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Conditional siphon priming for multi-step assays on centrifugal microfluidic platforms

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ABSTRACT

Centrifugal microfluidics has proven to be successful in biomedical diagnostics, biological analysis and environmental monitoring. However, the automation of multi-step sample processing, reaction and detection remains a great challenge. In this study, a conditional siphon priming technique is introduced for multi-step liquid addition or selective routing. Since the siphon channel is locally modified or venting is blocked by liquid in another chamber, siphon priming can be triggered by liquid addition or venting at low frequency. Using this technique, sequential release of liquids and selective routing in multiple manners were successfully achieved. As a proof of concept, a centrifugal microfluidic platform was designed for on-site ammonium analysis in water samples. The linear range of ammonium concentrations is extended by integration of a dilution process. This novel valving technique provides new solutions for integration of complex liquid handling processes on centrifugal platforms.

1. Introduction

Centrifugal microfluidics has been of great interest for both academia and industry over the last few decades [1,2]. Unlike most lab-on-a-chip devices which use syringe pumps to drive fluids thus require fluidic connectors between the chip and the periphery, liquid propulsion on centrifugal platforms can easily be performed by intrinsic centrifugation, making centrifugal microfluidic systems especially suitable for point-of-use applications. Centrifugal microfluidic technologies have been employed in biomedical diagnostics [3–5], biological analysis [6,7] and environmental monitoring [8–10]. However, as the integration of various laboratory unit operations such as metering, mixing, dilution, reagent release and particle handling remains a challenge on centrifugal platforms, robust valving techniques are hence in great need.

Up to now, multiple types of valves have been developed on centrifugal microfluidic platforms. A number of demonstrations have shown great flexibility by using sacrificial materials such as wax to transiently block the microchannels for flow control [3,10–12]. However, external power and control systems are required for the operation of these active valves, which introduces complexity to the peripheral instrument. Another category of valves, known as passive valves, can be actuated simply by changing rotational frequencies. Hydrophobic valves or capillary valves, which rely on the counteraction of the capillary pressure and the hydrostatic pressure at hydrophobic constrictions or hydrophilic expansions of microchannels, can hold the liquid until the rotational frequency exceeds a critical value [13,14]. Recently, dissolvable films combined with pneumatic chambers are also utilized as valves which can be opened at designated frequencies [4,15]. Although these valves have been proven successful in a number of demonstrations, the number of valves or processes that can be integrated on a single disk may be limited. In these cases, the burst frequency is largely dependent on the radial position of the valve on the disk and the rotational frequency has to be increased from low to high for the sequential operation of valves, not *vice versa*. On the other hand, siphon valving, which is actuated at low frequencies and is usually independent of the radial location, provides a solution for applications that require high rotational frequencies in early steps [16]. As siphon valving relies on the interplay between the capillary force and the centrifugal force in the inbound part of the siphon channel, surface treatment is usually necessary for the slightly hydrophobic materials that are used in centrifugal microfluidics. To eliminate surface treatment, centrifugo-pneumatic strategy has

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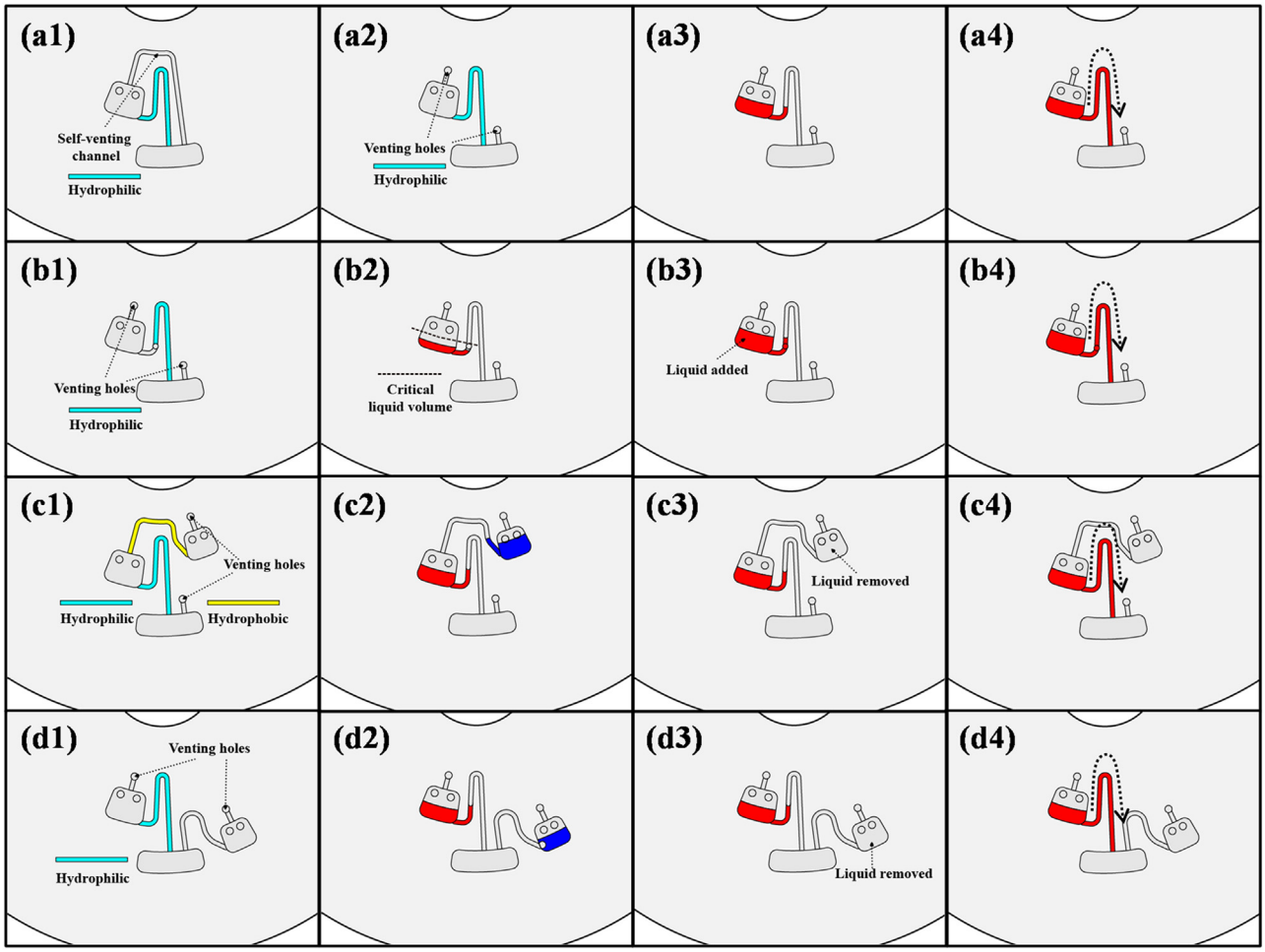

