Adaptable Stimulus Driver for Epileptic Seizure Suppression

Ming-Dou Ker[1,2], Wei-Ling Chen[1], and Chun-Yu Lin[1]

[1] Institute of Electronics, National Chiao-Tung University, Hsinchu, Taiwan
[2] Department of Electronic Engineering, I-Shou University, Kaohsiung, Taiwan

Abstract – The novel implantable stimulus driver for epileptic seizure suppression with low power design and adaptive loading consideration was proposed in this work. The stimulus driver consisted of the output stage, charge pump system, and adaptor can constantly provide 40-µA output stimulus currents, as the electrode impedance varies within 10~300 kΩ. The performances of this design have been successfully verified in a silicon chip fabricated by a 0.35-µm 3.3-V/24-V CMOS process. The power consumption of this work was only 1.1~1.4 mW. The proposed stimulus driver has been integrated into closed-loop epileptic seizure monitoring and controlling system for animal test.

I. INTRODUCTION

Epilepsy, one of the common neurological diseases, is caused by transient abnormal discharge in brain [1]. There are more than 40 types of epilepsies, and these epilepsies classify by location of seizures, syndromes, and causes. Each of epilepsies has unique seizure type, age group, diagnosis, and treatment. Epilepsy is usually treated by pharmacologic treatments. However, every kind of medicines may lead to side effects, such as blurry vision, dizziness, headaches, and fatigue [2]. Besides, some patients do not respond to medicines. For these patients, they may take surgical treatment. However, surgical treatment is not suitable for every patients, because it is risky that may cause functional loss.

Except for pharmacologic and surgical treatments, the electrical stimulations have been investigated recently [3]. It has been demonstrated that the abnormal discharge signal to cause epilepsy can be suppressed by electrical stimulation before epileptic seizures happen. Advantages of electrical stimulation are flexible, recoverable, and non-destructive. Fig. 1 shows the block diagram of an implantable stimulus driver for epileptic seizure suppression. The considerations of stimulus driver include safety, reliability, charge balance, voltage compliance, and density of stimulus site. Some studies revealed that unbalanced stimulus current causes net charge stores in body and leads to problems of pH shift, ionic charges near the implanted electrodes, and erosion of the electrode material [4]. To prevent from these problems, several implantable stimulus drivers have been presented. The aim of these works concentrated on balance of anodic pulse and cathodic pulse. The methodology, dynamic current balancing [5], and feedback DAC calibration, have been used for minimizing mismatch between anodic and cathodic currents. Besides, in order to achieve large voltage compliance to close fixed power supply and maintain high output impedance to hold the constant stimulus current irrespective of highly variety of stimulus site and tissue/electrode impedances, improved current sources have been presented. The fully cascade and wide swing cascade current sources are used in output stage of stimulus driver to increase output resistance [6]. Another voltage controlled resisters (VCR) current source gains large voltage compliance close to the fixed power supply by utilizing MOS transistors in deep triode region [6]. However, if variance of output voltage caused by variety of electrode impedance exceeds fixed power supply, stimulus current will decreases dramatically.

In this work, the implantable stimulus driver for epileptic seizures with low power design and adaptive loading consideration is proposed. The new stimulus driver with adaptor can detect the variation of electrode impedance to minimize power consumption. This proposed stimulus driver can deliver charge-balanced bi-phase stimulus current by two leads electrode per stimulus site with single supply voltage (V_{DD} = 3.3V). A 0.35-µm 3.3-V/24-V CMOS process is used in this work for the chip implementation.

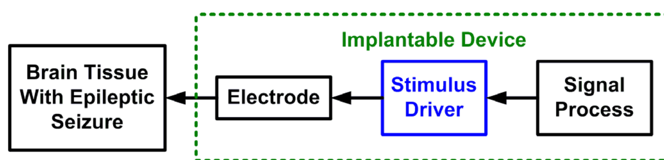

Fig. 1. Block diagram of implantable stimulus driver.

II. NEW PROPOSED DESIGN

The new implantable stimulus driver for seizure control with consideration of power consumption and adaptability on electrode impedance is proposed. As shown in Fig. 2, the proposed stimulus driver consists of the output stage, charge pump system, adaptor, and two leads electrode set. The output stage is realized with 24-V devices, while the adapter is realized with 3.3-V devices. The targeted stimulus current is 40 µA, which is able to suppress epileptic seizures of Long-Evans rats [7]. The effective electrode impedance is fully resistive and it will vary from 100 kΩ to 250 kΩ [7]. That

This work was partially supported by National Science Council (NSC), Taiwan, under Contract of NSC 99-2220-E-009-021, and by the "Aim for the Top University Plan" of National Chiao-Tung University and Ministry of Education, Taiwan.

