Thermal Characterization for COVID-19 Point of Care Testing Device

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***Abstract*—In this project, development of a point of care (PoC) device for COVID-19 saliva testing is being refined through thermal characterization. Loop-mediated isothermal amplification (LAMP) is the method used in the device for SARS-CoV-2 DNA amplification. In future work, we anticipate applying machine learning (ML) methods in order to optimize thermal design.**

Index Terms— COVID-19, saliva test, machine learning, LAMP, primer design

I. Introduction

Throughout the COVID-19 pandemic, fast and accurate testing has been crucial. Though infection has recently slowed in the United States due to the widespread availability of vaccines, countries with less robust healthcare frameworks have seen increased infection at an alarming rate. Point of care (PoC) COVID-19 testing may provide a way for countries such as these to effectively monitor infection rates and triage symptomatic individuals. PoC devices are appealing in countries with less advanced healthcare infrastructure as they may be deployed without the need for lab testing. Preservation of biochemical reagents by lyophilization [2] is a necessary precaution when exporting sensitive chemicals over large distances and will be explored for use in our PoC device in another study.

Current popular COVID-19 testing methods include the use of either a reverse transcriptase-polymerase chain reaction (RT-PCR) [] for detection of the viral genetic code or antibody testing [], which detects viral proteins. However, we chose another method for COVID-19 detection. Loop-mediated isothermal amplification (LAMP) [1], shown in Figure 1, is a method of DNA amplification in which carefully designed primers separate DNA strands and align in such a way that loop structures are formed. Then, elongation takes place at multiple sites and amplified DNA content is generated. Due to the specific thermal conditions necessary for successful DNA amplification by LAMP, thermal characterization and design was crucial to the PoC reader's robustness.

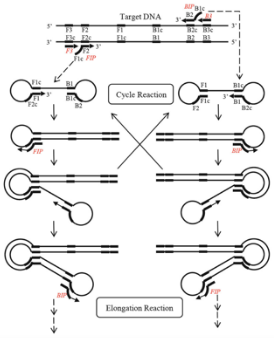

Figure 1: *Targeting, cycling, and elongation lead to DNA amplification using LAMP (figure obtained from [1]).*

Thermal characterization and thermal design [4] of the printed circuit board (PCB), heat spreader, saliva capsule, and chip is a crucial part of the PoC device's design process. A diagram of the apparatus used for thermal characterization can be seen in Figure 2. Tests were completed in order to ensure the viability of biochemical reactions that need to take place for COVID-19 detection in the POC device. Also, the materials used in both the saliva vial and chip needed to be tested for structural integrity under elevated temperatures. A proportional-integral-derivative (PID) controller is used in order to automatically regulate temperature within the PoC saliva reader. A set point of 63 degrees Celsius was chosen, as this is the ideal temperature for activation of LAMP reagents and thus allows for proper DNA amplification and subsequent SARS-CoV-2 detection. Additionally, self-heating and thermal throttling of the PCB components must be considered and may be addressed using ML [3].

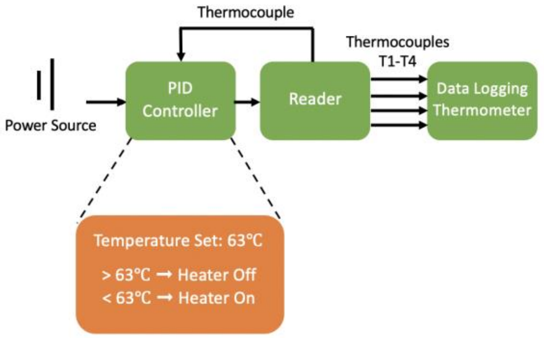

Figure 2: *Diagram of the apparatus used for thermal characterization. A feedback loop involving the temperature of the heat spreader within the reader and the PID controller is necessary for maintaining an ideal temperature for LAMP.*

A. Heat Transfer Modeling

Calculations were made in order to estimate thermal constants that were valuable to the study. Using known laws and equations of thermodynamics, as well as easily attainable values such as the reader's side lengths, theoretical heat dissipation data was generated. This was done in order to obtain baseline values in a fast manner before experiments started taking place. These thermal constants can be found in Table 1.

