AN ACTIVE, INTEGRATED BUBBLE TRAP AND DEBUBBLER FOR MICROFLUIDIC APPLICATIONS

Alison M. Skelley[1,2] and Joel Voldman[1,2,3]

[1]Research Laboratory of Electronics, MIT Cambridge, MA 02139;
[2]Microsystems Technology Laboratory, MIT, Cambridge, MA 02139;
[3]Electrical Engineering and Computer Science Department, MIT, Cambridge, MA 02139

ABSTRACT

We present a novel, fully integrated microfluidic bubble trap and debubbler. The 2-layer structure, based on a PDMS valve design, utilizes a featured membrane to stop bubble progression through the device. A pneumatic chamber directly above the trap is evacuated, and the bubble is pulled out through the gas-permeable PDMS membrane. Normal device operation, including continuous flow at atmospheric pressure, is maintained during the entire trapping and debubbling process. We present a range of trap sizes, from 2- to 10-mm diameter, and can trap and remove bubbles up to 25 μL in under 3 hours.

KEYWORDS: Bubble removal, bubble trap, PDMS valve, perfusion culture

INTRODUCTION

Microfluidic cell-culture perfusion systems provide an enabling platform for studying cell biology because they allow fine control over the microenvironment. We and others have used microfluidic perfusion for applications ranging from stem cell biology to neurobiology [1, 2]. Because assays may require cell growth for days (or even weeks), these systems are exquisitely sensitive to failure due to even a single bubble introduced into the device at any time during culture. Indeed, bubble introduction is the predominant failure mode for these (and many other) types of microfluidic systems.

There are two general approaches to bubble removal in a microfluidic system: trapping versus debubbling. A bubble trap is a structure that halts the progress of a bubble through the device [3]. The alternative is to actively remove the bubbles from the system, for instance by using PDMS' gas permeability to push bubbles out of the system [4]. Instead, we present an integrated device that combines trapping and debubbling, providing the ability to *continuously* trap and remove bubbles from the system, *always* under normal device operation.

RESULTS AND DISCUSSION

The trap is modeled after the valves demonstrated by Irimia *et al*. [5] (Figure 1). Upon entering the chamber, a bubble is corralled into a trapping area defined by a circular ridge (Figure 2, 45 s). The bubble continues into the trapping region until the back end of the bubble has just entered the chamber (Fig. 2, 1.5 min); at this point a fluidic connection is established underneath the circular ridge and around the bubble,

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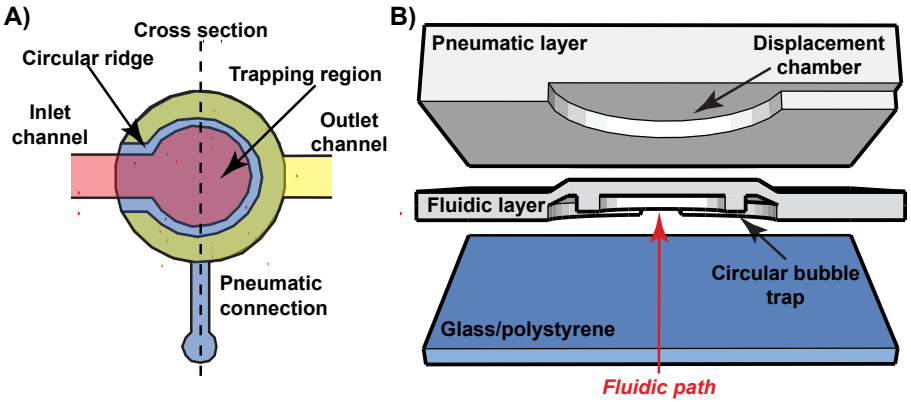

Figure 1. Top (A) and 3-D view (B) of the bubble trap, consisting of pneumatic and fluidic layers. The pnematic layer contains the displacement chamber, and the fluidic layer contains the inlet and outlet channels and circular ridge.

