The SoC Design of a Versatile Biomedical Signal Processor for Potentiostat

Chun-Po Huang, Ya-Ting Shyu, Tsung-Yu Hsieh, Chieh-Wen Cheng, Wei-Chiun Liu, Hao-Ting Jian, Ying-Wei Wang, Bin-Da Liu[1], Soon-Jyh Chang[2], Lih-Yih Chiou[3], and Chung-Ho Chen[4]
Department of Electrical Engineering, National Cheng Kung University, Tainan, Taiwan
bdliu@mail.ncku.edu.tw[1], soon@mail.ncku.edu.tw[2], lihyih@mail.ncku.edu.tw[3], chchen@mail.ncku.edu.tw[4]

***Abstract*—This paper presents a versatile and portable System on a Chip (SoC) biomedical signal processor which collects and analyzes biomedical signals in real-time. Measurements of the melatonin-mixed potassium ferrocyanide solution and patient specimen experiment are presented for verification. The measurement results show that this proof-of-concept prototype functions as a traditional potentiostat with high precision discrete components.**

Keywords—cyclic voltammetry; biomedical signal processor

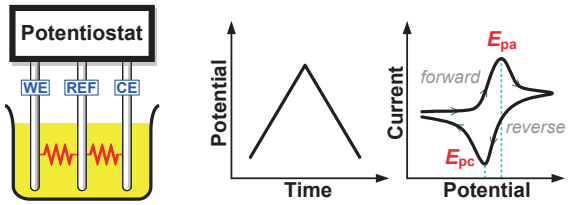
I. INTRODUCTION

A biomedical signal processor is an electrochemical device composed of an electrochemical biosensor and signal processor which measures biomedical signals and analyzes patient data in real-time. In a biomedical signal processor, the electrochemical biosensor is an analytical device for the investigation of reaction mechanisms related to electrochemical or biochemical phenomena. This function is commonly provided by potentiostat [1][2][3] because of the reliability and ease of manufacture. A typical potentiostat measurement system is shown in Fig.1(a). The labels *CE*, *REF*, and *WE* denote the counter, reference, and working electrodes. The analyte is placed into contact with the three electrodes. By controlling the potential across the analyte, the biomedical reactions (such as reduction-oxidation reaction) of the analyte can be measured by the current-sensing electrodes. The potential between electrodes is controlled by potentiodynamic electrochemical measurement methods. One of the common measurement method is cyclic voltammetry [4]. A typical cyclic voltammetry potential waveform and voltammogram are shown in Fig. 1(b). After the measurement process, the biomedical signal is passed to processor for analysis.

A potentiostat capable of performing cycle voltammetry with specific measurement parameters, such as waveform or signal swing of potential across analyte, can only be applied to corresponding types of biomedical solution. If the system measurement parameters are modifiable, the biomedical signal processor can support biomedical sensing and analysis for various kinds of solutions.

This paper implements a versatile biomedical signal processor composed of system on a chip (SoC) and external EEPROM. The SoC includes a microcontroller unit (MCU), XRAM, and analog potentiostat circuit. The SoC is fabricated with 180 nm CMOS technology and occupies 8.343 mm^2. The measurement method can be implemented as a program saved on the on-chip XRAM or off-chip EEPROM. The default electrochemical measurement method implemented in this system is cyclic voltammetry. With external EEPROM, the measurement program can be re-written and the experimental parameters can be adjusted according to the analyte or measurement method. The performance of this prototype is verified by comparing the melatonin concentrations measured from potassium ferrocyanide solution and patient specimen.

This work was supported in part by National Science Council (NSC) of Taiwan under Grant MOST 104-2220-E-006-006.



(a) (b)

Fig. 1. (a) Potentiostat measurement system. (b) Cyclic voltammetry potential waveform and typical cyclic voltammogram.

The rest of this paper is organized as follows: Section II describes the system architecture, implementation of key building blocks, and the system operations of potentiostat. Section III presents the measurement results. Conclusions are given in Section IV.

