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Multi-channel bio sensing and stimulation LSI chip using 0.18 μm CMOS process

Masaya Yamaguchi[1], Akiyoshi Shimada[2], Keiichi Torimitsu[2] and Nobuhiko Nakano[1*]

[1]Keio University, Dept. of Electronics and Electrical Engineering, Faculty of Science and Technology
3-14-1, Hiyoshi, Yokohama, Kanagawa 223-8522, Japan
Phone: +81-45-566-1543 E-mail[*]: nak@elec.keio.ac.jp
[2]NTT Basic Research Laboratories, NTT Corporation,
3-1 Morinosato- Wakamiya, Atsugi, Kanagawa 243-0198, Japan

1. Introduction

Neural sensing and stimulation techniques using a microelectrode array (MEA) are very important as regards the development of a brain-machine interface. We have already developed neural sensing and stimulation systems with an MEA [1]. The system has functions for recording and stimulating a neural signal on the same electrodes.

However the equipment constituting the system is very large and therefore unsuitable for future mobile applications. CMOS technology has the potential for high-density integration and complicated digital or analog processing on an LSI chip with low power consumption. We have developed 8-channel preamplifiers with stimulation signal formation circuits on a 2.4 × 2.4 mm^2 CMOS LSI chip.

2. LSI Chip design and evaluation

Chip functions

The designed chip is fabricated with a 0.18 μm CMOS triple-well process and is 2.4 mm square. Figure 1 shows the designed LSI layout. The chip consists of 8-channel low noise amplifiers designed to sense small neural signals and stimulation signal formation circuits. This chip makes it possible to realize multisite stimulation and neuron sensing through the MEA.

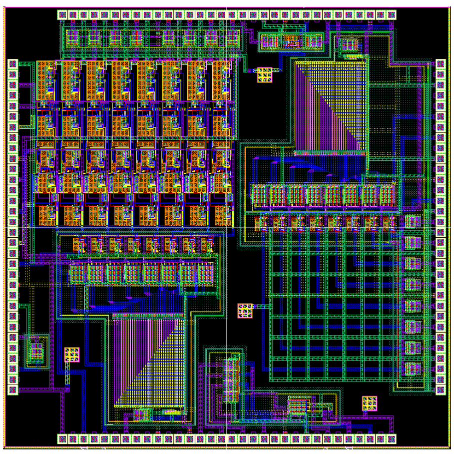

Fig. 1 Designed 2.4 mm square LSI layout.

Low noise pre-amplifier design

Figure 2 shows the circuit diagram of one channel. The blue zone is a preamplifier block for neural signal sensing and the red zone is a DC store / adder block for handling stimulation signals. In the sensing mode, the DC voltage of the input signal is stored at the capacitor. The stored DC voltage is then added to the stimulus signal to reduce the possibility of damage occurring in the stimulation mode.

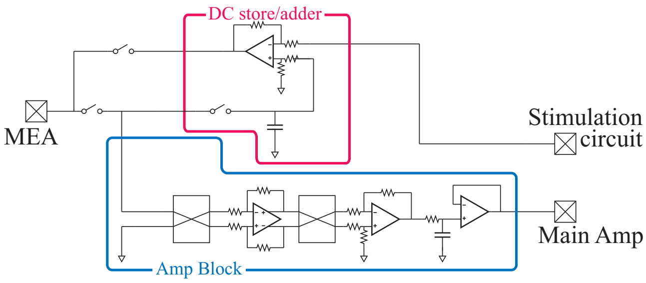

Fig. 2 Circuit diagram of a one-channel preamplifier with stimulation signal handling circuits.

The developed LSI preamplifier circuit includes a chopper circuit to prevent the relatively large flicker noise that is commonly exhibited by CMOS devices. The chopper circuit converts the input signal frequency to the chopper frequency to avoid the frequency domain, which is governed by flicker noise. Here the chopper frequency is 1 MHz. In Fig. 3 the red and blue lines show the noise floor of the preamplifier without and with the chopper circuit, respectively. These results show that the chopper circuit reduces the flicker noise to –10 dB at 100 Hz.

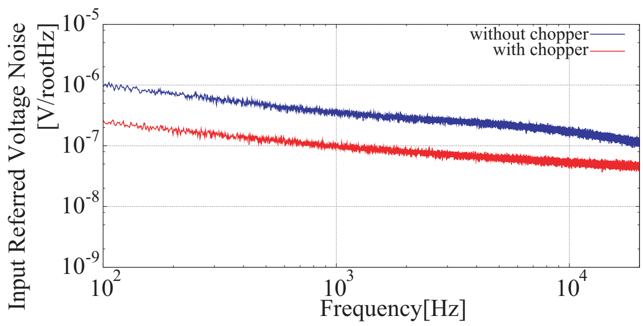

Fig. 3 Measured noise floors of preamplifiers with and without chopper operation.

We measured the neural signals with the current system, which includes a main amplifier, a band pass filter and D/A converters. The sampling frequency is from 100 Hz to 20 kHz and the neural signal amplitude is from several tens to several hundred μV. The bandwidth of the preamplifier is from DC to 150 kHz, the gain is 24.6 dB and the power consumption is 2 mW per channel. According to these results the amplification performance of the developed LSI preamplifier is sufficient for it to substitute for the current preamplifier.

