Medtronic Summit RC + S

Medtronic Summit RC + S experimental prototype DBS device has the ability to both deliver stimulation to and record electrical signal directly from the brain.

It attempts to bring the capability and flexibility of a microprocessor to a prosthesis embedded within the nervous system.

Chronically implantable, closed-loop neuromodulation devices with concurrent sensing and stimulation hold promise for better understanding the nervous system and improving therapies for neurological disease. Concurrent sensing and stimulation are needed to maximize usable neural data, minimize time delays for closed-loop actuation, and investigate the instantaneous response to stimulation. Current systems lack concurrent sensing and stimulation primarily because of stimulation interference to neural signals of interest. While careful design of high-performance amplifiers has proved useful in reducing disturbances in the system, stimulation continues to contaminate neural sensing due to biological effects like tissue-electrode impedance mismatch and constraints on stimulation parameters needed to deliver therapy. In this work, we describe systematic methods to mitigate the effect of stimulation through a combination of sensing hardware, stimulation parameter selection, and classification algorithms that counter residual stimulation disturbances. To validate these methods we implemented and tested a completely implantable system for over one year in a large animal model of epilepsy. The system proved capable of measuring and detecting seizure activity in the hippocampus both during and after stimulation. Furthermore, we demonstrate an embedded algorithm that actuates neural modulation in response to seizure detection during stimulation, validating the capability to detect bioelectrical markers in the presence of therapy and titrate it appropriately. The capability to detect neural states in the presence of stimulation and optimally titrate therapy is a key innovation required for generalizing closed-loop neural systems for multiple disease states [1)]

Some devices, including the Medtronic PC+S and NeuroPace RNS store data onboard the implanted hardware that can be transferred to an external computer after data collection. Other devices, including the Medtronic Summit RC+S [2)] , the Medtronic Percept PC and the CereplexW enable real-time streaming of neural data to external devices meters away. These devices can be used to collect chronic neural recordings in natural environments, enabling the identification and development of personalized biomarkers and therapies.

Stanslaski et al. describe the updated system architecture for the Summit RC+S system, the five custom integrated circuits required for bi-directional neural interfacing, the supporting firmware/software ecosystem, and the verification and validation activities to prepare for human implantation. Emphasis is placed on design changes motivated by experience with the CE-marked Activa PC+S research tool; specifically, enhancement of sense-stim performance for improved bi-directional communication to the nervous system, implementation of rechargeable technology to extend device longevity and application of MICS-band telemetry for algorithm development and data management. The technology was validated in a chronic treatment paradigm for canines with

naturally occurring epilepsy, including free ambulation in the home environment, which represents a typical use case for future human protocols [3)]

Mivalt et al. tracked brain impedance, sleep-wake behavioral state, and epileptiform activity in five people with epilepsy living in their natural environment using an investigational device. The study identified impedance oscillations that span hours to weeks in the amygdala, hippocampus, and anterior nucleus thalamus. The impedance in these limbic brain regions exhibits multiscale cycles with ultradian (~ 1.5 - 1.7 hr.), circadian (~ 21.6 - 26.4 hr.), and infradian (~20 - 33 days) periods. The ultradian and circadian period cycles are driven by sleep-wake state transitions between wakefulness, non-rapid-eye-movement (NREM) sleep, and rapid-eye-movement (REM) sleep. Limbic brain tissue impedance reaches a minimum value in NREM sleep, intermediate values in REM sleep, and rises through the day during wakefulness reaching a maximum in the early evening before sleep onset. Infradian (~20 - 33 days) impedance cycles were not associated with a distinct behavioral correlate. Brain tissue impedance is known to strongly depend on the ECS volume, and the findings reported here are consistent with sleep-wake dependent ECS volume changes recently observed in the rodent cortex related to the brain glymphatic system. We hypothesize that human limbic brain ECS changes during sleep-wake state transitions underlie the observed multiscale impedance cycles. Impedance is a simple electrophysiological biomarker that could prove useful for tracking ECS dynamics in human health, disease, and therapy.Significance StatementThe electrical impedance in limbic brain structures (amygdala, hippocampus, anterior nucleus thalamus) is shown to exhibit oscillations over multiple time scales. We observe that impedance oscillations with ultradian and circadian periodicities are associated with transitions between wakefulness, non-rapid-eye-movement (NREM) and rapid-eye-movement (REM) sleep states. There are also impedance oscillations spanning multiple weeks that do not have a clear behavioral correlate and whose origin remains unclear. These multiscale impedance oscillations will impact extracellular ionic currents that give rise to local field potentials, ephaptic coupling, and the tissue activated by electrical brain stimulation. The approach for measuring tissue impedance using perturbational electrical currents is an established engineering technique that may be useful for tracking extracellular space (ECS) volume [4)]

