_K - I_T - I_{ahp} - I_{Syn} - I_{app} - I_{DBS}$$

$$I_L = g_L(V - V_L), \quad I_{Na} = g_{Na} m_\infty^3(V) h (V - V_{Na})$$

$$I_K = g_K n^4 (V - V_K), \quad I_{Ca} = g_{Ca} s_\infty^2(V)(V - V_{Ca})$$

$$I_{T/STN} = g_T a_\infty^3(V) b_\infty^2(r)(V - V_{Ca})$$

$$I_{T/GPe} = g_T a_\infty^3(V) r (V - V_{Ca})$$

$$I_{ahp} = g_{ahp}(V - V_K)(Ca/Ca + K_I), \quad \epsilon \frac{dCa}{dt} = --I_{Ca} - I_K - K_{ca}Ca$$

**LFP Measurement**

$$LFP(t) = \frac{1}{N} \sum_{n=1}^{N} s_n(t)$$

**Filtered and Non Linearly Delayed LFP Signal**

$$\ddot{x} + \alpha \dot{x} + \omega^2 x = \alpha LFP(t)$$

**Frequency Modulation of the DBS Signal**

$$Z_c(t) = k\dot{x}(t-\tau)\left(\dot{x}^2(t) - \dot{x}^2(t - T_q)\right) + 2k\dot{x}(t)\dot{x}(t - T_q)\dot{x}(t - T_q - \tau)$$

