A Micromachine-based On-Chip Temperature Control System for Biomedical Applications

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Outline

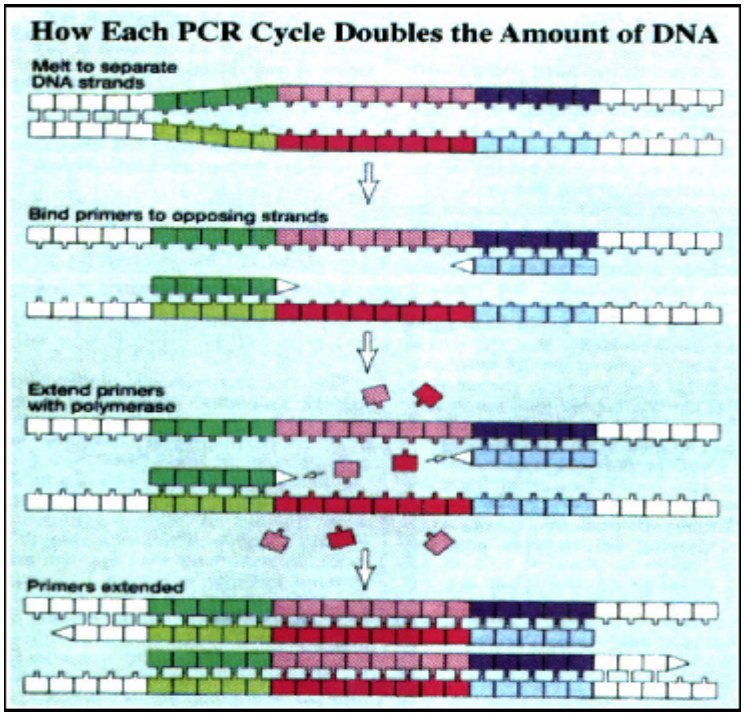
- Introduction and Motivation
- Design
- Fabrication
- Results and Discussion
- Conclusions

Introduction

- Applications in micro PCR chips, micro incubators, micro fermentors and other micro bioreactors which need precise temperature control.
- Advantages of Micromachine-based Temperature Control System

	Conventional Instruments	Micro Temperature System
Temperature Rising Rate	1 °C/sec	> 10 °C/sec
Sample volume	> 25 μL	≤ 5 μL
Power	High	Low
Integration	Separated Devices	Integrated
Others	Stationary	Portable

PCR (Polymerase Chain reaction) – Kary Mullis, 1984

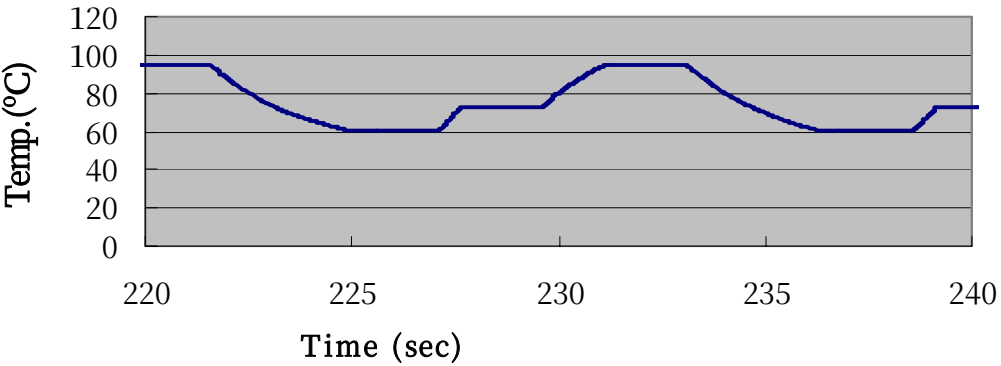


Denaturation- **95ºC**

Annealing- **60ºC**

Chain Extension- **72 ºC**

Repeat



Motivation

Typical PCR Cyclers

-take more than 2 hours

-Require more than 25 μL DNA samples

-Large-scale, bulky systems

Micro PCR systems

•Heaters and sensors located inside PCR chamber

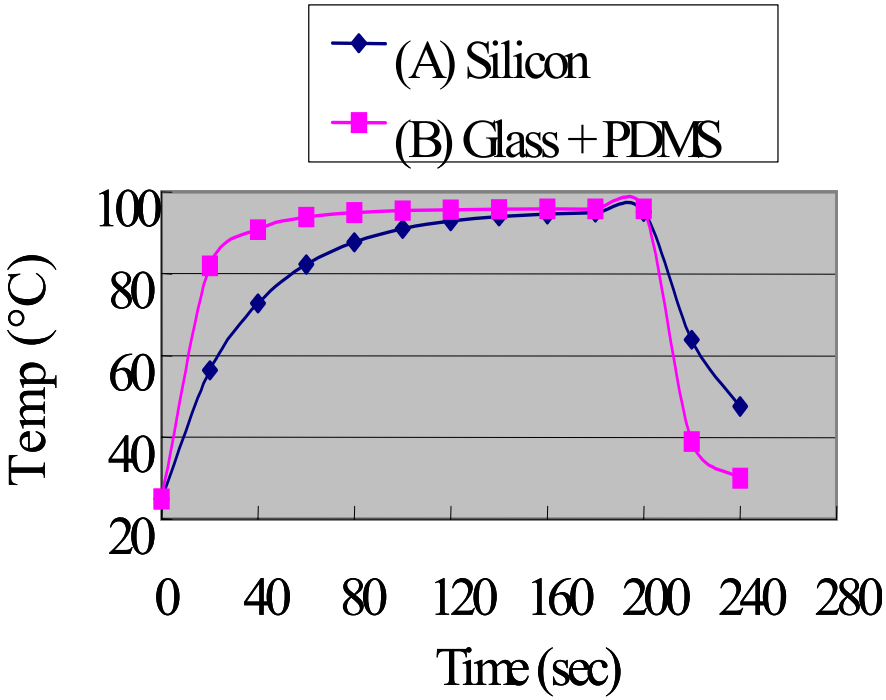
=> precise temperature control

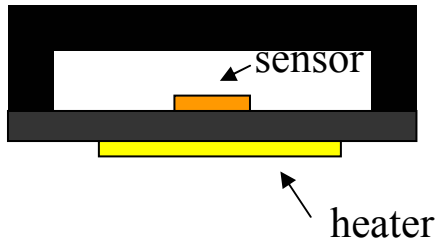
•Simpler fabrication process

•Glass substrates => biocompatible

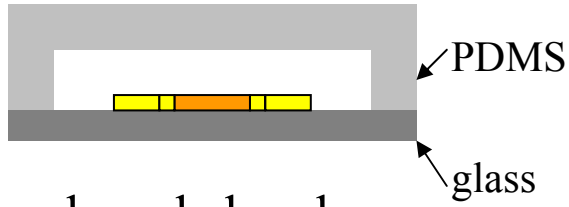
Design

- Heaters and sensors located inside the chamber
- => small thermal inertia, higher rising and cooling rates