Parameter	**Value**
Energy input per cycle	3265.36 J
Fraction of heat loss due to convection	0.50
Power balance error	0.01%
Case temperature rise	3.3℃

Table 1: *Table of values calculated for a heat transfer model of the reader used in later experiments.*

II. RELATED WORK

This study is largely based upon work done to design, construct, and test the PoC reader for point of care health applications other than COVID-19 []. The main goal of the study was to improve upon the accuracy of standard methods, such as lateral flow assays []. Also, the authors sought to develop a low-cost system without many bulky parts. They were able to execute this plan by utilizing an Arduino Uno microprocessor. Use of LEDs in conjunction with multiple types of filters eliminated the need for including laser inside the reader, which most likely would have taken up more space and raise the overall cost of reader production.

III. METHODS

Thermal experimentation was conducted using multiple sets of apparatus. In order to obtain a standard range of error for the thermocouples and thermometer used for thermal experiments, several thermocouples went through a standard calibration process. Each type K thermocouple was taped to a heat sink using polyimide tape, while connected to the digital thermometer, and left until its temperature equalized. The steady state temperature of the thermocouple was recorded. The thermocouple was then inserted into each of the four channels of the digital thermometer in order to measure the thermocouple-specific channel to channel error. Both steady state temperature differences and channel-to-channel error were taken into account when drawing conclusions from thermal data. All thermocouples used in later experiments were calibrated using this process.

The apparatus shown in Figure 3 consisted of the COVID-19 PoC reader, an OMEGA digital thermometer, four type K thermocouples, a PID controller, and a voltage source. This apparatus was used to measure temperatures at multiple sites within the reader when a standard heating cycle was run. A standard heating cycle included a full-voltage ramp to 63C at 0.7 amps and 5.0 volts and a 30-minute steady-state period at 63C. These particular values for temperature, time, voltage, and current were chosen in order to mimic the user settings once the reader is being utilized in real-world situations.

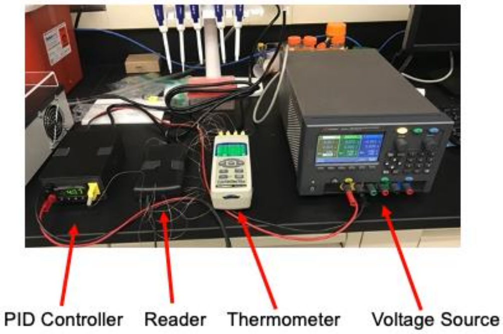

Figure 3: *Apparatus used for PoC reader temperature experiments.*

Thermal imaging, shown in Figure 4, was conducted using a FLIR ETS320 test bench thermal camera. Thermal imaging was conducted in order to determine the presence of any hotspots on the reader's PCBs. Hotspots were monitored because unequal distribution of heat within the reader may lead to unequal heating of the saliva and reagents, which could cause either an unsuccessful proteolysis or improper LAMP reaction. Both the reader's upper PCB, containing photodiodes, and the reader's lower PCB, containing LEDs, were tested for hotspots. In addition to the reader's PCBs, the heater and heat spreader were imaged.

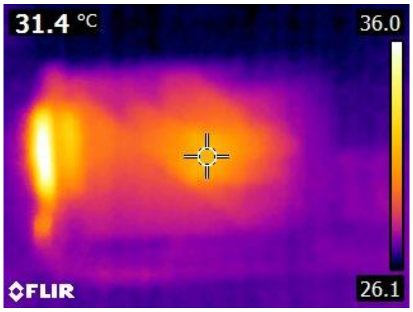

Figure 4: *A thermal image of the COVID-19 PoC reader's upper circuit board, taken using a FLIR ETS320 thermal camera.*

IV. RESULTS

A. Thermal Testing Results

Temperatures were taken at four locations-T1, T2, T3, and T4-within the reader during an extended heating cycle. T1 was a control thermocouple, placed on the heat spreader at a position symmetrical from the thermocouple connected to the PID controller. T2 was placed in the center of row one on the microfluidic chip. Row one of the chip is further toward the center of the reader when the chip is inserted. T3 was placed in the center of row four, the row of the microfluidic chip which was further from the center of the reader when the chip was inserted, compared to row one. T4 was placed on the upper PCB in the space in between rows one and four.

