IR thermocycler for centrifugal microfluidic platform with direct on–disk wireless temperature measurement system

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Abstract

We present a novel **infrared (IR) thermocycler** for **centrifugal microfluidic platforms** [1]. It allows to **directly heat liquids in reaction containers within** microfluidic polymer film disks [2] **for polymerase chain reactions (PCR) with average heating gradients of up to 4 K/s**. This thermocycler mainly consists of an **IR ring-heater, a direct on-disk wireless temperature measurement system with a resolution of 0.1 K and an embedded adaptive PID controller**. That enables to **precisely control the temperature of the liquid even at variant conditions** e.g. manufacturing tolerances, different cavity locations, ambient temperature changes, whereas state-of-the-art thermocyclers with indirect air temperature measurement are inflexible due to static thermal energy flow models. Hence our system has the potential for a higher **efficiency, accuracy and robustness,** thus for a **better PCR reproducibility**.

1 Introduction

In centrifugal microfluidic lab-on-a-chip systems both for the processing of immunoassays [3] as well as PCR the tempering of the reagents is essential. These reagents are generally kept in cavities made of polymers with volumes of few microliters. Polymer cartridges with microfluidic control structures and cavities could be either injection-moulded or blow-moulded of films. The efficiency and reproducibility of the PCR thermocycling process in centrifugal microfluidic analysers can be increased by employing an IR radiator combined with a direct measurement of the reaction temperature and closed-loop control.. Heating by direct IR radiation also has the benefit that a much lower thermal load has to be thermo-cycled, since no heat transport medium like air or a thermoblock have to be heated and cooled. In our setup, rapid cooling is realized by components with low thermal capacity, cool air ventilation and disk rotation. Adaptive PID control based upon direct on-disk temperature measurement [4] in the reagent cavity grants for robustness and the system reproducibility.

2 System specification and design

Average heating rates of 3 K/s and cooling rates of 1 K/s should be achieved. The liquid temperatures in the cavities subject to the thermocycling process should be approached without significant overshooting and stable at the setpoint value within a tolerance of +/- 0.2 K.

We choose an IR ring heater (Fig. 1) with an electrical power of 1700 W and a peak wavelength of ~ 2 µm. It has an inner diameter of 170 mm, half of the ring shaped glass body is gold plated such that the radiation emitted by the electrical coil of 560 mm length is focused to the reagent cavities. This radiator is fixed into the housing of a centrifugal analyser (Fig. 2), additionally a fan of 2 W was built into the lid. A carrier for the COC polymer film disk (diameter 210 mm) sealed by a COC polymer film of 150 µm thickness is connected to the motor spindle. The rotating components of the temperature measurement system (Fig. 2+3) are fixed in the center of this carrier. A SMD low-cost (0.15 US$) thermistor as temperature sensor is put to the microcavity (Fig. 4) of the COC disk. A microcontroller MSP430 communicates via a CC2500 radio transceiver with the rotating platform, receives temperature data at sampling rate of 8 Hz and runs an adaptive PID controller which controls both the IR ring heater and the ventilator.

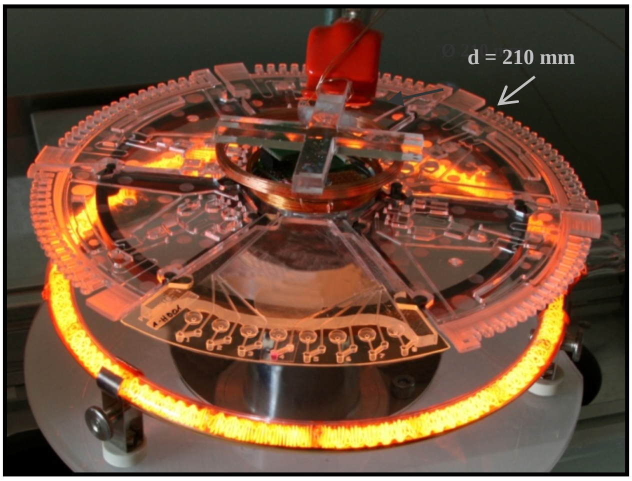

Fig. 1: IR ring heater with on-disk temperature measurement system - first prototype

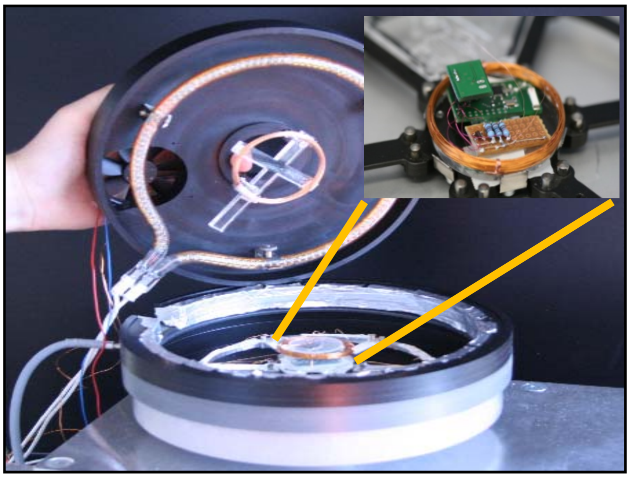

Fig. 2: Closed system with IR heater, fan and temperature measurement system on rotary platform

