## Responsive neuromodulation for a dynamic and distributed mental state

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Selecting and acting on salient features in a complex, dynamic environment is a critical skill of all animals, including humans, in order to survive and thrive. The ability to both accumulate sufficient evidence to accurately estimate the probability of success and then appropriately balance the reward and risks associated with the decision are key features of successful action selection and actuation, and must occur rapidly, within a changing environment. Although the human nervous system operates on the millisecond timescale, current neuromodulation treatments of nearly all neurological insults and injuries are titrated over weeks to months. Electrophysiological interrogation of the nervous system is today limited by our inability to probe the brain with high spatial and temporal precision, and across large spatial and temporal scales. For example, deep-brain stimulation (DBS) treatment for Parkinson's disease, essential tremor, and obsessive-compulsive disorders is set and adjusted through infrequent visits by the patient to a trained physician. Likewise, epidural electrical stimulation of the spinal cord (SCS) for treatment of pain is titrated via infrequent visits to clinics.

A more responsive form of DBS and SCS could offer improved therapy by sensing changes in neural activity, or biomarkers of disease, and then adjusting the amplitude, frequency, or pattern of stimulation in response. Such a system should ideally be able to detect both the onset of pathological network activity and act within a meaningful timeframe to provide effective titration of treatment. In this presentation, I will discuss prior work on developing a closed-loop spinal cord neuromodulation platform for the recovery of lower limb function after spinal cord injury, and the development of a fully-implanted brain-spinal interface. I will further discuss our more recent efforts to migrate such concepts to the treatment of severe obsessive-compulsive disorder in humans. Finally, I will discuss a technological platform we are pursuing that may provide observation of, and interaction with, neurons at the cellular level across many areas of the brain simultaneously, paving the way for new neuroscience discoveries and therapeutic opportunities.