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Advancements in Mathematical Approaches for Deciphering Deep Brain Stimulation: A Systematic Review

Luan Yang[1], Jingdong Zhang[1,2], Shijie Zhou[1,4] and Wei Lin[1,2,3,4,*]

[1] *Research Institute of Intelligent Complex Systems, Fudan University, Shanghai 200433, China.*
[2] *School of Mathematical Sciences, Shanghai Center for Mathematical Sciences, and LMNS, Fudan University, Shanghai 200433, China.*
[3] *MOE Frontiers Center for Brain Science, Institutes of Brain Science, Fudan University, Shanghai 200032, China.*
[4] *Shanghai Artificial Intelligence Laboratory, Shanghai 200232, China.*

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Abstract. Deep brain stimulation (DBS) is a prominent therapy for neurodegenerative disorders, particularly advanced Parkinson's disease (PD), offering relief from motor symptoms and lessening dependence on dopaminergic drugs. Yet, theoretically comprehending either DBS mechanisms or PD neurophysiology remains elusive, highlighting the importance of neuron modeling and control theory. Neurological disorders ensues from abnormal synchrony in neural activity, as evidenced by abnormal oscillations in the local field potential (LFP). Complex systems are typically characterized as high-dimensional, necessitating the application of dimensional reduction techniques pinpoint pivotal network tipping points, allowing mathematical models delve into DBS effectiveness in countering synchrony within neuronal ensembles. Although the traditional closed-loop control policies perform well in DBS technique research, computational and energy challenges in controlling large amounts of neurons prompt investigation into event-triggered strategies, subsequently machine learning emerges for navigating intricate neuronal dynamics. We comprehensively review mathematical foundations, dimension reduction approaches, control theory and machine learning methods in DBS, for thoroughly understanding the mechanisms of brain disease and proposing potential applications in the interdisciplinary field of clinical treatment, control, and artificial intelligence.

AMS subject classifications: 00A71, 97P70, 68T05

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*Corresponding author. *Email addresses:* wlin@fudan.edu.cn (W. Lin), sj_zhou@fudan.edu.cn (S. Zhou)

1 Introduction

Increasing evidence suggests that both invasive and non-invasive modalities [14, 27, 36, 57, 109] of brain stimulation present viable therapeutic avenues for addressing neurodegenerative disorders. Deep brain stimulation stands as the gold standard therapy for neurodegenerative disorders, notably advanced Parkinson's disease [4, 128]. The therapeutic efficacy of DBS often yields remarkable outcomes, ameliorating parkinsonian motor symptoms while concurrently reducing reliance on dopaminergic medications [96,97]. Nevertheless, the underlying mechanism through which DBS operates and the complete neurophysiological underpinnings of Parkinson's disease remain incompletely understood. Thus, the realms of neuron modeling and control theory assume substantial significance in deciphering the fundamental mechanisms governing DBS.

The brain, an intricately structured entity, emerges as a complex hierarchical network of interconnected neuronal networks [9, 70, 135]. Neurons assemble into distinct neuronal ensembles, whose interplay engenders larger, more complex assemblies [40,44,112]. While considerable insight has been garnered into the microscopic scale regarding the dynamics of individual neurons, the understanding of macroscopic behavior of such interacting populations of neurons remains extremely limited. It is widely postulated that the functional and information processing capabilities of the brain, spanning from basic perception to the realms of consciousness, emanate from the emergent collective dynamics of these neuronal assemblies. The basal ganglia circuit [20], comprised of pivotal nuclei such as the subthalamic nucleus (STN) and the internal segment of the globus pallidus (GPi), assumes a critical role in the expression of movement disorder. Ongoing endeavors are directed towards addressing dysfunction within this circuit, as a foundational strategy for the design and implementation of DBS.

Symptoms of various neurological disorders, such as PD, are believed to stem from overly synchronous activity within neural ensembles. The severity of clinical impairment in PD is widely recognized to correspond with an increase in the beta (13-15 Hz) oscillations in the local field potential (LFP) and in the activity of individual neurons within the basal ganglia circuit [102]. Simultaneously, abnormal synchrony patterns are associated with malfunction in disorders such as epilepsy and PD [123]. Biological and neural systems can be seen as networks of interacting periodic processes. A computational network model of the STN and the GPi within the indirect pathway of the basal ganglia can be aptly characterized by the Hodgkin-Huxley (HH) model [102].

The human brains comprises a multitude of dynamical units, this naturally and urgently calls for developing efficient methods for properly extracting and quantifying the collective behavior of the complex spatio-temporal dynamics of neuronal oscillators. Although the dimensional reduction for large-scale neural oscillators from the perspective of clinical experiments have been comprehensively investigated [41, 103], theoretical dimensional reduction of the complex mathematical formulation of neuronal dynamics still remains a gap. The basic idea of dimensional reduction is to replace the original high-