A Fully Integrated 8-Channel Closed-Loop Neural-Prosthetic CMOS SoC for Real-Time Epileptic Seizure Control

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ABSTRACT

In this paper, an 8-channel closed-loop neural-prosthetic SoC is presented for real-time intracranial EEG (iEEG) acquisition, epileptic seizure detection, and adaptive feedback stimulation control. The SoC is composed of 8 energy-efficient analog front-end amplifiers (AFEAs), a 10b delta-modulated SAR ADC (DMSAR ADC), a configurable bio-signal processor (BSP), and an adaptive high-voltage-tolerant stimulator. A wireless power-and-data transmission system is also embedded. The noise-efficiency-factor (NEF) of the AFEA is 1.77. A constant 30 µA stimulus current is delivered by closed-loop control. The acquired signals are transmitted with on-off keying (OOK) modulation at 4Mbps over the MedRadio band for monitoring. A multi-LDO topology is adopted to mitigate the interferences across different power domains. The proposed SoC is fabricated in 0.18µm CMOS and occupies 13.47 mm^2. Verified on Long Evans rats, the proposed SoC achieves more than 92% detection accuracy within 0.8s with a power consumption of 2.8 mW.

1. INTRODUCTION

Epilepsy is a one of the common neurological disorders. Around 1% of the world population is affected which can be characterized by recurrent seizures. Currently, numerous antiepileptic drugs are available for seizure control, but approximately 30% of epileptic patients remain drug-resistant. Conventional resection surgery might be beneficial to patients who respond poorly to medical treatment. However, only a part of patients are suitable for resection surgery. Electrical neuromodulation to control drug-resistant epilepsy has been attempted due to several potential advantages over conventional surgery, such as reversible characteristic [1], [2].

In the proposed neuromodulation treatments such as peripheral vagus nerve stimulation, preliminary results show that electrical stimulation of the central nervous system is a promising solution. It delivers electric impulses to a selected brain region in response to epileptic or pre-epileptic activities [3]. For epilepsy therapy, a responsive neural stimulation system can detect epileptic activities to achieve higher treatment efficacy.

Several works have been developed for neural signal acquisition and seizure detection [4], [5]. An EEG acquisition SoC with seizure classification achieves 84.4% detection accuracy within 2s [4]. A seizure onset detector with 100% accuracy has been presented in [8], but the detection latency is 13.5s [5]. In the prior works, either detection accuracy is moderate or the detection latency is too long. Moreover, the responsive neural stimulation function has not been included.

To address these issues, we have developed a fully-integrated SoC composed of analog front-end amplifiers, an ADC, a bio-signal processor, and an electrical stimulator for closed-loop epileptic seizure control [6]. More than 92% detection accuracy within 0.8s has been achieved for real-time neuromodulation on animal experiment of Long Evans rats. With the inclusion of wireless power and data transmission, the proposed SoC is a promising solution for implantable devices of epilepsy treatment.

2. SYSTEM ARCHITECTURE

The proposed 8-channel closed-loop neural-prosthetic SoC is composed of two major parts: 1) a closed-loop signal-processing path including an 8-channel iEEG acquisition unit consisting of an 8-channel AFEA and a 10b DMSAR ADC, a BSP, and an adaptive high-voltage-tolerant stimulator; 2) a wireless transmission link including a MedRadio-band transceiver and a wireless power supply system.

The iEEG signals are sensed by the electrodes and acquired by the AFEA. The DMSAR ADC performs fine and coarse conversion operations, the signals are resolved to obtain 10-bit digital codes. The digitized 10-bit iEEG signals are further fed to the BSP to extract the epileptic features in time-domain entropy and frequency spectrum. Once a seizure has been detected, the BSP sends a command to activate the adaptive stimulator to deliver stimulus currents to suppress the aberrant brain activities. To adapt to a wide range of load impedances of the electrode-tissue interface, an adaptive stimulator is designed to deliver constant 30µA stimulation current. Thus, the closed-loop seizure control is carried out by a sequence of operations from signal acquisition, seizure detection, to electrical stimulation.

The recorded iEEG signals are transmitted at a data rate of up to 4MHz over the MedRadio band (401-406 MHz) for signal monitoring. The transmitted signals are encoded with reliable cyclic redundancy check for error checking. The encoded data are sent to an OOK modulator. For an implanted system supported by a battery, the voltage and power of the battery decrease as time passes after implantation. Moreover, frequent battery replacement surgery increases the risk for the patients. Therefore, a wireless power supply system has been designed to supply a steady power to the implanted device and hence maintain signal quality and system performance.