(A) Si-based chamber with external heaters



(B) Glass-based chamber with internal heaters

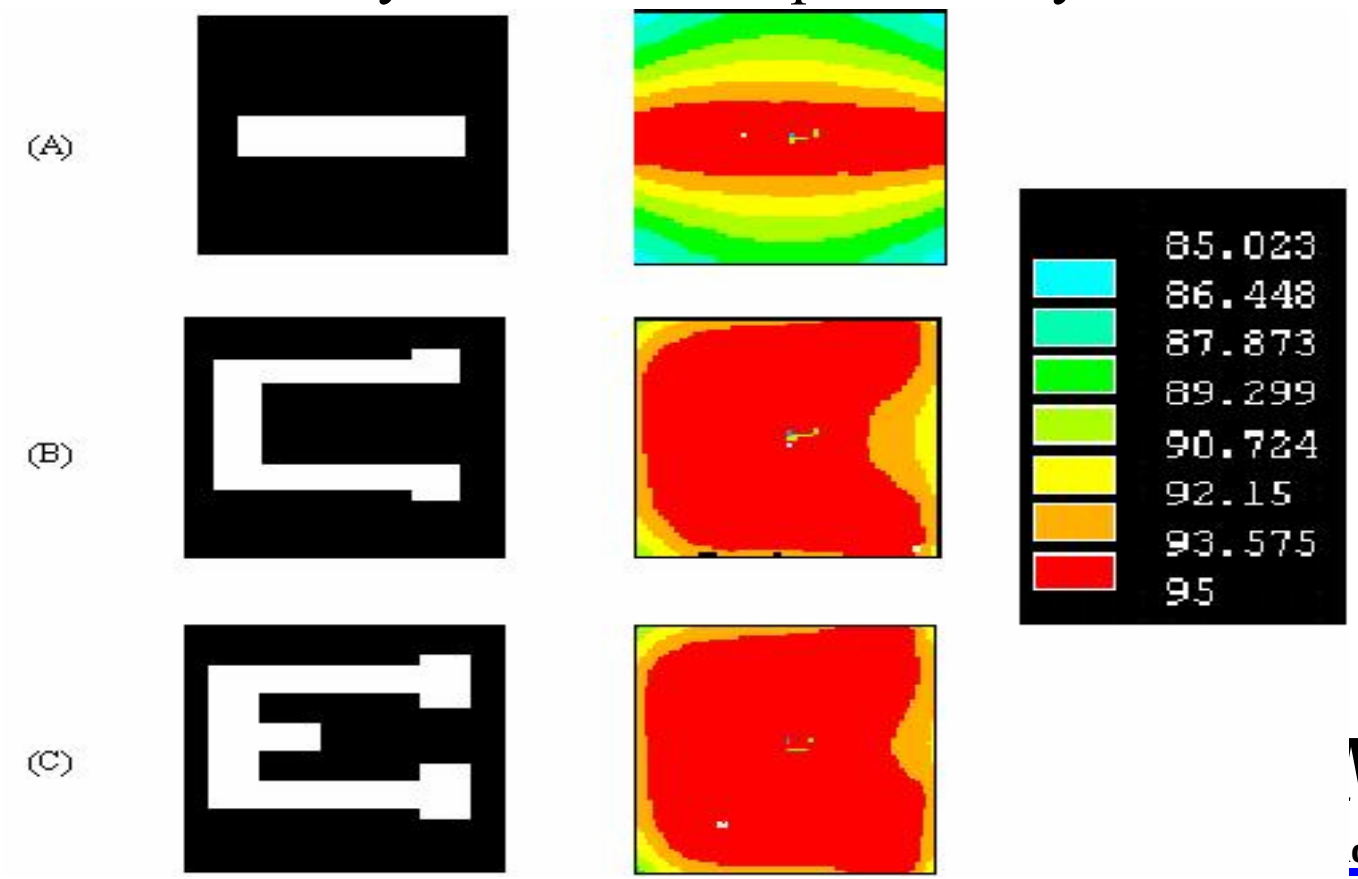
Power = 2.8 W

Chamber Size = 3 mm X 3 mm X 0.1 mm

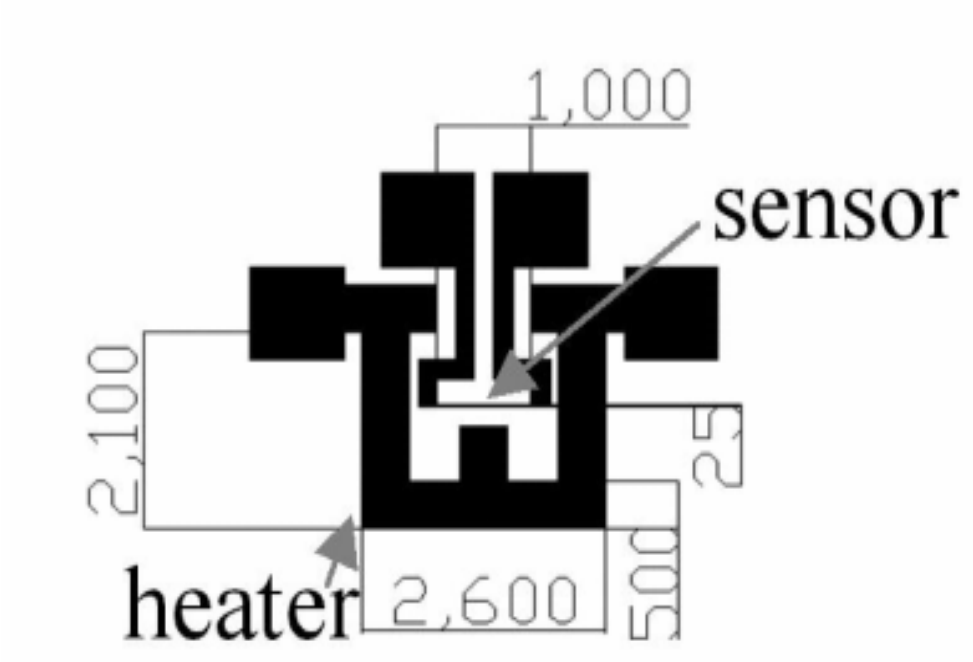
Heater Design

•Percentage within 1.5 ° of the set-up temperature was used to evaluate the performance of the heaters (Area Percentage of $0<\Delta T<1.5^{o}C$)

