US-Japan NSF IRES Program for Developing Portable Point-of-Care Testing Devices: Research Outcomes of Year 1

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Abstract

Supported by the International Research Experiences for Students (IRES) program of National Science Foundation (NSF), this program aims to develop a portable point-of-care testing (POCT) device for detection of pathogens by integrating a filter-free wavelength complementary metal-oxide-semiconductor (CMOS) optical sensor and a microfluidic device in a portable platform. For the first year of the program, a cohort of four students successfully conducted their summer research with mentors at Toyohashi University of Technology (TUT) in Japan. This paper reports on the research outcomes of the first year of the program.

Keywords

Undergraduate student poster, International research experiences, Microfluidics, CMOS sensor, Research abroad

Introduction

The recent global COVID-19 pandemic has shown the need for a fast, reliable, and accurate diagnostic method for detecting pathogens. Portable point-of-care testing (POCT) devices provide a possible low cost, easy-to-use solutions with a high detection success rate and accessibility to low-resource areas of the world. Despite the progress made in recent years, POCT devices still may require skilled technicians and external power supplies [1].

Microfluidic channel devices allow for the miniaturization of larger-scale applications, such as pathogen detection. Thus, utilizing the advantages of microfluidics results in a reduction of time, cost, and resources necessary for wide-scale testing [2]. The filter-free wavelength (FFW) complementary metal oxide semiconductor (CMOS) sensor can detect multiple wavelengths in the incident light without any optical filters [3], which makes it ideal for POCT devices as it cuts down on both the size and cost of the sensor.

Therefore, this IRES program aims to address the current limitations of POCT devices by combining microfluidics and the FFW CMOS sensor in a portable platform and to develop a portable POCT device for efficient detection of infectious pathogens. The first cohort of students conducted an eight-week-long summer research program at Toyohashi University of Technology (TUT) in Japan to integrate microfluidics and the CMOS sensor. This paper aims to document their research outcome for the first year of the IRES program.

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Methods

FFW CMOS sensor preparation

The FFW CMOS sensor was pre-made at TUT's Institute for Research on Next-generation Semiconductor and Sensing Science ($IRES^2$). First, a microcircuit with two sensors was attached to a breakout PCB with a light cyanoacrylate adhesive. The sensors were wire-bonded to the PCB using an ultrasonic wire bonding machine (Westbond Model 7KE) and aluminum wire (Figure 1A). Then, a thin layer of polydimethylsiloxane (PDMS) was applied on top of the sensors and the wire bonded connections for protection. This breakout PCB was integrated into a larger PCB for signal conditioning. It uses an Op Amp (Figure 1B) to convert measured currents into voltages. Analog-to-digital converters (Texas Instruments ADS1255) were used to change these voltages into 16-bit digital signals for a microcontroller to read. The microcontroller sent the values to a Bluetooth transmitter which can then be read via a terminal emulator using a UART serial port connection..

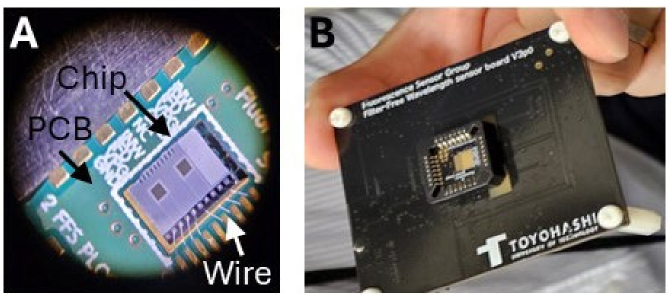

Figure 1. CMOS sensor. (A) A chip of two sensors wire-bonded to PCB. (B) Full sensor PCB.