978-1-4244-9021-9/11/$26.00 ©2011 IEEE

is to say, stimulus voltage and required power supply are much higher than the operating voltage (V_{DD} = 3.3V). Depending on electrode impedance, the proposed stimulus driver with the adaptor regulates the high operating voltage for output stage of 24-V devices by feedback of the adaptor. The charge pump system is designed to control the charge pump circuit to generate the required high operating voltage (V_{CC}).

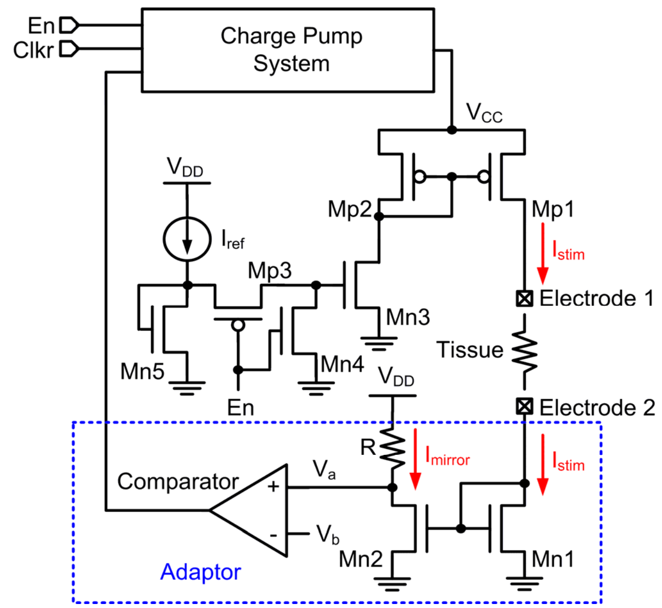

Fig. 2. Circuit schematic of the proposed stimulus driver.

The stimulus current source consists of a current mirror (Mp1 and Mp2) and bias circuit. During the stimulus driver "turn-on" interval, enable (En) is low (0V), Mn4 is switched off, Mp3 is switched on, and Mn3 is biased through Mp3. The stimulus current (I_{stim}) is delivered by Mp1. During the stimulus driver "turn-off", enable (En) is high (3.3V), Mn4 is switched on, and Mn3 is connected to ground through Mn4, no stimulus current is delivered.

The proposed stimulus driver adopts two leads electrode set per stimulus site (electrode 1 and electrode 2) to generate bi-phase stimulus current. Whenever the stimulus current is delivered by Mp1 and flows into electrode 1, the direction of stimulus current is controlled by the on-chip switches of two leads electrode set. As illustrated in Fig. 3, two leads electrode set consists of four switches and two electrodes. While anodic current is required, the switch_anodic is switched on and switch_cathodic is switched off. Anodic stimulus current flows from the top site of tissue to the down site of tissue. While cathodic current is required, the switch_anodic is switched off and the switch_cathodic is switched on. The cathodic stimulus current flows from the down site of tissue to the top site of tissue. After stimulus current passes through tissue, electrode 2 is used to collect the stimulus current back to the adaptor.

The adaptor of stimulus driver consists of a current mirror (Mn1 and Mn2), resistor (R), and comparator. While stimulus current (I_{stim}) is collected by electrode 2 to pass through Mn1 of current mirror, the gate of Mn2 is biased to induce the proportional current (I_{mirror}). The adaptor utilizes I_{mirror} flowing through poly resistor (R = 41.25kΩ) to generate a voltage signal (V_a), which can be expressed as

$$V_a = V_{DD} - I_{mirror} * R \quad (1)$$

Another voltage signal (V_b) which is used to compare with V_a is $0.5 \text{x} V_{DD}$. Whenever the stimulus driver is turned on to stimulate the tissue, the comparator in the adaptor compares these two voltage signals (V_a and V_b) and distinguishes the amplitude of stimulus current. The operating voltage (V_{CC}) for stimulus driver is controlled by the output of comparator.

When the electrode impedance is increasing, the stimulus current is decreased. The insufficient stimulus current leads to V_a higher than V_b, the output of comparator will become high (3.3V), and charge pump system is activated to provide stimulus current source with higher voltage until stimulus current reaches 40 μA. When electrode impedance is decreasing, the V_a is also decreasing. The larger stimulus current leads to V_a lower than V_b, the output of comparator will become low (0V), and charge pump system is inactivated to provide stimulus current source with lower voltage until stimulus current returns 40 μA.

