# MINIATURIZED ENDOTHERMIC COOLING MODULE FOR DENATURATION OF ON-CHIP PCR PRODUCT AND ITS ELECTRICAL DETECTION USING NANOWIRE BIOSENSOR

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## ABSTRACT

This work presents a miniaturized endothermic cooling module (Fig.1) for denaturation of on-chip polymerase chain reaction (PCR) product and its electrical detection using nanowire biosensor [1] at the downstream of integrated microsystem for application in infectious disease diagnostics, by directly detecting the viral ribonucleic acid (RNA) from blood samples.

**KEYWORDS:** Endothermic Cooling, Denaturation, Nanowire Biosensor, Integrated Microsystem

## INTRODUCTION

Recent technological advances have enabled automation and miniaturization of some of the steps [2], such as cell lysis, viral RNA extraction, nucleic acid (NA) amplification, and NA detection, etc. Among those steps, hybridization-based electrical detection device, such as silicon nanowire biosensor, has been highlighted due to its high sensitivity and multiplexing capability [1]. In order to realize a fully integrated microsystem having DNA hybridization-based detection method, implementation of DNA denaturation process, so-called super-cooling process (graph in Fig.1(a)), is crucial. The conventional ways for reaching below room temperature are using either Peltier thermoelectric cooling (TEC) devices [3] or Joule-Thomson (JT) devices [4]. Both methods are well-known but have difficulties in integration with other microfluidic components. Thus, this paper proposes a novel cooling module which has a two-step cooling function (Fig.2) – heat-sink and super-cooling.

## WORKING PRINCIPLE

Working principle of miniaturized endothermic cooling module is: 1) the metallic chamber, which pre-contains the endothermic chemicals, covered by a top-cap (Fig.1(b)); 2) during PCR cycling, contact plate (Fig.1(c)) of the cooling module contacts microPCR chamber thermally. Even though there are endothermic chemicals inside the chamber, the metal chamber can dissipate the heat effectively due to its high thermal conductivity and large surface area; 3) for the super-cooling of dsDNA product, pre-contained endothermic chemicals start to react with injected water into the chamber.

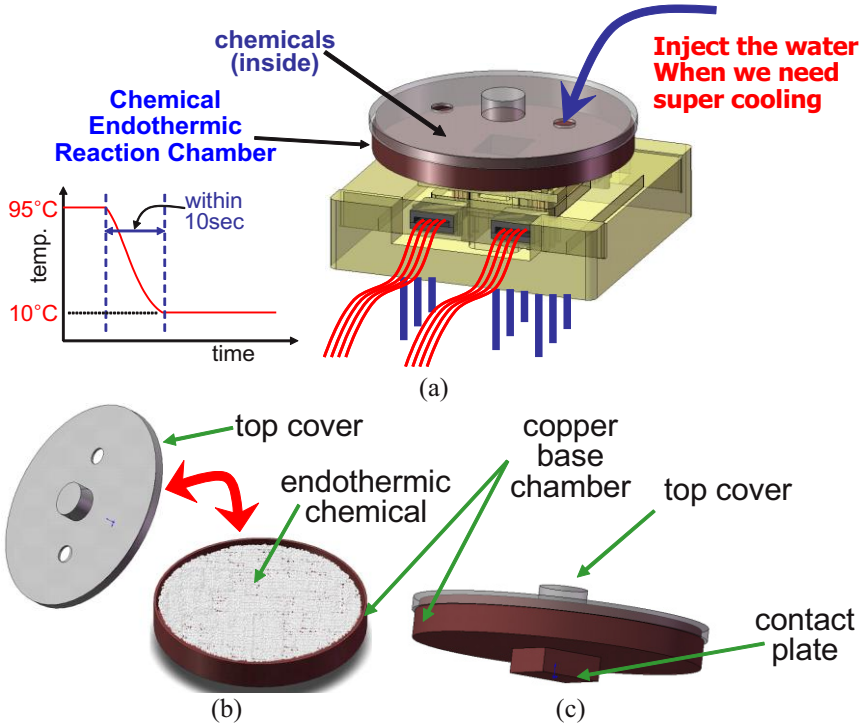



*Figure 1: Conceptual design of the miniaturized endothermic cooling module: (a) miniaturized endothermic cooling module assembled with integrated microPCR system. The graph on the left hand side illustrates the thermal requirement, which is on-chip PCR product could be denatured into ssDNA after rapid cooling; (b) endothermic chemicals in the copper base chamber of the cooling module; (c) perspective bottom view.*

## EXPERIMENTAL RESULTS AND DISCUSSION

Figure 3 shows the integrated micro sample preparation silicon device and its packaging, which is compatible with proposed miniaturized endothermic cooling module by assembling (Fig.4). In this paper, we present three major experimental results regarding the two-step cooling performance of proposed miniaturized endothermic cooling module. First of all, as shown in Fig.5, we demonstrated the heat-sink capability of the metal chamber with endothermic powder inside. As a result, we can cool down the microPCR chamber temperature from 93°C to 58°C within 5sec, during the PCR thermal cycling without any endothermic chemical reaction. Figure 6 shows the super-cooling experimental results with comparison to different cooling conditions including without cooling chamber, with cooling chamber only, with water injection to the chamber without endothermic chemical, as well as with different amount of endothermic chemicals. As shown in the graph, we can reach to around 10°C from 95°C within 10sec, which is the required condition for DNA denaturation. We have also conducted DNA denaturation test (Fig.8) with nanowire biosensor (Fig.7). As shown in the Fig.8, integrated process of on-chip super cooling in the microPCR chamber shows comparable level of nanowire relative resistance change with the conventional cooling method.