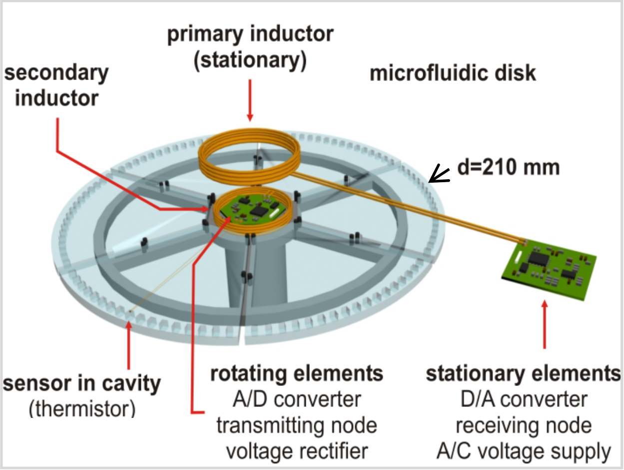

Fig. 3: Setup with thermistor, A/D converter, transmitting node, primary and secondary coils

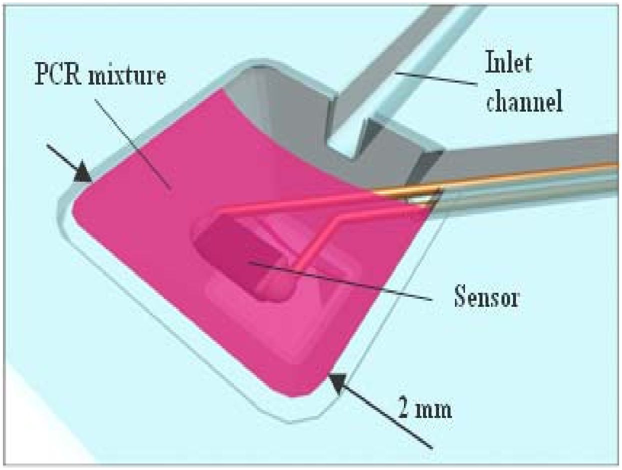

Fig. 4: Illustration of a thermistor with a volume of 54 nl fixed in sealed reaction chamber of polymer film cartridge

3 Experiments and simulations

The peak intensity of the IR radiator hits an absorption maximum of water and a transmission maximum of the COC sealing film at a wavelength of ~ 2 µm (Fig. 5).

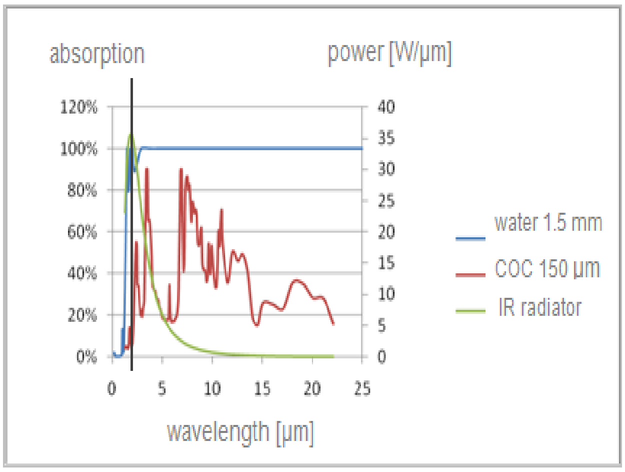

Fig. 5: Absorption spectra of water and COC film in comparison to emission spectrum of IR radiator

At 1940 nm ~15 % of the radiation energy is absorbed by the COC sealing film (Fig. 6). Simulations show that thermal conduction from the sealing lid and the cavity walls to the reagent contribute little to the heating process.

