Implantable ECoG Measurement Device for Localized Epilepsy Detection and Treatment

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***Abstract*—We present an implantable ECoG (electrocorticogram) measuring device that can detect localized epilepsy from a specific brain region and apply deep brain stimulation as a counteractive measure to an epileptic seizure. Specifically, we stimulate the monitored brain region with a counter-phase version of the measured epileptic waveform in an effort to dampen the seizure activity. The ECoG device triggers this response when there is an increase in 200-400Hz activity and a measured max potential of at least 1 mV which captures the frequency composition and amplitude of common epileptiforms. Considering the patient-to-patient differences in epilepsy, our device lends itself to changes to meet patient-specific needs through the use of off-the-shelf components. To minimize the post-operative disruption of the patient and the device, we also provide a compatible wireless power delivery antenna.**

I. Introduction

Localization-related epilepsy (LE) is a type of focal epilepsy where seizures arise from specific parts of the brain. They are characterized as either idiopathic–seizures with an unknown cause–or symptomatic–seizures caused by an underlying brain lesion or disorder. Focal epilepsy is a neurological condition where the predominant symptom is recurring seizures affecting one hemisphere of the brain [1].

Since LE can originate from any part of the brain, seizure symptoms are dependent on the location of the seizure onset and can affect different functions such as vision, movement, memory, or emotions. Notable regions in which LE can harm include the frontal lobe, the parietal lobe, and the occipital lobe. LE in the frontal lobe, the area of the brain responsible for planning, movement, and personality, can have a significant impact on a patient's quality of life. In the parietal lobe, the brain region responsible for combining and interpreting sources of stimuli, LE can cause hallucinations, numbness, and space-perception issues. Symptoms of LE in the occipital lobe, the brain region that controls visual processing, include visual distortions in the left or right of the patient, depending on whether LE occurs in the left or right cortex. In any case, LE originating from any brain region can impact critical cognitive function for the duration of a seizure. Moreover, it has been shown that seizure activity can worsen via activity-regulated myelination, the same mechanism that supports healthy synchronization in neural networks [2]. Medication is a common form of treatment, but, for more than 30 percent of those with a form of epilepsy, this medication may not be effective in eliminating seizure activity [3].

For patients with a form of LE that are resistant to pharmacological intervention, an invasive solution via an ECoG (electrocorticogram) based measurement and detection system may be more effective in preventing seizure activity. ECoG has already been shown to be pivotal in detecting seizure onset regions; however, this information is often used to surgically eliminate the affected brain region [4]. A crucial problem with this approach is that it would only be effective in cases where the onset region is sufficiently small. Otherwise, the brain could be damaged. It is then imperative that there is a generalizable method for the treatment of LE for those that can not be treated with medication that, with minimal alterations, can be made to fit the needs of any patient without surgical intervention. Therefore, we propose an implantable ECoG electrode designed to both detect and counteract localized epileptic seizures from specific brain regions. We achieve this by continuously monitoring activity in targeted regions and then stimulating with a counter-phase version of the measured electrical potential, a method for invasively treating epileptic seizures [5]. It should be noted that our design assumes that we have prior knowledge of the affected brain region which can be done non-invasively.

Our design considers a variety of observed information about epilepsy. Regular brain activity is represented by the center frequencies of five frequency bands, namely delta 2–4 Hz, theta 4–8Hz, alpha 8–12 Hz, beta 16–25 Hz, (low) gamma 30–50 Hz [6]. This means we can reasonably expect to place regular cognitive processing within the 2-50Hz band. Within this band, we do not activate counter-phase stimulation. Epileptic seizures, on the other hand, tend to be a coherent disruption of normal brain activity categorized by a sudden increase in measured potential and frequency. During an epileptic seizure, an increase in high-frequency gamma (60-150Hz) and periodic ripples at 250–500 Hz are observed at the onset of an epileptic seizure [7]. Furthermore, epileptic responses are patient sensitive [8].