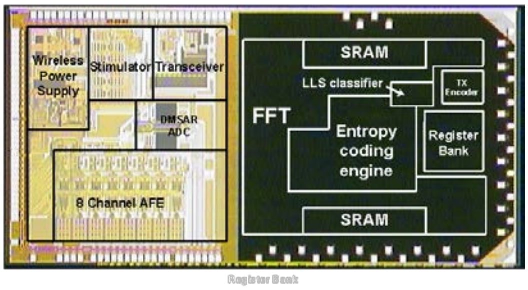

Fig. 1. Chip photograph of the SoC.

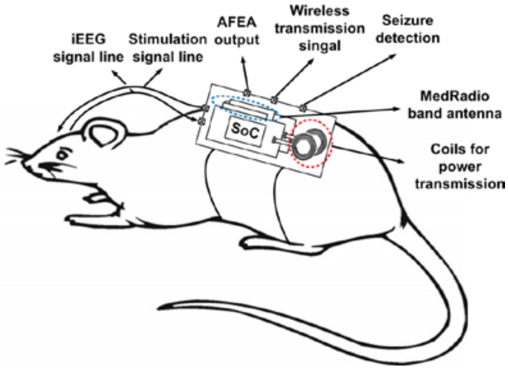

Fig. 2. The measurement setup of the microsystem with SoC on a freely-moving Long-Evans rat.

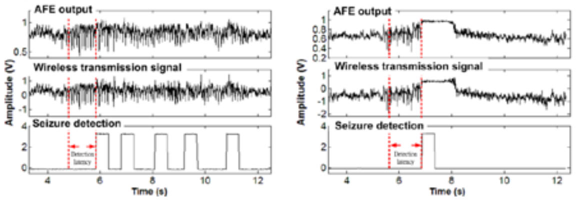

Fig. 3. Spontaneous spike-wave discharges at the output of the analog front-end amplifier (AFEA), digitized wireless transmission signal with the (a) absence and (b) activation of ZI stimulation.

3. EXPERIMENT RESULTS

Figure 1 shows the chip photograph. The proposed SoC was fabricated in a 0.18μm CMOS process and the total chip area is 13.47 mm^2 including the ESD pads. Each subsystem was tested separately and the function of the whole system was verified in an animal experiment. The experimental results are described as follows. The AFEA provides 3-step gains (41 dB, 50 dB, and 61 dB). The NEF with a 7 kHz bandwidth for the AFEA stage is 1.77. The DMSAR ADC operates at 500 kSample/s and the measured ENOB is 9.57 bits with power of 3.0 μW. The measured INL/DNL of the DMSAR ADC is 0.32/0.08 LSB. The MedRadio-band transceiver was tested at a data rate of 4Mbps through the MedRadio band. The output power of the TX is -17.2 dBm and the sensitivity is -45.7 dBm. With a data rate of 4 Mbps, the energy-per-bit of the TX and RX is 0.16 nJ/b and 0.07 nJ/b, respectively.

The amplitude of the signal received by the receiver coil is 2.45 V. After being rectified, the output DC voltage becomes 2 V with 10.2 mV ripples. The LDOs regulate the noisy voltage to sustain a steady voltage of 1.8 V with 5.9/72.4/1.4 mVp-p in ALDO/DLDO/RLDO regions. The power consumption of the proposed SoC is 2.8 mW.

Figure 2 shows the measurement setup of the microsystem with SoC on a freely-moving Long-Evans rat. The microsystem with SoC was tested 72 hours and powered wirelessly. Figure 3 shows the received and digitized iEEG waveforms of the spontaneous SWDs. Figure 3 (a) shows the case when the stimulator is turned off. As can be seen, the epileptic seizures are detected successfully. When the stimulator is turned on, the seizures are suppressed through the closed-loop control, as shown in Fig. 3 (b).

3. CONCLUSION

An 8-channel closed-loop neural-prosthetic SoC has been implemented to perform real-time seizure-triggered neuromodulation. Entropy-and-spectrum-aided seizure detection and adaptive neural stimulation have been also presented. The SoC integrates 8 AFEAs, a DMSAR ADC, a bio-signal processor, and an electrical stimulator. The AFEA features with configurable gain and bandwidth. The DMSAR ADC operates at 500k Samples/s with an ENOB of 9.57b. The BSP implements an efficient seizure detection algorithm and achieves more than 92% detection accuracy in 0.8s. The stimulator delivers a constant 30 μA stimulation current. In addition, a wireless power-and-data transmission system, including a MedRadio-band transceiver and an inductive link power supply system, has been embedded for signal monitoring and wireless power transmission. It has been demonstrated that the proposed SoC is able to successfully suppress epileptic seizures of Long-Evans rats. Based on the preliminary results, the developed closed-loop seizure control SoC is a promising solution for treating epilepsy. For future applications on human implants, the chip package, antenna, and coils will be carefully designed to meet all the system-performance and regulatory requirements.

4. REFERENCES

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