Low-power CMOS-based epileptic seizure onset detector

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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 mainstay 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 electrographic 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 scalp 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 stabilizer 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 hyperexcitation. Significant duration of the detected hyperexcitation 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, focality, 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 (NCSOD) 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 hyperexcitation 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.

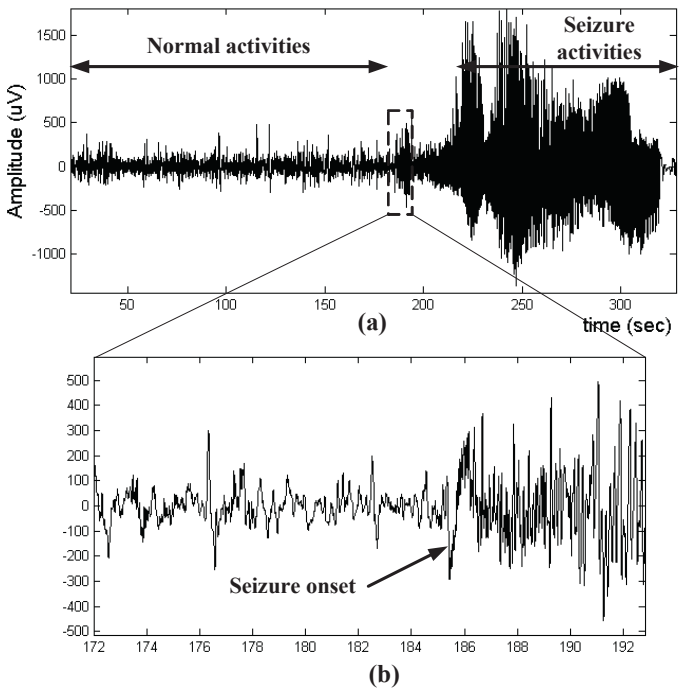

Fig. 1. Invasive EEG of an actual epileptic seizure: (a) start of seizure activity is characterized by low-amplitude fast activity and (b) zoom inset shows seizure-onset.

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_{HETi}) 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

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

where n= 1, 2, 3 ….N.

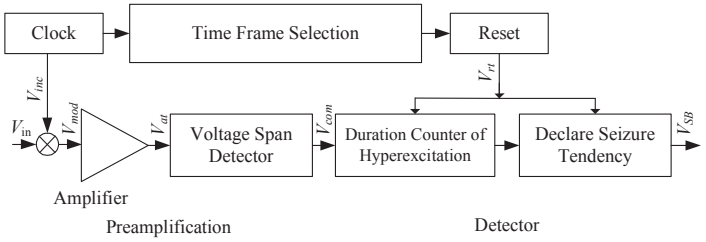

Fig. 2. Block diagram of the proposed detector.

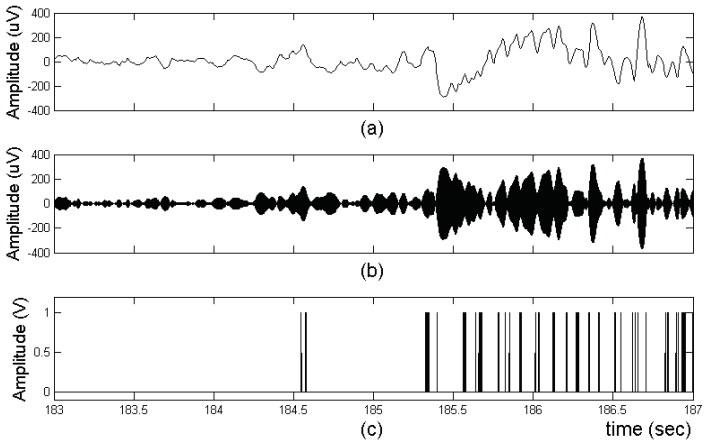

Fig. 3. Detection of epileptic seizure onset in Fig. 1: (a) is seizure onset (x); (b) is modulated seizure onset signals (V_{mod}); (c) is detected hyperexcitations (V_{com}).

The detected hyperexcitation signal is

$$V_{com}(n) = \begin{cases} '1', & for \;\; V_{HET1} > V_{\mathrm{mod}}(n) > V_{HET2} \\ '0', & Otherwise \end{cases} \qquad (2)$$

In a T_f, durations of the detected hyperexcitation is T_1 (=t_{11}+t_{12}+ t_{13}….+t_{1N}). If the hyperexcitation time threshold is T_{HET}, seizure prediction V_{SB}(n) is

$$V_{SB}(n) = \begin{cases} '1', \; Seizure, & if \;\; T_1 > T_{HET} \\ '0', \; No \;\; Seizure, & Otherwise \end{cases} \qquad (3)$$

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_k 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.

