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A Multimodal Lab-On-CMOS based Biosensor System

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***Abstract*—This paper presents the design of a multimodal sensor in CMOS integrated circuits for biosensor applications. The system consists of five sensor modalities: temperature, impedance, pH, electrochemical, and optical. The sensor electrode topology was simulated using COMSOL Multiphysics for an active electrode area of 100 $\times$ 100 μm^2. The readout was designed in a commercial 0.18 μm CMOS technology. Monte Carlo simulation was performed on the individual modalities, considering process variations. The pH sensor sensitivity was 91 mV/pH over the 5.71 to 7.31 range. The sensitivity of the temperature sensor was 0.6 mV/°C over a 10 °C to 50 °C. The electrochemical sensor has a current range of 10 nA and 5 μA over the 0.2–1.2 V range for cyclic voltammetry and amperometry.**

***Index Terms*—Multimodal Sensors, Lab-on-CMOS, temperature sensor, pH sensor, electrochemical sensor, impedance sensor, SiPM, COMSOL.**

I. Introduction

Auobioluminecsent bioreporter cells, created using Luciferase gene cassette, have been used to understand biomolecular processes underlying cellular drug response, disease progression, and gene function [1]. CMOS technology can be used to design multimodal sensors with reduced size, weight and power (SWAP) compared to implementing discrete sensors [2]. The sensitivity, linearity, and dynamic range of each individual sensor are considered in a co-design sequence with the other sensors.

There is significant research on multimodal systems consisting of multiple sensors. Many systems are implemented with discrete components or benchtop equipment. State-of-the-art, low-SWAP, CMOS-based multimodal sensor systems typically consist of two to three sensors in a single package [3]–[8]. However, to monitor the local environment of cells, including the growth medium, five sensors are needed. The light emitted from the auto-bioluminescent cells carries vital information [9]. Biochemical processes are also sensitive to temperature and pH, thus requiring monitoring of those quantities [10], [11]. Cell impedance monitors, in real time, the viability and motility of cells [12]. Electrochemical detection quantifies various analytes using cyclic voltammetry or amperometry [13]. The novelty of this design is the combination of these five sensors in one single package, which can provide all the necessary information for a lab-on-CMOS system. This approach can be used in a wide range of applications, including robotics, surveillance, healthcare, and smart homes [14]–[16].

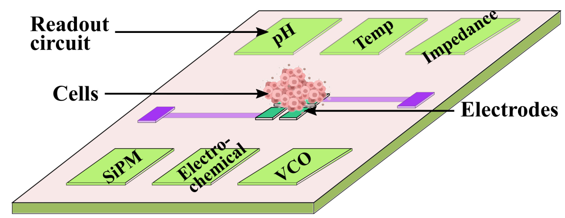

Fig. 1. System overview of the multimodal sensor. pH, electrochemical, impedance, temperature, and optical sensor are designed. The readout circuits are placed along the periphery of the chip. The electrodes of all five sensors are placed in the center. Biological cells are placed on the electrodes for measurement.

Autobioluminescent cells, in growth medium, are placed on top of the electrodes as shown in Fig. 1. The five sensors capture the respective signals, and the readout circuits convert them into voltages. An analog to digital converter (ADC) can be used to digitize the output [5], [17]. We report on the design of a low power multimodal sensor for real-time *in situ* monitoring of autobioluminescent cells. To reduce area and power consumption, a voltage-controlled oscillator (VCO) is used for voltage-to-frequency conversion instead of a power hungry and space intensive ADC. The novelty of this work lies in the development of the five sensors together with finite element analysis simulations to understand the interaction of multiple sensor electrodes.

The paper is structured as follows: Section II details the multimodal sensor system and individual sensor designs. Section III presents the electrode design and simulation experiment. Section IV covers the circuit simulation results for each sensor. Finally, Section V offers concluding remarks.

II. System Design

Fig. 1 shows the placement of sensor electrodes at the center of the chip and the analog front-end readout circuits along the periphery. The sensor area consists of electrodes for a pH sensor, a silicon photomultiplier (SiPM) based on a 2$\times$2 single-photon avalanche diode (SPAD) array, three metal electrodes (Working (WE), Reference (RE) and Counter (CE)) for the electrochemical sensor, and electrodes for the impedance sensor. The area also includes a temperature sensor.

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