II. SYSTEM ARCHITECTURE AND OPERATIONS

The system architecture of the prototype biomedical signal processor is composed of SoC and off-chip EEPROM as shown in Fig. 2. The SoC circuit can be categorized into digital and analog parts. The digital part consists of a programmable MCU (PACMP-S51), and the analog part consists of digital-to-analog converter (DAC), analog-to-digital converter (ADC), and three operational amplifiers (OPamp). To perform cyclic voltammetry, the PACMP-S51 sends digital signals to the DAC to create a linear and continuous scanning potential between the *REF* and *CE* electrodes of the electrochemical biosensors. The potential waveform is triangular as shown in Fig. 1(b). During the reduction-oxidation reaction of the solution, the current is sensed by the working electrode. According to the range, the current is transferred to voltage with proper resistance selected by the MCU. This voltage signal is converted to digital by the ADC and then passed to the MCU. Finally,

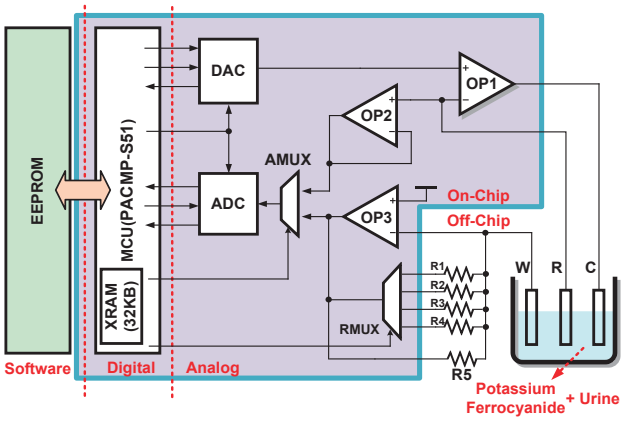


Fig. 2. The architecture of versatile biomedical signal processor.

the MCU analyzes the received electrochemical potential information from the ADC output.

A. Digital Block

The PACMP-S51 is an 8051-compatible MCU integrated with a digital-analog interface. It provides various measurement methods. The data received from the ADC is stored on the 32-kB on-chip XRAM or outputted to other devices via standard UART, SPI, or I^2C. Fig. 3 is the system block diagram of the PACMP-S51, including MCU core, 256-byte SRAM, 32-kB XRAM for storing data, EMIF for accessing external EEPROM, and standard interfaces such as UART, SPI, and I^2C.

B. Analog Block

The analog block consists of a 12-bit DAC, three high-gain (>100 dB) OPamps, and a 12-bit ADC. This subsection shows the detailed specifications and structures of these circuits. The SoC was fabricated with 180 nm CMOS process. The analog block uses I/O devices and 3.3 V supply for application.

- DAC: The structure of the DAC is illustrated in Fig. 4(a). It consists of a high DC-gain and wide-output-swing Opamp, a 12-bit binary-weighted capacitor array, clock divider, and digital control circuit. The DAC has two phases of operation, sample phase and hold phase. During sample phase, the bottom-plates of the capacitors connect to ground or VDD according to the 12-bit digital code input. During the hold phase, the bottom-plates of the capacitors are flipped to the output of Opamp. To relax the OPamp design difficulty, the operation frequency of the DAC is set to the system frequency divided by 128.

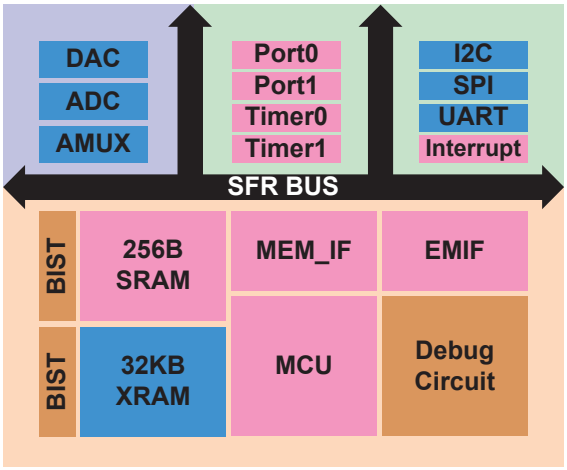


Fig. 3. PACMP-S51 architecture

- Opamp: The structure of Opamp is shown in Fig. 4(b). The folded-cascode structure is adopted to achieve high DC-gain. The combined p-type and n-type input pair supplies consistent high linearity over the wide input voltage range. The output stage is sized allowing the Opamp to achieve wide output swing (0.45 to 2.85 V) and high slew-rate (with a 100 pF output capacitor loading) operation.
- ADC: Successive approximation register (SAR) ADC is chosen for this application due to low power consumption. Fig. 4(c) shows the structure of the SAR ADC. Two input channels can be selected by the MCU. The SAR ADC executes analog-to-digital conversion with switchback switching scheme [5]. The operation speed of the ADC is the same as the system clock. The ADC has two operation states controlled by the enable

