MICROFLUIDIC FINITE STATE MACHINE
FOR AUTONOMOUS CONTROL OF INTEGRATED FLUID NETWORKS
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ABSTRACT
We present a significant advance in microfluidic digital logic that brings us very close to achieving fully autonomous microfluidic systems. Specifically, we demonstrate the first true finite state machine controller in microfluidics, along with an asynchronous counter and a semi-autonomous fluid handling system.

KEYWORDS: Microfluidic Large-Scale Integration, Digital Logic, Finite State Machine, Fluid Handling

INTRODUCTION
Microfluidic large-scale integration achieves highly complex fluid control, but typically relies upon unwieldy off-chip pneumatic and electronic components that interface to the chip through a maze of tubing [1]. Digital logic constructed out of microfluidic valves and channels could potentially enable fully self-contained microfluidic systems that are controlled by onboard circuitry. While a number of digital logic components have been demonstrated in microfluidics [2-6], a true digital microcontroller has remained out of reach. Removing this dependence on external control would take a step toward the creation of a truly portable, integrated lab-on-a-chip.

THEORY
Our digital logic implementation is based upon a pneumatic valve design originally reported by Jensen et al. These valves, seen in Figure 1, can be treated analogously to NMOS transistors in the construction of digital circuits [2].

Using this technology, we intend to integrate pneumatically driven logic circuits with fluid handling components such as peristaltic pumps to create a system capable of complex operations with minimal dependence on external connections. The end goal of this digital logic integration is to reduce off-chip complexity to the point where only a single chip-to-world connection to a constant vacuum is required to serve as the power source for such a device. To achieve this goal, we propose a fully autonomous system as schematically diagrammed in Figure 3, consisting of an on-chip oscillator (presented at µTAS 2010 [3]), a timer, a finite state machine (FSM), and a fluid handling system.

The core of our control system is the finite state machine. In this microcontroller architecture, the system steps between a series of states, each of which define a specific function. The FSM must store its current state in memory and also calculate its next state based upon the current state. We have implemented a 2-bit FSM, which provides four individual states: metering, mixing, incubation, and flushing, for example. The circuit schematic for the FSM is presented in Figure 5, along with a timing diagram that shows the system stepping through four discrete digital states.

For proper operation, the FSM must remain in each of its four states for predetermined intervals of time. In order to achieve this, a timing system is required. We demonstrate a binary counter circuit that can tally a series of pulses from a timing reference in order to measure a longer period of time. The building block of the counter circuit is the T flip-flop, a memory element that toggles between its two binary states (on, off) with each input. A 2-bit asynchronous counter was created by cascading two T flip-flops, with a pulse transition detector in front of each flip-flop (Figure 4). While a greater number of bits will eventually be required, for example to provide timing for chemical reactions in point-of-care diagnostics, this counter circuit can be scaled by simply cascading additional stages.

Figure 1: Normally closed pneumatic valves act as the fundamental building block of microfluidic digital logic. Left: Blowup of the three-layer valve. Right: Cross sectional diagram of constructed valve. Vacuum applied to one side of the PDMS layer causes the membrane to deform, connecting the two microfluidic channels on the opposite side.

Figure 2: Microfluidic networks of pneumatic valves and channels behave analogously to electronic digital circuits. Shown here is an electronic inverter and its pneumatic counterpart.
Finally, we have implemented a semi-autonomous fluid handling system capable of four functions: metering, mixing, incubation, and flushing (Figure 6). Only four connections are required to control a network of 30 on-chip valves. One vacuum connection serves as the power source, while the other three connections are static on/off inputs that select between each function (incubation is essentially a wait state that requires no active control). Complex behavior such as peristaltic rotary pumping is completely controlled by internal circuitry [7].

EXPERIMENTAL

At a high level, digital design is similar between electronic and pneumatic circuits, granting the ability to pull from a wide library of previously established designs and information. Pneumatic circuits are roughly modeled with PSPICE/OrCAD (Cadence Design Systems Inc., San Jose, CA, USA), translating pneumatic resistance into electrical resistance based off of various geometric factors such as channel depth and length [8]. This allows for optimal sizing of resistor lengths in the pneumatic circuits for proper operation.

Device fabrication is as previously described for microfluidic channels on a glass substrate [2]. Briefly, microfluidic channels and valves are patterned and etched into glass wafers (Telic Co., Valencia, CA, USA) via photolithography and wet etching.

Data for the timing diagram in Figure 5 was obtained by video analysis of light reflection off of individual valves in a running circuit. Briefly, a script in MATLAB (The MathWorks Inc., Natick, MA, USA) was written to plot normalized pixel intensities of selected regions of interest over the course of the video.

Figure 3: Block diagram of proposed autonomous microfluidic system, integrating digital logic control and fluid handling on a single chip. We have demonstrated three components, as detailed in the following figures. The on-chip oscillator, which serves as the system clock reference, was presented at µTAS 2010 [3].

Figure 4. Timing is achieved by tallying clock cycles in a counter circuit. Left: Schematic of 2-bit asynchronous counter. Additional pulse transition detectors and T flip-flops can be cascaded to increase the number of bits. Right: With each rising edge in the 2-bit counter’s input, the outputs will count from 0 to 3 in binary.

Figure 5. Left: Schematic of 2-bit finite state machine (FSM). When given an input pulse, the FSM transitions from one state to the next based off of its current state. The 2 FSM outputs, labeled Q0 and Q1, will be used to send the fluid handling device into 4 states, with each state corresponding to a different fluid handling operation. Right: Timing diagram of FSM. Values represent intensity of light reflected from outputs.
RESULTS AND DISCUSSION

We have presented several pneumatically driven microfluidic circuits that utilize conventional digital logic design to minimize off-chip complexity. Significantly, we have demonstrated the first finite state machine in microfluidics.

The complete proposed system operates as follows: the on-chip oscillator, acting as a stable clock, is fed into a timer circuit that counts oscillation cycles to measure periods of time. At the correct moments in time, the timer sends a signal to the FSM, which transitions from state to state based off of its built in logic. Finally, the FSM’s output state sends the fluid handling circuit into one of its four states, causing the circuit to execute one of its four fluid handling operations.

The combination of these components creates an autonomous, pneumatically driven microcontroller for fluid handling control. We have demonstrated the four components of this autonomous system (oscillator, timer, FSM, fluid handling) operating individually. Future work will involve integration of all four components into a single chip, resulting in a fully autonomous fluid handling solution.

CONCLUSION

The integration of large-scale digital logic into microfluidic chips aims toward complete elimination of off-chip control elements such as valve manifolds and computers, and also paves way for a fully contained lab-on-a-chip without dependence on electricity. With further integration of more complex circuits, devices capable of intricate fluid handling operations can be run with a simple, modest vacuum source, such as a syringe or a portable pump.

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REFERENCES


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