## Scalable Integration of Elastomeric Components for Self-Regulating Microfluidic Devices

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One main research focus in microfluidics has been enhancing both the use and capabilities of devices through development of control systems<sup>1</sup>. Typically these systems achieve dynamic on-chip fluid regulation by utilizing computerized external actuators which directly valve and pump fluids in the device<sup>4,5</sup>. Although these systems provide immensely versatile microfluidic control, their external control setups limit their scalability and convenience for use by non-specialists. This shortcoming has motivated efforts to design control systems that passively/automatically regulate fluid flow on-chip<sup>2,3</sup>. Currently methods have only been able to passively regulate fluid in response to a dynamic input signal. Previously our group has shown the use of an elastomeric passive check-valve to temporally regulate the output of a fluid that is infused at a constant rate and therefore requires no dynamic input<sup>4</sup>. We demonstrated that a network of these valves could sequentially release and switch fluids in a finite step process.

We have advanced this methodology by systematically using two types of elastomeric components (Fig.1) to make a continuous oscillator that switches flow between two fluids that are infused simultaneously at a constant flowrate (Fig 2A,B). Figure 2C shows ten different frequencies that can be attained within the operating range of this particular circuit design. The operating range is dictated by the resistance provided by the component and channel geometries since that facilitates proper timing of the pressurizing and depressurizing of the fluids in the device. In addition, data from a developed model is used to corroborate the mechanism of oscillation which results from the passive regulation of the pressurized fluids by the elastomeric components (Fig. 2C). Currently the automatic oscillation of two fluids in a microfluidic device without any dynamic input signal is unprecedented. This capability enables on-chip generation of a basic clock-signal that can be used to drive and regulate other components in a synchronous manner. In addition, we have developed a fabrication scheme which enables efficient large-scale integration of these components on a single substrate (Fig. 3). The key to this largescale integration is a fabrication procedure which selectively deactivates oxidized PDMS layers so that the middle membrane layer does not bond to the part of the PDMS that forms the gap between interrupted channels (Fig. 4). This is done by exploiting the known contamination of residual PDMS monomer from the surface of a nonoxidized PDMS stamp used for micro-contact printing<sup>5</sup>. Therefore, momentary contact of a PDMS stamp patterned with extruded features that match the gap regions negates bonding of the oxidized PDMS membrane within that area. As with electronics, the efficient integration of components in large-scale is vital for enabling wide-spread use of microfluidic systems since it significantly increases functionality and decreases cost.

Word Count: 444

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Fig. 1. Passive Elastomeric Components. Two types of components are shown, a check-valve and switch-valve, each in their two different on and off states. Each component is comprised of two PDMS layers with a disconnected channel in one layer and a cavity in the other, separated by a thin PDMS membrane. Upon pressure, the component will deform the membrane into the cavity, allowing fluid to bypass the gap. The check-valve has a hole after the gap directing any back-pressure to pinch the membrane against the gap, negating back-flow. The switch-valve has access channels to the cavity allowing alternate pressurized fluids to close the valve.



Fig. 2. Microfluidic Oscillator. (A) Circuit diagram of both states of a microfluidic oscillator consisting of two switch-valves and two check-valves. Two fluids are simultaneously infused at a constant flowrate. The four components translate the constant input signal into an oscillating output of the two fluids. (B) Actual images of the two different states and the transitions between those states. (C) Graph of actual and simulated flowrate versus frequency plot for the given circuit design. Inset graph is a model of the flowrate of each fluid in the outlet channel over time.



Fig. 4. Selective Bonding Fabrication Steps. The gold color represents oxidized PDMS and the light blue represents unoxidized PDMS. First the bottom layer is bound to a thin PDMS membrane (shown as red) by oxygen plasma, and then holes are punched where required. The top layer is oxidized by oxygen plasma and then the gap regions between disconnected channels are rendered unable to bond by stamping residual PDMS monomer. PDMS monomer is transferred by momentary contact with an unoxidized PDMS stamp. Both layers are subsequently bonded together.

Fig. 3. Large-Scale Integration. Four separate circuits, each  $\sim 250$  components, are fabricated on a single substrate within the area of a dime.