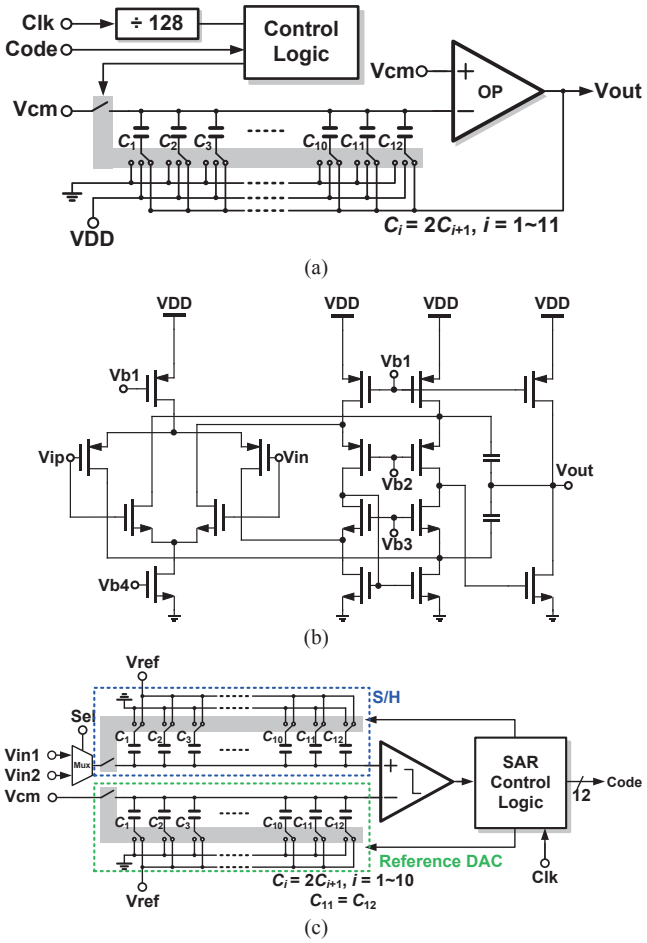


Fig. 4. Building blocks of analog part. (a) DAC. (b) Opamp. (c) ADC.

signal from the MCU. When the enable signal is on, the ADC operates normally; otherwise, the ADC enters and stays in idle state to save power.

C. *Interface between Digital and Analog Blocks*

There is an interface circuit between the digital and analog blocks. Because the voltage domain of digital block (1.8 V) and analog block (3.3 V) are different, level-up/down shifter circuits are needed (see Fig. 5). A handshaking protocol is used for the MCU to communicate with the analog components. During data transfers, a control bit from the MCU is asserted and waits for the ready signal from the ADC/DAC as shown in Fig. 6. After the ready signal is detected, the control bit is de-asserted and the communication is complete.

III. Experimental Results

This SoC was fabricated using 180 nm CMOS process by TSMC. The digital circuits use core devices with 1.8 V supply and the analog circuits use I/O device with 3.3 V supply. Fig. 7 shows a die photo of this SoC and a detailed view of the analog blocks. The area of the whole chip is about 8.343 mm^2, and the active area of the analog blocks is about 0.285 mm^2. In this section, the experiments of measuring the melatonin concentrations in potassium ferrocyanide solution and patient specimen are presented. The setup environment and the detail of experiments are described in the following.

A. *Experiment Environment and Setup*

The measurement environment and setup are shown in Fig. 8. A power supply provides 1.8 V for the digital part and 5 V for on-board low-drop regulators (LDOs) which provide analog supply (3.3 V) and bias voltages. A clock generator gives a 1 MHz clock signal for system. An oscilloscope is used to probe the voltages on the DAC's output and ADC's input for observing the reduction-oxidation reaction. The printed circuit board (PCB) and its connection look complex due to extra design for sub-block testing. The measured solutions in this experiment include potassium ferrocyanide with melatonin and patient specimen. The electrodes used include carbon and gold electrodes.

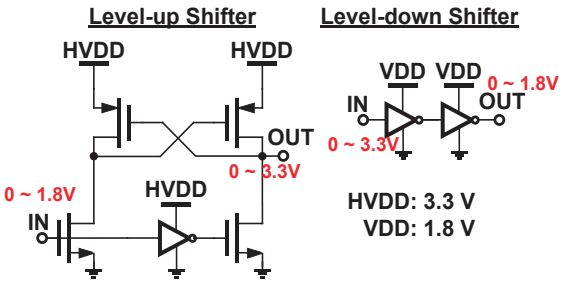


Fig. 5. Level-up/down shifter.

