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Abstract: Deep brain stimulation (DBS) is clinically recognized to treat movement disorders in Parkinson’s disease (PD), but its therapeutic mechanisms remain elusive. One thing is clear though: high frequency periodic DBS (130-180 Hz) is therapeutic, while low frequency DBS (i.e., 100 Hz or less) is not therapeutic and may even worsen symptoms. So, what is so special about high frequency? We address this question by focusing on the effects of DBS on the cortico-basal ganglia-thalamo-cortical (C-BG-T-C) loop in the brain, which provides a major contribution to motor control. Thalamic cells play a pivotal role in performing movements, as they selectively relay motor-related information back to cortex under the control of modulatory signals from the basal ganglia (BG). PD affects the BG signals and this may ultimately impair the thalamic relay function. Through single unit recordings from healthy and PD primates, and a detailed computational model of the C-BG-T-C loop under PD conditions, we show that DBS pulses evoke multiple inputs that propagate through the C-BG-T-C loop both orthodromically (i.e., forward) and antidromically (i.e., backward) and fade away within a few milliseconds thus having little effects on the BG signals. However, if the latency between consecutive DBS pulses is small (DBS is high frequency) and constant over time (DBS is periodic), then orthodromic and antidromic effects can positively overlap (reinforcement) within the loop and result into a strong, long-lasting perturbation that ultimately drives the BG signals and restores a more normal activity in the thalamic neurons. This suggests that (i) DBS globally impacts the entire C-BG-T-C loop, (ii) the therapeutic merit of clinically-used DBS settings depends on the anatomical properties of the loop, (iii) DBS in different individuals may require slightly different settings, and (iv) the therapeutic effects may be preserved even though the entry point of the DBS input is moved along the C-BG-T-C loop, which are all consistent with the clinical practice.

Bio: Sabato Santaniello is Assistant Professor in the Biomedical Engineering Department, University of Connecticut. He received undergraduate and master degree with honors in Computer Engineering from University of Naples (Italy), and Ph.D. degree in Systems and Control Engineering from University of Sannio (Italy). He was postdoctoral fellow (2009-2013) and research scientist (2013-2014) in Neural Engineering and Computational Neuroscience in the Institute for Computational Medicine, Johns Hopkins University. His research interests include modeling, estimation, and control of neural systems, biomedical signal processing, and neural stimulation, with applications to movement disorders and epilepsy.