Chemical Engineering Science 186 (2018) 191–198

Contents lists available at ScienceDirect

Chemical Engineering Science

journal homepage: www.elsevier.com/locate/ces

Thermal analysis of the photothermal effect based droplet microfluidic system

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HIGHLIGHTS

- Photothermal effect based droplet microfluidic system is proposed for PCR applications.
- Thermal analysis of the proposed droplet microfluidics is performed.
- A linear relationship between the droplet temperature rise and laser power is found.
- Typical thermal cycle with quick response can be achieved.

ARTICLE INFO

Article history:
Received 3 December 2017
Received in revised form 8 February 2018
Accepted 21 April 2018
Available online 25 April 2018

Keywords:
Droplet microfluidics
Rail and anchor
Photothermal effect
PCR
Thermal analysis

ABSTRACT

In this work, the photothermal effect based droplet microfluidic system with the incorporation of the rail and anchor is proposed to complete the thermal cycle for the polymerase chain reaction (PCR) applications. Using the photothermal effect of the laser enables non-contact control of the droplet temperature with quick response, while the rail and anchor enables precise control of the droplet movement and easy focus on the droplet, respectively. With the proposed droplet microfluidic system, the thermal analysis towards the PCR application is then performed. It is found that when the *Biot* number of the droplet is less than or equal to 0.1, the uniform temperature distribution in the droplet can be ensured by selecting suitable carrying oil. A linear relationship between the droplet temperature rise and laser power is found, by which each characteristic temperature required in the PCR thermal cycle can be controlled by adjusting the laser power. The minimum temperature response time constant can be as low as about 0.175 s. The first thermal cycle with the consideration of the enzyme activation can be finished in 48.8 s and the following each thermal cycle can be completed in 28.6 s. The results obtained in this work have demonstrated the feasibility of the photothermal effect based droplet microfluidic system for the PCR applications.

1. Introduction

Since the development by Kary Mullis in 1983 (Bartlett and Stirling, 2003), the polymerase chain reaction (PCR) has been widely used to amplify DNA with several orders of magnitude for medical and biological applications (Jiang et al., 2014; Shu et al., 2014). In recent, the incorporation of the microfluidics technology into the PCR technology leads to the microfluidic PCR (Kopp et al., 1998; Beer et al., 2007). This new technology holds great advantages, in that it can be performed with a small fraction of reagents and much less reaction time (Lin and Lee, 2010). However, this new technology still faces some shortcomings of the surface inhibition and contamination (Guo et al., 2012). Fortunately, these shortcomings can be overcome by the droplet microfluidics because it presents the need of much short time, low cost and high sensitivity, nanoliter or picoliter volume and contamination avoidance (Thorsen et al., 2001; Anna et al., 2003). For this reason, the droplet microfluidics for the PCR application has received ever-increasing attention all over the world (Bu et al., 2003; Zhu et al., 2012).

In general, the PCR requires the repeated thermal cycle of a sample through a denaturation (94–98 °C), an annealing (50–65 °C) and an extension (70–80 °C) to achieve an exponential increase in target DNA (Li et al., 2013). In this case, the heating and cooling devices are usually required. However, it is difficult to incorporate multiple heating or cooling devices into a microfluidic chip. In addition, they also bring substantial obstacles against

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https://doi.org/10.1016/j.ces.2018.04.049
0009-2509/

implementing PCR because of special equipment needed (Jiang et al., 2014). Recently, the incorporation of optics into microfluidics has resulted in several novel microfluidic systems by using various interactions between light and fluids (Hunt and Wilkinson, 2008; Fan and White, 2011). The photothermal effect is one of the important interactions, which quickly converts the light energy into the thermal energy. The use of the light as the heating source can realize non-contact heating, quick temperature response and precise control without significant effect on the carrying fluid and the substrate (Terazono et al., 2008). For example, Reinhardt et al. (2007) presented a simple, fast and localized heating approach relying on the strong absorbance of infrared (IR) light by microsized patterned surfaces. Li et al. (2013) reported a gold nanorod-facilitated optical heating method.

In addition, using the light source to realize the non-contact thermal cycle for the PCR amplification of target DNA has also been reported by Oda et al. (1998). In this work, the feasibility of shortening the thermal cycle time to enable more rapid reaction without critically compromising detect ability was demonstrated. Hühmer and Landers (2000) also demonstrated the thermal cycle of nanoliter volume (160 nL) using infrared-mediated temperature control. Terazono et al. (2008) developed a rapid real-time PCR system using the direct absorption of an IR laser beam by water droplets. Besides, Kim et al. (2009a, 2009b) also reported a high-speed real-time PCR amplification in nanoliter droplets dispersed in the oil phase, in which the thermal cycle relied on an IR laser. More recently, Hettiarachchi et al. (2012) presented a platform for performing real-time PCR of breast cancer cell DNA within the droplet-in-oil microreactors. Illumination to the droplets by a low-power IR laser with the wavelength of 1460 nm provided a simple approach for the droplet manipulation and rapid thermal cycle. The above works indicate that using the IR laser functioned as the heating source is feasible for the PCR applications. However, it should be pointed out that the location of the droplet in the above-mentioned works may change with the fluid flow, which will result in the laser beam not to be easily focused on the droplet and thus limit this application. Fortunately, this problem can be avoided by the anchor or rail, which corresponds to cavity or groove on the microchannel (Fradet et al., 2011). Abbyad et al. (2011) demonstrated the manipulation of droplets by using rails and anchors. Lee et al. (2012) studied the interface induced recirculation within a droplet fixed by the anchor. Fradet et al. (2011) demonstrated the integration of rails and anchors into microfluidic system enabled the creation of highly controllable 2D droplet arrays. Therefore, it can be concluded that the anchor and rail have the potential to solve the problem encountered in the droplet microfluidics with a laser as a heating source.