To account for this information, we defined the onset of an epileptic seizure to be a rise in 200–400 Hz activity with a peak amplitude of 1mV and selected parameters to activate treatment when this response is detected and deactivate when the seizure ends. We acknowledge that depending on the patient, the frequency composition of epilepsy may differ. To this end, our design lends itself to straightforward alterations that can meet patient-specific needs. Moreover, we provide a compatible inductive power antenna to maximize uptime and minimize the postoperative disruption of both the patient and the device.

II. Design

A. ECoG Electrode

Our design consists of a flexible implantable ECoG electrode array with a polydimethylsiloxane (PDMS) base and platinum-iridium contacts. A flexible base will allow the electrode to make as much contact with the cortical surface as possible while minimizing breakage and damage to surrounding tissue. PDMS was chosen for this design due to its flexibility, biocompatibility, and compatibility with microelectromechanical systems fabrication (MEMS) techniques used in the fabrication of the electrode array [9].

Platinum-iridium contacts were chosen for this design due to their conductivity and charge-injecting capabilities as well as their resistance to corrosion in the body. Platinum has a high charge injection capacity, therefore it is able to inject large amounts of charge. This is critical for our circuit design, which requires the feedback of a counter-phase version of the measured seizure response back into the affected brain region. Additionally, precious metals such as gold and platinum are resistant to corrosion and oxidation in the body, which is key when selecting a metal for an electrode. While other metals such as iron or silver perform poorly in the body due to corrosion, platinum does not. Platinum also has high radiopacity, meaning that it is easily visible on X-ray imaging [10]. Because of this, it will be easier to tell if there are any issues with the electrode placement or if it has migrated over time.

Placement of the electrode will vary from patient to patient, as the electrode will be placed over zones of seizure origin. Placing an electrode array over the entire cortical surface would be neither safe nor feasible, so specific regions of the brain must be isolated as potential regions of seizure origin, something that can be determined via scalp EEG or analysis of patient symptoms [11]. This means that our electrode is designed only for use in LE where the area of seizure origin can be easily located, and cannot be used to treat generalized epilepsy where the entire brain is affected.

B. ECoG Measurement and Seizure Detection Circuit Design

To process the potential measured by the electrode, the circuit is designed to detect LE waveforms in the 200–400 Hz range with an amplitude of 1mV. We accomplish this by applying a bandpass filter to our signal to detect brain measured ECoG potentials in the desired frequency band and a Schmitt hysteretic comparator to detect an amplitude of ± 1 mV. The output of this hysteretic comparator is a counter-phase version of the measured potential with a an amplitude of ± 1 mV. The entire circuit design is shown in Fig. 1.

Due to intrinsic loss within the operational amplifier model used in simulation, a gain of 2 V/V per stage is needed. Thus, $R_2 = 2R_1$. The capacitor C_1 controls the first cutoff frequency (200 Hz) and C_2 controls the second (400 Hz).

$$H(s) = \frac{-Z_f}{Z_i} = \frac{-R_2}{R_1} \cdot \frac{sR_1C_1}{(1+sR_2C_2)(1+sR_1C_1)} \quad (1)$$

From that and the overall transfer function of the bandpass filter in Eqn. (1), the values of the passive components were calculated. The entire circuit as shown in Fig. 1 consists of four second order active bandpass filters, meaning the overall transfer function of the filtering stage is given by:

$$(H(s))^4 = (\frac{-R_2}{R_1} \cdot \frac{sR_1C_1}{(1+sR_2C_2)(1+sR_1C_1)})^4 \quad (2)$$

A steep roll-off is needed to ensure we only activate a seizure response in the desired frequency band. The output of the filtering stage is passed into a Schmitt Trigger Comparator with transfer function as shown in Fig. 3 [12]. The Schmitt Trigger Comparator activates at a measured amplitude of ± 1 mV and produces a counter-phase version of the measured epileptic response as in Fig. 2.