Multisite stimulation circuits

Figure 4 shows the circuit diagram of the multisite stimulator. To realize multisite stimulation using a small number IO pad, we designed the serial-parallel digital converter and a 4-bit digital analog converter (DAC). This circuit system can supply a voltage to the 8-channel pad connected to the MEA. The maximum stimulation signal voltage amplitude that can be employed with a bi-phase voltage waveform is ±700 mV (see Fig. 5). The typical time slot width is 20 μs, and this is adequate for neural stimulation. As regards the stimulation, first the mode is switched from the sensing mode to the stimulation mode, then a reset signal is applied to the serial to parallel controller, and finally continuous serial digital data are converted to an analog voltage waveform for stimulation at any channel with any timing.

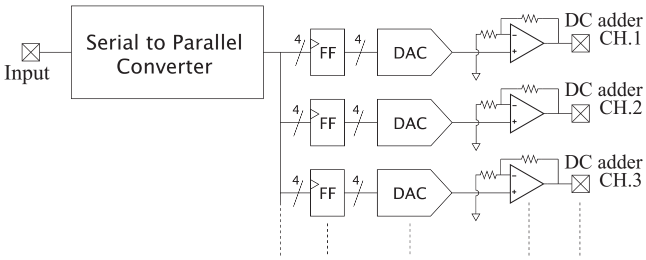

Fig. 4 Coded waveform and the circuit diagram of multisite stimulator.

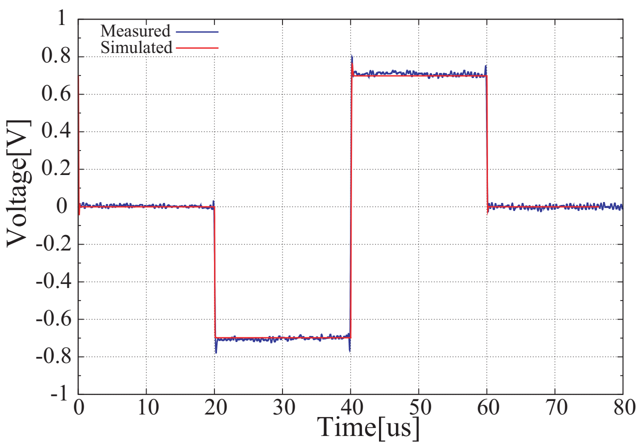

Fig. 5 Measured voltage waveform formed by multisite stimulation circuit. Here one site is stimulated and the other sites are grounded.

3. Measurement results

To confirm the stimulation performance, dissociated cerebral cortical neurons from Wistar rat embryos (embryonic day 18) were cultured on the polymer MEA. The LSI chip was connected to our conventional system. A stimulation signal was formed on the chip with serial data by using a PC controlled digital signal generator. The signal was applied to neurons cultivated on the MEA for 23 days in vitro. Figure 6 shows the neural response with and without stimulation. Before and after applying stimulation, spontaneous periodic bursts were observed. During the stimulation period, a number of spikes were evoked as shown at the bottom of Fig. 6. This result demonstrates the stimulator of the LSI chip can induce the neural activity without any damage.

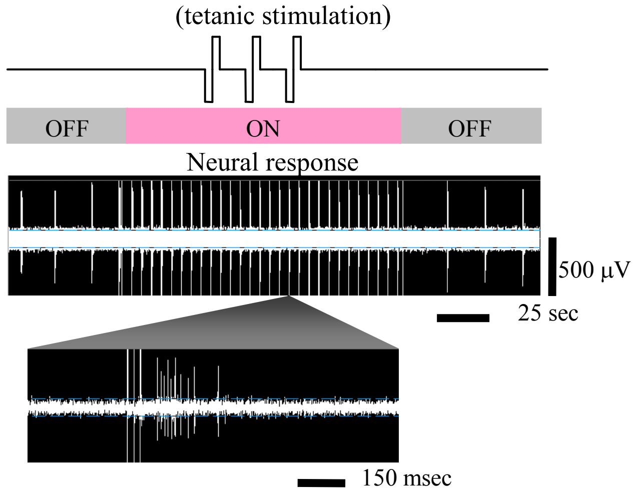

Fig. 6 Measured extracellular action potential.

4. Conclusion

We designed 8-channel preamplifiers and multisite stimulation circuits on a 2.4 mm square LSI chip using a 0.18 μm CMOS triple-well process. The preamplifier circuits can amplify a small neural signal with low power consumption and 1 MHz chopper operation. The stimulation circuits can apply a voltage between -700 and +700 mV to any channel and with any timing using serial digital data. The bi-phase stimulation waveform formed by the designed LSI has the same performance as that formed with a conventional stimulation system. This function was confirmed by connecting the LSI to a conventional sensing and stimulation system. The miniaturization of the system by using the custom LSI will offer great advantages for future brain machine interface applications.

Acknowledgements

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The experiments were conducted in accordance with the regulations on animal care of the ethical committee of Laboratory Animals, NTT Basic Research Laboratories.

Reference

[1] Yasuhiko Jimbo, Nahoko Kasai, Keiichi Torimitsu, Takashi Tateno, and Hugh P. C.Robinson "A System for MEA-Based Multisite Stimulation" IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING, VOL.50, NO.2, FEBRUARY 2003, pp. 241-248