•Better uniformity achieved for optimum layout of heaters.



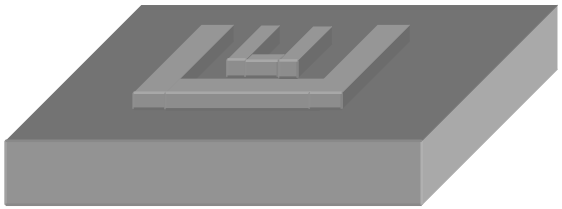
Layout of Heaters and Sensors



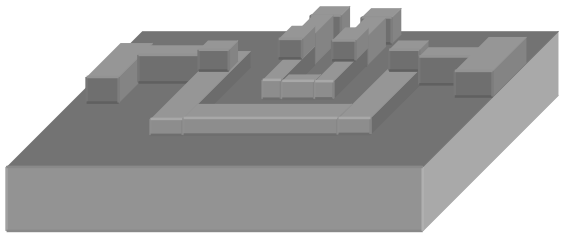
- Heaters and sensors using the same material (Pt)
- Simpler process
- Sensing temperature inside the chamber

Fabrication – glass substrates

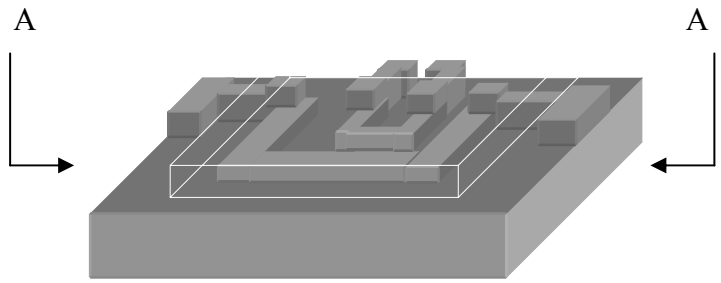
- Heaters and sensors fabricated on glass substrates
- Au as metallization lead
- Polyimide as isolation layer
- PDMS upper plate



(a) Electron-beam evaporation/patterning of Pt/Cr



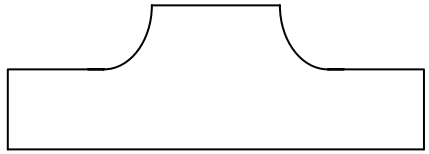
(b) Electron-beam evaporation/patterning of Au/Cr



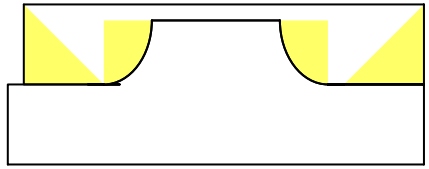
(c) Spin-coating/patterning of polyimide

(d) Bonding of a PDMS upper plate with a chamber (A-A section)

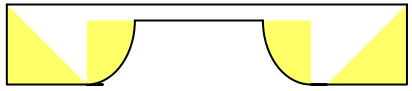
Fabrication – PDMS Upper Plates



(a) Glass template formed by wet chemical etching



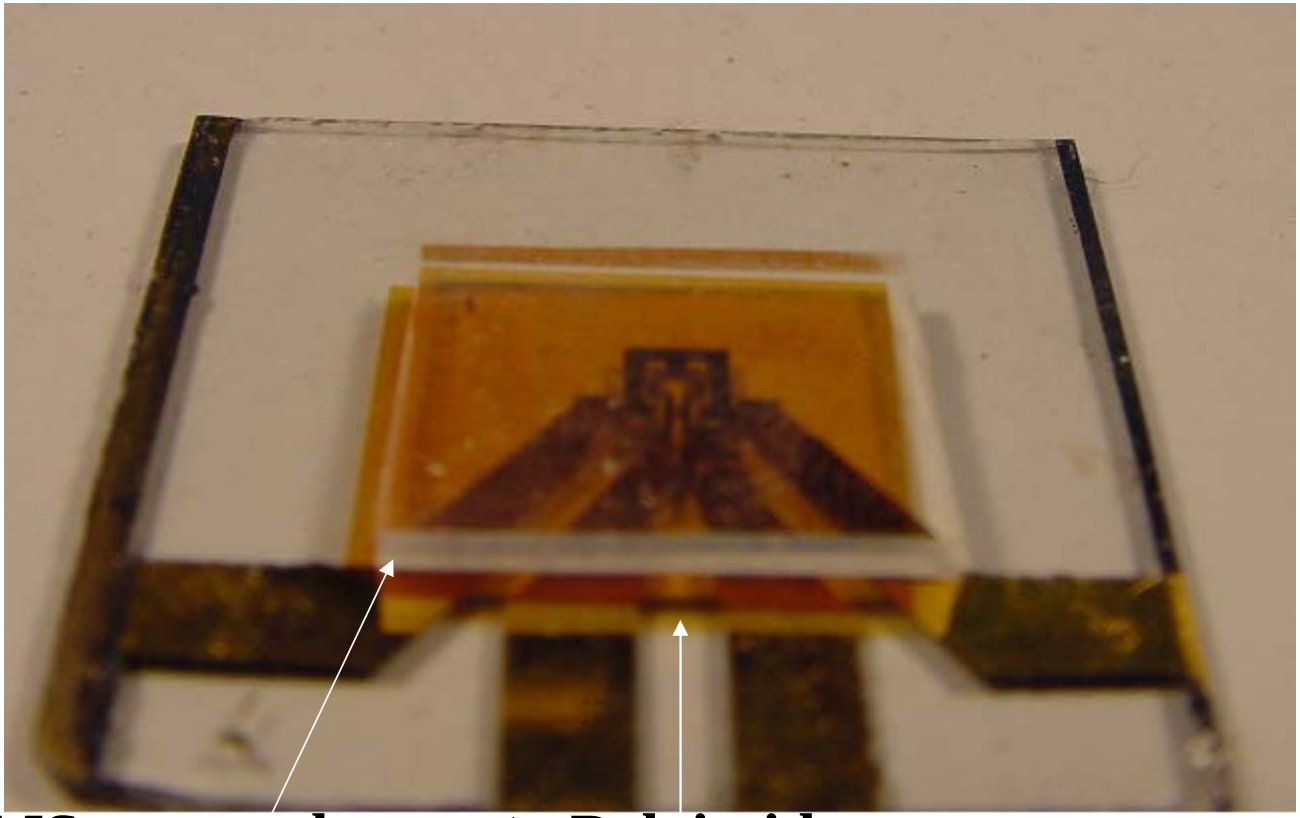
(b) Inverse structures formed by PDMS casting process