The full cycle included a fully powered ramp to 63C at 5 volts and 0.7 amps, followed by two hours of continuous heating at 63C. This temperature of 63C was automatically maintained by the PID controller. The results of this experiment can be seen in Figure 5. A discrepancy of about 6.7 degrees Celsius was found between the control steady state temperature and the reaction well steady state temperatures.

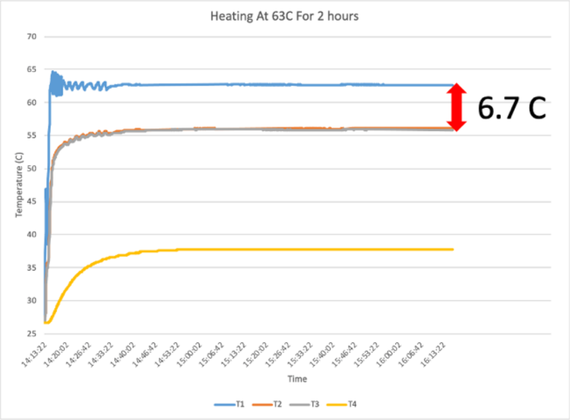

Figure 5: *A heating cycle was performed in which the reader was operated by a PID controller. Firstly, the heaters were powered at 3.5 watts to reach the set point of 63 degrees Celsius. Then, the set point was maintained by the PID controller in conjunction with an electrical relay. A discrepancy of 6.7 degrees Celsius between the reaction well temperatures and control temperature was observed.*

B. Heat Spreader Redesign

In an effort to reduce the discrepancies found between reaction well temperature and heater temperature, a new design was devised for the heat spreader. The initial design of the heat spreader included small circular perforations in a flat aluminum heat spreader with bottom-mounted heaters. The microfluidic chip sat on top of this heat spreader and a separate spring was positioned on top of the microfluidic chip. A new design for the heat spreader was generated in which the heat spreader was combined with the spring and heaters were instead top-mounted. Perforations in the new heat spreader design are larger than the old perforations and rectangular in order to maintain access to the photodiodes upon the spring's compression. The old and new designs can be seen in Figure 6.

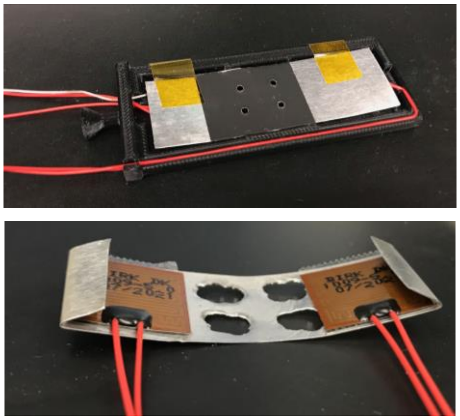

Figure 6: *Heat spreader with bottom-mounted heaters (top) compared to the newly designed heat spreader-spring combination with top-mounted heaters (bottom). The heaters have not yet been compared in formal testing.*

V. CONCLUSION

Investigation of thermal characterization and thermal design of the PoC reader were important for successful heating of the biochemical reagents, and therefore, a successful DNA amplification reaction in the presence of viral content. Further, successful DNA amplification is necessary for the accuracy of the COVID-19 tests performed using the PoC reader. However, further thermal experiments on and redesigns of the reader must be conducted in order to fully optimize heating temperature of the reagents.

VI. FUTURE WORK

One main area for future improvement in the reader's thermal design may be metal composition of the heat spreader-spring combination. Thus far, only heat spreaders constructed from aluminum have been tested. One strong consideration of a metal for future testing is phosphor bronze. Usage of metals other than aluminum has been suggested to improve thermal conductivity of the heat spreader, such as in [7], in which the authors describe using natural graphite for effective heat spreader construction

Additionally, the old and new heat spreaders must be formally compared in experimental trials. The rationale behind the redesign of the heat spreader is general principles of thermal conductivity and must be validated using data comparisons and statistical analysis.

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