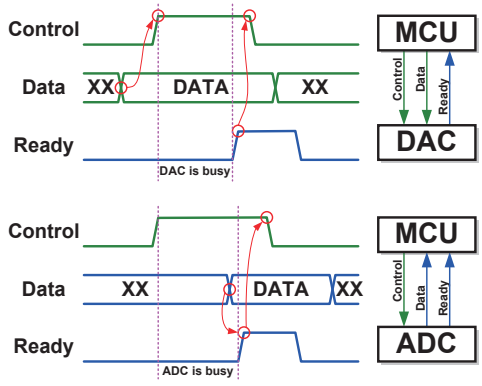


Fig. 6. PACMP-S51 and DAC/ADC handshaking protocol

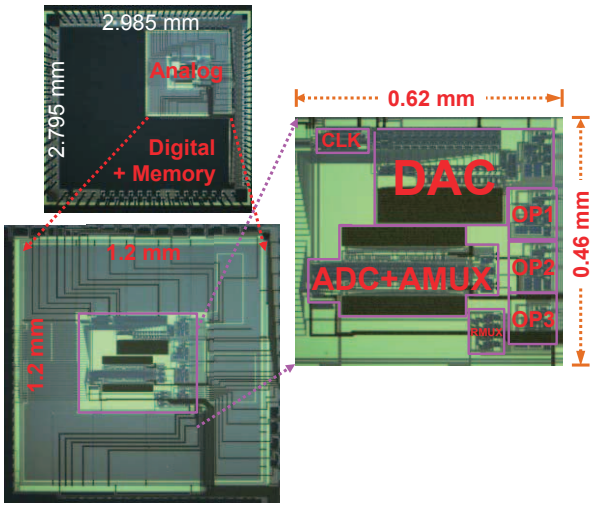
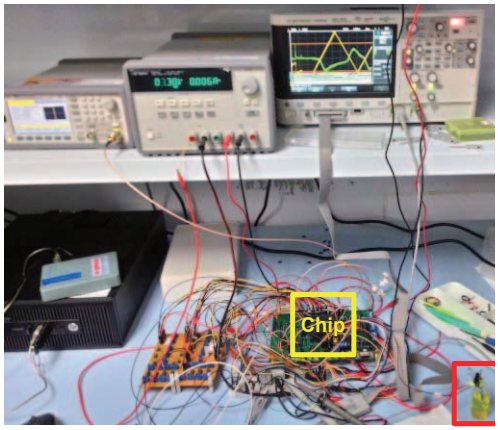
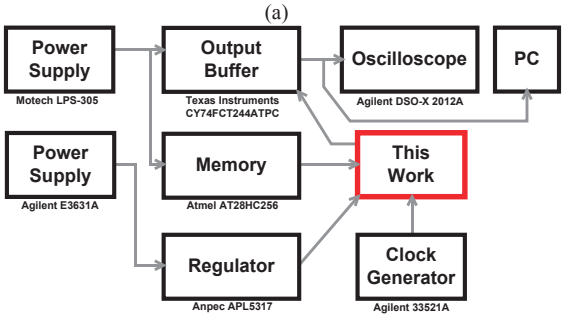


Fig. 7. Die photo of SoC and its analog blocks.



(a)



(b)

Fig. 8. Experiment environment and setup. (a) Photo (b) Configuration.

B. *Measurement of Potassium Ferrocyanide Solution with Melatonin*

This experiment uses a gold electrode to measure the reduction-oxidation reaction of potassium ferrocyanide solution mixed with different concentrations of melatonin. The time-domain measurement results of potassium ferrocyanide solution without melatonin are shown in Fig. 9. The x-axes of all plots show time. The y-axes of the plots from top to bottom show the output voltage of DAC, and the output code of ADC. In the top plot, the scan rate and signal swing of the triangle potential waveform are 41.7 mHz and 1.2 V (1.05 V to 2.25 V). The bottom plot reveals the result of the reduction-oxidation reaction. Fig. 10 shows the transfer curves of reduction-oxidation reaction with various concentrations of melatonin. It shows that the heavier concentration of melatonin will result in higher peak current. The relationship between concentration and the peak current difference (with respect to buffered solution) is illustrated in Fig. 11.