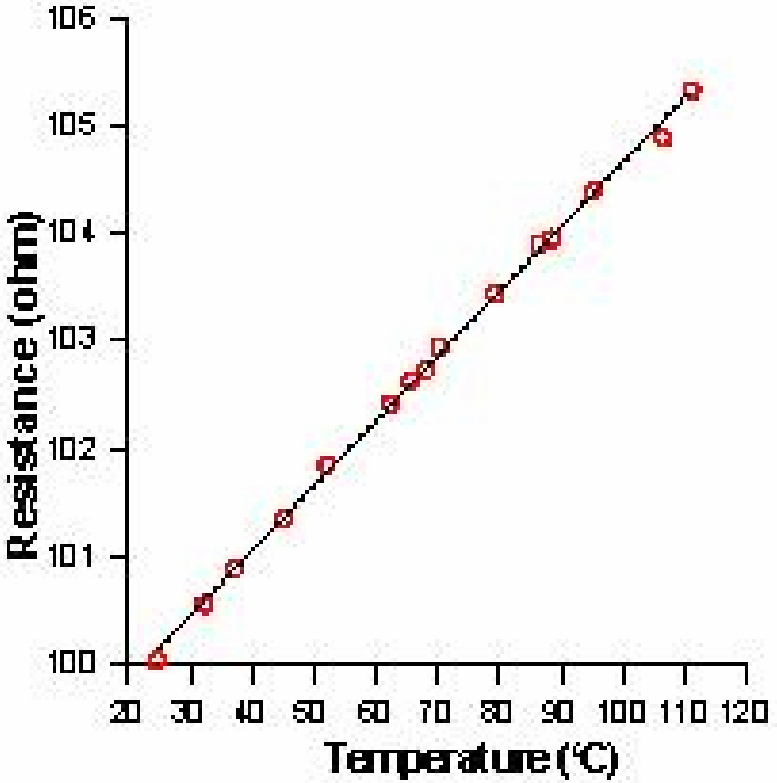
(c) Peeling of PDMS upper plate

PCR chips

Oxygen plasma used for glass/PDMS bonding



Sensor Testing

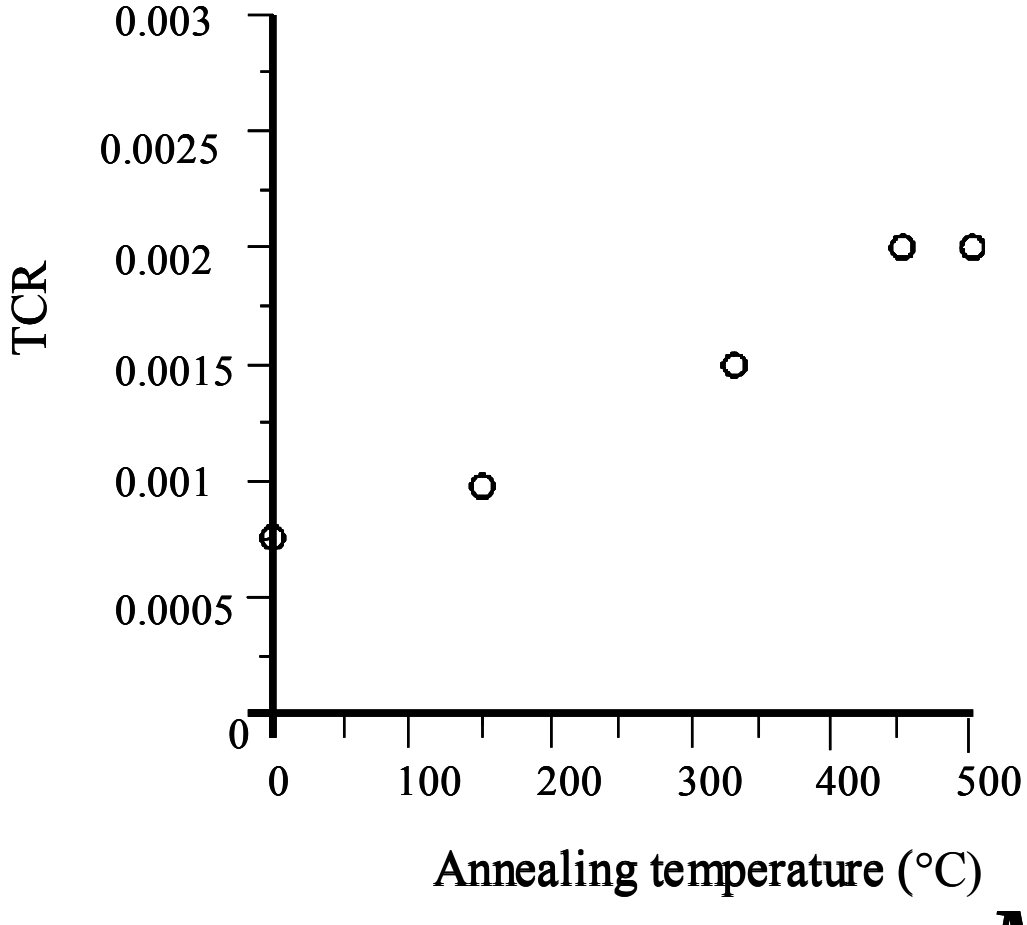


