MICROFLUIDIC TEMPERATURE BEHAVIOR IN A MULTI-MATERIAL 3D PRINTED CHIP

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ABSTRACT

As analysis systems shrink in size to microfluidic scales and devices, there is a need to improve temperature control in the microscale for temperature sensitive processes. Technology that combines accurate temperature measurement and 3D spatial control of the temperature distribution is limited by common 2D layer-based microfluidic fabrication techniques but can be realized with 3D printed microfluidic chips. This work presents an iterative process to create a microfluidic chip using multi-material 3D printing to improve temperature sensing and create an even temperature around a target volume. Through an iterative process, verification is presented of fluorophore viability (specifically CdTe quantum dots) after being secured in place by cured PR48 3D printing resin, thus confirming the possibility of fluorescent thermometry as an accurate non-contact temperature sensing method. Numerical analyses of various geometries of chip design iterations are also presented verifying spatially even heating due to the placement of non-contact heating sources in the microfluidic chip. Combining the fluorescent thermometry and improved heating will lead to improved temperature control in microfluidic devices.

INTRODUCTION

Typical microfluidic chips are made from 2D layers combined to form 3D geometries [1]. This method of construction can lead to uneven heating and inaccurate temperature sensing

through induced temperature gradients due to the 3D volume being heated from a single 2D heater location [2]. Additionally, devices made this way are often expensive and time consuming to create due to the use of a clean room. Two examples where evenly heated microchannels are necessary include polymerase chain reaction (PCR – amplifying a sample of DNA) and high-resolution melting analysis (HRMA – analyzing DNA sequences) [3, 4]. Advances made in microfluidic 3D printing should be utilized to create truly 3D designs that can evenly apply heating to microfluidic channels instead of continuing use of 2D heaters [2, 5]. This has the benefit of reducing the cost of microfluidic devices [6] and increasing the precision of their temperature control. These advances in 3D printing have been most successful with the use of custom 3D printers and resin compared to using PDMS and has allowed the resolution of 3D printers to be reduced to the tens of micrometers scale [7, 5].

Microfluidic temperature control methods vary in how the temperature is measured and how the temperature is adjusted. Temperature sensing can be done by both contact and non-contact methods. Thin film platinum resistors, thermocouples, and thermistors are commonly used for contact temperature methods, but as fluid amounts get smaller, the thermal mass of the sensor becomes more significant lag and uncertainty [8]. Non-contact methods do not suffer from these same drawbacks and common methods are IR-sensing, Raman thermometry, and fluorescent thermometry. Fluorescent thermometry can provide the spatial resolution and reduced time lag inside of microfluidic devices, which both IR (can only see the surface) and Raman (long integration times) cannot. Fluorophores that can be chosen

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for fluorescent thermometry differ in stability, specifically that organic fluorescent dyes experience photobleaching (a weakening in fluorescent signal over time) as they are exposed to the excitation laser while non-organics like quantum dots (QDs) have been proven to be consistent over extended periods of laser exposure [9, 10]. The research presented in the paper will use QDs as the source of fluorescent thermometry.

Microfluidic channel heating is commonly done through external Peltier elements, endo/exothermic reactions in the chip, passing current through conductive materials such as conductive films, and focusing lasers on liquid water drops in the microfluidic chips [8]. These methods focus on heating the entire chip or a significant region, increasing temperature lag (the time needed for the effects of the heater to reach the target volume) as the thermal mass is increased [11]. Using the precision of 3D printing, local heating can be accomplished by filling channels with different materials and focusing the heating to an area of interest. One such possibility is Joule heating with a liquid metal. The liquid metal is advantageous because it can fill the channel no matter how complex the design. Recently a metal alloy was inserted at an elevated temperature, which then solidified and was used for heating a microchannel [12]. For a simpler process, alloys that are liquid at room temperature can also be used. Of particular interest is the idea of using gold nanorods (GNRs) suspended in resin. The GNRs have been proven to be an efficient heating source by converting NIR light into local heat [13], yet application of the GNRs into an injectable resin for microfluidics has not been published. Having precise control of channel geometry allows the GNRs to be placed where desired to focus the heating on a target volume.

This paper details several iterations of microfluidic designs that have successfully used 3D printing to integrate multiple materials into a single microfluidic chip. By embedding temperature sensitive materials and efficient heating materials in a 3D geometry around the target volume, this research works to advance temperature control by improving temperature sensing and heating in microfluidic chips. Through an iterative process, through both experimental results and numerical modeling, advances have been made in the design stage and will shortly be validated.