$$I_{DBS}(t) = P_{bi}(|\widehat{Z_c(t)}|t)$$

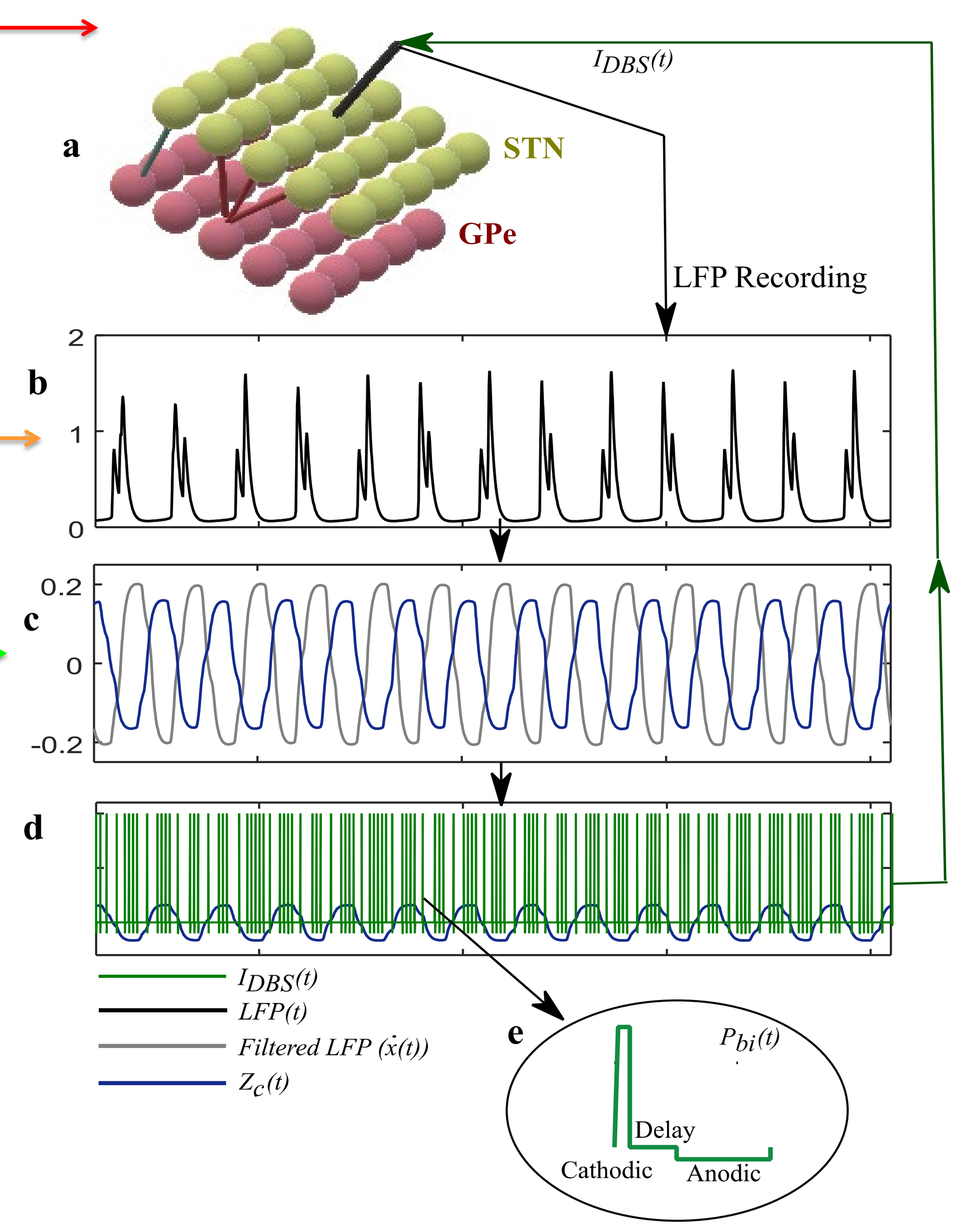



**Fig. 1. The schematic of the delayed feedback frequency adjustment protocol**

**Results**- We have measured the synchrony Index (SI) and Energy Consumed (EC) for the proposed frequency adjustment protocol. Therefore, we were able to compare our method with widely used delayed feedback amplitude modulation protocols [3]. Additionally, we have tested the effect of DBS Interphase delay length on the desynchronization efficiency of our method. Adapted signals in a delayed feedback method can reduce the side effect of tissue damage, enhance the desynchronization performance and increase the battery life. The FAS protocol has shown to be more efficient in the suppression of the STN oscillations along with generating a mixture of firing responses, which has been associated with the efficiency of DBS

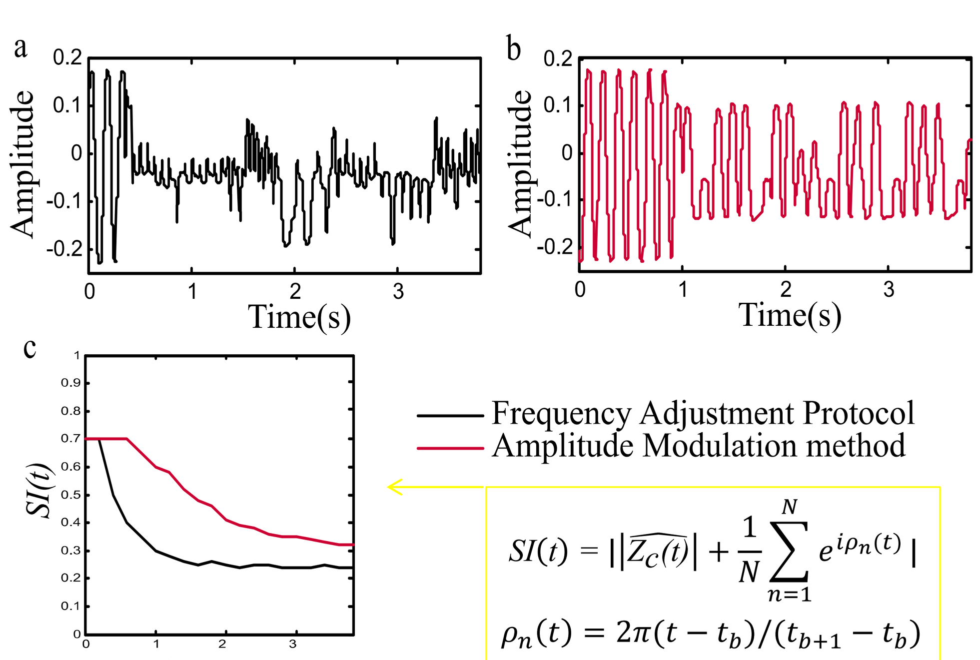



**Fig. 2. Desynchronization results of delayed feedback frequency adjustment (a) and amplitude modulation (b) protocols. $I_{DBS}$ is applied 0.2 s after simulation and while frequency adjustment method rapidly starts to desynchronize, the amplitude modulation protocol seems to begin the desynchronization after almost 1 s. The slope of $SI(t)$ in (c) shows that frequency adjustment is quicker in desynchronizing the oscillation. The optimum $SI(t)$ for our proposed method was 0.24 compared to 0.32 for amplitude modulation [3].**