The charge pump system of stimulus driver consists of the 4-stage charge pump circuit, buffer, clock control, and on-chip output loading capacitance (CL), as shown in Fig. 4 [8]. The 4-stage charge pump circuit uses 24-V devices with deep N-well, and the rests of the circuit use 3.3-V devices. The clock control is utilized to generate interweaved clock signals which depends on the reference clock (Clkr), enable signal (En), and the feedback signal from the comparator. There is a compromise between CL size and clock frequency, so the used clock frequency is 25 MHz.

At the beginning of stimulation, there is no charge stored at the output loading capacitance (CL) of charge pump system, and output voltage of charge pump system (V_{CC}) is initially 0V. The stimulus current is approaching 0 A; therefore, as Eq. (1) shown, V_a is higher than V_b and charge pump system is activated. Therefore, the output voltage of charge pump system increases and stimulus current is delivered by the current source. The charge pump system keeps activated until the stimulus current is slightly higher than 40 μA to cause V_a lower than V_b, that leads to the output of comparator becomes low (0V). Meanwhile, the stimulus current reaches the designed amplitude, and the output voltage of charge pump system equals to the required operating voltage (V_{CC}). The inactivated charge pump system causes that stimulus current and output voltage of charge pump decrease again. Therefore, by changing state of charge pump system constantly, the output voltage of charge pump system, as well as the operating voltage for stimulus driver, keeps at the required operating voltage.

The stimulus driver with the adaptor can match the least required voltage. The proposed stimulus driver with adaptor

978-1-4244-9021-9/11/$26.00 ©2011 IEEE

provides any amplitude of electrode impedance with least operating voltage for 24-V device, which is sufficient to deliver the designed stimulus current, but not provides a fixed operating voltage for 24-V devices.

The proposed bi-phase stimulus driver to suppress epileptic seizure with adaptive loading design and low-power consideration has been fabricated in a 0.35-µm 3.3-V/24-V CMOS process. Fig. 5 shows the chip photograph of the fabricated stimulus driver. The layout size of the proposed stimulus driver is about 1000 × 700 µm^2.

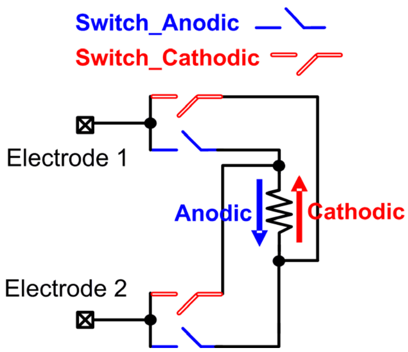

Fig. 3. Two leads electrode set consists of four switches and two electrodes.

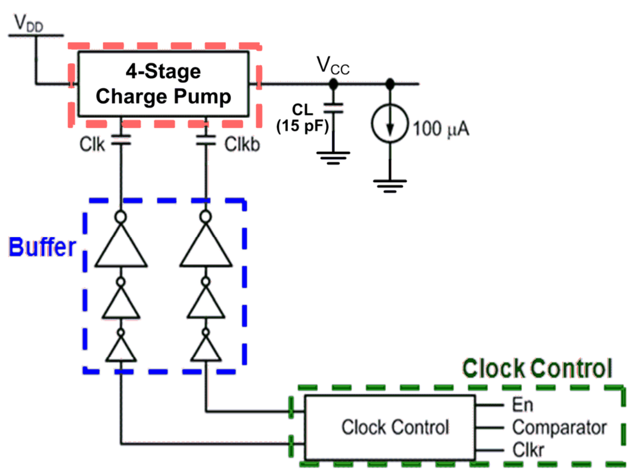

Fig. 4. Circuit schematic of charge pump system.

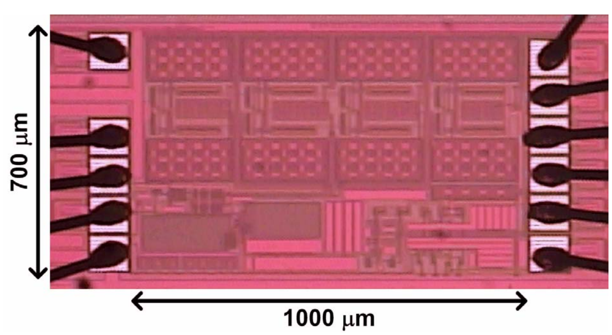

Fig. 5. Chip photograph of the fabricated stimulus driver in a 0.35-µm CMOS process.

