

Rapid Temperature Cycling Miniaturized PCR Thermocycler with Switchable Heat Pipe Cooling

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Summary:

We present a highly miniaturized PCR thermocycler based on an aluminum oxide ceramic with an integrated micro-well structure, integrated heating and switchable thermal coupling for cooling. A platinum microheater enables rapid temperature changes, while pneumatically coupled heat pipes provide efficient heat dissipation during the cooling phase. The combination of low thermal mass and actively controllable heat transport enables significantly accelerated thermal cycling compared to conventional systems. Process monitoring is performed using fluorescence-based real-time detection. This approach offers potential for compact and high-performance point-of-care diagnostic systems.

Keywords: PCR, Thermal Cycler, Heat Pipe, Microheater, Point-of-Care

Background, Motivation and Objective

Fast and portable PCR (Polymerase Chain Reaction) systems are becoming increasingly important for point-of-care diagnostics and decentralized applications [1,2,3]. However, conventional thermocyclers are limited by large thermal masses and slow temperature transitions.

Advances in microsystem technology enable compact systems with significantly improved heating and cooling rates [4,5]. Nevertheless, efficient and controlled cooling in particular remains a key challenge.

The goal of this work is to develop a miniaturized PCR thermocycler based on a well-integrated ceramic structure with an embedded heating function and actively controlled thermal coupling for rapid temperature cycling. In particular, the decoupling of heating and cooling remains challenging, as continuous thermal coupling leads to parasitic heat losses and limits achievable temperature ramp rates.

Description of the New Method or System

To address this limitation, a thermocycler concept with switchable thermal coupling is proposed, enabling active control of heat transfer during different phases of the PCR cycle. The overall architecture is shown in Fig. 1. The system is based on a $5 \times 5 \times 5 \text{ mm}^3$ Al_2O_3 cube with an integrated microcavity. Heating is provided by a platinum-based microheater. Cooling is achieved by pneumatically coupling two heat pipes to the ceramic, thereby establishing a switchable thermal contact. An integrated fluorescence detection unit enables real-time

monitoring of DNA amplification, thereby combining rapid thermal cycling and optical readout within a compact system.

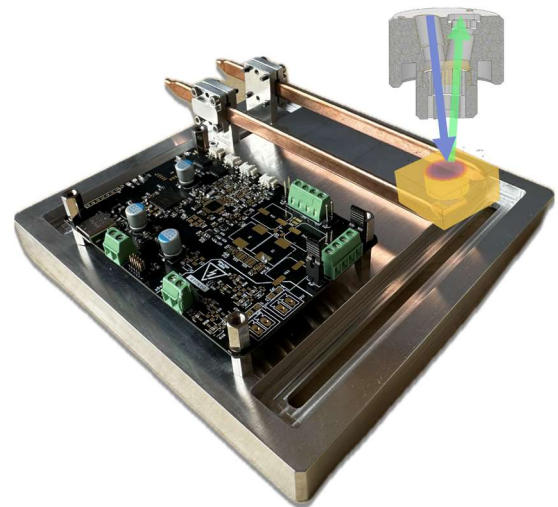


Fig. 1. Design of the miniaturized Thermocycler with integrated microheater, switchable heat pipe cooling, and fluorescence detection.

As illustrated in Fig. 2, the heat pipe operates on a closed two-phase cycle. A working fluid evaporates at the hot contact surface and transports latent heat along the heat pipe. At the cold end, the fluid condenses and releases the heat. The condensate is returned to the evaporation zone by capillary forces, enabling highly efficient heat transfer with low thermal resistance.

This principle allows heat transfer to be activated only during the cooling phase, while thermal coupling is minimized during heating. The thermal

behavior of the thermocycler can be approximated using simplified heat transfer models.

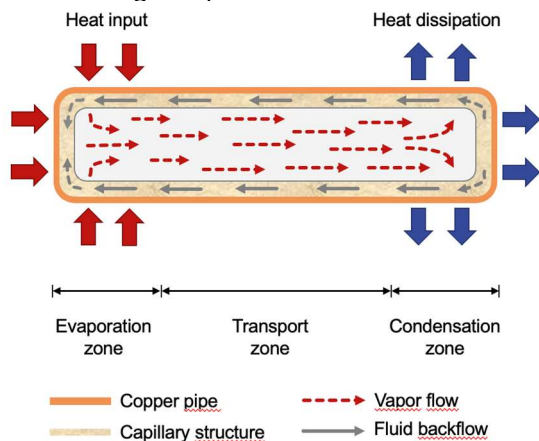


Fig. 2. Schematic illustration of the operating principle of a heat pipe.

Heat transfer within the system can be approximated by Fourier's law

$$q = -k \cdot \nabla T \quad (1)$$

where q is the heat flux, k is the thermal conductivity, and ∇T is the temperature gradient. However, heat pipes exhibit a significantly higher effective thermal conductivity k , which can exceed that of solid materials [6]. The amount of heat transferred can be described simply by

$$Q = h \cdot A(T_{hot} - T_{cold}) \quad (2)$$

where Q is the heat transfer rate, h is the effective heat transfer coefficient, A is the effective heat transfer area, T_{hot} is the temperature of the hot side, and T_{cold} is the temperature of the cold side. The effective heat transfer coefficient h is significantly enhanced by phase-change processes within the heat pipe. Pneumatic coupling specifically reduces the thermal resistance R_{th} during the cooling phase

$$R_{th} = \frac{\Delta T}{Q} \quad (3)$$

where R_{th} is the thermal resistance and ΔT is the temperature difference across the thermal interface. This minimizes heat loss during the heating phase while enabling high cooling rates.

Results

To evaluate the thermal performance of the proposed concept, the PCR protocol, including temperature levels and typical dwell times, is summarized in Table 1. As shown in Fig. 3, the normalized cooling curves demonstrate a significant improvement in thermal dynamics due to the use of heat pipes. Once the denaturation temperature is reached, cooling occurs significantly faster than without a heat pipe. This leads to accelerated transitions between the denaturation and annealing temperatures. Without a heat pipe, cooling proceeds significantly slower and exhibits lower effective cooling rates. The

improved heat dissipation reduces cycle times and increases the overall efficiency and performance of the PCR process. These results demonstrate the effectiveness of the proposed switchable

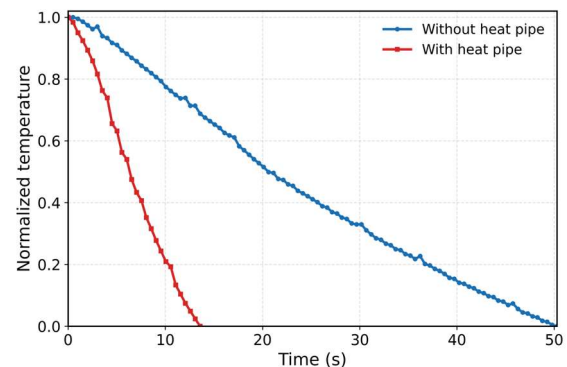


Fig. 3. Normalized cooling curves from 96 °C to 55 °C for operation without and with heat pipe.

heat pipe cooling concept for enabling rapid and efficient PCR thermal cycling in miniaturized systems.

Tab. 1: Process parameters for a PCR cycle, including the respective temperature steps and durations.

Process step	Temperature T / °C	Typical duration
Denaturation	96	10 – 30 s
Annealing	55	10 – 30 s
Elongation	68	20 – 60 s

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