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PCR thermal management in an integrated Lab on Chip

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Abstract. Thermal management modelling and simulations of a polymerase chain reaction (PCR) device to be integrated on a lab on chip (LOC) have been carried out and presented. A typical MEMS PCR in symmetrical configuration is the base model for this study. When the PCR device is integrated on a fluidic chip with many other bio-analysis components such as DNA extraction, RNA extraction, electro-chemical sensor, flow through components and channels etc., thermal symmetry required for uniform temperature across the PCR chamber is normally lost. In this paper, ANSYS 8.0 simulations in varying conditions and corresponding physical basis have been investigated and presented. Model optimizations are carried out when PCR chamber is placed, one, in the centre (symmetry) and two, in the corner (asymmetry) of the integrated chip. In both cases, temperature uniformity within ±0.5 °C variation is obtained.

1. Introduction

Polymerase chain reaction (PCR) chamber technology for DNA amplification is well established and has been around for almost two decades. Over the years many groups have developed miniaturized PCR chips using MEMS technology [1-4], temperature uniformity has been improved tremendously and miniaturization has played a key role in this advancement. In our previous work [3-4], we had reported silicon and plastic MEMS PCR technologies with very good DNA amplification results. Cycle time was reduced to few seconds and temperature uniformity within ±0.5 °C was achieved.

Research focus has moved forward with bio fluidic analysis integration emerging as a new research paradigm [5-7]. Automation is very important for handling many dangerous bio-analytes and so is the speed of bio analysis, thus, there is an increasing demand for multifunctional integrated bio-chips. This involves combining channels/valves, bio-analysis chambers, electrochemical/optical detection systems, fluidic controls into one functional chip. Temperature control and processes are very critical in such multifunctional chips. This paper is an attempt to tackle thermal optimization in a typical integrated bio-chip.

This paper presents thermal management mechanism in an integrated bio-fluidic microchip using a simple PCR model, which may also have other multi bio-analysis fluidic /non-fluidic components. Integration adds new constraints and asymmetries, which requires thermal model optimization to maintain temperature uniformity inside the PCR chamber. It is very likely that PCR placement is unsymmetrical and even chamber shape itself can be unsymmetrical. Packaging conditions are always different for different integrations. This paper investigates these varying conditions and constraints, and presents issues and mechanisms to achieve thermal optimization.

2. Experimental model design

A typical integrated chip PCR model was designed as shown in Figure 2.1. It has a silicon-glass integrated bio-fluidic chip with a PCR chamber placed in one of the corners. The whole bio-fluidic chip is encapsulated in a 2.5 mm thick PDMS polymer material. PCR area of the chip is exposed to the air through an opening on the back side. Another window in PDMS package opens the bio-fluidic chip on the front side. These exposures to surrounding environment can be used for forced convection cooling for the PCR chip. Dimensions of the bio-chip and PDMS package have been depicted in Figure 2.1.

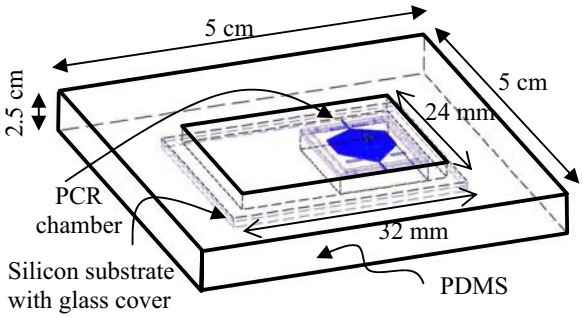

Figure 2.1 A typical integrated bio-fluidic chip with miniaturized PCR device

A series of simulation models were designed and carried out to understand the importance and to incorporate necessary modalities to manage thermal budget of the system optimally. Thermal symmetry is an important consideration for achieving desired temperature uniformity of about less than 1 °C. In simulation studies model parameters such as, shape of the chamber, placement of the chamber with respect to the whole chip, placement of heaters, and symmetry of thermal loss paths were investigated to understand their significance. Design methodologies for optimal design were carried out and discussed.

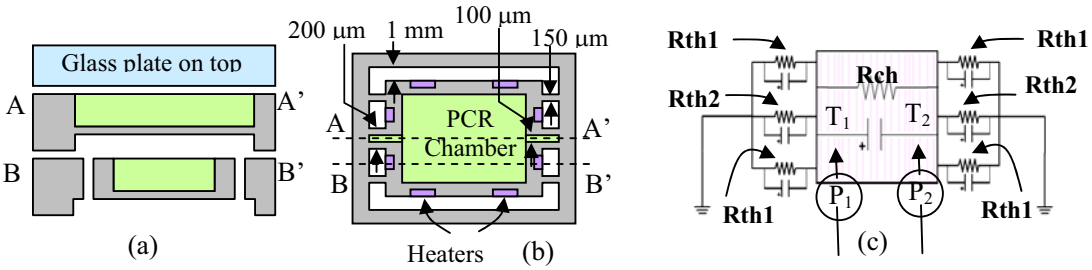

Figure 3.1 A typical symmetrical PCR, (a) cross section, (b) top view, and (c) equalent circuit

