WIRELESS INTEGRATED MICROSYSTEMS LAB

A Pulsed Electrochemistry Readout IC for Single-Transistor-based Biosensor

I. Introduction

In recent years, researchers have discovered more and more biomarkers in body fluids as a diagnostic index of diseases . In the medical system, blood tests and urine tests have been widely used due to their accessibility and accuracy. However, current equipment for these tests is usually bulky and expensive. Besides, the test equipment requires medical professionals to operate the devices carefully, causing the whole process time-consuming. With the demands of portable devices for real-time point-of-care, the devices should be low power, reconfigurable, sensitive, and selective to the target biomarkers. In chemical analysis, the electrochemical method has advantages in good repeatability, accuracy, direct access to body fluids, low cost, and low power consumption . Amperometry is one of the popular sensing methods. By applying a constant or pulse voltage to the sensor or transducer, the current changes over time represent the dynamics of chemical reactions.

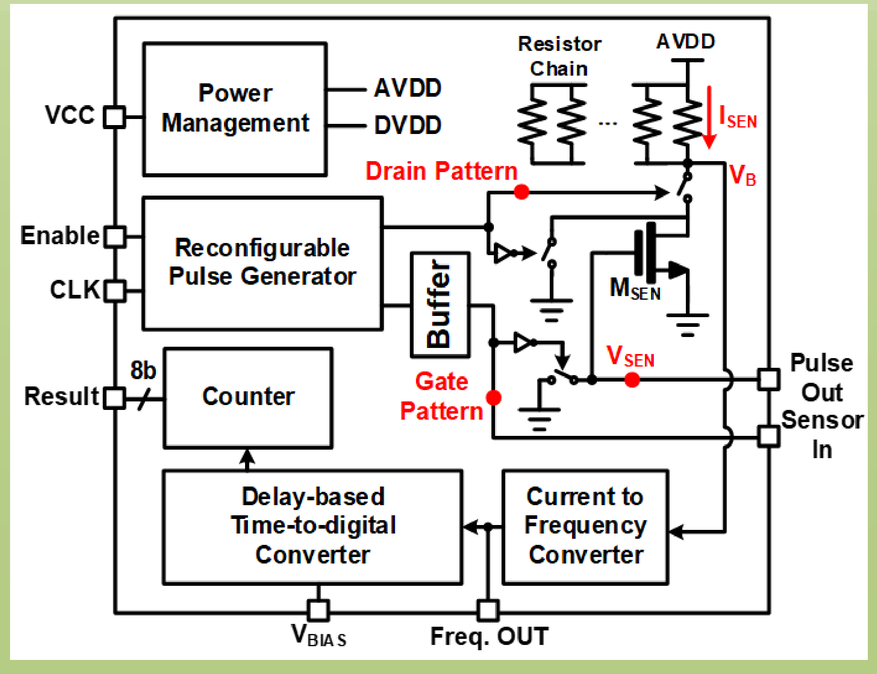

Fig.1 Block diagram of the proposed circuit

II. Design of Readout IC

Fig. 1 shows the block diagram of the proposed readout circuit, mainly includes a reconfigurable pulse generator, current-to-frequency converter, and a time-to-digital converter.

Fig. 2 shows the schematic of a reconfigurable pulse generator. The proposed system measures the concentrations of an analyte by using the double-pulse mechanism , which can mitigate the screen effect. One pulse serves as the stimulus signal, and the other pulse is for the enable and reset signals of the sensing transistor. Two 4-bit multiplexors and a D flip-flop chain are implemented for generating two pulse signals. In the proposed design, the drain and gate pulses can be adjusted from $8T_{clk}$ to $25T_{clk}$, where T_{clk} is the unity delay of 10 μs. A timing gap is devised between the rising edge and falling edge of two pulses and is realized by shifting two inputs of the two MUXs and two NOR gate. The amplitude is adjustable through a supply-shifting mechanism for applying to different sensors. By changing the V_{DD} of the buffer, the amplitude of the gate pulse varies.