TCR : temperature coefficient of resistance

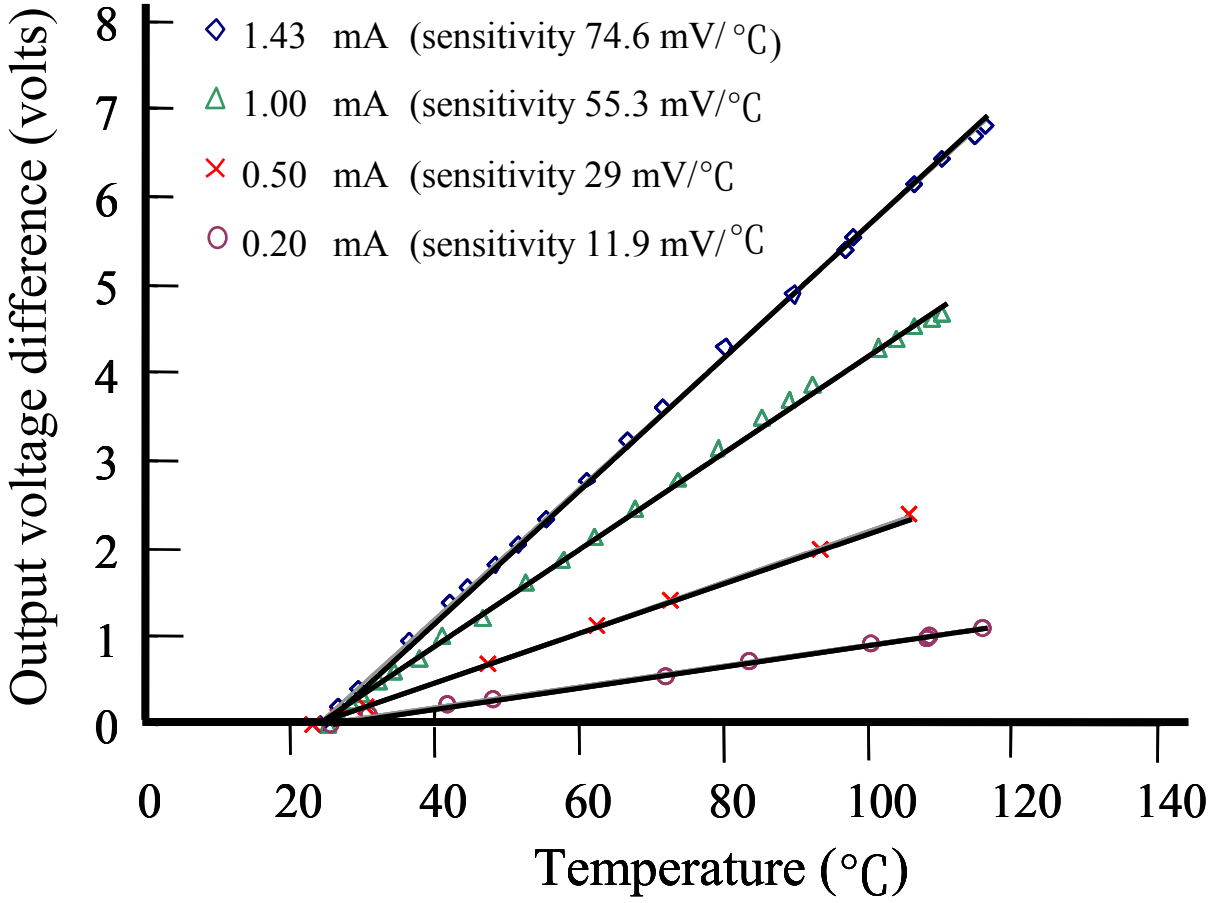
$$TCR = \frac{\Delta R / R_0}{\Delta T} = 0.00315\ /^{o}C$$

Linear relationships of R(T)

