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Closed-Loop DBS with Movement Intention

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Abstract— **In this paper we present a prototype proof-of-concept for a closed-loop deep brain stimulation system for patients with essential tremor. This system makes use of sensed movement intentions via EEG to determine when stimulation is required and automatically enables stimulation only when needed. We demonstrate this system using a healthy subject and a benchtop experimental prototype. By limiting stimulation to only when it is therapeutically required, implanted neurostimulators can be more power efficient and potentially limit the period where patients experience side-effects to only the time when therapy is needed.**

Keywords*: *Deep Brain Stimulation, Implantable Systems, Neurological disorders

I. Introduction

Neurological movement disorders are among some of the most debilitating diseases that have a dramatic effect on the quality of life of patients. While medication can be used for treatment for a time, often as the disease progresses these treatments become ineffective at suppressing symptoms. Deep brain stimulation (DBS) has been shown to treat even medication-resistant neurological movement disorders [10] including Parkinson's disease and essential tremor [6].

A DBS system consists of implanted electrodes in the brain connected to an implanted neurostimulator in the chest through a wire routed under the skin. A variety of neurological disorders can be treated depending on where the electrodes are implanted. This includes movement disorder symptoms such as tremor, but DBS has also been shown to potentially treat other disorders such as chronic pain [13].

However, there is still considerable room for improvement in deep brain stimulation for movement disorders. Increasing power efficiency extends the lifetime of the implanted devices and would correspond to fewer battery-replacement surgeries. Additionally, stimulation of these deep-brain structures can cause a variety of side-effects that can include tingling, trouble speaking, or a multitude of other possible symptoms [9]. Current systems are "open-loop" in that no measurement of tremor or treatment effectiveness is used to modify the stimulation levels [6]. These parameters are set by the clinician, and run without changes until the next clinical visit. While some patents can make minor adjustments to their stimulation settings, commonly used to turn the device off while sleeping, these require manual intervention which can be difficult for patients with movement disorders.

A potential solution to increasing power efficiency and lowering stimulation side-effects is to be more selective with how and when stimulation is delivered [6]. By incorporating sensors and communication channels to the implanted device, a "closed-loop" system could be developed where stimulation is dynamically adjusted to the immediate needs of a patient.

For this paper, we will narrow our focus to kinetic essential tremor. While other work has used the sensing of physical manifestations of tremor in the limb to perform closed-loop DBS [19], we propose to use cognitive signals not directly associated with tremor to perform this same closed-loop functionality. A patient with kinetic essential tremor experiences uncontrollable rhythmic motions whenever the limb is volitionally moved [3]. By sensing when a patient intends to move the limb, a system could predict when a patient needs stimulation without directly sensing experienced tremor.

There are several important design requirements of such a system to consider while designing experimental platforms. The detection or prediction of tremor must be done in such a way as to reduce the burden on the patient and needs to be specifically tuned to the tremoring region of the body. The system also needs the ability to respond with stimulation within strict time limits. This requires real-time telemetry links between computational elements and implantable hardware. Finally, appropriate stimulation patterns need to be utilized that will effectively treat the incipient tremor.

In this paper, we demonstrate a prototype system where we use electroencephalography (EEG) as a minimally invasive method to prototype the use of sensed movement indicators to trigger electrical stimulation from a DBS implant. While this is a benchtop experiment using a healthy subject, this system functions in real-time using implantable hardware. This work represents an important proof-of-concept for developing closed-loop DBS systems that utilize movement intention to trigger stimulation.

II. Background

Essential tremor (ET) is an extremely common neurological movement disorder and is estimated at affecting more that 5 million people in the United States alone [8]. It primarily effects the elderly and the estimated incidence of the disease is at least 13% for those over 60 [11]. One of the most common forms of tremor is kinetic tremor in a single limb [3]. A patient with kinetic tremor experiences uncontrolled tremors whenever they attempt to volitionally move the effected limb. ET is a progressive disorder without a cure and over time the tremor can slowly grow in amplitude and spread to other parts of the body [5].