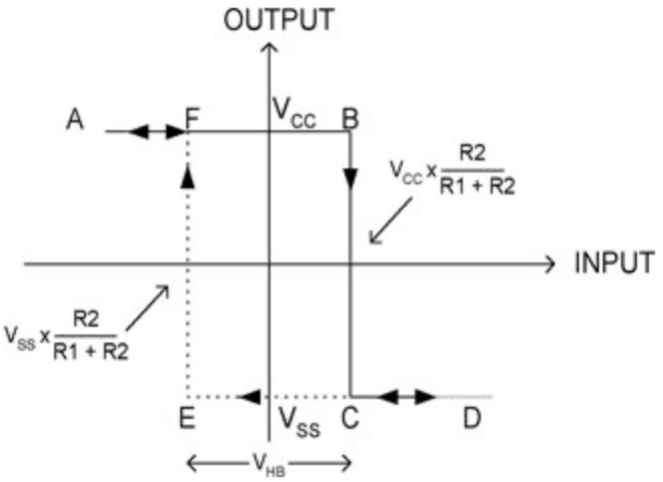

Fig. 3. Output of Schmitt Trigger Comparator [12]

To both feed back the counter-phase potential into the brain at seizure onset and to stop stimulation at seizure termination, we include a DC-blocking capacitor $C_f = C_9$ as our last stage chosen according to the following Eq. (3)

$$|Z_{C_f}| = (2\pi f_{DC} C_f)^{-1} \approx 1\text{G}\Omega \quad (3)$$

The entire circuit is powered with a 20 mV supply.

C. Wireless Power Antenna

In the design of the power supply for the operational amplifiers and comparator detailed in the primary circuit, a power circuit model is presented in Fig. 4. This power circuit consists of four key components: an antenna model, a half-wave voltage doubler, a voltage divider acting as ground, and another voltage divider.

The antenna model serves as the initial stage in the power circuit, replicating the transfer of AC voltage from an external antenna to one located within the device, akin to the induced current observed between coupled inductors. The antenna model includes an inductor with inherent resistance and is responsible for receiving AC voltage, as depicted in the

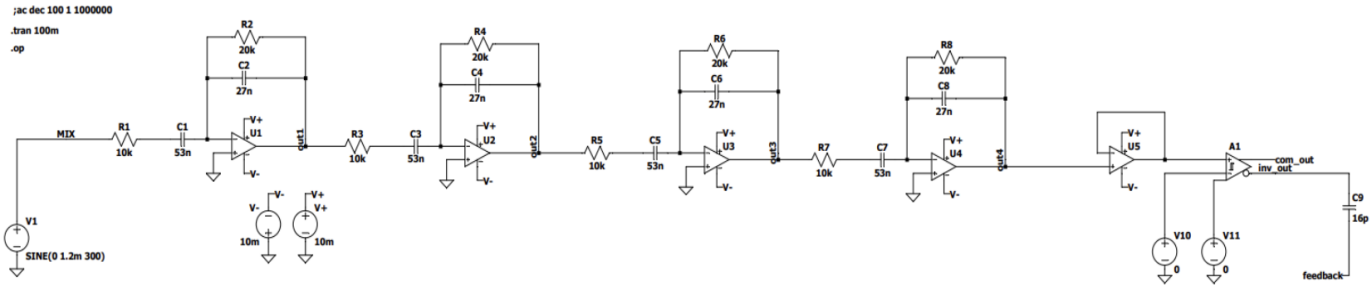

Fig. 1. 4 active second-order bandpass filters buffered into Schmitt Trigger Comparator with feedback into the brain upon seizure detection.