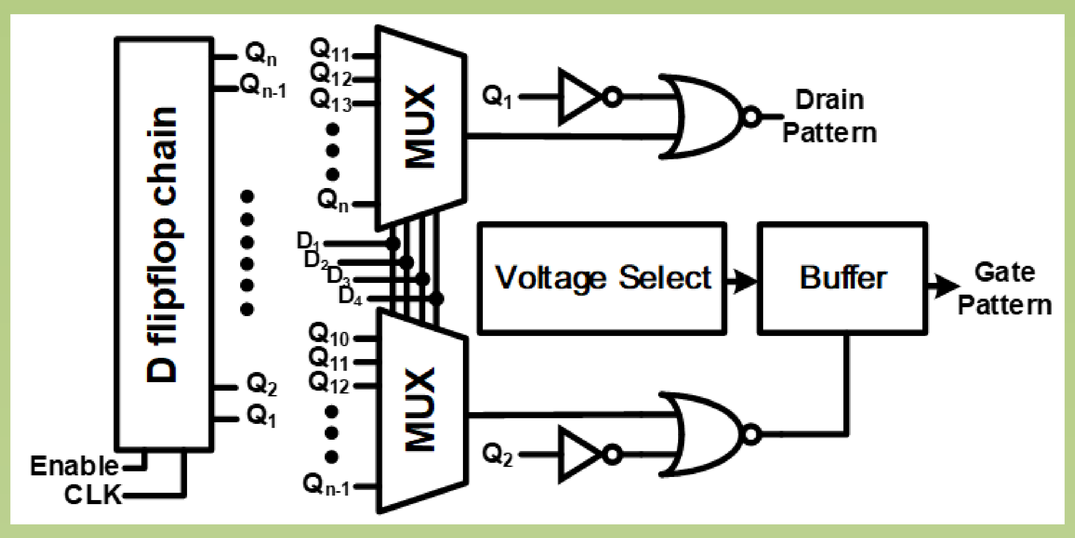

Fig. 2 Schematic of reconfigurable pulse generator

Fig. 3 shows the schematic of the current-to-frequency converter. The charging time of the capacitors (C_c) determines the output frequency . The gate voltage to the bio-sensing transistor changes with different concentrations of the analyte on the sensing electrodes. The voltage is amplified by the transconductance of the bio-sensing transistor and converted to a current that charges the timing capacitance. The state transition is controlled by a comparator combined with a Schmitt trigger and a non-overlapping clock generation. When the voltage on one of the paths is higher than the other, the comparator changes the state. The Schmitt trigger increases noise tolerance during the transition state. The non-overlap circuit not only provides two charge/discharge signals for the two paths, but also prevents the short circuit at the transitions between charging and reset phases.

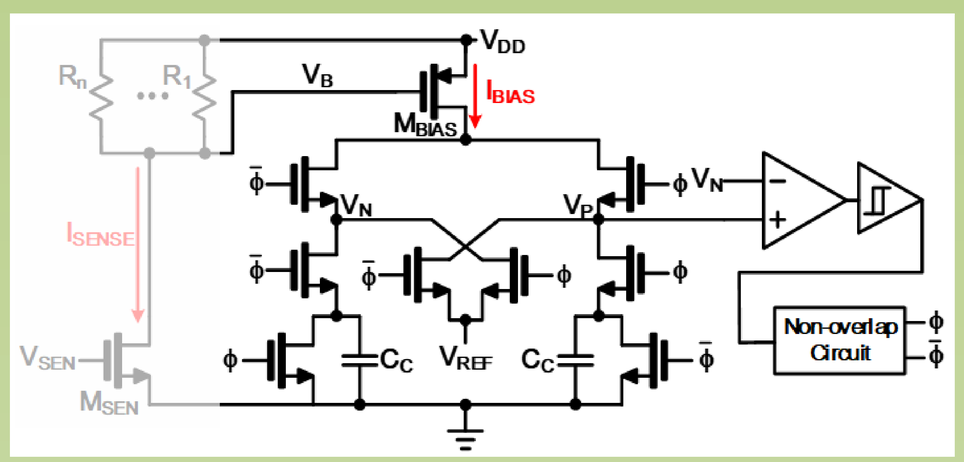

Fig. 3 Schematic of the current-to-frequency converter

In order to sense the frequency change of the I-to-F, a time-to-digital converter (TDC) is employed. Fig. 4. shows the schematic of the TDC design. The delay line chain is responsible for the pulse width sensing. The delay chain is divided into coarse and fine-tuning schemes for saving power and area. The coarse delay line helps to eliminate the baseline width of the output duration and to reduce the required numbers of stages in the fine delay line for an extensive range detection. In the fine delay chain, delay blocks sense the difference of the pulse width. Then, the delay chain produces thermometer codes according to the length of the input signal. Finally, the 8-bit counter converts the thermometer codes into binary codes. Therefore, by reading out the counter output, the information of the analyte concentration can be obtained.

