Low-power CMOS-based epileptic seizure onset detector

Muhammad Tariqus Salam¹, Mohamad Sawan¹, Anas Hamoui², and Dang Khoa Nguyen³

¹Polystim Neurotechnologies Laboratory, École Polytechnique de Montréal
²Department of Electrical Engineering, McGill University, Montréal
³Neurology, CHUM Notre-Dame Hospital, Montréal

tariqus.salam@polymtl.ca

Abstract – In this paper, we present an implantable CMOS integrated device that automatically detects epileptic seizure onsets. By recognizing partial-onset seizures, it can improve epilepsy treatment. The circuit consists of a chopper stabilized preamplifier, comprising a modulator, an amplifier, a high-pass filter with low cut-off frequency, and a voltage span detector. The proposed low-power detector extracts seizure onset information from neural signals and monitors the signals over a time period to capture seizure events. Signals are analyzed and the mathematical model is validated in Matlab. Circuits are implemented in a CMOS 0.18-μm process. Total power consumption of the preamplifier and detector are 6.72 uW and 55.51 nW, respectively. Detection performance was verified using intracerebral electroencephalographic recordings from epileptic patients, and the detector accurately identified seizure onsets.

I. INTRODUCTION

Epilepsy is a common chronic neurological disorder characterized by a predisposition to unprovoked recurrent seizures. A seizure is the manifestation of an abnormal, hypersynchronous discharge of a population of cortical neurons. Antiepileptic drugs are the mainstream of treatment but many suffer from systemic side effects and a third is non-responsive. Some of these refractory patients may benefit from epilepsy surgery but others exhibit an epileptogenic zone overlapping eloquent areas (language, motor, visual) which cannot be removed without significant neurological deficits. Over the last few years, there has been growing interest in developing responsive epilepsy therapy devices that could deliver focal electrical stimulation, drugs or even alter the cortical temperature to stop seizures at their onset. Responsive stimulation requires systems that detect abnormal electrophysiological activity to provide focal treatment.

Many mathematical models have been developed to detect seizures, of which intracerebral EEG-based models have shown better performance than shield EEG-based models. Several models have shown impressive ability to predict seizure onset, e.g., wavelet decomposition [1], mean phase coherence measurement [2], and signals synchronization [3]. These models have been translated into band pass filters and desktop software that are useful for short-term applications. So far, very few implantable microelectronic devices have been proposed in the literature. One implantable seizure detection device [4] uses an FIR band-pass filter with 15 amplifiers to implement the algorithm. However, this integrated circuit is considerably larger than a low power microelectronic circuit (e.g. 2/3 Gm-C circuits and logic gates).

Neural signal amplification is a critical issue, because the relatively poor noise performance of CMOS technology causes several types of unwanted noise, modulates the signal and decreases the signal-to-noise ratio. Many neural signal preamplification methods have been proposed, and some have shown impressive abilities to amplify very low-amplitude action potentials. The chopper stabilized preamplifier is a classic model that is widely used to reduce amplifier-generated noise such as low frequency (1/f) and offset voltage noise [5]. The Chopper stabilized circuit consists of a modulator, an amplifier, a demodulator, and a low-pass filter [6].

This paper presents a method to detect epileptic seizures upon their occurrence. We propose an epilepsy seizure onset detection system implemented in CMOS technology for an implantable device. A new preamplifier is applied to reduce design complexity, power, and noise compared to the classical chopper stabilized preamplifier. The proposed detector monitors neural signals over a period of time, using two low-power Gm-C circuits to measure the duration of hyperexcititation. Significant duration of the detected hyperexcititation indicates a definite seizure event and locks the decision until the time period ends. Epileptic signals and the mathematical model are analyzed in Matlab, and the corresponding simulation results on the CMOS circuits are presented. The superiority of the proposed system is demonstrated by comparing our results with existing solutions [4]. The novel preamplifier incorporated in the seizure onset detection application considerably improves detection performance.