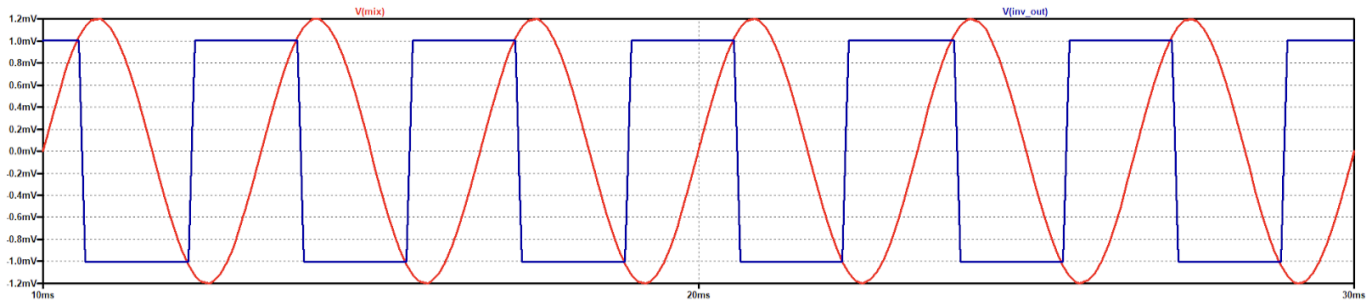

Fig. 2. Example seizure response (red) and the counter-phase stimulation waveform (blue)

leftmost part of Fig. 4. The presence of resistance in the inductor necessitates the inclusion of both inductance and resistance in the antenna model.

Next, the half-wave voltage doubler converts the AC voltage input into a DC voltage output, roughly double the peak voltage (V_{peak}) of the input. This is achieved by exploiting the characteristics of sinusoidal waves and the unidirectional conductivity of diodes. During the negative phase of the input wave, diode D_{vd1} allows current to charge capacitor C_{vd1}. Conversely, in the positive phase, diode D_{vd2} enables the charging of capacitor C_{vd2}, incorporating voltage from both the source and C_{vd1}, ultimately yielding an output approximately equal to twice V_{peak}. The functionality of this circuit persists in both the forward region, with an output of $2 \cdot V_{\text{peak}} - 2 \cdot V_{\text{threshold}}$, and the non-conducting region, where a reduced yet continuous current produces a diminished DC-like voltage. In our application, a 20 mV output is attainable from this stage [13, 14, 15].

To derive the supply voltages for the op-amps, the voltage across C_{vd2} is divided equally by two resistors, establishing a ground reference and providing $\pm 10mV$ supply voltages, denoted as $V_{+\text{Opamp}}$ and $V_{-\text{Opamp}}$. It is important to note that the presence of minimal ripples in the output may require an increased AC V_{peak} input to achieve a standard output of $2V_{\text{peak}} - 2\ V_{\text{threshold}}$ with diminished ripples.

Finally, for the comparator supply voltage of 1mV, options such as a buck converter or a voltage regulator are considered. However, given considerations of circuit size and complexity, a simple voltage divider is selected to produce the $\pm 1mV$ supply voltages across resistor R5.

III. Discussion

The proposed ECoG device is an example of closed-loop stimulation where electrical stimulation is only applied during the period of seizure activity, as oppose to open-loop configurations which provide a constant stimulus. Research has shown that open-loop stimulation is a harm-prone approach, as it has the capacity to interrupt vital cognitive processes and provide discomfort to the patient [5]. Excessive open-loop stimulation has also been shown to accelerate the habituation of symptoms or cause symptoms to rebound [16]. Although open-loop stimulation can be done in a non-invasive manner, the propensity for this methodology to harm the patient compared to closed-loop stimulation make it a poor choice for interrupting LE.

Closed-loop stimulation is used in our design to minimize unnecessary harm to the patient. Though it is possible to provide closed-loop stimulation through a method known as transcranial electrical stimulation, an invasive, ECoG-based approach suits the goal of mitigating LE by being able to provide more targeted, direct stimulation to affected brain regions [5]. This has been shown to be a safe and effective method of preventing drug-resistant epilepsy [17].

Another vital aspect of the proposed closed-loop design is the usage of counter-phase stimulation to interfere with LE as soon as it is detected. This is known as phase-targeting stimulation, and it can be used either to destruct or restore physiological oscillations in the brain [5]. In the context of our design, the aim is to destruct LE behavior in affected brain regions. Therefore, stimulation with a waveform that is out-of-phase with the detected seizure response is applied.