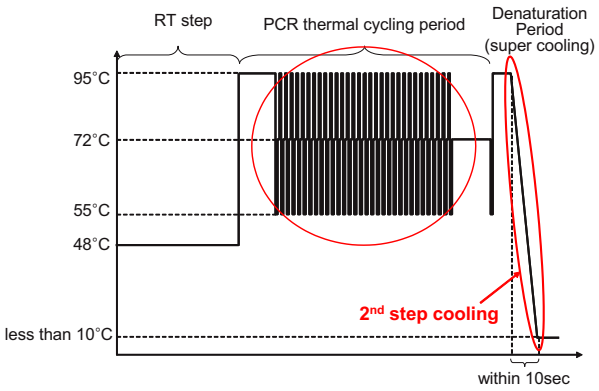



*Figure 2: Schematic view of temperature profile for RT-PCR cycling and on-chip DNA denaturation.*

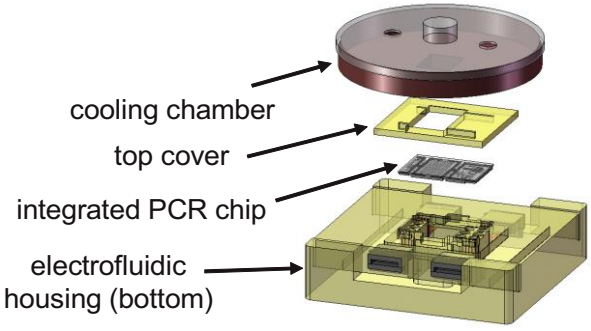



*Figure 4: Assembly map of miniaturized endothermic cooling module with microPCR module.*

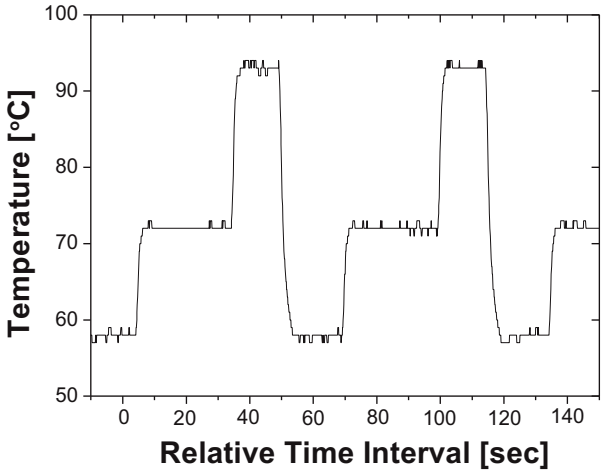
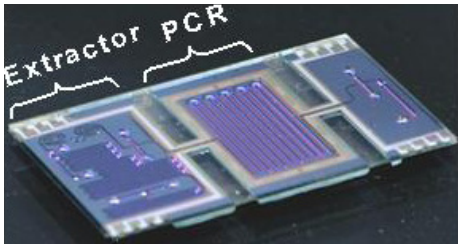
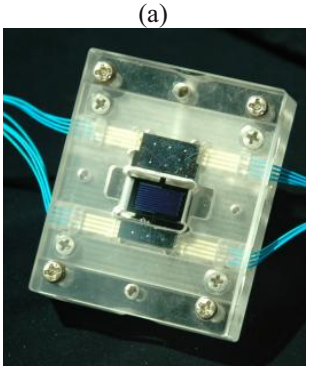



*Figure 5: An example of controlled temperature profile during PCR cycling period, in which miniaturized endothermic cooling module takes heat-sink role.*




(a)



(b)

*Figure 3: Photographs of the integrated micro sample preparation module: (a) monolithically integrated microfluidic device for NA extraction with PCR; (b) microelectrofluidic packaging for integrated sample preparation module – miniaturized endothermic cooling module (Fig.1) contacts the PCR chamber through the hole at the center part.*