3. Theoretical considerations

A typical symmetrical PCR chamber is shown in Figure 3.1 (a) to (c). Typical dimensions are also mentioned. This chamber can be modeled theoretically by using electrical analogy of thermal heat flow. Temperature will replace voltage, thermal power will replace current, thermal resistance will replace electrical resistance, and thermal capacity will replace electrical capacity. Electrical equalent model of thermal circuit is shown in Figure 3.1 (c), where Rth1 and Rth2 represent resistances of the links at both sides of the chip and Rch represents the resistance of the chamber. In symmetrical conditions, the model can be considered as one dimensional and thermal resistances on both sides of the PCR chamber can be replaced by equalent thermal resistance R_{th}. Temperature distribution of this simplified one dimensional PCR system can be given by [4]

$$T(x) = \int_0^x P_l.\left(R_{th} + \frac{L_{ch} - x}{L_{ch}}.R_{th}\right)dl + \int_x^{l_{ch}} P_l.\left(R_{th} + \frac{L_{ch} - l}{L_{ch}}.R_{ch}\right)dl$$

$$= P.(R_{th} + R_{ch}) - \frac{P.R_{ch}}{2.L_{ch}^2}\left(x^2 + L_{ch}^2\right) \qquad (1)$$

Where P and Pl (=P/Lch) are heating power (for half-branch) and uniform heating power per unit length, respectively. x is distance of a point from centre of the PCR chamber (along length in one

dimensional system). L_{ch} is the channel length. The relative temperature deviation in the reaction chamber will therefore be

$$\frac{\Delta T}{T} = \frac{R_{th}}{2(R_{th} + R_{ch})} \tag{2}$$

Heat flow is given by the following, Newton's law of cooling states.

$$Q = hA(T_s - T_{ref}) \tag{3}$$

Where h is the heat transfer coefficient, A is the surface area, T_s is the surface temperature and T_{ref} is the reference temperature. In PCR thermal cycle, maximum temperature is approximately 95°C. If room temperature is assumed to be 25°C, maximum temperature difference for heat loss will be approximately 70°C. Theoretical calculations can be used to estimate maximum thermal power loss through conduction links (to sink) due to temperature difference between chamber and the sink. To maintain uniform temperature, a thermal power equalent to thermal loss power has to be supplied to the system and this supplied power corresponding to maximum loss (at maximum temperature) will be the maximum power required by the PCR system.

4. Understanding thermal asymmetries using FEA simulations

As explained in previous sections, symmetry is critical for achieving uniform temperature across the chamber. Figure 4.1 shows ANSYS FEA simulation results of a typical model when chamber does not have thermal symmetry. This model has multiple asymmetries, namely related to, corner placement, chamber shape, heater placements, and heat loss links to sink. The effect of these asymmetries on temperature uniformity is clearly shown in the FEA simulation results given in Figure 4.1. Temperature variation is about 3.0°C, which is considered quite large in miniaturized MEMS PCR devices, where a temperature variation across the chamber should be less than 1°C.

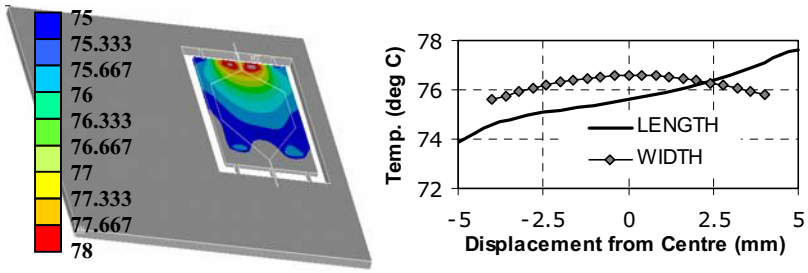

Figure 4.1 FEA simulation results of an asymmetric PRC chamber model. Chart in (b) shows temperature from centre of PCR across length (5 mm), and width (4mm).

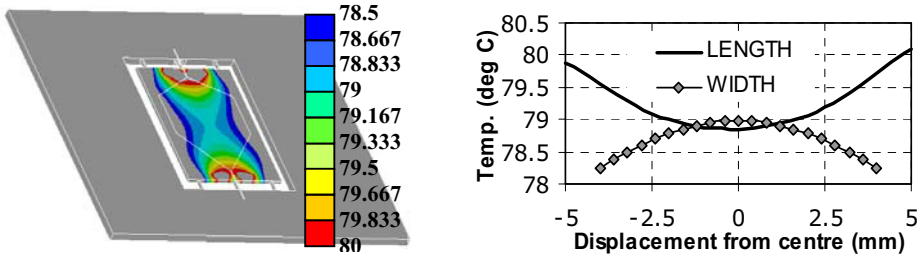

Figure 4.2 (a) Simulation results with chamber shape asymmetry.