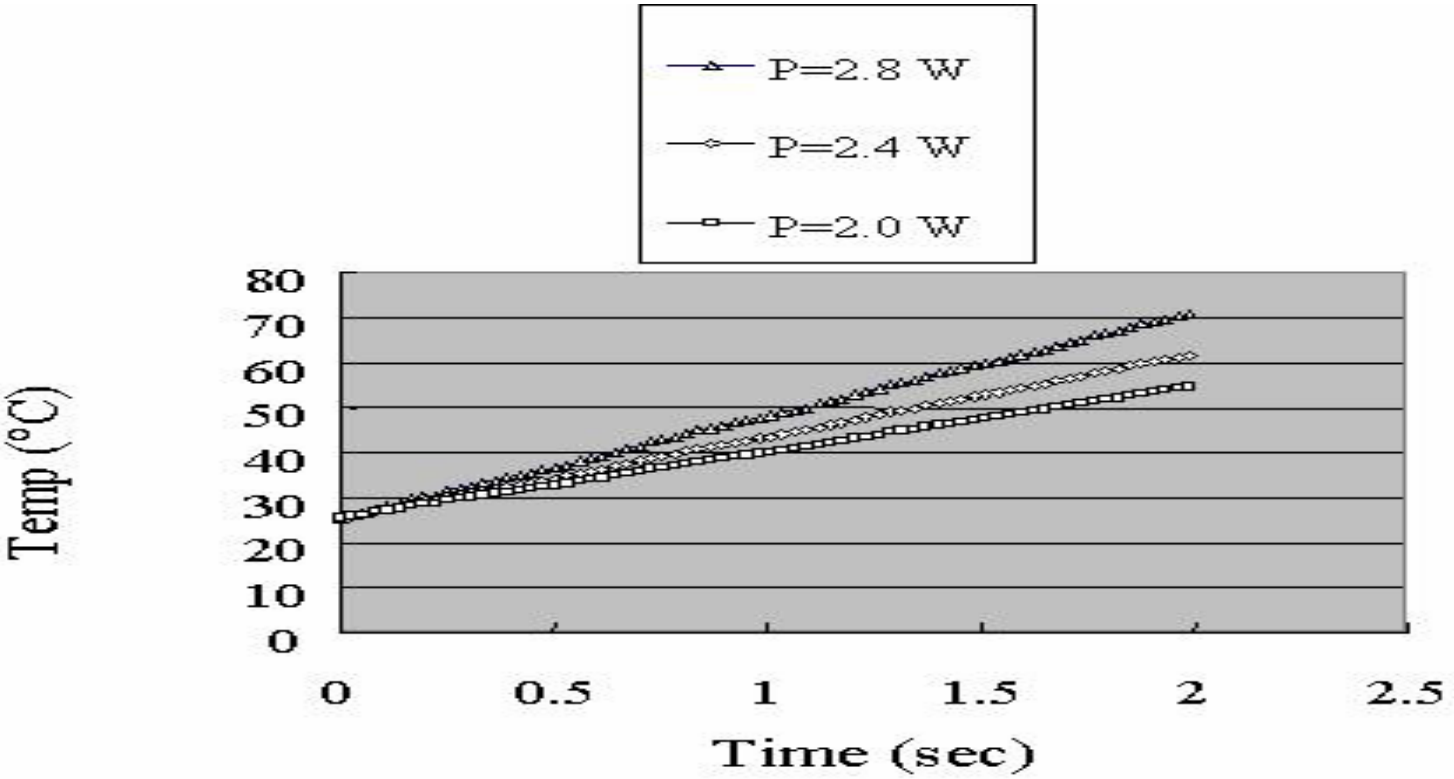
Effect on Sintering on TCR



Testing Results of the Sensor



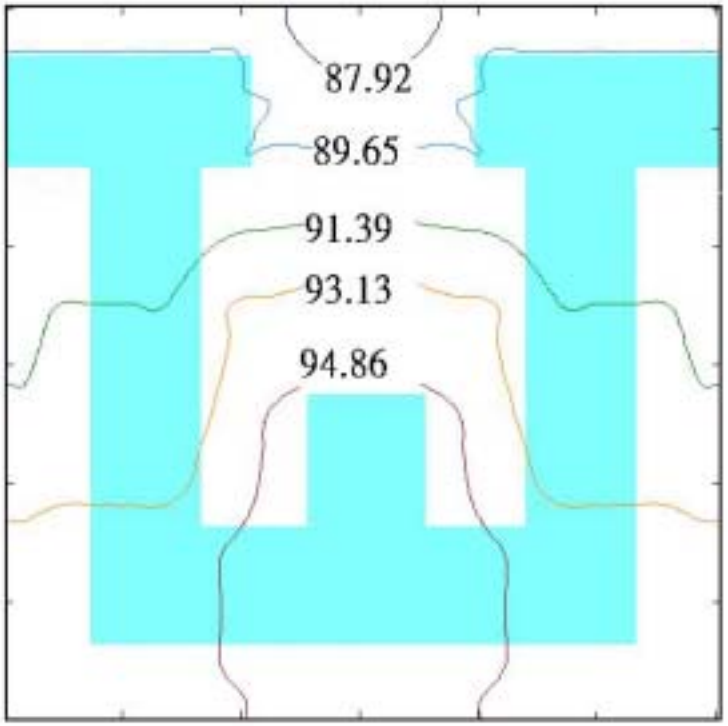
Heater Testing



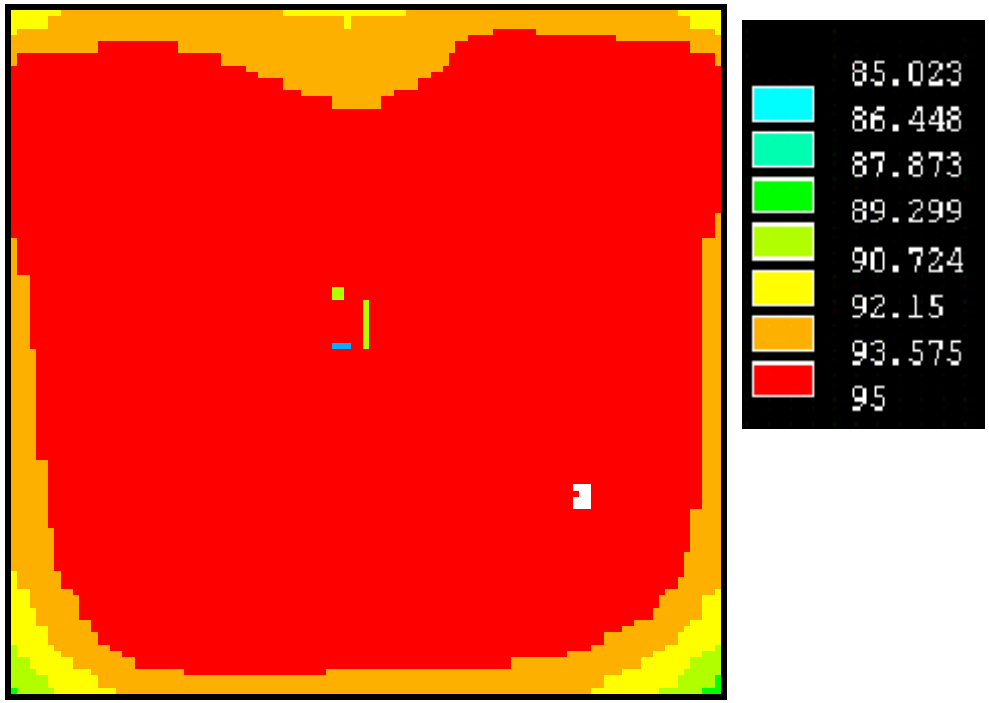
Temperature rise rate : 20 °C/sec @ P=2.8 W