II. PROPOSED SYSTEM

Seizure activities begin in an epileptogenic zone and spread to the adjacent regions. From patient to patient, seizure onsets may vary in terms of onset morphology, discharge frequency, foci, and spread pattern. The most common seizure onset is characterized by a low-voltage high-frequency discharge. Fig. 1 shows the sudden appearance of this typical low-voltage fast activity recorded from an intracerebral contact positioned over the epileptogenic zone, increasing in amplitude, and spreading to other contacts (not shown). In order to identify the seizure-onset (thus allowing early responsive abortive therapy), a system should meet certain conditions. A necessary condition for seizure onset detection (NCSD) is that a group of neurons is hyperexcited. Because interictal epileptic spikes or other physiological rhythm such as sleep spindles may cause false alarms for seizure detection, the sufficient and necessary condition for seizure onset detection (SNCSOD) is hyperexcititation of a neuron group over a period of time. Fig. 2 presents a block diagram of the SNCSOD showing the global architecture of the proposed detector.
Normal activities
Seizure activities

Seizure onset

Fig. 1. Invasive EEG of an actual epileptic seizure: (a) start of seizure activity is characterized by low-amplitude fast activity and (b) zoom inset shows seizure-onset.

In Fig. 2, input signals are divided into time frames and monitored over a time period. If the satisfied amount of seizure activities is detected in a time frame, seizure tendency is declared. Consequently, false alarms are avoided by analyzing the signals in a given time frame and low-voltage high-frequencies are detected by a voltage span detector (VSD). A detailed discussion is given below.

III. DETECTION ALGORITHM

Seizure onset signal is initially analyzed in Matlab software and a seizure detection algorithm for partial-onset seizures is proposed. Fig. 3 demonstrates seizure onsets detection of an EEG ($x(t)$). The input signal (Fig. 3(a)) is modulated to a high frequency ($F_s = 1/T_s$) so that instrumentation low-frequency noise of does not affect the signal. Moreover, this modulation (Eq. (1)) converts negative signal amplitudes to positive amplitudes (Fig. 3(b)). Thus, threshold voltages ($V_{HET}$) of a VSD are positive values. Fig. 3(c) shows that VSD detects seizure activities following Eq. (2). Mathematical models of the algorithm are described below.

The discrete modulated signal ($V_{mod}$) in a time frame ($T_f$) is

$$V_{mod} (n) = \sum_{n=1}^{T_f/T} x (nT_s)(-1)^n$$

where $n=1, 2, 3 ..., N$.

The detected hyperexcitation signal is

$$V_{com}(n) = \begin{cases} 1, & \text{for } V_{HET1} > V_{mod}(n) > V_{HET2} \\ 0, & \text{Otherwise} \end{cases}$$

In a $T_s$ durations of the detected hyperexcitation is $T_1 (=t_{i1}+t_{i2}+t_{i3}+...+t_{iN})$. If the hyperexcitation time threshold is $T_{HET}$, seizure prediction $V_{SA}(n)$ is

$$V_{SA}(n) = \begin{cases} 1, & \text{Seizure} \\ 0, & \text{No Seizure} \end{cases} \text{ if } T_i > T_{HET}$$

The advantages of this algorithm are accurate seizure onset detection, prevention of false alarms in seizure prediction, and implementability in analog circuits (low noise and low power consumption). Analog circuit implementation of the algorithm is presented below.

IV. CIRCUIT IMPLEMENTATION

This system comprises two main parts: preamplification and detection of seizure onset. Details are given below.