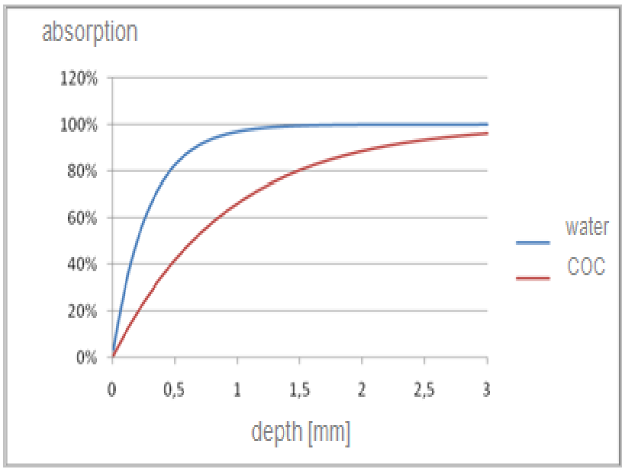

Fig. 6: Absorption rates of water and COC for a wavelength of 1940 nm at various depths

Average heating rates of up to 4 K/s for step responses from room temperature to 50, 70 and 92 °C could be achieved with low overshoots (Fig. 7). Cooling is controlled by both air ventilation and the disk rotation frequency. Increasing the rotation frequency from 3 Hz to 30 Hz reduces the thermal resistance by ~ 60 % (Fig. 8). PCR thermocycling with a free choice of temperature settings, holding times and cycle numbers is flexibly programed by a C# process controller communicating via a UART interface with the embedded temperature controller (Fig. 9).

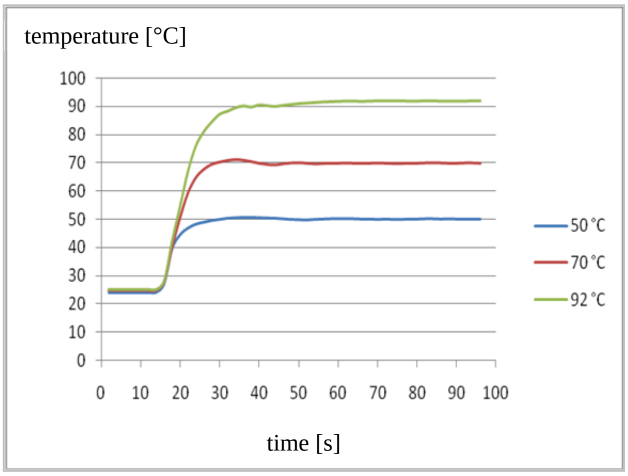

Fig. 7: Step responses of closed-loop PID controlled system measured in microcavity

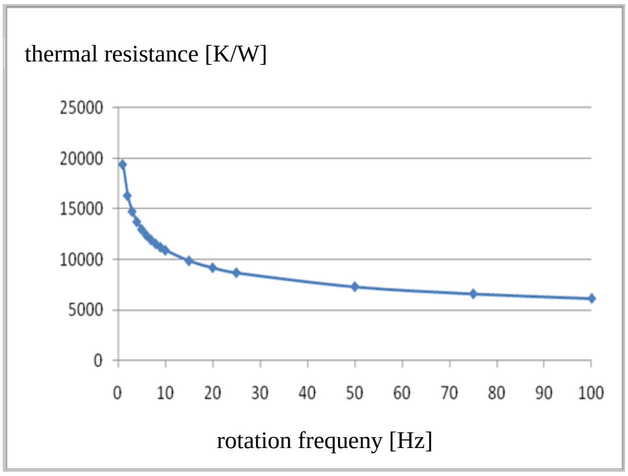

Fig. 8: Thermal resistance of COC polymer film disk cavities at different rotation frequencies

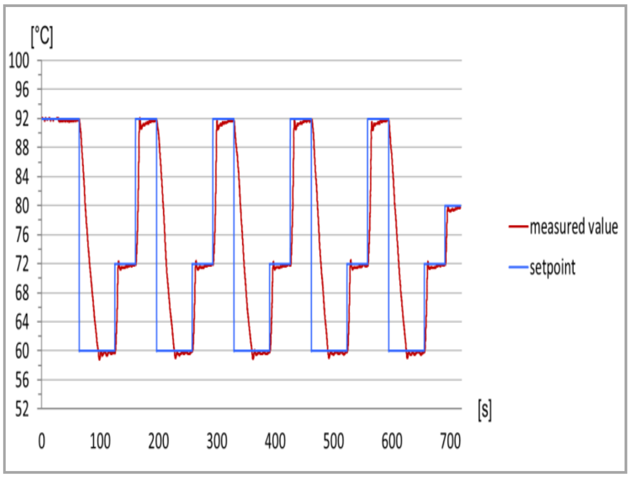

Fig. 9: Thermocycling in polymer film cavities filled with 10 µl of water

4 Conclusion

IR radiation is capable to directly and rapidly heat water-based reagents in cavities of microfluidic polymer film disks. Both controlling the fan and the disk rotation frequency enhances the cooling process. Directly measuring the reagents temperature leads to robust systems with low overshoots of less than 1 K and stable values at the set-points during the holding times of the thermocycling process. Thus this system has the potential to reduce PCR cycling times significantly and also decrease the thermal load for the surrounding laboratory.

5 Acknowledgements

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6 References

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