$$V_{HETi} = \frac{V_{DD} - |V_{tp}| + V_{tn}\sqrt{K_n/K_p}}{1+\sqrt{K_n/K_p}} \qquad (4)$$

where V_{tp} and V_{tn} are the threshold voltage of the NMOS and PMOS device, respectively, and $K_{\mathrm{n}} = (\mathrm{W/L})_{\mathrm{n}}\, \mu_{\mathrm{n}}\, C_{\mathrm{ox}}$ and $K_{\mathrm{p}} = (\mathrm{W/L})_{\mathrm{p}}\, \mu_{\mathrm{p}}\, C_{\mathrm{ox}}$. Eq. (4) determines the comparator threshold settings, as required.

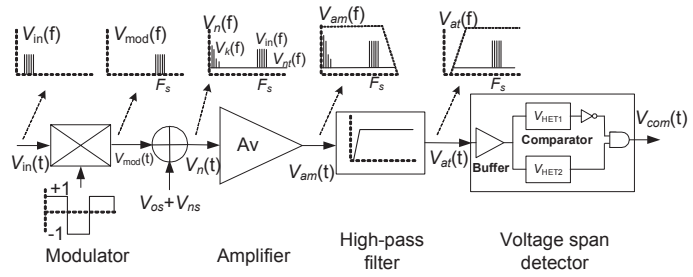

Fig. 4. Modified chopper stabilizer circuit and corresponding frequency analysis of signals in different nodes.

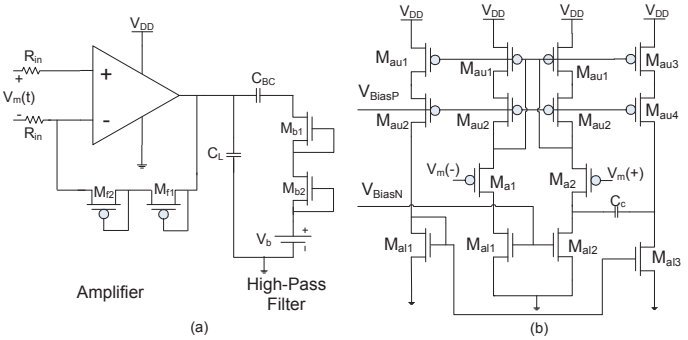

Fig. 5. Preamplification front-end: (a) Band-pass filter comprising an amplifier and a high-pass filter, (b) OTA used in the amplifier.

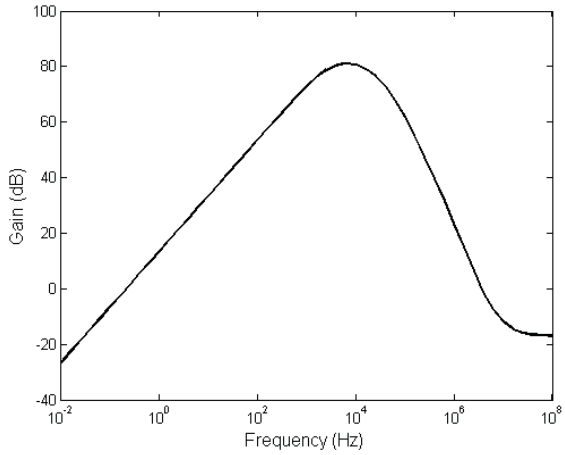

Fig. 6. Gain response of the band-pass filter.

Fig. 5(a) illustrates the preamplifier construction, which comprises an OTA, as shown in Fig. 5(b). Briefly, a band-pass frequency response (Fig. 6.) is produced by the amplifier and high-pass filter (Fig. 5(a)). The band-pass filter has 81 dB midband gain and 15 KHz (2 KHz to 19 KHz) bandwidth with 6uVrms input-referred noise.

B. Gm-C circuits

The seizure onset signal is extracted (Fig. 4) by a VSD. V_{com} duration is measured by a Gm-C circuit, in which output current I_{cgm} is precisely controlled by circuit conductance g_m. If I_{cgm} passes through a capacitor (C), the change in voltage across C is

$$\frac{dV}{dt} = \frac{1}{C} g_m V_{com} \tag{5}$$

Eq. (5) shows that voltage change due to V_{com} is proportional to g_m. 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_m block of Fig. 7(a), and the detector (Fig. (8)) is formed by combining the two circuits.