A. Preamplification

Fig. 4 depicts the new chopper stabilized preamplification method, where the demodulator and low-pass filter of a classical chopper stabilized preamplifier [6] are replaced by a high-pass filter and a VSD. This method reduces power dissipation, noise, and design complexity. Fig. 4 shows that the preamplifier input signal is modulated to frequency $F_s$, and the flicker noise $V_f$ and dc-offset voltage noise $V_{os}$ of the amplifier are attenuated by the high-pass filter, while the finite bandwidth of amplifier bandlimits the thermal noise $V_{nt}$. Amplified hyperexcited signal ($V_{at}$) is detected by a VSD (Fig. 4), and seizure onset information ($V_{com}$) is extracted from the input signals. A VSD consists of a buffer, logic gates, and two comparators. A comparator is comprised of two cascaded CMOS inverters, with threshold voltage set by the aspect ratio of the transistor.

$$V_{HET} = \frac{V_{DD} - V_{tp} + V_{in} + \sqrt{K_n/K_p}}{1 + \sqrt{K_n/K_p}}$$

where $V_{tp}$ and $V_{in}$ are the threshold voltage of the NMOS and PMOS device, respectively, and $K_n = (W/L)_n \mu_n C_{ox}$ and $K_p = (W/L)_p \mu_p C_{ox}$. Eq. (4) determines the comparator threshold settings, as required.
duration is measured by a Gm-C circuit, in which output current through a capacitor (C), the change in voltage across C is proportional to

\[ \frac{dV}{dt} = \frac{1}{C} g_{mc} V_{com} \]  

Eq. (5) shows that voltage change due to \( V_{com} \) is proportional to \( g_{mc} \). The Gm-C circuit in Fig. 7(a) illustrates the measurement of input voltage duration. In order to calculate the duration of seizure onset within a given time frame, the Gm circuits in Fig. 7(b) and (c) are used to implement the \( g_{mc} \) block of Fig. 7(a), and the detector (Fig. 8) is formed by combining the two circuits.

According to Eq. (5), accumulated charge in \( C_1 \) (Fig. 7(a)) is proportional to input voltage, and \( C_2 \) maintains charge balance. If the charge accumulation exceeds a certain limit, the transistor \( M_{t1} \) discharges the capacitor completely and resumes accumulating. Two separate Gm circuits (Fig. 7(a) and (b)) provide high input voltage and low output current in order to calculate the duration of seizure onset (\( T_{HET} \)) and the time frame (\( T_f \)) of the monitoring period. In Fig. 7(b), the \( g_{mt} \) of transistor \( M_{t1} \) determines \( T_{HET} \), and in Fig. 7(c), the \( g_{mc} \) of transistor \( M_{t2} \) determines \( T_f \). The discharging paths (three cascodes) of the Gm circuits have high output impedance to compensate linkage currents.

C. Detector

The preamplifier identifies the dynamic changes of the hyperexcited signal, while the detector (Fig. 2) monitors seizure onsets over a given time period (\( T_f \)), and the predetermined amount of abnormal activity in a \( T_f \) defines a seizure onset. Duration of seizure activity (\( T_f \)) is measured by a duration count detector (DCD) (Fig. 8). If \( T_f > T_{HET} \) in a \( T_f \), seizure tendency is declared. Fig. 8 shows that \( g_{mt} \) accumulates charge (proportional to \( V_{com} \)) in a capacitor \( (C_{cl1}) \) until it reaches a predefined threshold voltage \( (V_{thp}) \), at which time it locks the hyperexcitation signal \( (V_{det}(t)) \). Similarly, \( g_{mc} \) stores the clock pulse in a capacitor \( (C_{cl2}) \) and restarts the program after \( T_f \). These detector parameters will be chosen according to the patient’s seizure onset information.

---

**Fig. 4.** Modified chopper stabilizer circuit and corresponding frequency analysis of signals in different nodes.

**Fig. 5.** Preamplification front-end: (a) Band-pass filter comprising an amplifier and a high-pass filter, (b) OTA used in the amplifier.

**Fig. 6.** Gain response of the band-pass filter.

**Fig. 7.** (a) Gm-C circuit used to calculate the hyperexcitation duration, and schematic of the \( g_{mc} \) block in Fig. 7(a) is realized in Fig. 8: (b) \( g_{mt} \) identifies seizure onset and (c) \( g_{mc} \) calculates time frame.

