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Simulation guided-design of a microfluidic thermal reactor for polymerase chain reaction

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A B S T R A C T

Microfluidics have been developed as a major platform for chemical/biochemical reactions because of several major advantages: low reagent usage, fast reaction rate, less labor involved to minimize the contamination, and the potential to achieve a "lab-on-a-chip". One such application will be the polymerase chain reaction (PCR) which requires repeated thermal cycling. One cycle includes 90–95 °C for denaturation, 50–70 °C for renaturation, and 70–75 °C for extension to amplify the DNA fragments of interest. Two numerical simulations based on finite element analysis (FEA) were conducted: (1) a device simulation was realized to understand the temperature uniformity of the micro-channels on a polydimethylsiloxane (PDMS)-glass format; (2) a single micro-channel simulation was realized to understand the temperature distribution of the flowing reagent inside the micro-channel, which led to elucidate the impact of the thermal convection to the temperature distribution of the reagent. The device simulation results show three distinct and uniform temperature zones on a designed hybrid continuous flow PCR (CFPCR) device. For the micro-channel simulation, results show that the dwell time of the chemical reagents at each target temperature zone at higher flow velocities is reduced. It also shows the importance of the flowing reagent's thermal convection to the temperature distribution of a microfluidic thermal reactor. To verify the simulation results, a hybrid, 40-cycle continuous flow PCR (CFPCR) was designed and fabricated for experiments using photolithography and polydimethylsiloxane (PDMS) casting techniques. A 99 bp lambda DNA fragment was successfully amplified on this hybrid device at different flow velocities from 4 mm/s to 20 mm/s. This confirms the (1) success of the simulation-guided design for a microfluidic thermal reactor and that (2) insufficient dwell time for the PCR reaction at higher flow velocities lead to a lower amplification efficiency.

Keywords: Continuous flow polymerase chain reaction (CFPCR); Numerical simulations; Microfluidic thermal reactor

1. Introduction

Microfluidic technology has been developing for three decades since the first micro-gas chromatograph was reported in 1979 (Terry et al., 1979). This elucidated that a bio/chemical reaction can be realized on a small footprint with the benefits of lower reagent demand, faster reaction rate, minimized labor to reduce the contamination, and the potential to integrate with other functional components as a micro total analysis systems (μTAS). The original microfabrication techniques were derived from the semiconductor industry and the major substrate materials in the late 90s were silicon and glass. To obtain the goal of developing a microfluidic device that is low-cost, disposable, less hazardous fabrication processes, and mass produced, new substrate materials with associated fabrication techniques were explored such as polycarbonate, poly(methyl methacrylate) (PMMA), polydimethyl-siloxane (PDMS) (Soper et al., 2000), and even paper (Martinez et al., 2008; Mantinez et al., 2008).

After the polymerase chain reaction (PCR) was reported in 1987 (Mullis and Faloona, 1987), the methods of disease diagnosis have been moving from conventional cell-culture processes to molecular level detection (Robertson and Nicholson, 2005). PCR exponentially amplifies the DNA

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