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Development of bifurcation microchannel to uniformly distribute a liquid plug

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ABSTRACT

This study developed a Y-bifurcation microchannel to enhance uniformity and reduce losses associated with the distribution of liquid plugs. Bifurcation geometry can be integrated within the design of high-throughput systems to enable the precise distribution of reagents used in parallel reactions. Numerical simulations were used to evaluate the geometry-dependent pressure distribution inside the splitting liquid plug, the results of which were used as a reference for the modification of the Y-bifurcation microchannels. Four geometries were tested in the simulations to elucidate the relationship between bifurcation geometry and distribution performance. A Y-bifurcation microchannel with rounded corners (2 mm radius) and a separator (0.5 mm in height) resulted in the smallest pressure difference within the splitting liquid plug. Thus, this design was adopted for the fabrication of devices used in subsequent experiments. The proposed Y-bifurcation microchannel was manufactured on a PMMA substrate using a micromilling machine in conjunction with a thermal bonding technique. The results of fifty experiments using the Y-bifurcation microchannel revealed an average variance of 2.13% (standard deviation of 3.94%) in distribution uniformity and an average residual liquid volume of 95% (standard deviation of 4.3%). The performance of the proposed Y-bifurcation microchannel proved significantly better than that of existing T-bifurcation microchannels.

1. Introduction

Microfluidic technology has been steadily progressing since the first micro-gas chromatograph was developed in 1979 (Terry et al., 1979). The benefits of microfluidics include a reduction in the amount of reagent that is required, accelerated reaction rates, and minimal handling to reduce cross contamination. Microfluidic devices can be extended from micro-total-analysis-systems (μTAS) to high-throughput platforms (Chen et al., 2010; Park et al., 2010), making them applicable in large-scale screening as well as drug synthesis operations. Most large-scale applications operate in parallel, and therefore require the ability to simultaneously manipulate reagents in multiple streams with a high degree of accuracy and within a volume ranging from nanoliters to microliters (Hong and Quake, 2003; Breslauer et al., 2006). This necessitates the means to distribute a fixed-volume reagent plug rapidly and uniformly into multiple microchannels simultaneously.

Microfluidics is a promising tool for the processing of tiny quantities of reagents, even in high-throughput microfluidic devices (Whitesides, 2006; El-Ali et al., 2006; Luo et al., 2008). Researchers have been using microfluidics to achieve parallel reagent distribution using highly integrated devices with soft PDMS (polydimethylsiloxane) as valves (Unger et al., 2000; Thorsen et al., 2002; Liu et al., 2003), as well as devices capable of continuously forming droplets for large-scale screening applications (Song et al., 2003; Chen et al., 2008; Schmitz et al., 2009; Kim et al., 2011). Taking full advantage of a microfluidic platform for high-throughput applications requires a reliable

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mechanism capable of distributing a fixed volume of reagent into multiple reaction zones rapidly and with a high degree of uniformity, as opposed to using manual pipettes for the repeated dispensing of reagents. Some researchers have used microfluidic devices to demonstrate the capability of parallel reagent distribution (Unger et al., 2000; Thorsen et al., 2002; Liu et al., 2003; Song et al., 2003; Chen et al., 2008; Schmitz et al., 2009; Kim et al., 2011), while others have focused on the geometry of microfluidic devices and its effect on the rapid manipulation of droplets (Wang et al., 2009; Tan et al., 2004). A continuous nanoliter microfluidic dispenser was fabricated for the loading of reagents on an instrument platform (Wang et al., 2009). This solution provides an inexpensive and compact solution for reagent distribution with accuracy on the scale of tens to hundreds of nanoliters. The polydimethylsiloxane (PDMS) microfluidic device in that study is able to load 32 drops of reagent into 32 micro chambers simultaneously. Each droplet is expected to measure 115 nl with a coefficient of variance (CV) of less than 6%. Another study focused on the geometry of microchannels used to control fission, fusion, and the sorting of continuous nanoliter droplets (Tan et al., 2004). Using PDMS, microfluidic devices with a variety of geometries have been designed and fabricated with the aim of elucidating the influence of individual geometric factors on the manipulation of droplets at the nanoliter scale. An understanding of the fundamental principles in the manipulation of droplets has made it possible to develop several applications, including those for the control of chemical concentration, droplet circulation with specific concentration, and droplet rearrangement.