Microfluidics

Microfluidic channel devices with a channel height of 100 μm (Figure 2) were designed using computer aided design (CAD). The mold was printed using a 3D printer (Phrozen Sonic Mini 8k) with a 5:1 mixture of white and gray resins (SK Honpo Optical Modeling, DLP 3D Printer High Toughness Ultra Resin, White and Gray) to achieve an ideal rigidity. After curing, the mold was washed several times with IPA, followed by drying with compressed nitrogen gas after each wash. After 30 min-long UV treatment, the mold was soaked in fresh isopropyl alcohol (IPA) for 1.5 hours and then heat treated at 80°C for 30 minutes.

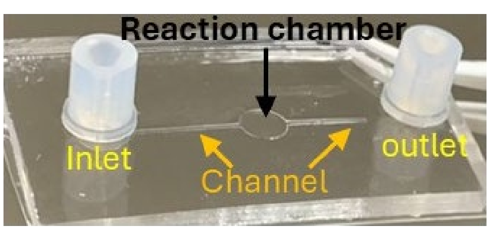

Figure 2. Microfluidic device used in testing

For PDMS casting, PDMS was vacuum centrifuged (EME V-mini 300) for 5 minutes at 1,500 rpm and then poured into the mold. The PDMS cured for two hours at 80°C, and the cast was removed from the mold. Lastly, 1 mm-diameter inlet and outlet holes were punched into the PDMS cast. The cast and a separately prepared PDMS substrate were bonded together through plasma bonding

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(J-Science Lab, JPA 300). The microfluidic channel device was then heat treated at 80°C for full bonding.

3D printed case

The base of the case (80 mm × 90 mm) included side venting features for heat removal and access holes for the PCB external power cord and switch. The base used heat-set inserts and standoffs to mount PCB (Figure 3A). The base was printed using a 3D printer (Elegoo Saturn 3 Ultra) and the white resin described previously. The stage consisted of two layers to adjust the microfluidic channel device in the x and y directions independently. The first stage used four small dowel pins directed downward that interfaced within slots on the base, to allow a 9 mm range of motion in the x-direction. Then, four more dowel pins were used directed upward, interacting with slots in the second stage, which allowed 10 mm of motion in the y-direction (Figure 3B). The second stage had a cavity (35 mm × 55 mm) for placing the microfluidic device and a 3 mm diameter light inlet for an external light source to excite the sensor. The stage layers were printed using the Phrozen printer and the mixed white and gray resins described previously.

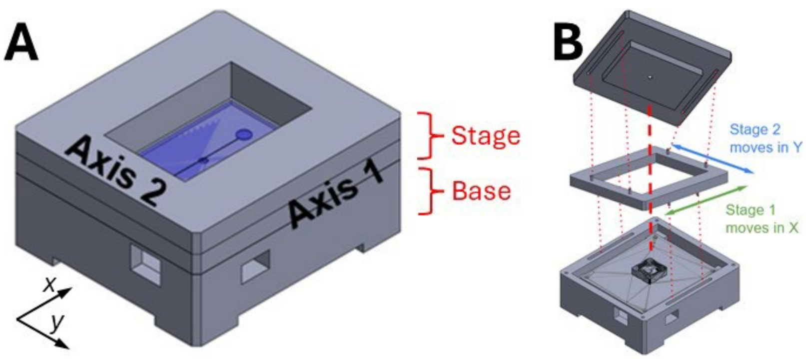

Figure 3. 3D printed case. (A) The case consisted of the base and the two-layered stage. (B) Exploded view.

Testing

Figure 4 shows the set-up used for system testing. A fluorescent sample (concentrations: 1, 10 and 100 µg/mL), Texas Red (Sulforhodamine 101 Acid Chloride) or FITC (Fluorescein Isothiocyanate), was flowed through the microfluidic device with a flow rate of 0.1 mL/min using a syringe pump. A 5× objective lens was used on the microscope (Olympus BX43) to focus the light source through the microfluidic device onto the sensor, and a halogen light source (X-Cite exacte) with a UV Filter (Wavelength: 365nm, Intensity: 48µW) was used to fluoresce the reagents.