While pharmacological medicine can suppress symptoms, it is estimated that pharmaceutical treatment will be eventually ineffective for between 25-55% of essential tremor patients [10]. There are two surgical methods that are used for these cases of otherwise untreatable tremor, both of which target the ventral intermediate (VIM) nucleus of the thalamus. The first of these surgical methods is a thalamotomy: a surgical lesioning of the VIM thalamic nucleus. However, the removal of tissue from the brain is permanent and there is a significant incidence of long-term side-effects associated with the procedure [16]. The second surgical therapy is thalamic stimulation using a chronically-implanted deep brain neurostimulator. While a more complicated procedure, DBS has become the more attractive surgical treatment due to the reduced number of adverse events and because the stimulator settings can be periodically tuned and modified after implantation by clinicians [5] [10]. Similar to how the exact mechanisms and causes of essential tremor are poorly understood, the mechanism by which DBS treats tremor is also unclear. Regardless, DBS has a dramatic improvement in tremor symptoms for many essential tremor patients [2].

Electroencephalography (EEG) is the measuring of the electrical signals on the surface of the scalp generated by the brain. It is a well established fact that it is possible to predict periods of limb movement by using EEG [14]. This is accomplished by monitoring the area directly over the area of the motor cortex where limb movement processing occurs. When a patient moves their limb, there is a general desynchronization in the contralateral (opposite side of the brain from the limb) motor cortex [18]. A drop in alpha and beta band power can be measured as the movement-processing neurons begin firing more stochastically as movement is executed. Interestingly, imagined movement also has this same desynchronization effect [15].

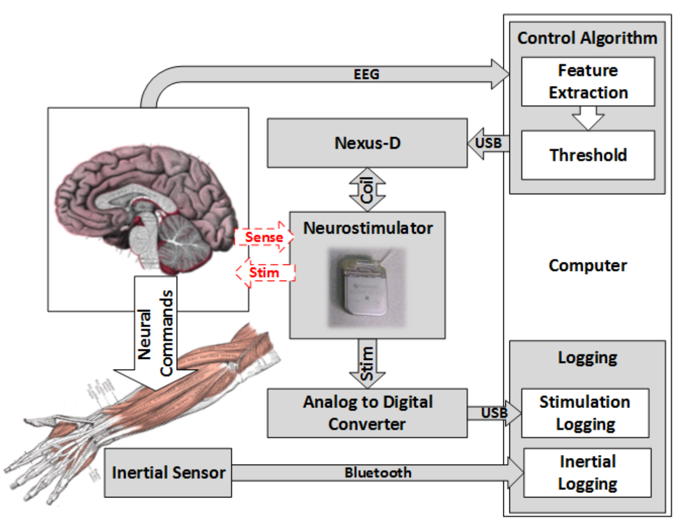

Fig. 1. **Experimental Setup:** A system block diagram showing the connections between various components for this experiment. Grayed blocks are used in this proof-of-concept setup. Dashed lines indicate the ability for a future implanted system to perform sensing and stimulation directly without need of worn EEG.

Even while experiencing tremor, ET patients exhibit this motor cortex desynchronization during movement [4]. Since a patient who suffers from kinetic tremor only experiences symptoms when they perform volitional movements, it is feasible to use intentions measured through EEG as a prediction for when deep brain stimulation should be triggered.

III. Methods

A block diagram of our experimental prototype is illustrated in Figure 1. EEG data is being collected from a healthy subject while wearing an inertial motion tracker on the right arm. This inertial data is logged and for allows precise monitoring of when the patient is moving their limb. The EEG data is processed in order to make control decisions as to when the stimulation should be turned on or off. These control decisions are used to update the stimulation parameters of a Medtronic Activa PC+S with the Nexus-D communication link (described below). Finally the output stimulation leads are connected to an USB analog-to-digital converter to log the final stimulation waveform. This extensive system logging allows for post-experimental analysis of overall performance.

To sense movement intention with EEG, we are using the gTec Mobilab battery-powered bioamplifier. The device samples up to eight EEG channels at 256Hz to be recorded. By making use of the code provided with this device, the data can be accessed in real-time through a desktop computer for our control algorithm. To sense motor intention of the right arm and hand, we place electrodes on top of the limb's primary motor cortex as shown in Figure 2. In order to reduce common-mode noise, a ring of electrodes is placed around the center electrode located at C3. The ring electrodes are then weighted by 1/4 and subtracted from the center electrode. Using the signals of the surrounding neighboring electrodes in this manner is a method for spatial filtering to increase EEG performance [12]. Due to the noisy nature of EEG, the subject kept the rest of their body at rest and their eyes closed and still for the duration of the experiment.