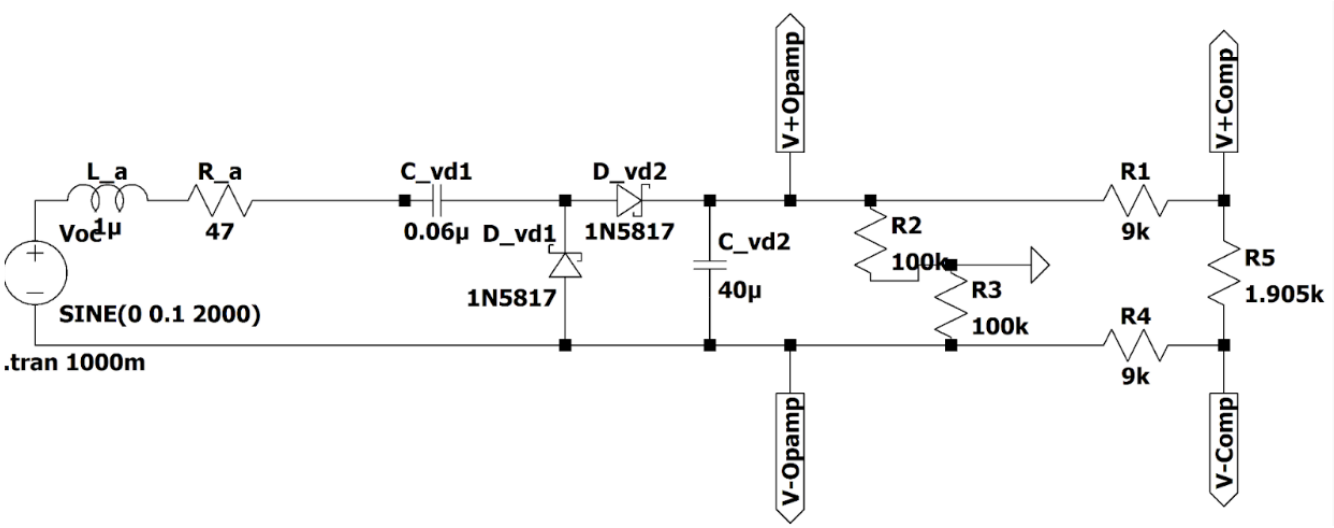

Fig. 4. Wireless power delivery schematic

The short term benefit of the proposed device are that those with drug-resistant LE would experience less significant seizure episodes without having to rely on the creation of an effective pharmacological intervention for treatment. The long term benefit of such a device is that the disease progression of LE would be interrupted. Research indicates that activity-regulated myelination, the natural process by which the brain strengthens neural networks in the brain, can promote seizure progression in affected patients [2]. Effective intervention prevents the myelinated pathways involved with LE from getting excessive use, stifling the progression of the LE in the patient.

IV. Conclusion

In this work, we have presented an ECoG measurement device for localized epilepsy detection and treatment. The design consists of 4 second-order band-pass filters buffered into a Schmitt hysteretic comparator that provide counter-phase electrical stimulation into the affected brain region that activates at seizure onset. We defined the seizure activity be an ECoG signal that has frequencies in the 200-400 Hz band and an amplitude greater than or equal to ± 1 mV. Our closed-loop approach to LE treatment can provide relief to those with a drug-resistant variant of the illness, and it has the capacity to prevent the progression of the illness in the future. When used with the ECoG electrode array with PDMS base and platinum iridium contacts, the device is able to function in the brain undisturbed for a prolonged period of time while ensuring we can inject enough charge into the affected regions. This is further supported by our compatible wireless power delivery antenna, which circumnavigates the issues associated with battery or wired power delivery approaches. Although our design makes assumptions about the frequency and amplitude composition of LE, the equations that describe the dynamics of the circuit make it relatively easy to manipulate. Therefore, the design is generalizable to patient-to-patient differences in LE by only altering resistor and capacitor values in both the comparator and bandpass filters.

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