III. Experimental Results

Under measurement, Agilent E3631A is used to provide the fixed 3.3-V V_{DD}. Hp 33120A is used to supply the 25-MHz clock signal and to enable the implanted stimulus driver. Tektronix 3054B is used to observe stimulus voltage/current of the stimulus driver.

While enable signal is given, the proposed design starts to deliver the stimulus current. Fig. 6 summarizes the measurement results of stimulus currents when the electrode impedance varies from 10 kΩ to 300 kΩ. The anodic and cathodic stimulus currents match the specification of 40 µA under the various range of electrode impedance. Fig. 7 summarizes the operating voltage verses electrode impedance. The average power consumption of the stimulus driver is 1.1~1.4 mW. All of measurement results are summarized in Table I.

The proposed stimulus driver is further integrated into closed-loop epileptic seizure monitoring and controlling system for animal test [7]. The sketch diagram of measurement setup for animal test is shown in Fig. 8. In this experiment, the stimulus current is conducted by a 4-microwire bundle, each made of Teflon-insulted stainless steel. Whenever the system detects an epileptic seizure, the proposed stimulus driver is activated by a trigger signal to stimulate the Long-Evans rat. Fig. 9 shows the test result, where the epileptic seizure with abnormal discharge was detected during 1~6 seconds, and the system triggered the proposed stimulus driver to stimulate the Long-Evans rat. After stimulation, the intensive and rapidly brain activity was suppressed.

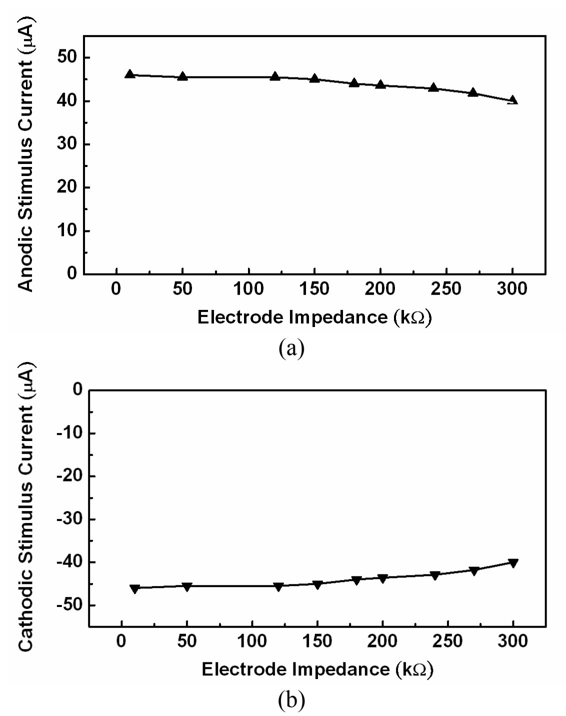

Fig. 6. (a) Anodic and (b) cathodic stimulus currents under different electrode impedances.

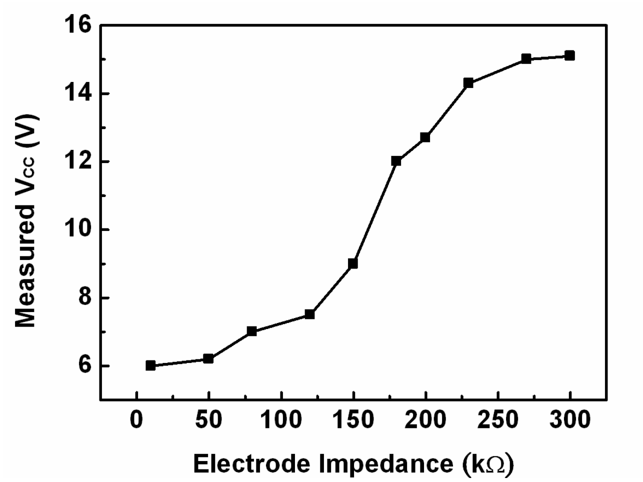

Fig. 7. Output voltage of charge pump system under different electrode impedances.

