A CLOSED-LOOP NEUROSTIMULATOR TO TREAT EPILEPSY

1 Supervising staff

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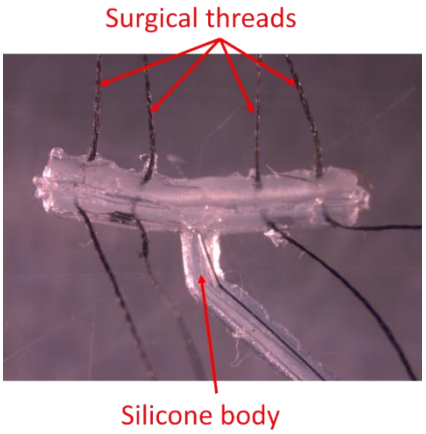
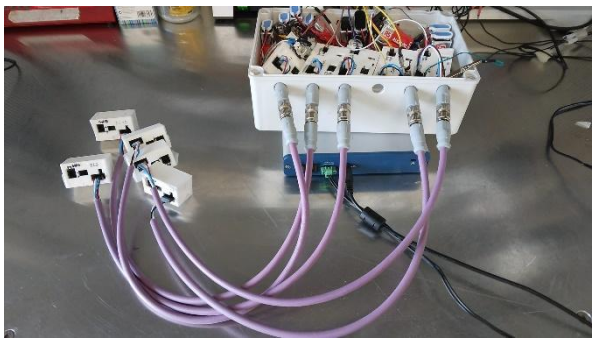
2 Context

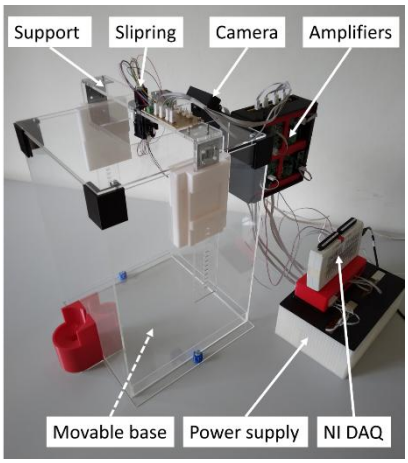
Epilepsy is the second most common chronic neurological disease, associated with stigma and high economic costs. Worldwide, 50 million people are affected by epilepsy, and one-third do not respond to antiepileptic drugs [1]. These patients should be referred for a presurgical evaluation to identify and subsequently remove the epileptogenic focus surgically. If surgery is impossible, neuromodulation can be offered as an adjunctive treatment [2]. In particular, Vagus Nerve Stimulation (VNS) is an attractive neuromodulation technique, as it is less invasive and/or more convenient than other alternatives, i.e., responsive neurostimulation (stimulation is applied directly to the seizure focus), deep brain stimulation of the anterior nucleus of the thalamus, and transcranial direct current stimulation. VNS consists of an implanted pulse generator that delivers trains of electrical pulses to the left vagus nerve, which induces antiepileptic effects for both focal and generalized seizures [3]. Up to 6-9% of patients are rendered seizure-free [4], [5], and approximately half of the treated patients achieve a good clinical response (>50% seizure frequency reduction) [5]. However, despite 30 years of experience in using VNS for epilepsy, the mechanisms of action of VNS remain to be fully elucidated [6]. Nearly one-third of patients do not respond to VNS, and very little is known about why this occurs [4]. Moreover, until now, the titration of VNS parameters is performed empirically, with current intensities raised until the patient's tolerance or a clinical effect is reached. It may lead to administering unnecessarily high currents, resulting in avoidable side effects and a waste of battery energy [4].

The abortive effect of VNS is confirmed by several human and animal studies [7]–[9]. These publications strengthen the expectation that an automated seizure detection controlling on-demand VNS would significantly increase the treatment's efficiency and provide a warning possibility. Within this context, the vagus nerve is a key bidirectional information pathway between the brain and different visceral organs. For this reason, exploiting the vagus nerve traffic related to seizures might offer a novel method for the early detection of seizures as needed to control an on-demand therapeutic stimulation of the same nerve.

We implemented and validated a chronic recording setup, including specific microcuff electrodes [10], [11]. Our recording systems allow free motion and real-time physiological data acquisition and transfer (including the vagus nerve activity - VENG, electroencephalography - EEG, the video, etc.). It contains a Raspberry Pi, which captures the physiological signal. To do a chronic recording, the user uses a software interface to control the Raspberry Pi from an external server.







The setup does not, however, include the stimulation module, which is the missing piece of the puzzle to reach a closed-loop stimulation therapy.

From a technical point of view, closed-loop stimulation is challenging. When the nerve is activated by an electrical stimulus and electrophysiologic activity is recorded by electrodes, the stimulus artifact contaminates the recording. This can be problematic for the design of an implantable device able to simultaneously monitor and stimulate the nervous system (i.e., working in a closed loop). The artifact has several causes, including the voltage gradient induced between the recording electrodes due to the current flowing around the stimulation site, the impedance imbalance between the recording electrodes, and the capacitive coupling between the stimulating and recording leads.

Artifact suppression in neural recording systems is critical, particularly for low-voltage signals such as electroneurogram, where even minimal artifacts from the stimulation can negatively impact the recorded signals.

3 Work

This project aims to adapt the chronic recording setup, adding a neural stimulator, to reach a closed-loop stimulation therapy.
Major steps will include:

- Understanding the chronic recording setup
- Designing and implementing a stimulation device
- Adding an artifact suppression system to record and stimulate simultaneously from the same electrode
- Validating the design on a phantom and then in real conditions.

Students have at their disposal all the project outputs from previous teams.

4 References

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