

Towards The Functionalization of MIDA: Computational Modeling of Basal Ganglia Indirect Pathway

Vlad Dobrin¹, Ayan Kazi¹, Mahir Sudad¹, Noriana Jakopin¹, Malath Al Matoq¹, Josselyn Marroquin¹, Nevine El-leithy¹, PhD

¹University of Maryland, College Park, Deep Brain Neurotech, Electrical and Computer Engineering Department

Introduction: The Multimodal Imaging-based Detailed Anatomical (MIDA) model of the human head and neck is one of the most detailed computational models of the human brain, with 153 structures and a resolution of 0.5 mm [1]. It has been used for the testing of various brain stimulation devices, such as Deep Brain Stimulation (DBS). DBS is widely used for the treatment of Parkinson's Disease (PD), however, the mechanism behind the intervention is not well understood. Functionalizing MIDA by integrating microscopic neuronal structures and dynamics with the macroscopic anatomy would allow for a deeper analysis of how electromagnetic stimulation would alter the electrophysiology of the brain. This study is focused on inserting biologically realistic neurons from pathways targeted by DBS, such as those in the Globus Pallidus externus (GPe), the neostriatum, and the thalamus, into their appropriate structures using NEURON and Sim4Life. Functionalizing such pathways could possibly lead to understanding the mechanism of Deep Brain Stimulation in treating basal ganglia disorders such as Parkinson's Disease.

Materials and Methods: Computational neuronal models from pathways in the neostriatum [2], globus pallidus externus (GPe) [3], and the thalamus [4] were used. Electrophysiology for GABAergic and Glutamatergic neurons was incorporated into the model. After conversion to hoc format, the neuron models were imported into their respective regions of the MIDA and connected to form the indirect pathway network using Sim4Life's NEURON solver. Simulation of neuron-electromagnetic (EM) interaction was performed using the EM Low-Frequency solver in Sim4Life to assess the effects of electromagnetic fields from stimulation devices.

Results and Discussion: Insertion of a network of four neurons into the basal ganglia structures has been accomplished, as shown in Figure 1 and 2, and the effect of EM stimulation on neural activity was assessed. This attempt is proof of the possibility of computational modeling of the effect of EM fields on neuronal signaling. Each individual cell has near accurate biophysical and electrophysiological properties. While these are preliminary results, it is evident this could be extrapolated for more involved networks of neurons. The current limitation is that the positioning of neurons may not be accurate due to the lack of access to DTI data for the MIDA model. Neuron-EM interaction was simulated using the low-frequency Ohmic Quasi-Static solver of Sim4Life.

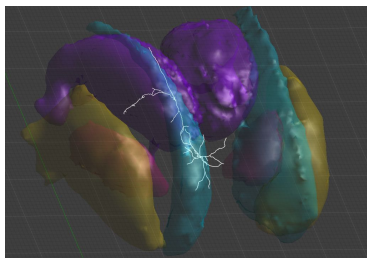


Figure 1: Simulation of the Indirect pathway of the Basal Ganglia in MIDA.



Figure 2: Biologically realistic Indirect pathway network.

Translational Impact: A network of striatal-pallidal-thalamic neurons was constructed using NEURON and Sim4Life. This first step underscores the possibility of elucidating how aberrant microscopic neural activity in pathological conditions can be recalibrated or modulated using EM stimulation. Future incorporation of unmyelinated fibers within basal ganglia mesoscale anatomy, obtained in collaboration with University of Maryland Medical School, will shed more light on the full impact of EM stimulation.

References: [1] Iacono M.I. et al., *PLoS One*, 2015, 10(4):e0124126 [2] McDonald C.G., et al., *Brain Res.*, 2007, 1151:211-8 [3] Johnson M.D. et al., *J Neurophysiol.*, 2008, 100(5):2549-63 [4] Berning M. et al., *Neuron.*, 2015, 87(6):1193-1206

Disclosure Statement: The mention of products, their sources, or their use in connection with material reported herein is not to be construed as either an actual or implied endorsement of such products by Deep Brain Neurotechnologies.

Acknowledgments: Dr. Antonino Cassara, Zurich Med Tech for Sim4Life, Dr. Cha-Min Tang (UMMC), Dr. Leonardo Angelone (FDA).