DROPLET-ON-DEMAND FOR REALIZING FLEXIBLE AND PROGRAMMABLE LAB-ON-CHIP-DEVICES

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ABSTRACT

Passive microfluidic networks have recently been introduced as a promising approach for realizing flexible and programmable droplet-based microfluidic devices that target various biomedical applications. For the practical realization of such networks controllable and reliable droplet generation, so-called Droplet on Demand (DoD), is crucial. For this purpose, we developed a novel, high-precision technique for generation of individual droplets of desired volumes, at prescribed times of emission and with precisely controlled droplet distances which enables performing highly flexible droplet generation protocols. We verify the proposed method through experiments, showing the successful generation of droplets of arbitrary volumes and distances.

KEYWORDS: Microfluidic networks, Droplet-on-Demand, Lab-on-Chip

INTRODUCTION

Microfluidic network refers to multiple Lab-on-chip (LoC) devices connected together on a single microfluidic platform in order to perform complex laboratory analyses [1]. Here, micro- to nanoliter droplets are generated with high precision and selectively carried inside closed microchannels to different locations on the chip. Having the possibility to employ multiple LoC devices on a single platform, and to selectively generate and deliver droplets to these devices, provides the opportunity to implement highly flexible and programmable droplet-based microfluidic systems.

An example of a microfluidic network used for high-throughput antibiotic susceptibility and toxicity testing is shown in Fig. 1 [1]. Using the DoD, droplets that carry different antibiotics, or different concentrations of the same antibiotics, are generated and carried throughout the network towards the targeted LoC for processing. Using microfluidic control units (µfSwitches) the droplets are selectively directed towards the targeted LoC where biochemical reactions take place. Since the system employs multiple LoC devices in parallel, where each LoC devices can host different biological samples (i.e. bacteria, proteins or cells), true high-throughput testing becomes possible.

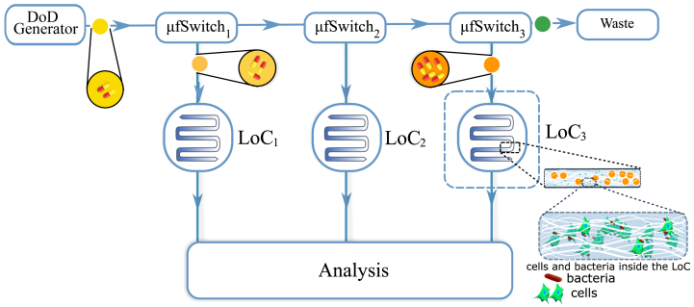

Figure 1: Schematic of a microfluidic network for high-throughput drug screening application. Multiple LoC devices interconnected on a single platform enable parallelism while the DoD system enables performing arbitrary protocols of droplet formations.

A key element in the microfluidic network is highly controllable and reliable droplet generator. Over the years, only a few microfluidic systems for the generation of droplets on demand have been proposed [2]. However, established DoD systems are dominantly active systems that integrate electrodes and microvalves to enable customized droplet generation. This approach greatly reduces the biocompatibility of the microfluidic device and reduces its applicability to only applications where the effect of electric field on the biological samples is an acceptable risk. Moreover, the multi-layer fabrication and process, as well as experimental equipment needed, become very complex and expensive.

DROPLET ON DEMAND

The technique presented in this work is unique in its ability to completely passively (without any active components on the chip) manipulate the droplet generation and therefore enable achieving fully customized droplet parameters. The method utilizes simple T-junction geometry to bring two immiscible phases into contact, where due to the competition between viscous shear stress and interfacial tension droplets are generated.

Initially, the two phases are brought into the equilibrium state (a completely stable interface) by precisely controlling the applied pressures coming from the external pump. The droplet generation is initiated by overcoming the equilibrium state and applying a series of positive pulses to the dispersed phase while maintaining the continuous phase flow constant (Fig. 2). At the end of the droplet generation process, the system returns to the equilibrium state. Full customization of the droplet parameters (size, content and inter-droplet distance) is ensured by precise control of the equilibrium pressures and by varying the duration of the pulse and the period between successive pulses. This way, single or multiple droplets of arbitrary volumes and distances are generated.

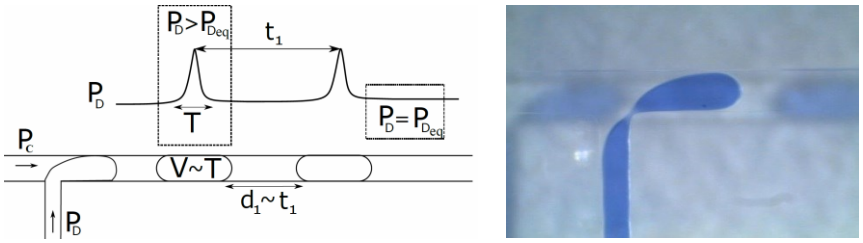

Figure 2: Working principle of the novel DoD method. a) A series of positive pulses is applied to the dispersed phase to generate droplets; b) Microscopic image of the droplet generated when the positive pulse is applied.

EXPERIMENTAL

The DoD system was fabricated in polydimethylsiloxane polymer using standard soft lithography methods. A pressure controller (Elveflow, OB1MK3) was used to induce input pressures. For the evaluation of the DoD system, we used an optical microscope and to automate the system, a programmed sequence of the pressure pulses was applied through the Elveflow Smart Interface Microfluidic Software. We used silicone oil as a continuous phase and dyed water as a dispersed phase in order to visualize the droplet generation process.

RESULTS AND CONCLUSION

In this work, we have proposed, and experimentally verified, a novel method that enables absolute customization of the droplet generation process. Using the method, droplets of arbitrary sizes and inter-droplet distances were generated as shown in Fig. 3. By precisely controlling the droplet generation process, it is possible to achieve other microfluidic operations, such as droplet merging, mixing and multistep reactions on the demand. In contrast to conventional techniques, the method offers simplicity in its design, it is passive and therefore offers a high degree of biocompatibility and applicability in numerous microfluidic applications. The technique offers high reproducibility of the generation conditions which allows for creating droplets that can act as an isolated, perfectly controlled reactors, and lastly, due to simple fabrication the method is economical and supports rapid prototyping of the DoD device.

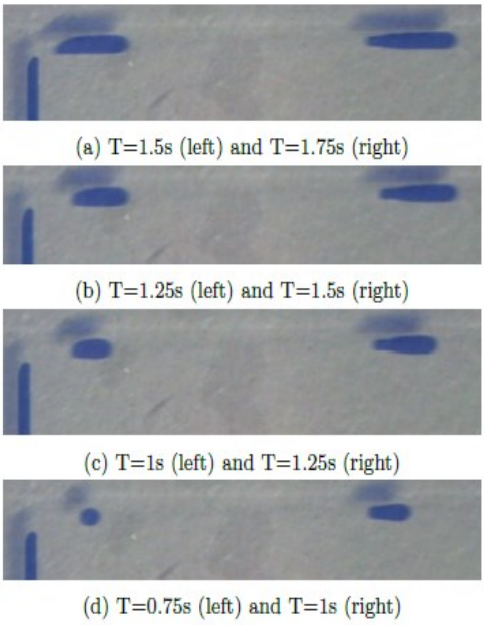

Figure 3: Microscopic images of the droplets generated when pulses of different durations are applied. Decreasing the pulse duration linearly from T=1.75s to T = 0.75s decreases the droplet diameter from D = 400 μm to D = 170 μm.

REFERENCES

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