C. *Measurement of Urine Sample*

This experiment uses a gold electrode to analyze the patient specimen. The target is to estimate the concentration of melatonin in the patient specimen. The measured transfer curves of the urine sample and buffered solution are illustrated in Fig. 12. The difference between the peak values of these curves is about 0.0468 mA. The concentration of melatonin in the urine sample is estimated at 143.19 pg/ml according to the corresponding x-axis value by mapping the value with the point that has the identical y-axis value on the curve in Figure 11.

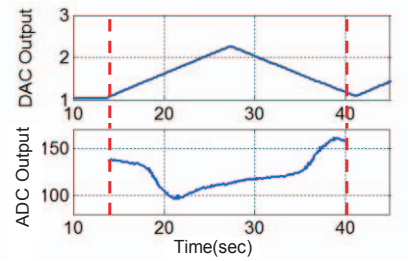


Fig. 9. The measurement results of potassium ferrocyanide buffered solution.

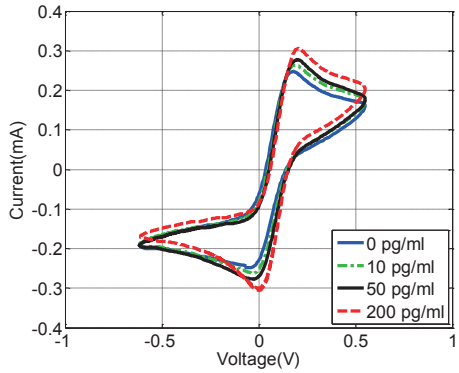


Fig. 10. Cyclic voltammetry of melatonin solutions measured by using this SOC chip.

IV. Conclusion

This paper implements a versatile and portable biomedical signal processor realized by a SOC chip that can perform biomedical analysis. Two experiments were presented for performance verification. The first experiment measured potassium ferrocyanide solution mixed with different concentrations of melatonin. The second experiment measured a patient specimen, and estimated the concentration of melatonin. The measurement results show that the performance of this prototype can satisfy the requirement of patient specimen measurement and analysis.

References

[1] J. C. Fidler, W. R. Penrose, and J. P. Bobis, "A potentiostat based on a voltage-controlled current source for use with amperometric gas sensors," in *Proc. Instrum. Meas. Technol. Conf.*, May 1991, pp.456–459.

[2] J. Zhang, N. Trombly, and A. Mason, "A low noise readout circuit for integrated electrochemical biosensor arrays," in *Proc. IEEE Sensors*, Oct. 2004, pp.36–39.

[3] C. Y. Huang, Y. C. Huang, T. Y. Lin, C. H. Chang, and X. F. Li, "An SOC-based portable cyclic voltammetry potentiostat for micro-albumin biosensors," in *Proc. IEEE Conf. Ind. Electron. Appl.*, May 2007, pp.604–609.

[4] J. Wang. *Analytical Electrochemistry,* Second Edition, New York: John Wiley & Sons, 2000.

[5] G.-Y. Huang, S.-J. Chang, C.-C. Liu, and Y.-Z. Lin, "10-bit 30-MS/s SAR ADC using a switchback switching method," *IEEE Trans. VLSI Syst.*, vol. 21, no. 3, pp.584–588, Mar. 2013.

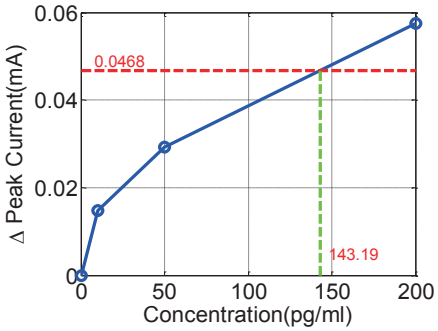


Fig. 11. The relationship between concentration and the peak current difference (with respect to buffered solution).

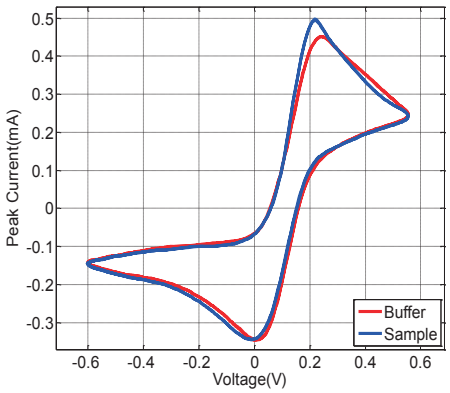


Fig. 12. Cyclic voltammetry of urine sample and buffered solution.