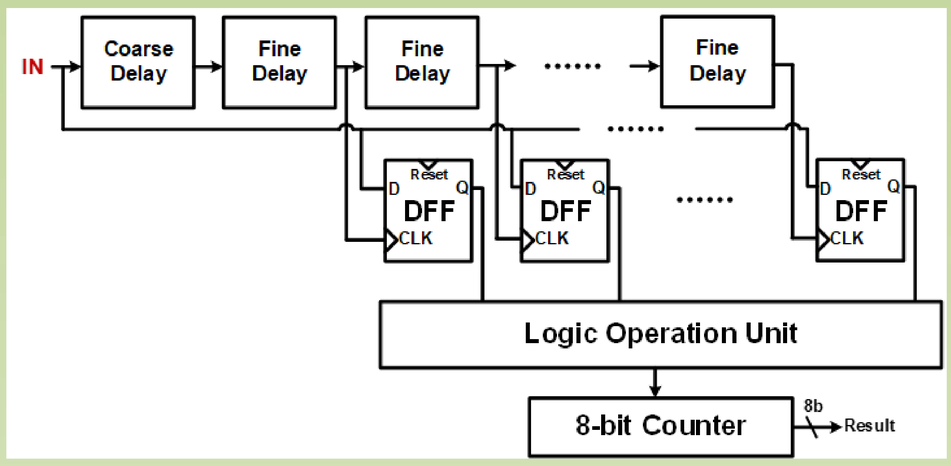

Fig. 4 Schematic of TDC

III. Implementation & Measurement Result

Fig. 5 shows the chip photograph of this design. This chip was fabricated in a 0.18 μm CMOS process, and the chip area is 1.3 mm x 1.2 mm. The chip consumes 14μW at a supply voltage of 1.2V. The chip was mounted on the printed circuit board (PCB) for the test. In addition, the test chip was sealed with epoxy to reduce the noise coupling from the environment, such as light interference. To verify the function of the proposed circuit, we measured the analyte concentrations of potassium ferricyanide using two gold electrodes. Fig. 6 shows the measurement results. Before the measurement, the duration and amplitude of the gate pulse are set to 170 μs and 0.6 V. A two-electrode electrochemical sensor is used to translate the chemical reactions to electrical signals. The results show that the designed circuit can detect the analytes in a range of 1nM ~1mM $K_3[Fe(CN)_6]$ concentration.

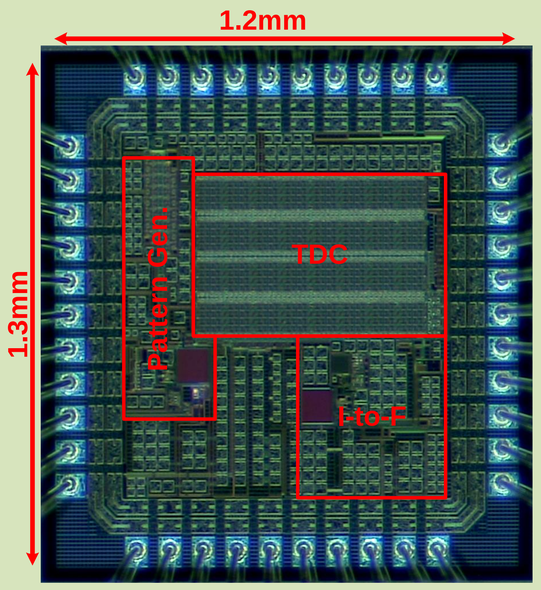

Fig. 5 Chip photograph

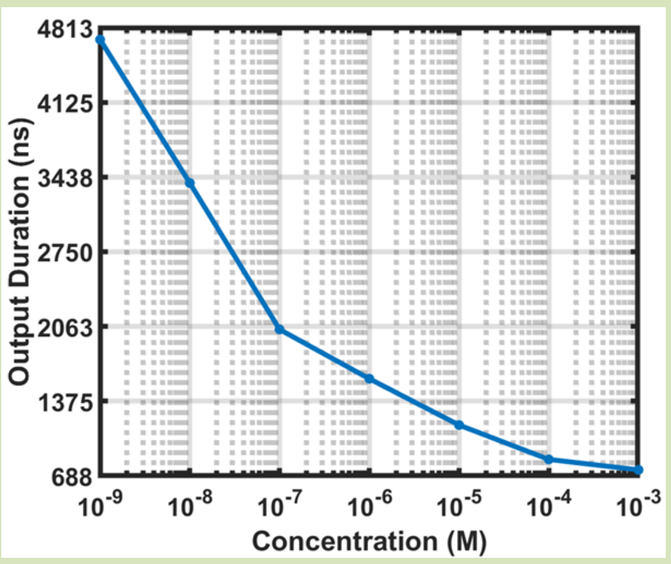

Fig. 6 Measurement results of $K_3[Fe(CN)_6]$ concentration