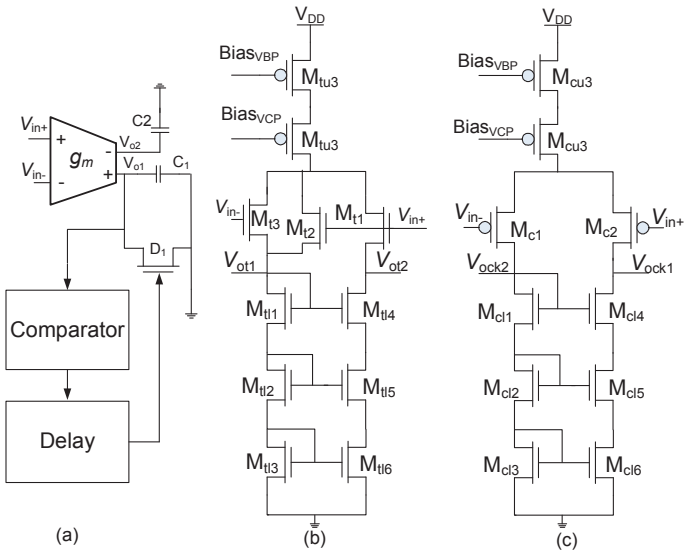

Fig. 7. (a) Gm-C circuit used to calculate the hyperexcitation duration, and schematic of the g_m block in Fig. 7(a) is realized in Fig. 8: (b) g_{mt} identifies seizure onset and (c) g_{mc} calculates time frame.

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 (D_1) 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_{c2} 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_1) is measured by a duration count detector (DCD) (Fig. 8). If $T_1 > T_{HET}$ in a T_f, seizure tendency is declared. Fig. 8 shows that g_{mt} accumulates charge (proportional to V_{com}) in a capacitor (C_{t1}) until it reaches a predefined threshold voltage (V_{thp}), at which time it locks the hyperexcitation signal (V_{SB}(t)). Similarly, g_{mc} stores the clock pulse in a capacitor (C_{cl1}) and restarts the program after T_f. These detector parameters will be chosen according to the patient's seizure onset information.

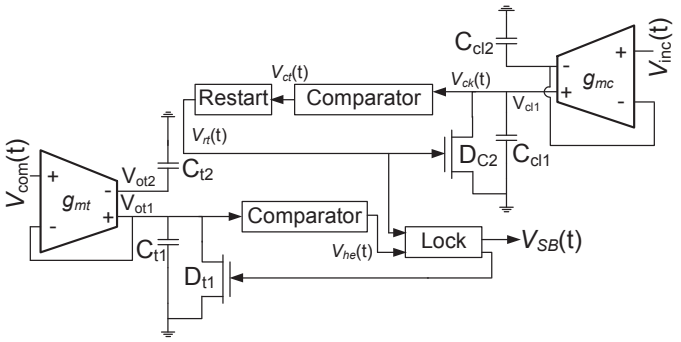

Fig. 8. Block diagram of the duration count detector.

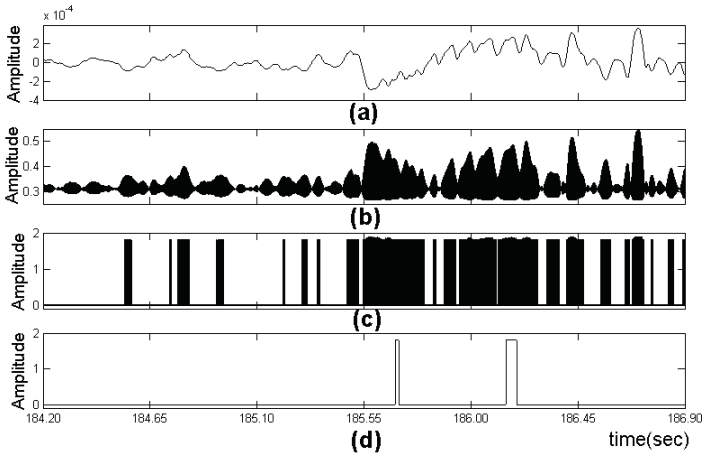

Fig. 9. Transient analysis of the implemented circuits: (a) seizure onset of Fig. 1, (b) is modulated amplified seizure signal V_{at}, (c) is detected hyperexcited signal V_{com} and (d) shows detection of the seizure event V_{SB}.

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_{os}, V_k, and V_{nt}) are attenuated by the band-pass filter, and the modulated signals are amplified to the desired level. Consequently, a certain DC offset (320 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. 5(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.

TABLE I.

SIMULATED POWER CONSUMPTION (PC) (V_{DD} = 1.8V)

Preamplification blocks		PC (W)	Detector blocks	PC (W)
Amplifier		6.70u	OTA (g_{mc})	8.30n
VSD	Buffer	22.95n	OTA (g_m)	38.70n
	Comparators	2x166.20p	Comparators	2x166.20p
	Inverter	32.50p	Restart	2.70n
	AND gate	46.70p	Delay or Lock	2.74n
Total power consumption			6.78u	

VSD: Voltage Span Detector.

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.

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