To understand the effect of asymmetries independent to one another, FEA simulations were carried out with one asymmetry at a time while removing rest of the asymmetries from the model. The FEA simulation results are shown in charts Figure 4.2 (a) to Figure 4.2 (d). Results in the charts clearly explain that all the asymmetries are detrimental to temperature uniformity. The effect of asymmetries

in heater (heat supply) and thermal resistive links to sink is much more critical. Color graphs of temperature distribution across the PCR chamber in these two cases clearly signify the need for symmetry or thermal optimization should be carried out by introducing opposing factors in the model.

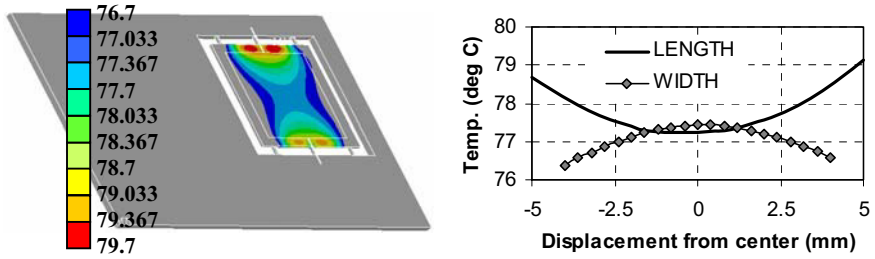

Figure 4.2 (b) Simulation results with chamber location in the corner of chip.

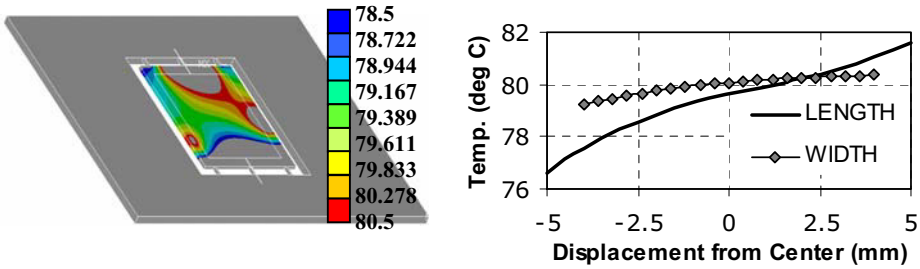

Figure 4.2 (c) Simulation results with heater asymmetries

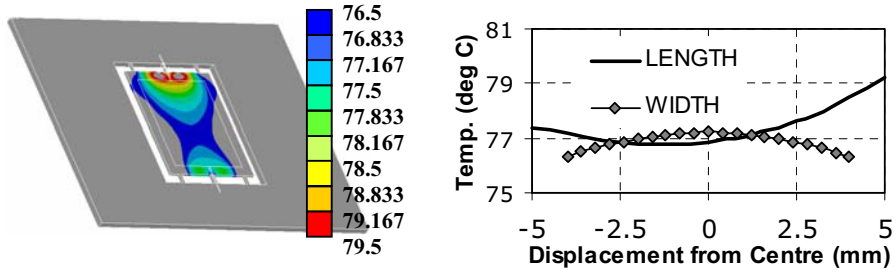

Figure 4.2 (d) Simulation results with thermal loss links to sink not symmetrical.

5. Model optimization and discussions

Model optimization was carried out in two stages; first, system was optimized with PCR placed in the centre of the chip, which means chamber placement was symmetrical. Chamber shape, heaters, and thermal loss links, were also designed to be symmetrical. In the second stage, optimized PCR chamber was moved to one of the corners of the chip. This introduced placement asymmetry, which was balanced by introducing opposing asymmetries in heaters power and thermal loss resistances (links).

5.1. Stage 1: Centre placement

Simulation with four heaters showed a variation of more than 1°C across length and width as shown in Figure 5.1.1 (b). The thermal loss through the cover glass plate seems to be the most appropriate explanation for this undesired variation. From chart, a highest temperature on the two ends along the length and lowest temperature on the two ends along the width is clearly evident, which explains a heat flow from two length ends (this is where heaters are placed) of the chamber to the two width ends. Another four heaters of same power rating were introduced on the sides. FEA simulation

temperature color profile and charts for eight heaters are shown in Figure 5.1.1 (a) and (b) respectively. Very good temperature uniformity within 0.3 °C can be seen here.