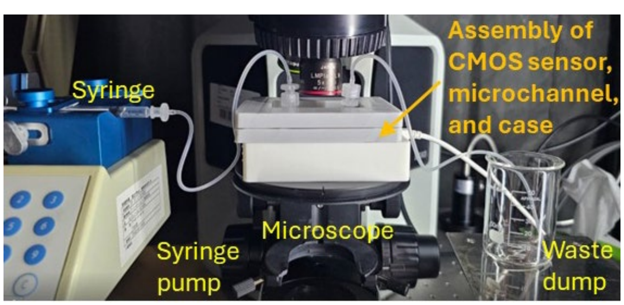

Figure 4. Test set up.

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Results and discussion

The Year 1 cohort focused on the integration between the CMOS sensor and a packaged microfluidic device and on the detection of fluorescent dyes using the integrated system. Detection of the dyes was defined by sensor current ratio readings rising above the system noise (~0.348) in response to a stimulus. Both the FITC and the Texas Red were detectable at various concentrations (shown in gray in Table 1). Additionally, both reagents were tested quite far from their optimal excitation spectra (365 nm), yielding approximately 10-20% of the maximum possible emission intensity. It is likely that much lower concentrations of these reagents would likely be detectable if excited at their optimal wavelengths. Although shorter wavelengths are more ideal for sensor detection (e.g., FITC), Texas Red performed better in this study. There were several factors confounding this result: the non-ideal excitation wavelength used, the molecule size and concentration of the reagent molecules, and the lack of external verification of light intensity magnitude during the test.

Table 1. The current ratio of the CMOS sensor as a function of dye concentration

	1 µg/mL	10 µg/mL	100 µg/mL
Texas Red	0.348	0.363	0.498
FITC	0.348	0.348	0.355

Summary

The Year 1 cohort gained a unique experience of going through the research process in such a short time. After literature review and brainstorming, the team realized that it was critical to develop an engineering solution for well-controlled alignment between the microchannel device and the CMOS sensor. Therefore, they focused on the integration between the CMOS sensor, the microfluidic device, and the 3D printed case. The cohort successfully designed, fabricated, and tested a prototype of the integrated system.

Acknowledgement

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Jonathan Janecek

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Jonathan Janecek is a fourth-year electrical engineering student at UNL, with a focus in circuit design and embedded systems. He is a math and engineering tutor at UNL and spent this past summer as a participant in the 2024 NSF IRES Japan program gaining research experience at Toyohashi University of Technology designing a portable device for pathogen detection. On campus he is an active member in the Aerospace and Institute of Electrical and Electronics Engineers/Eta Kappa Nu (IEEE/HKN) clubs.

Christian Sunderland

Christian Sunderland is a senior student studying physics and data analytics at Nebraska Wesleyan University. He completed two months of interdisciplinary research in Toyohashi, Japan. He hopes to continue research of different physical fields before moving onto graduate school to study astrophysics.

Laurel Sky Wagner

Laurel Wagner is a senior undergraduate student studying chemical engineering at UNL. At UNL, she is an introductory chemical engineering teaching assistant, an executive officer in the UNL Society of Women Engineers, and a team lead in the University of Nebraska Engineers Without Borders Student Chapter. She was a visiting scholar in the 2022 University of California San Diego Advanced Materials Research Experiences for Undergraduates (REU), 2023 Materials REU at the University of California, Irvine, and the 2024 NSF IRES Japan program at Toyohashi University of Technology.

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Rachael Wagner is a biomedical engineering Ph.D. student at UNL. Her research interests include medical devices, space technology, and surgical robotics. She graduated with a bachelor's from UNL in 2018 and worked at Virtual Incision in Lincoln, Nebraska before pursuing a graduate degree.

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Moeto Nagai

Dr. Moeto Nagai is a Professor at the Institute for Research on Next-generation Semiconductor and Sensing Science (IRES^2) and the Department of Mechanical Engineering at TUT. He received his Ph.D. in Engineering from the University of Tokyo in 2009. He has been recognized with several awards, including the MEXT 2018 Science and Technology Prize. Dr. Nagai was also selected as part of the Leading Initiative for Excellent Young Researchers (LEADER) program.

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