**Fig. 8.** Block diagram of the duration count detector.
low amplitude neural signals are modulated into high frequency \( (DKN) \). These signals are fed into the system (Fig. 3), whereupon seizure onset was determined and marked by an epileptologist.

V. SIMULATION RESULTS

Fig. 9 shows the invasive EEG recording of Fig. 1. The seizure onset was determined and marked by an epileptologist (DKN). These signals are fed into the system (Fig. 3), whereupon low amplitude neural signals are modulated into high frequency (\( F_s = 7 \) KHz) to prevent amplifier flicker noise from mixing with the original signal. Various noises \( (V_{noi}, V_{si}, \text{and } V_{an}) \) are attenuated by the band-pass filter, and the modulated signals are amplified to the desired level. Consequently, a certain DC offset \( (320 \text{ mV}) \) of \( V_{at} \) is created by adding a voltage source \( V_{b2} \) that adjusts the magnitude of \( V_{at} \) as required. Moreover, Fig. 9(b) shows that the negative side of the input signal is attenuated by \( M_{b1} \) and \( M_{b2} \) transistors (Fig. 8(a)) and that the resultant \( V_{at} \) contains all seizure-onset information. Hyperexcitation of \( V_{at} \) is detected by the VSD, and the threshold voltages \( V_{HET1} \) and \( V_{HET2} \) of the VSD are determined by the frequency- or time-domain analysis of \( V_{at} \).

It is seen that amplitude of the ictal pattern at onset for this patient is mainly between 320 mV and 460 mV. On the other hand in the detector, the duration of the detected hyperexcitation \( V_{com} \) within a \( T_f \) (110 msec) exceeds \( T_{HET} \) (80 msec), the DCD (Fig. 8) follows Eq. (3) and locks its \( V_{SB} \) to ‘1’, thus signaling a seizure. Fig. 9(c) shows that \( V_{SB} \) has determined the seizure tendency at 185.60 sec and 186.20 sec, and has locked the channel until the end of \( T_f \). Overall, the system has detected 2 pulses during this 2.70 sec simulation. A threshold number of pulses will be defined prior to triggering an appropriate seizure abortive therapy. During this experiment, it is seen that the low-frequency signal \( V_{at} \) with an amplitude between the threshold voltages of VSD and the low-frequency amplifier noise could cause unwanted warning messages. However, \( T_{HET} \) and \( T_f \) are tuned to seizure onset frequency of the patient, such that no false alarms occur in the entire experiment. Depending on the patient, \( V_{HET1}, V_{HET2}, T_{HET} \) and \( T_f \) values may differ, and multi-channel signal acquisition and seizure detectors could be needed, depending on number of epileptogenic foci.

Table I summarizes the power consumed by the various blocks of the proposed preamplifier and detector. A comparison to existing systems shows that the preamplifier dissipates less power \([6, 4]\), the detector is more compact \([4]\), and the overall noise is reduced.

VI. CONCLUSION

The proposed system demonstrates accurate detection of partial-onset seizure characterized by initial low voltage fast activity. However, the automated detector system provides patient-specific tunable parameters to adjust to other seizure onset patterns with distinct amplitudes and frequencies. The preamplification circuits sufficiently attenuate flicker noise, dc offset noise, and thermal noise, and the digitally controlled low-power Gm-C circuits precisely defined the seizure onset. Moreover, the new preamplification method reduces power dissipation, noise and design complexity compared to the classical chopper stabilized preamplifier. Several other advantages of the proposed circuits were noted: low power consumption of the detector, no false alarms and negligible effect of the flicker noise on the detector. This system should prove to be useful in the long-term treatment of epilepsy.

ACKNOWLEDGEMENTS

The authors are grateful for support from NSERC, the Canada Research Chair in Smart Medical Devices, the Microsystems Strategic Alliance of Québec (ReSMiQ), and the EEG technicians at Notre-Dame Hospital, Montreal.

REFERENCES