Temperature Distribution around Micro Heaters

arrayed temperature sensors

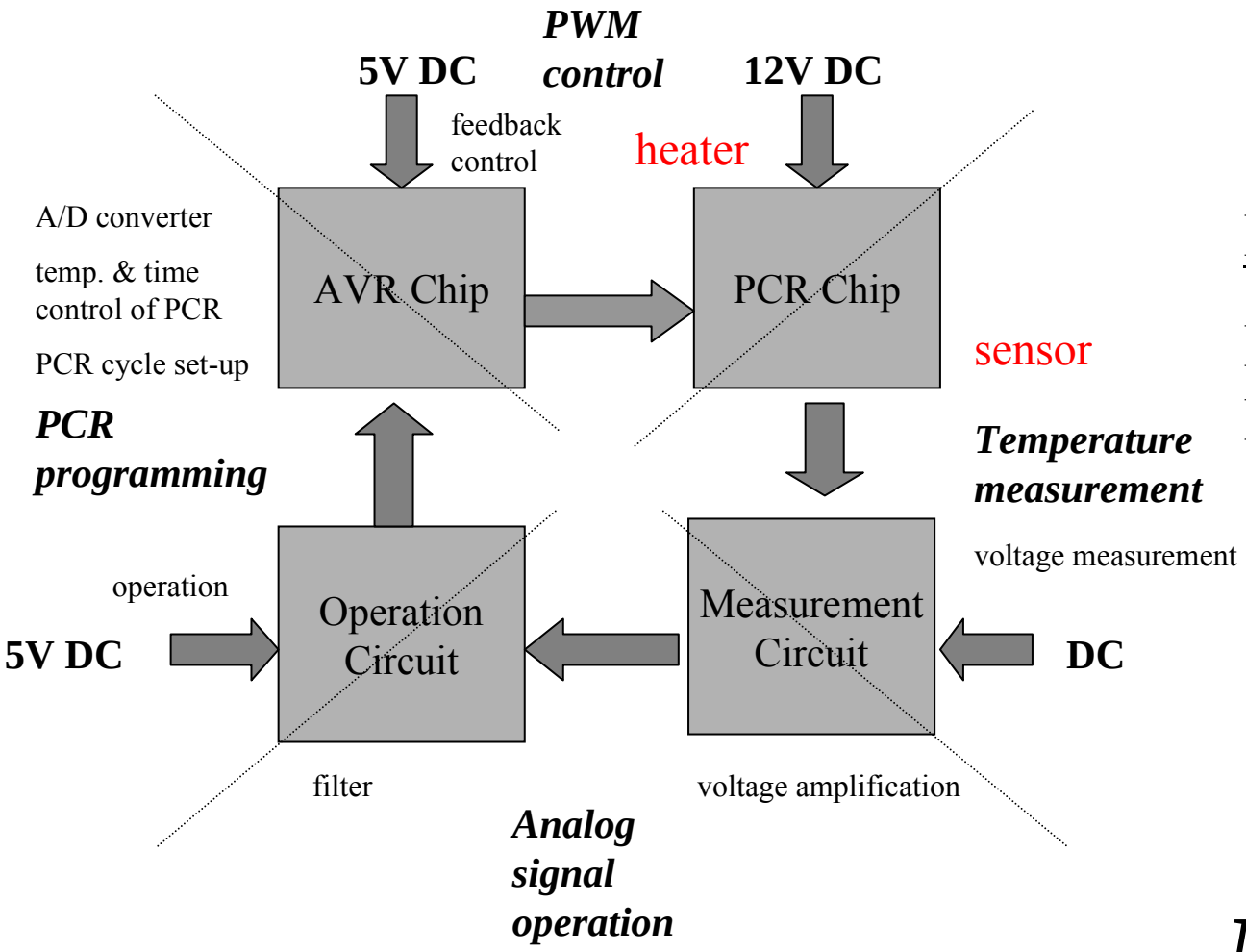


IR thermal imager



Temperature distribution around a micro heater with a set-up temperature of 95 ^{0}C

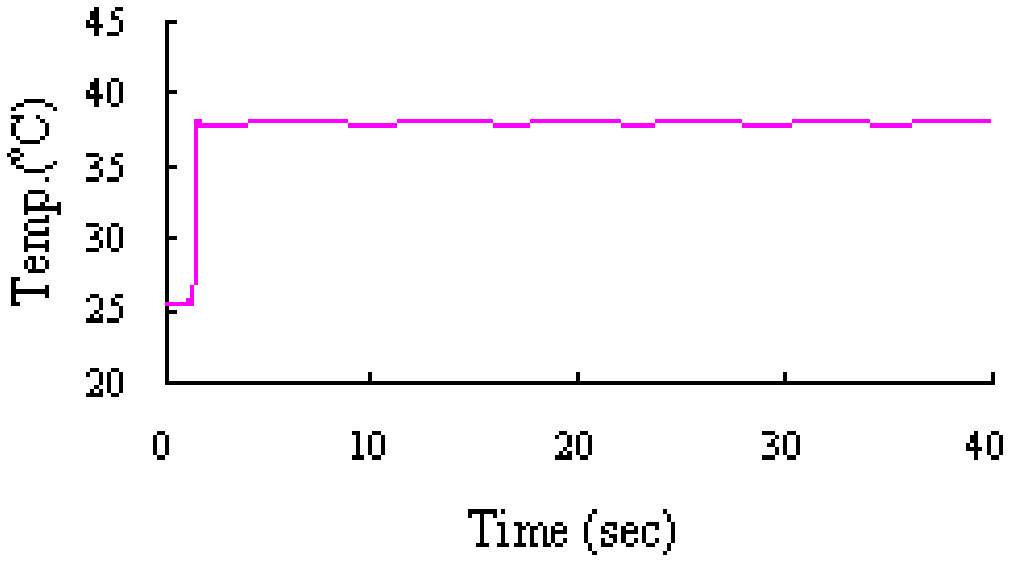
Control System



PWM Control :