Methods

Several iterations of microfluidic chips are present in this work, with modifications based on temperature sensing and heating needs. Our microfluidic chips have been printed using a commercial Asiga 3D printer with PR48 resin, incorporating fluorescence in specific locations due to Rhodamine B (RhB) dye and QDs. Our iteration process is separated into two focuses, with the CAD models shown in Fig. 1. Iterations I1.1 and I1.2 have been printed and tested with the goal of selecting and validating the fluorophore for fluorescent thermometry. The

design of iterations I2.1 and I2.2 were focused on selecting a geometry for accurate temperature data, and although their temperature distributions have been analyzed with a finite element model, printing and testing will be part of a future work.

3D Printing

The Asiga printer we used has a resolution of $27\text{ }\mu\text{m}$ in the X-Y plane and as small as $9\text{ }\mu\text{m}$ in the Z-axis [14]. The printer uses stereolithography based on digital light processing to cure photo-sensitive resin in layers to create the 3D geometry in a single process, after many layers are created [14].

With the use of 3D printing, we were able to create channels inside the chip that were then filled with UV light curable PR48 resins impregnated with other materials. For example, we have filled a channel in a microfluidic chip with CdTe QD-filled resin and cured the resin, suspending the QDs in a solid matrix. Future work will do the same with GNRs. Following impregnated resin injection, the entire chip was placed in a UV light source for 30 minutes to cure the resins. The complex geometries allowed by 3D printing allow us to place the channels, and hence the specific “doped” resins, in an arrangement that was beneficial for temperature control of a target volume. Reducing the spacing between the temperature sensor and target volume will increase temperature accuracy and reducing the spacing between the heating element will reduce temperature lag. The novelty of our method is in the geometry of those specific channels being designed and created in a truly 3D space.

Fluorescent Thermometry

In our first iteration (I1.1) of microfluidic chip, we used Rhodamine B (RhB)-filled resin (RB from Sigma Aldrich, $\lambda_{max}=570\text{ nm}$, mixed in PR48 resin). This doped resin was illuminated with a 532 nm LaserQuantum GEM laser (visible in Fig. 2), and the fluorescent spectra was acquired through a StellarNet GREEN-Wave16 spectrometer by means of a LabView program. The fluorescent intensity decayed through the expected photobleaching from exposure during temperature calibration (visible in Fig. 3), which created a need to change the fluorophore.

The next iteration (I1.2) used the same design of chip but the RhB was replaced with CdTe QD-filled resin (CdTe QDs from PlasmaChem, $\lambda_{max}=650\text{ nm}$, mixed in PR48 resin). These QDs used the same laser and spectrometer setup. There is an expected accuracy of $1\text{ }^{\circ}\text{C}$ [9] with QD fluorescent thermometry using only the emission peak wavelengths [15, 16] or emission intensity [10].

The subsequent iteration (I2) will also use QDs for fluorescent thermometry. The research presented here will build on that to further improve the temperature accuracy.

FIGURE 1. 3D PRINTED GEOMETRIES OF MICROFLUIDIC CHIPS, ITERATIONS I1.1/I1.2 (A), 2.1 (B), AND 2.2 (C). THE TARGET VOLUME OR SURFACE IS THE REGION ON THE CHIP WHERE ACCURATE TEMPERATURE CONTROL IS DESIRED

FIGURE 2. RHODAMINE B AND CDTE QD DOPED RESIN INJECTED INTO I1 CHIPS, WITH AND WITHOUT LASER ILLUMINATION. IMAGES WERE TAKEN THROUGH A 550 NM LONG-PASS FILTER

Temperature Measurement Setup

The first iterations (I1.1 and I1.2) microfluidic chip were placed on a resistance heating powered by a DC power supply (BK Precision 1096), which was controlled by a LabView PID program. The input for the PID and the values used to calibrate the fluorescence were from a thermocouple inserted into the chip (Type K from OMEGA). Data was collected from the spectrometer data once the chip temperature variation was less than 2% of the desire temperature. The peak intensity was determined as the maximum of a 3rd order fit and correlated to a temperature. Plotting the resulting correlation validated the temperature sen-

sitive nature of the Rhodamine B and QDs remained after being in resin and cured by UV light.

Numerical Temperature Analysis

The temperature distribution in the microfluidic chip designs were analyzed through COMSOL 5.3 multi-physics modeling. The properties of the chip were assumed to be similar to nylon because we are interested in how the temperature will behave in a similar plastic for which we do not have thermal property data. The channel that will hold the target volume was modeled as a heat outflow. The channel containing Rhodamine B or QD-filled resin was modeled as nylon because the concentrations of Rhodamine B and QD is not significant enough to significantly change the heat transfer characteristics of the channel [9]. The channels with running water were modeled with convection by calculating the heat transfer coefficient for the given dimensions and setting the water temperature. The channels that will contain the GNR-filled resin were modeled as a heat source with the heat generating only in a section modeled to be illuminated by the heating laser.