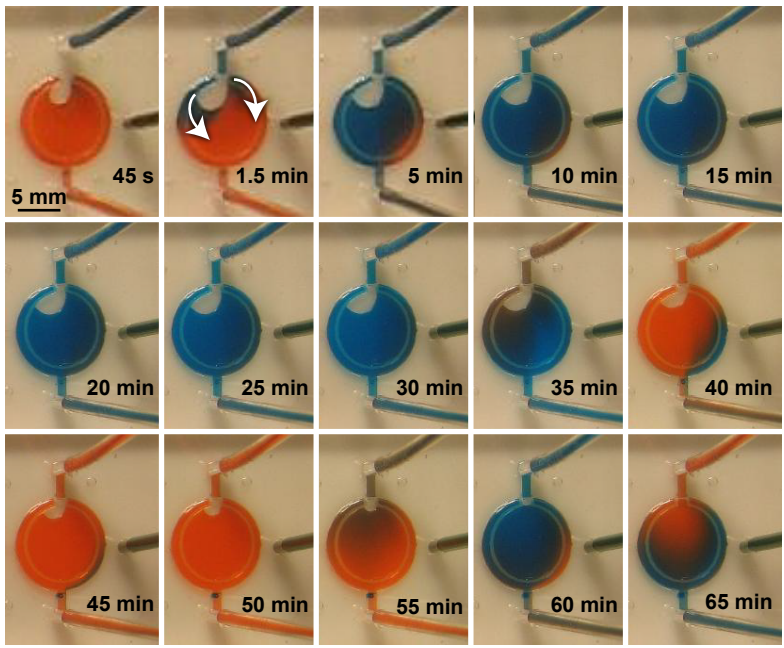

Figure 2. Images of the trapping and debubbling process. The bubble enters the valve (45 s) and is immobilized (1.5 min) while the solution is continuously exchanged (red to blue). At t=35 and 55 min the solution is again exchanged, indicating that continous flow is maintained. The bubble is gradually removed through the PDMS membrane via the vacuum applied in the pneumatic chamber. At t=65 min the bubble has been removed from the system.

so the bubble is immobilized and stable flow is maintained. Because the pneumatic chamber above the trapping region is constantly under vacuum, the bubble is degassed through the PDMS membrane. With valved traps ranging from 2 to 10 mm in diameter we can trap bubbles up to 25 µL and can remove the largest of these bubbles in under 3 hours (Figure 3). During this time there is steady, uninterrupted flow through the system.

CONCLUSIONS

These debubblers provide a stable, predictable trapping solution for microfluidic systems that can be incorporated directly upstream of sensitive cell-culture chambers. The debubblers have been integrated into our cell-culture systems and we routinely use them for multi-day experiments.

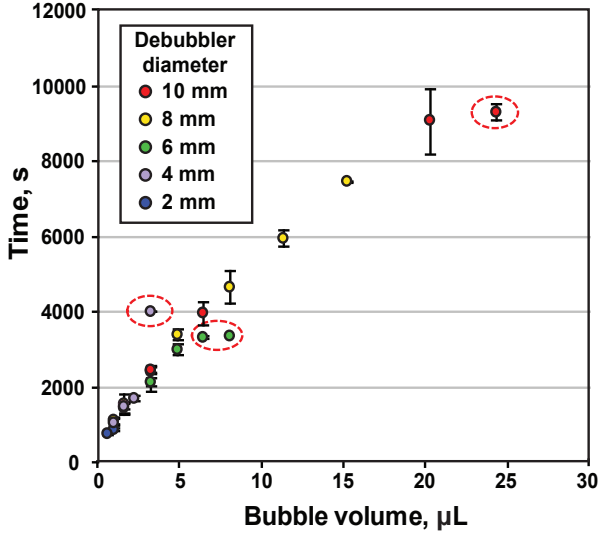

Figure 3. Bubble removal times for a series of different traps. The time to remove the bubble is linearly dependent on the bubble volume and independent of the trap size. Outlying points, indicated by red circles, demonstrate deviation from the linear relationship due to the bubble extending beyond the circular trap region.

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