To process the data, we preform a 1024-point FFT every 0.2 seconds. The spectral power is estimated by summing

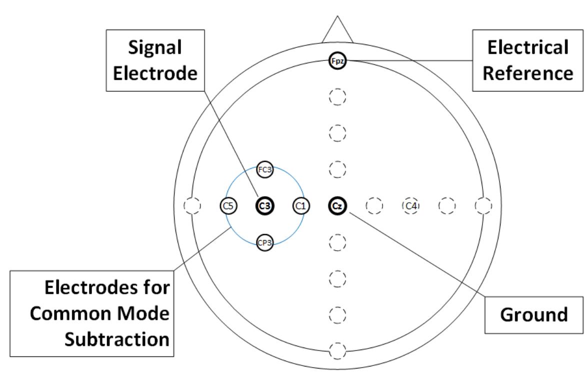

Fig. 2. **EEG Electrode Positions:** Map of EEG electrodes used. Ground was placed at Cz in the middle of the head. Electrical reference is on the forehead at Fpz. Sensing of motor intention was done with an electrode placed at C3 with a ring of electrodes surrounding it for common-mode subtraction.

the FFT output bins corresponding to the 14-25Hz band. When the bandpower falls below a calibrated threshold, the stimulator is enabled and the electrical stimulation is ramped up to a therapeutic level. After the band power recovers and remains above the threshold for two seconds, the stimulation is turned back off.

Once these control decisions have been made, they must be communicated to the implanted device. For this purpose, we have selected to use the Medtronic Nexus-D, which is an investigational communication and control link to implanted Medtronic Activa PC and PC+S neurostimulators. The Activa PC is a FDA approved device already available for clinical use. The Activa PC+S is an investigational implantable device with the additional ability to measure and communicate sensed electrical signals from the implanted electrodes. While this sensing ability will be useful for future work using neural signals to trigger stimulation, for these experiments we are not making use of this functionality. Using the Nexus-D, our host application running on a desktop PC has the ability to tune and adjust the stimulation parameters of the Activa PC/PC+S within bounds set up by a separate clinician programmer. This allows our program to control the timing of when and how stimulation is delivered. We have demonstrated and discussed the prototyping capabilities of this system previously [7].

During the trial run, the subject alternated between periods of rest and movement. The EEG movement intention was used to trigger stimulation in an unimplanted Activa PC+S. Since there is no patient in the loop receiving the stimulation, this is not representative of a truly closed-loop system. Instead it is an example of stimulation signals that would be sent while sensing this particular form of data.

IV. Results

The results of an experimental trial run are shown in Figure 3. The top graph shows the recorded periods of movement using an inertial sensor on the arm being moved. Approximately every ten seconds the subject alternated between periods of limb movement and rest. The middle graph shows the 14-25Hz bandpower estimate from the EEG used to trigger stimulation. As expected, a drop in this bandpower estimate can be used to predict periods when the subject was moving. The tuned threshold used to enable or disable stimulation is shown as the horizontal line in this plot. Finally, the delivered stimulation is shown in the bottom plot. The stimulator is turned on in response to predicted movement and disabled during periods of rest. The average total power used for stimulation for this experiment resulted in approximately 45% of the power used in an open-loop scenario, which is expected given the simulation conditions of a subject equally alternating between movement and rest.

V. Discussion

The use of sensors to determine when and how deep-brain stimulation should be delivered has the potential to