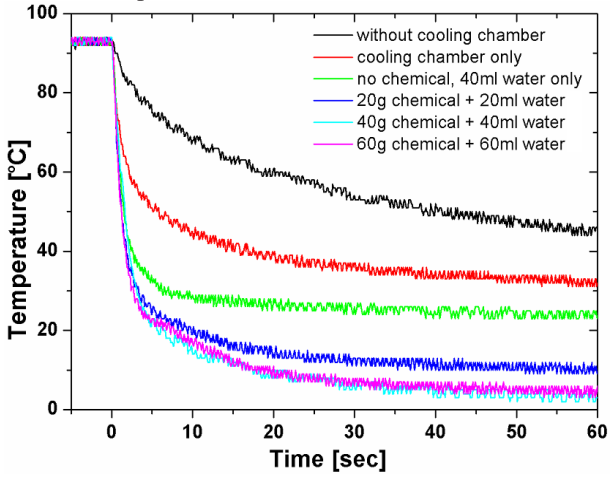
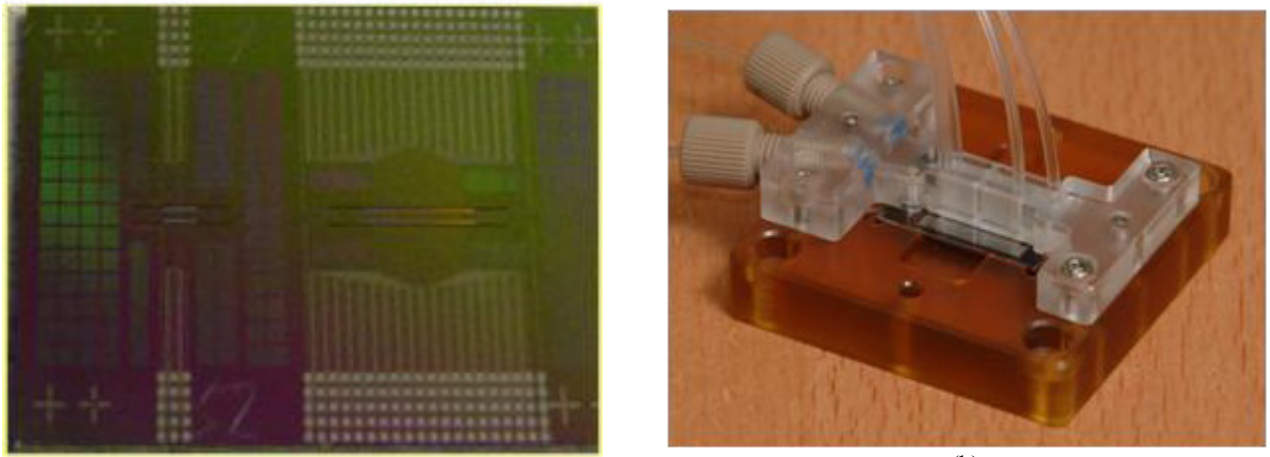



*Figure 6: Super cooling experimental results using miniaturized endothermic cooling module with comparison of different cooling conditions including without cooling chamber, with cooling chamber only, with water injection to the chamber, as well as with different amount of endothermic chemicals.*



(a) (b)

*Figure 7: Silicon nanowire photographs: (a) top view of the silicon nanowire biosensor; (b) customized plastic housing for denatured ssDNA detection experiment using nanowire biosensor.*

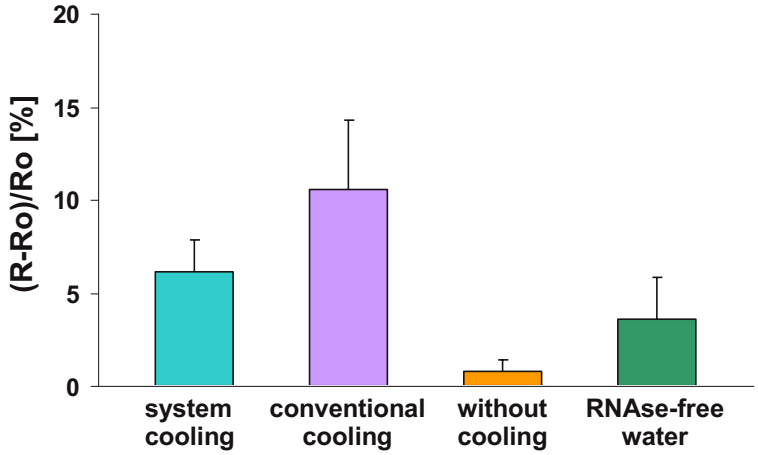



*Figure 8: Experimental results of the DNA denaturation test with nanowire biosensor: system cooling – sample from integrated microsystem including on-chip DNA denaturation process; conventional cooling – sample from conventional super cooling method including boiling water and ice water dipping; without cooling – sample from conventional PCR without post denaturation process; RNAse-free water – sample is just RNAse-free water as a control.*

## CONCLUSION

Consequently, we can conclude that present miniaturized endothermic cooling module has capability to denature on-chip PCR product for downstream electrical detection of ssDNA, thus is applicable to realization of integrated microsystem for nucleic acid based diagnosis of infectious disease.

## ACKNOWLEDGEMENTS

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