Inspired by this idea, we propose a droplet microfluidic system with the incorporation of the anchor and rail into a chip for the PCR application using the IR laser as the heating source in present study. In this system, the anchor is used to fix the droplet, and the rail is used to control the movement trajectory of the droplet. The IR laser is applied to heat the droplet for realizing the PCR thermal cycle. The thermal analysis of this droplet microfluidic system is then performed. The results indicate that the temperature rise is linearly increased with increasing the laser power, which is meaningful to control the droplet temperature corresponding to the denaturation, the annealing and the extension in the thermal cycle. Moreover, because the droplet microfluidics has excellent heat transfer ability, the temperature response is quick so that rapid PCR can be ensured with one thermal cycle less than 30 s and 48 thermal cycles finished within 23 min. The obtained results are helpful for the design and operation of the droplet microfluidics with the IR laser as a heating source for the PCR applications.

2. Droplet microfluidic system design

The droplet microfluidic system proposed in this study is schematically shown in Fig. 1, which consists of a liquid feeding compartment, a PCR microfluidic chip with the anchor and rail, a laser controlling system. The liquid feeding system contains three micro syringe pumps which are used to feed the reactant solution and oil. The laser controlling system is used to control the laser to heat the droplet. The PCR microfluidic chip consists of three parts: the droplet generation, the laser heating and the droplet collection, as illustrated in the Fig. 2. The droplets are generated using the cross-junction structure (Christopher and Anna, 2007), because this structure can ensure the uniform droplet generation. In the laser heating region, the rail and anchor are designed, where the anchor is used to fix the droplet during the PCR thermal cycles and the rail is used to control the movement of the droplet. The droplet collection section has the rail and sieve combined structure, in which the rail is used to collect the droplet and the sieve provides the pathway for the oil phase. In this design, to control the velocity of the carrying phase and the droplet generation, three inlets are designed on the PCR microfluidic chip, in which the inlet 1 and 2 are used to feed the reactant solution and oil for controlling the droplet generation. The inlet 3 is used to feed the oil for controlling the velocity of the carrying phase of oil in laser heating region. In order to ensure the flow uniformity, the tree shaped structures are used at the ends of the inlet.

During the working process, the reactant solution contained droplet is generated in the droplet generation part. Because of the existence of the rail and anchor, the generated droplet can have controllable movement trajectory along the rail. When the droplet

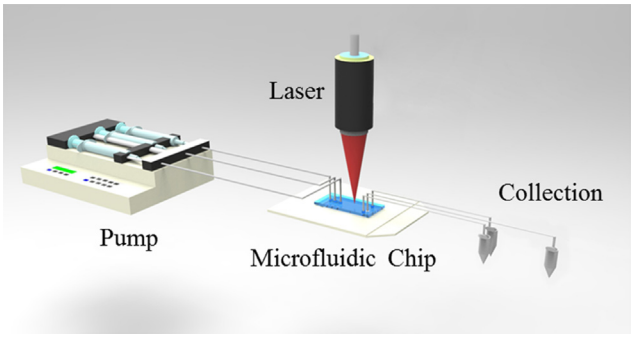

Fig. 1. Schematic of the photothermal effect based droplet microfluidic system for PCR application.

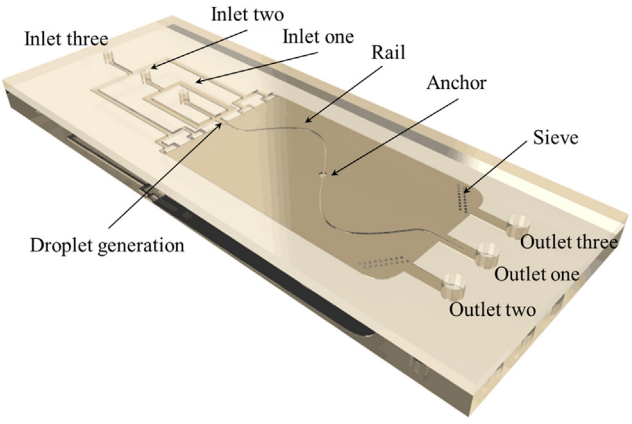

Fig. 2. Illustration of the microfluidic chip design.