Pulse –Width-Modulator

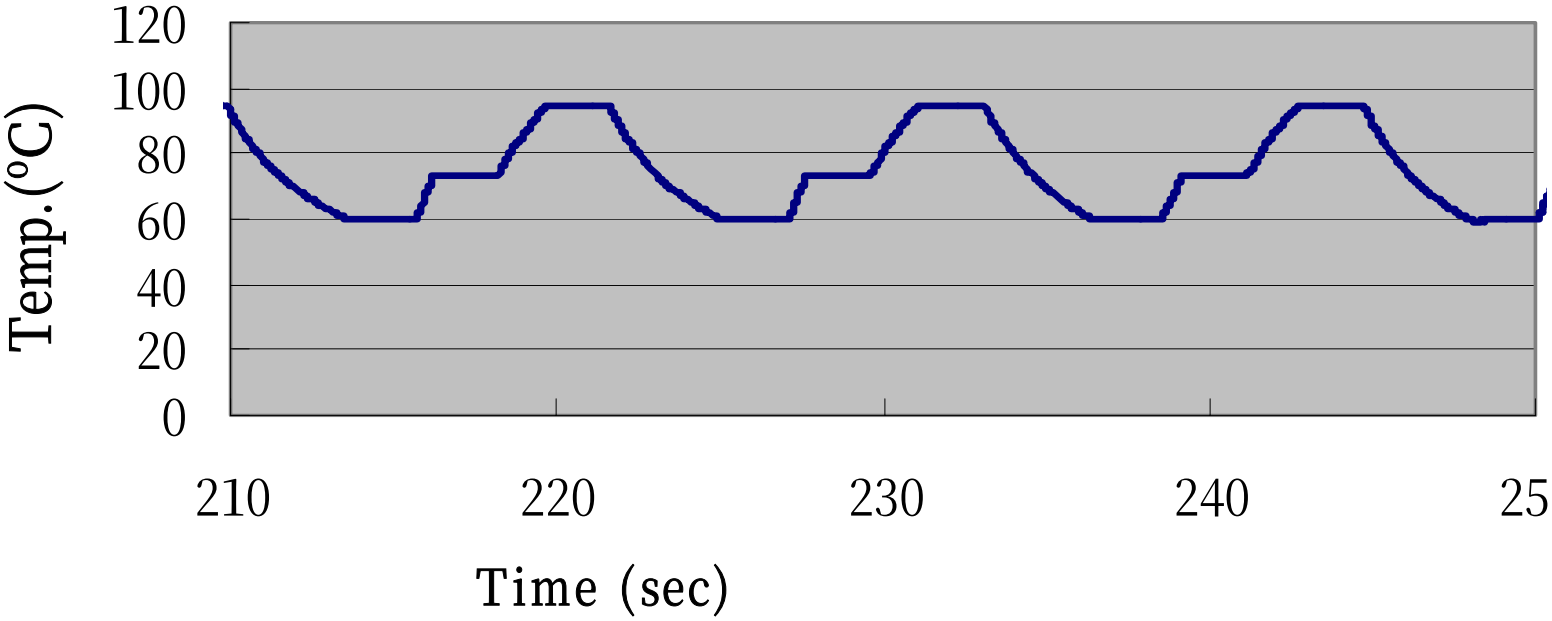
Biomedical Application (1)
Enzyme reactor



Variation : ±0.1 °C

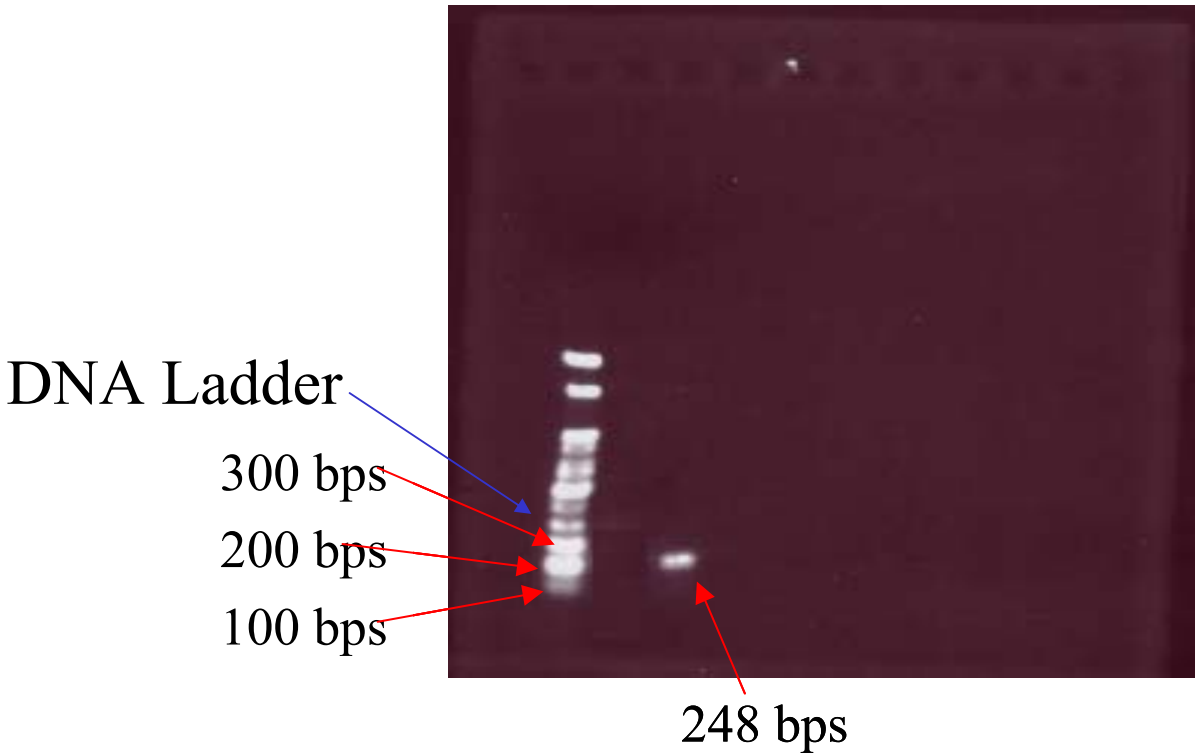
Enzyme Digestion Temperature = 38°C

Biomedical Application (2)
PCR Thermal Cycling



- Temperature Rise Rate : 20 °C/sec
- Temperature Drop Rate : 10 °C/sec
- Mean Power Consumption : 1.24 W
- 32 cycles in 15 minutes

Slab Gel Electrophoresis Results



- HTR6 receptor gene (248 bps)
- Volume of DNA samples = 900 nL
- 15 min, 32 cycles

Conclusions

A simpler fabrication process for micro temperature control system has been developed.

-Micro temperature sensors and heaters were fabricated on glass substrates, which are more bio-compatible.

-Fewer consumption of both samples and reagents

-Shorter cycle time - higher temperature rise and drop rates due to low thermal inertia.

-Less power consumption

-Accurate temperature control

- Development of the micro temperature control system is crucial for μ-TAS

Acknowledgements

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