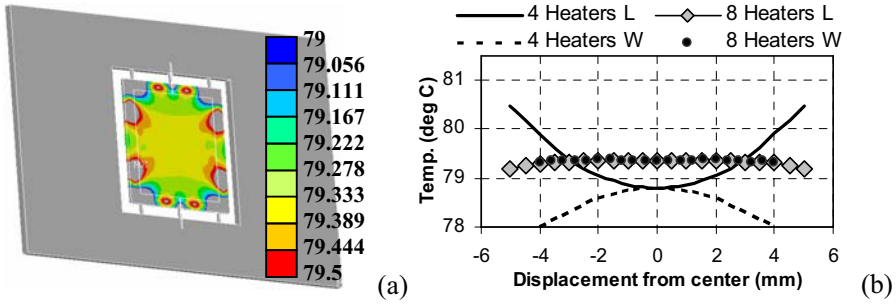

Figure 5.1.1 (a) ANSYS FEA simulation plot with 8 heaters, (b) Chamber temperature variations when four and eight heaters are used.

5.2. Stage 2: corner placement

The optimized PCR chamber discussed in previous section was moved to one corner. FEA simulations were carried out without changing any parameters, results are shown in Figure 5.2.1 (a) and (b). It can clearly be observed that the outermost (on the bio-chip) corner of the PCR chamber is relatively at higher temperature. This phenomenon can be understood with the help of Figure 5.2.1 (c). This outermost corner has additional thermal resister for the heat to pass to sink. So to achieve temperature uniformity across the PCR chamber either the thermal resistance is lowered in this corner or more heat is supplied on the other side (lower temperature side) of the PCR chamber.

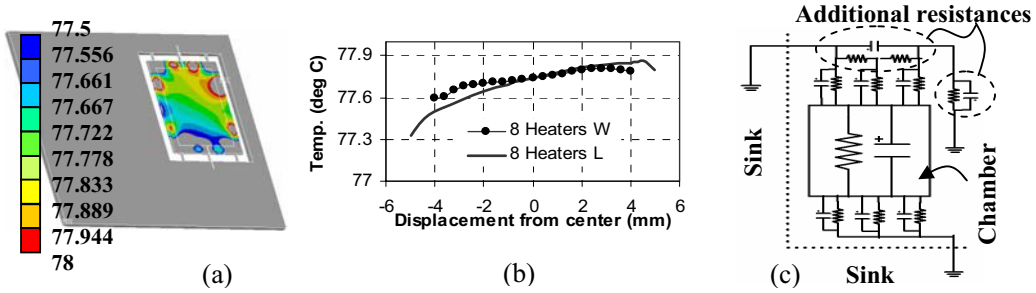

Figure 5.2.1 Temperature distribution of chamber with eight heaters before optimization (a) FEA color plot, (b) graphical representation, and (c) thermal equalent circuit.

In our study, to reduce temperature variation across the chamber and achieve very good temperature uniformity, heat supply from heaters on the other side (lower temperature side) was increased in steps and finally a very good uniformity as shown in the Figure 5.2.2 (a) and (b), was achieved.

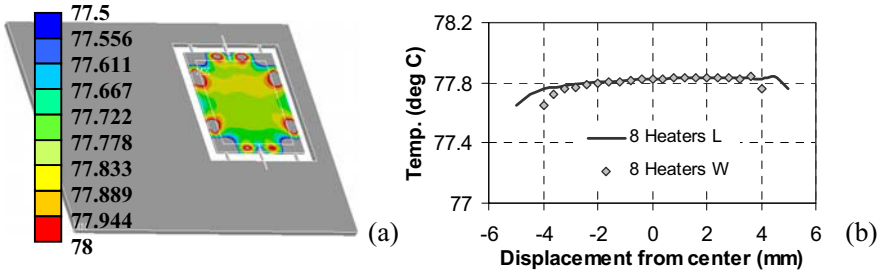

Figure 5.2.2 Temperature distribution simulation results with eight heaters after optimization (a) FEA simulation plot, (b) temperature distribution across length and width.

6. Conclusions

A typical integrated Bio-chip model having PCR device was used to investigate thermal management issues. The effect of various asymmetries such as location, shape of chamber, thermal power supply through heaters, and thermal power loss through thermal resistive links was studied in detail and critical issues related to these asymmetries were discussed. The symmetry of heat power supply and thermal resistive links was found to be very critical for achieving good temperature uniformity within ±0.5 °C. Additionally, it was also investigated that small thermal loss through thermal isolation materials such as glass can cause significant temperature variation; in our model a variation of more than 1 °C was observed. Four more heaters were introduced to make sure a more uniform thermal power supply to the bio-chip, this reduced the temperature variation to less than 0.3 °C. In case chamber is not placed symmetrically, e.g. moved to a corner, a mechanism to optimize such a typical real case has also been discussed. This optimized model has also been presented.

7. Acknowledgements

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8. References

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