Results

Iteration 1.1

Using the I1 chip design, we injected the temperature sensing channel with Rhodamine B doped resin, but photobleaching became a primary concern during temperature calibration (Fig. 3). Due to the amount of time required for temperature variation to subside, the fluorescent signal weakened drastically. This would reduce the accuracy of the calibration, preventing any useful fluorescent thermometry uses with the Rhodamine B resin.

Iteration 1.2

The next iteration (I1.2) changed the fluorophore from Rhodamine B to CdTe QDs. The purpose of this was to overcome the photobleaching concerns from the previous iteration. A second

FIGURE 3. NORMALIZED RHODAMINE B PHOTBLEACHING DATA. RHODAMINE B FLUORESCENCE PEAK INTENSITY AT A CONSTANT TEMPERATURE AND ILLUMINATION POWER

chip identical to the first was printed and the channel was filled with QD-filled resin and cured. After collecting temperature calibration data, we found that the temperature sensitive nature of the QDs was not affected by the curing process and that there is still the expected linear correlation with repeatable results (Fig. 4). However, COMSOL analysis revealed that this geometry would not work for our goal of controlling the temperature because of the significant space and thermal difference between the QDs and our target volume (Fig. 5).

Iteration 2.1

Having established the successful use of CdTe QDs to relate fluorescent intensities to temperature, the next iterations focused on selecting geometries to create an even temperature field for the target volume. Using COMSOL, a design was created placing three concentric helical channels around the target volume (Fig. 1b). Each channel contained either flowing cooling water, GNR heating channels, or QD temperature sensing channels. The goal of the helical channels was to create a radial temperature field with the target volume in the middle. However, by having the heating and cooling staggered, the temperature of the target volume fluctuated (Fig. 6).

Iteration 2.2

Continuing with the goal of creating a uniform temperature field radially around the target volume, we determined that a good geometric design for temperature sensing along the target volume is to have the QDs-filled resin in a helical channel that

FIGURE 4. THE AVERAGE OVERALL FLUORESCENCE EMISSION AT VARIOUS TEMPERATURES FROM 200 DATA SETS COLLECTED AT EACH TEMPERATURE (A), THE LINEAR CORRELATION BETWEEN PEAK INTENSITY AND TEMPERATURE (B). CDTE QD FLUORESCENCE KEPT ITS THERMAL SENSITIVITY AFTER BEING CURED IN PR48 RESIN

is wrapped around the target surface. The target volume would then be surrounded by eight equally spaced channels running parallel to the target volume channel (Fig. 1c). Four channels will provide a heating source, and the other four channels will have water passing through to provide the cooling. The models were run simulating a 785 nm laser uniformly illuminating GNR-filled resin. The simulations show that there will be a controllable and even temperature field around the target volume and that the embedded QDs and locations for the calibrating thermocouples will share a very similar temperature (Fig. 7).

FIGURE 5. COMSOL ANALYSIS OF I1.2. THE VARIATION IN THE QD CHANNEL AND TARGET VOLUME TEMPERATURE (AS SEEN BY THE DISSIMILAR ISOTHERMS) LED TO THE NEXT ITERATIONS ON CHANNEL GEOMETRY. COLOR BAR UNITS ARE °C

Future Work

Through an iterative process, we were able to create a design through numerical simulation that should achieve the goal of accurate temperature sensing and heating. To validate our I2.2 design, the microfluidic chip will be printed and filled with QD-filled resin and a heating source. As previously mentioned, liquid metal or GNR-filled resin can be used as the heating source. One possible alloy is galinstan, with a melting temperature of -20 °C [17] and high enough resistivity to allow Joule heating. A PID program will be created to control the illumination from a 785 nm laser directed at the GNRs or to control the current passed to the liquid galinstan. Temperature data will then be collected and compared to the numerical model. Additionally, to improve the temperature accuracy based on the QD fluorescence, we will use neural networks to analyzing fluorescence features (with previous implementations of this technique reaching an accuracy of ± 0.29 °C) [9].

Conclusion

The presented research has demonstrated that 3D printing can be used to integrate multiple materials into a single microfluidic chip, specifically temperature sensitive fluorophores useful for fluorescent thermometry. Additionally, using numerical models, a microfluidic chip design has been created that when filled with specific “doped” resins will provide an accurate temperature reading and a uniform temperature field around a target volume. Through this iterative process of numerical models and experi-

FIGURE 6. COMSOL ANALYSIS OF I2.1, SHOWING THE FLUCTUATING TEMPERATURE PROFILE OF THE TARGET VOLUME DUE TO HELICAL CHANNEL HEATING AND COOLING. COLOR BAR UNITS ARE °C

FIGURE 7. COMSOL ANALYSIS OF I2.2. THE TARGET VOLUME AND QD CHANNEL ARE SHOWN TO HAVE A VERY EVEN TEMPERATURE FIELD AND BE VERY CLOSE. COLOR BAR UNITS ARE °C

mental validation, advances will be made that will be combined to improve temperature control in microfluidic devices.

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