A study aims to identify changes in local field potentials (LFPs), specific electrical signals that are thought to represent how the brain communicates information from one region to another, to see how this relates to DBS parameter settings and patient depressive symptomatology. The goal of this study is to study LFPs before and during active DBS stimulation to identify changes that correlate with the antidepressant effects of SCC DBS.

The study team will recruit 10 patients with TRD and implant them with the Summit RC+S system. Participants will be asked to complete short questionnaires and collect LFP data twice daily for the first year of the study, as well as have weekly in-person research procedures and assessments with the study team for up to one year. These include meetings with the study psychiatrist, and psychologist, symptom ratings, and periodic EEGs (scalp brainwave recordings). A brief discontinuation experiment will be conducted after 6 months of stimulation, in which the device will be turned off and patterns of LFP changes will be recorded. The entire study is expected to last about 10 years, which is the expected life of the battery that powers the device. All participants are required to live in the New York metropolitan area for the first two years of the study
https://classic.clinicaltrials.gov/ct2/show/NCT04106466

Alarie et al. characterized artifact sources in recordings from a bidirectional DBS platform, the Medtronic Summit RC + S, with the goal of optimizing recording configurations to improve signal-to-noise ratio (SNR). Data were collected from three subjects in a clinical trial of DBS for obsessive-compulsive disorder. Stimulation was provided bilaterally to the ventral capsule/ventral striatum (VC/VS) using two independent implantable neurostimulators. They first manipulated DBS amplitude within safe limits (2-5.3 mA) to characterize the impact of stimulation artifacts on neural recordings. We found that high amplitude stimulation produces slew overflow, defined as exceeding the rate of change that the analog-to-digital converter can accurately measure. Overflow led to expanded spectral distortion of the stimulation artifact, with a six-fold increase in the bandwidth of the 150.6 Hz stimulation artifact from 147-153 to 140-180 Hz. By increasing sense blank values during high amplitude stimulation, we reduced overflow by as much as 30% and improved artifact distortion, reducing the bandwidth from 140-180 Hz artifact to 147-153 Hz. They also identified artifacts that shifted in frequency through modulation of telemetry parameters. We found that telemetry ratio changes led to predictable shifts in the center frequencies of the associated artifacts, allowing us to proactively shift the artifacts outside of our frequency range of interest. Overall, the artifact characterization methods and results described here enable increased data interpretability and unconstrained biomarker exploration using data collected from bidirectional DBS device [5].

With wireless transmission come potential failures in data transmission, and not all available devices correctly account for missing data or provide precise timing for when data losses occur. Our inability to precisely reconstruct time-domain neural signals makes it difficult to apply subsequent neural signal processing techniques and analyses. Here, our goal was to accurately reconstruct time-domain neural signals impacted by data loss during wireless transmission. Toward this end, we developed a method termed Periodic Estimation of Lost Packets (PELP). PELP leverages the highly periodic nature of stimulation artifacts to precisely determine when data losses occur. Using simulated stimulation waveforms added to human EEG data, we show that PELP is robust to a range of stimulation waveforms and noise characteristics. Then, we applied PELP to local field potential (LFP) recordings collected using an implantable, bidirectional DBS platform operating at various telemetry bandwidths. By effectively accounting for the timing of missing data, PELP enables the analysis of neural time series data collected via wireless transmission prerequisite for better understanding the brain-behavior relationships underlying neurological and psychiatric disorders [6].

Automated Artifact Injection could potentially be a method of introducing controlled disturbances or external signals into the brain modulation devices to study their effects on neural behavior [7]

[1]
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