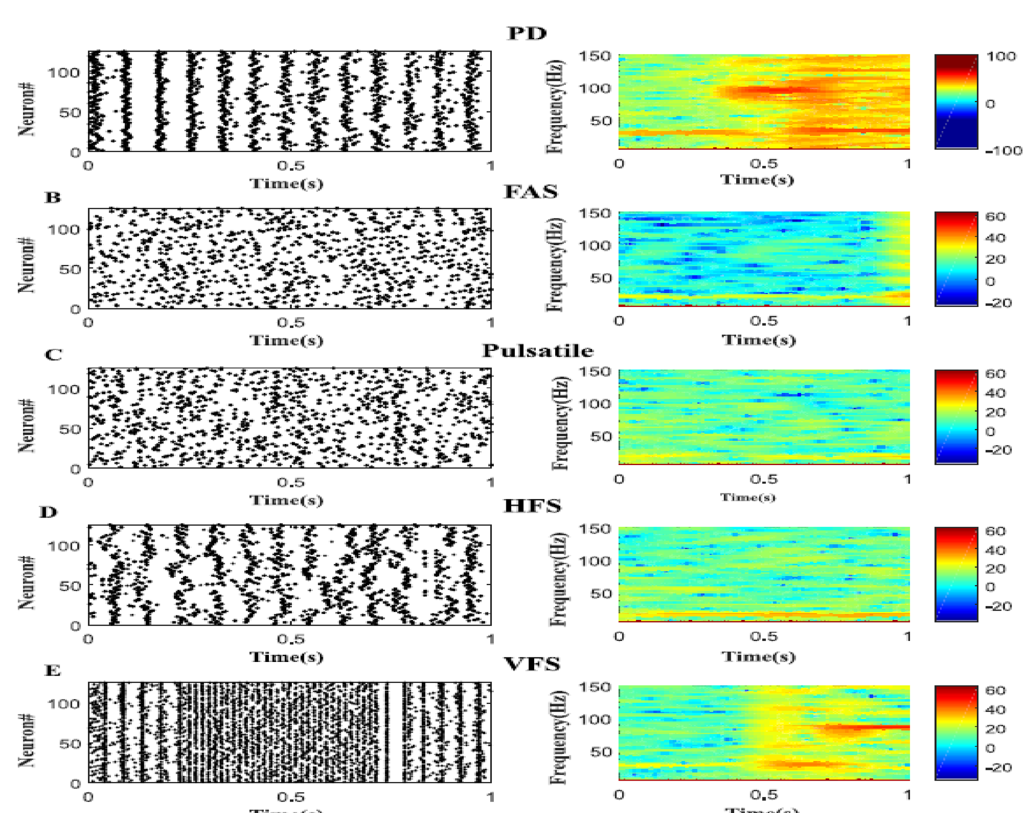



**Fig. 3. Power density of the filtered LFP signal is shown through spectrograms for PD condition, frequency adjustment protocol (FAS), Pulsatile, HFS and VFS methods. Oscillations at low frequencies seen in PD (a) are diminished by both protocols FAS and Pulsatile. However, desynchronization by the frequency adjustment method is more prominent.**

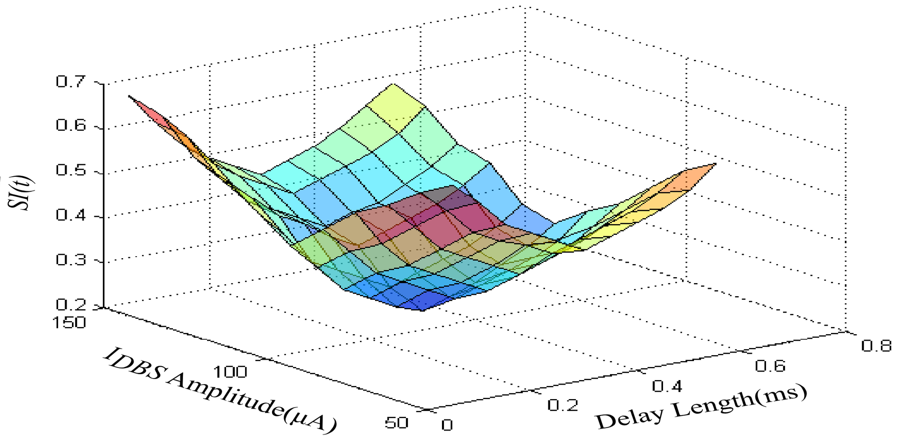



**Fig. 4. Average Synchrony Index based on the delay length and required stimulation amplitude. Too low or too high amplitudes of $I_{DBS}$ with any delay length does not show great desynchronization. However, minimum $\overline{SI(t)}$ of 0.24 was obtained by optimum delay length of 0.3 ms and $I_{DBS}$ amplitude of 100 $\mu A$.**

**Table I. Population Size Effect on *EC* and Neuronal Activation. The frequency adjustment method lowers the *EC* significantly compared to the amplitude modulation methods.**

| Stimulation Protocol | Performance Metrics | Population Size 25 | 100 | 500 | 1000 |
|---|---|---|---|---|---|
| Proposed Frequency Adjustment | EC($nJ$) | 61 | 102 | 231 | 407 |
| | % of activated neurons | 99 | 97 | 95.8 | 94.4 |
| Amplitude Modulation [4],[6] | EC($nJ$) | 74 | 151 | 302 | 595 |
| | % of activated neurons | 96 | 91 | 86.2 | 81.2 |

## References

[1] T. J. Foutz and C. C. Mcintyre, "Evaluation of novel stimulus waveforms for deep brain stimulation," *Journal of Neural Engineering*, vol. 7, no. 6, pp. 066008, 2010.
[2] D. Terman, J. E. Rubin, A. C. Yew, C. J. Wilson, "Activity patterns in a model for the subthalamopallidal network of the basal ganglia", *J. Neurosci.*, vol. 22, no. 7, pp. 2963-2976, Apr. 2002.
[3] O. V. Popovych, B. Lysyansky, and P. A. Tass, "Closed-loop deep brain stimulation by pulsatile delayed feedback with increased gap between pulse phases," *Scientific Reports*, vol. 7, no. 1, 2017.

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