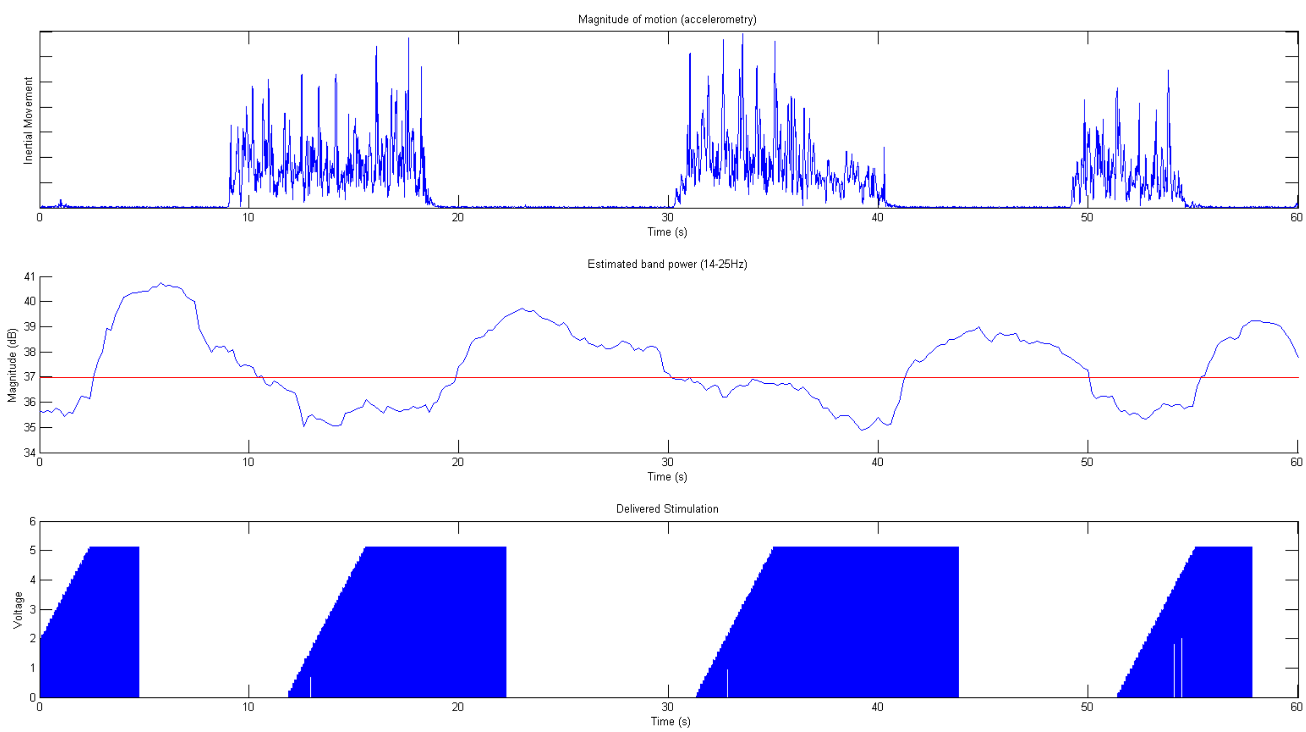

Fig. 3. **EEG Prototype Stimulation Results:** *Top:* Magnitude of actual movement using worn inertial system. *Middle:* EEG 14-25Hz bandpower estimate. Representative of sensed movement intention. Horizontal line indicates threshold for enabling/disabling stimulation. *Bottom:* Recorded stimulation response from the neurostimulator. There is a delay between threshold crossing and stimulation starting due to configurable state-transition latencies. The ramping up of stimulation is standard practice due to the way patients perceive stimulation.

dramatically upon improve current implanted neurostimulation. By selectively stimulating we will be able to extend the battery life of these devices, which will mean fewer battery-replacement surgery over the lifetime of patients. Additionally, for patients that experience side-effects from their stimulation, we will potentially be able to limit these side-effects to only the time when stimulation is necessary.

There of course are limits to using EEG as a signal source for these closed-loop DBS systems. Most patients would not want to wear a EEG cap in their daily life, surface EEG is noisy due to the impedance of the scalp, and variations in electrode positions would mean the system would have to be calibrated too often to be practical. Instead, this system should be considered a proof of concept for using recorded cortical movement intentions. EEG movement-related signals collected on the scalp are similar to electrocorticography (ECoG) movement-related recordings taken from the surface of the brain [18]. The advantage of ECoG is that the recordings from the surface of the brain are far less noisy and much more stable over time.

For future work, we propose the use of implanted cortical electrodes as a signal source to determine movement intentions. These implanted cortical electrodes could be placed upon a specific location of the motor cortex directly and an implanted neurostimulator could make use of sensed desynchronization as a trigger for stimulation to treat kinetic tremor. While there may be concerns of an implanted device's ability to sense cortical movement intentions during stimulation due to electrical noise, detecting cortical signals during DBS stimulation has already been shown to be possible [17]. Additionally, if these intention signals are sensed by the same implanted device, there would be no need to communicate with an external computation device. This would allow further reductions in power by removing the high-power real-time telemetry requirements, and the energy cost of performing this sort of spectral analysis on chip has been shown to consume as little as 5μW per channel [1].

This paper represents a first step towards the use of movement intentions to trigger deep brain stimulation for the suppression of kinetic tremor. The prototype system we have demonstrated fulfilled our design requirements for a closed-loop DBS system by being able to effectively identify periods of movement using scalp EEG and take action using an implantable neurostimulator. This EEG system was demonstrated in order to prepare for an eventual fully embedded system making use of cortical signals. Closed-loop DBS systems have the potential to improve treatment for a large number of essential tremor patients and may be generalizable to other disorders as we identify other symptom-specific neural predictors.

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