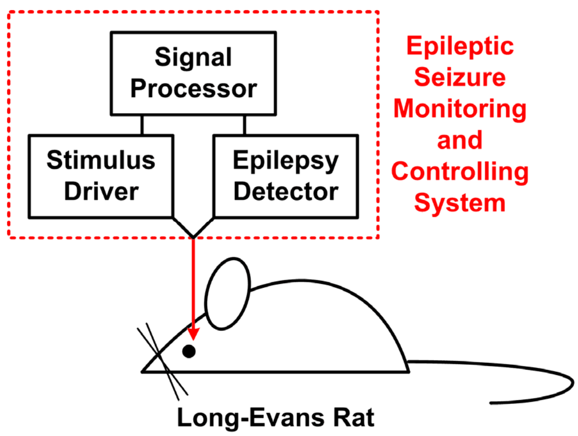

Fig. 8. Measurement setup for animal test.

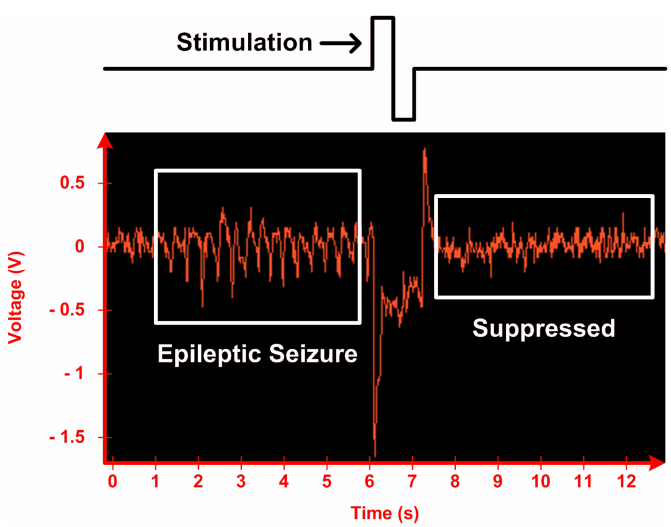

Fig. 9. Experimental result on EEG signal of Long-Evans rat.

Table I. Summary on the Proposed Stimulus Driver

Technology	**0.35-μm 3.3-V/24-V CMOS Process**
Layout Area	**1000 μm x 700 μm**
Available Stimulus Current	**~ 40 μA**
Electrode Configuration	**Two Interface Leads Per Site**
Electrode Impedance	**10~300 kΩ**
Supply Voltage	**3.3 V**
Power Consumption	**1.1~1.4 mW**

IV. Conclusion

Design of bi-phase stimulus driver to suppress epileptic seizure with adaptive loading consideration is proposed. The stimulus driver consists of the output stage, charge pump system, and the adaptor. While the electrode impedance varies from 10 kΩ to 300 kΩ, the proposed stimulus driver can constantly deliver 40-μA stimulus current. The power consumption of this work is only 1.1~1.4 mW. The stimulus driver is successfully integrated into closed-loop epileptic seizure monitoring and controlling system to verify its performance.

References

[1] P. Hese *et. al.*, "Automatic detection of spike and wave discharges in the EEG of genetic absence epilepsy rats from Strasbourg," *IEEE Trans. Biomedical Engineering*, vol. 56, no. 3, pp. 706-717, Mar. 2009.

[2] G. Cascino, "Epilepsy: contemporary perspectives on evaluation and treatment," in *Proc. Mayo Clinic*, 1994, pp. 1199-1211.

[3] W. Stacey and B. Litt, "Technology insight: neuroengineering and epilepsy - designing devices for seizure control," *Nature Clinical Practice Neurology*, vol. 4, pp. 190-201, Feb. 2008.

[4] J. Gwilliam and K. Horch, "A charge-balanced pulse generator for nerve stimulation applications," *J. Neuroscience Methods*, vol. 168, no. 1, pp. 146-150, Feb. 2008.

[5] S. Guo and H. Lee, "Biphasic-current-pulse self-calibration techniques for monopolar current stimulation," in *Proc. IEEE Biomedical Circuits and Systems Conference*, 2009, pp. 61-64.

[6] M. Ghovanloo and K. Najafi, "A compact large voltage-compliance high output-impedance programmable current source for implantable microstimulators" *IEEE Trans. Biomedical Engineering*, vol. 52, no. 1, pp. 97-105, Jan. 2005.

[7] C. Young *et. al.*, "A portable wireless online closed-loop seizure controller in freely moving rats," *IEEE Trans. Instrumentation and Measurement*, vol. 60, no. 2, pp. 513-521, Feb. 2011.

[8] M.-D. Ker *et. al.*, "Design of charge pump circuit with consideration of gate-oxide reliability in low-voltage CMOS processes," *IEEE J. Solid-State Circuits*, vol. 41, no. 5, pp. 1100-1107, May 2006.