The single droplet/plug fission process is an essential factor in microfluidic devices, particularly with regard to the distribution of reagents at fixed volumes. One common application of the single droplet/plug fission process involves the loading of specific volumes of a mixture into a high-throughput device. Generally, the operation of high-throughput instruments within a laboratory involves the manual mixing of reagents in a centrifugal tube followed by the manual loading of these mixtures into multiple centrifugal tubes using a pipette. Under these conditions, the loading and mixing steps are very time-consuming, experience-dependent, and incur a high risk of cross contamination. Compared to the fission process involved in continuous flow, a fixed-volume droplet/plug fission process is more sensitive to the effects of geometric design as well as the surface conditions, inlet/outlet conditions, and variations in fabrication. Thus, gaining an understanding of the influence of each parameter is crucial to the success of the resulting devices. Liu (2012) experimentally studied the droplet fission process in terms of differences in inlet/outlet boundary conditions, bifurcation angle, and the flow resistance ratio of the two distribution channels with a focus on the behavior of the reagent droplet under various bifurcation geometries. Chen et al. (2014a) developed a T-bifurcation microchannel, which achieved an average variance of 3.64% in distribution uniformity (STD = 3.81%) with a 7.9% loss of liquid volume (STD = 1.2%). They also used numerical simulations to help in the design of the bifurcation microchannels and conducted multiple experiments to characterize the device. They concluded that the geometry of bifurcation microchannels has a significant influence on the uniformity and loss associated with liquid plugs, due primarily to differences in pressure distribution within the plugs.

This study developed a Y-bifurcation microchannel to enhance uniformity in distribution and minimize losses associated with the use of T-bifurcation microchannels (Chen et al., 2014a). We employed finite element numerical simulation software to help in the evaluation of pressure distribution inside the splitting liquid plugs. The microfluidic devices were manufactured using a micromilling machine to cut a substrate of poly(methyl methacrylate) (PMMA), which was then sealed with another piece of PMMA by thermal bonding. We conducted fifty experiments to elucidate the uniformity in distribution and the volume loss associated with the use of liquid plugs in this newly developed Y-bifurcation microchannel. Our results were then compared with those obtained from previous devices based on T-bifurcation microchannels. We applied one-way analysis of variance (ANOVA) to ensure that the proposed Y-bifurcation microchannel is statistically superior to existing devices made with T-bifurcation microchannels.

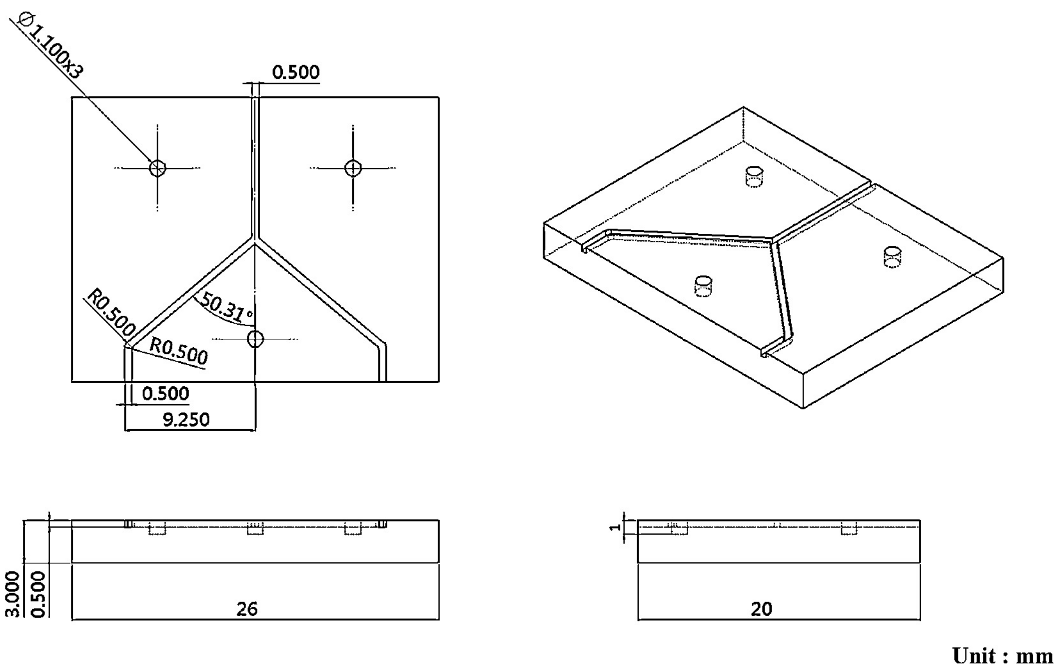

Fig. 1 – Design layout and dimensions of Y-bifurcation microfluidic device.