Fig. 1. Schematics of (a) typical siphon valving technique and (b-d) conditional siphon priming technique. Hydrophilic channels are shown in light blue and hydrophobic channels are shown in yellow. Main liquid is shown in red and ancillary liquid is shown in blue. The flow of liquid is indicated by dotted arrows. (a1) Schematic of a self-vented siphon. (a2) Schematic of a siphon vented to the atmosphere. (a3-4) Priming of siphon at low rotational frequency. (b1) Schematic of a locally modified siphon. (b2) No siphon priming at low frequency as the liquid is not sufficient to get access to the hydrophilic channel. (b3-4) Priming of siphon at low frequency once the liquid volume is above a critical value. (c1) Schematic of a siphon with an upstream chamber between venting holes. (c2) No siphon priming at low frequency as venting is blocked by the liquid in the upstream chamber. (c3-4) Priming of siphon at low frequency once the liquid in the upstream chamber is removed or pumped out. (d1) Schematic of a siphon with a downstream chamber between venting holes. (d2) No siphon priming at low frequency as venting is blocked by the liquid in the downstream chamber. (d3-4) Priming of siphon at low frequency once the liquid in the downstream chamber is removed or pumped out. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

been developed, which utilizes the energy of air compression stored during high-frequency rotation to prime the siphon channel [17]. However, it is very challenging to concatenate several centrifugo-pneumatic siphon valves for the implementation of more complex liquid manipulation in bioassays, such as immunoassays. In order to perform bioassays with more complex liquid handling protocols, serial siphon valving is employed to achieve sequential release of fluids [18,19]. The number of siphon crests in this technique determines the actuation sequence of valves, however, dead volume becomes larger when more siphon crests are involved in the valve. Lately, a water-clock-based flow sequencing technique has also been demonstrated, which relies on venting controlled by movement of liquid in a clock chamber [20]. Although various samples or reagents can be released in a simple network, the time-scale of the flow sequencing is still of the order of 100 s after increasing the viscosity of the fluid in the clock, which may not be sufficient for mixing or incubation steps in bioassays.

In this paper, a novel valving technique is proposed, which is based on conditional siphon priming triggered by either liquid addition or venting. First, the working principle is described in theory and validated by experiments. Then a microfluidic network is presented to implement sequential release of fluids, which is usually necessary in biological or chemical analyses. Subsequently, two networks are shown to demonstrate selective routing, which is also important for comprehensive liquid manipulation. Finally, as a proof of concept, a centrifugal microfluidic platform is designed and employed in the determination of ammonium in water, which has a potential for on-site analysis. Furthermore, the linear range of ammonium concentrations is extended by integration of a dilution process, making this platform applicable to a wider concentration range of ammonium-containing samples.

2. Working principle

In the common siphon valving technique (Fig. 1a), the loading chamber and the collection chamber which are self-vented or vented to the atmosphere, are connected by a hydrophilic siphon channel (Fig. 1a1–2). The siphon channel has a crest point located radially closer to the center of rotation than the liquid level in the loading chamber. Below a critical frequency, the capillary force in the inbound part of the siphon channel prevails over the counteracting centrifugal force, which thereby drives the liquid meniscus