PROGRAMMABLE MICROFLUIDIC DIGITAL LOGIC FOR THE AUTONOMOUS LAB ON A CHIP

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ABSTRACT

We present sequential logic circuits implemented in microfluidics rather than electronics. A programmable finite state machine and counter circuits are built out of pneumatic Boolean logic gates. Thus, we demonstrate microcontrollers built entirely out of microfluidic parts for autonomous regulation of microfluidic liquid networks.

KEYWORDS: Microfluidic Integration, Programmable Finite State Machine, Digital Logic

INTRODUCTION

Next generation integrated microfluidics with embedded control circuits will allow reduction and removal of external controllers and their interfaces [1]. Previously, we developed circuits including oscillators, timers and self-driving peristaltic pumps constructed out of microfluidic valves and channels[2-4]. Previous designs were only semi-autonomous, however, as an off-chip controller was still required for selecting between the different liquid handling steps. Here, we present a programmable finite-state machine (FSM) controller.

THEORY

The finite state machine (FSM) is a microcontroller architecture built around the concept of stepping through a series of program states. The FSM stores the current state and calculates the next state from a set of rules that can consider a user input plus the current state. We implemented a 2-bit FSM by using a pneumatic D flip-flop for each bit of the state register. Each D flip-flop consists of two stable D latches in a clocked master-slave configuration rendering the system robust against race conditions. A 2-bit machine is capable of stepping through 4 unique program states. Instead of hardwiring these steps and transitions between them in the combinatorial logic block of the FSM, we implemented a programmable logic array (PLA) that can be reconfigured by drilling holes in the elastomeric layer that is sandwiched in the middle of the device structure. Using a single device (Figure 1) we implemented 3 different FSM programs by drilling different patterns of holes in the networks of the PLA. Thus we demonstrated the first programable microfluidic computer. We are also in the process of integrating a controller with a liquid handling network for the goal of performing an ELISA as a series of dispensing, washing, and mixing steps (Figure 2).

Finally, the implementation of complex control programs will require large numbers of (100s) of gates to be integrated onto each device. Thus, we investigated the scalability of or pneumatic valves and circuit topologies for increased density. Compared to our wet-etch glass process, CNC machining offers wider tuning of channel resistance and more accurate placement of ports and vias. Figure 3 shows asynchronous counter circuits implemented in both processes and illustrates the more than 10-fold increase in circuit density achieved in the CNC process.

EXPERIMENTAL

Devices were fabricated by sandwiching a flat sheet of 250-µm PDMS between two etched glass plates or machined acrylic plates. Device fabrication in glass wafers (Telic Co., Valancia, CA, USA) was achieved by photolithography and HF wet etching [2]. PLA were programed by boring via holes in specific locations either by manual punching or laser ablation. Timing diagrams (Figures 1 and 3) were obtained by video analysis of light reflection from individual valves in a running circuit.

RESULTS AND DISCUSSION

We implemented 3 different FSM programs in a single fabricated device. State transition diagrams describing the branching decisions that govern stepwise progression through each FSM program are shown in Figure 1. Each sequence requires a unique connection of circuit nodes, which is achieved by punching different pattern of via holes through the membrane layer. Our FSM can take a single bit of user input, A, into account, which enables conditional branching at specific states of the transition diagram.

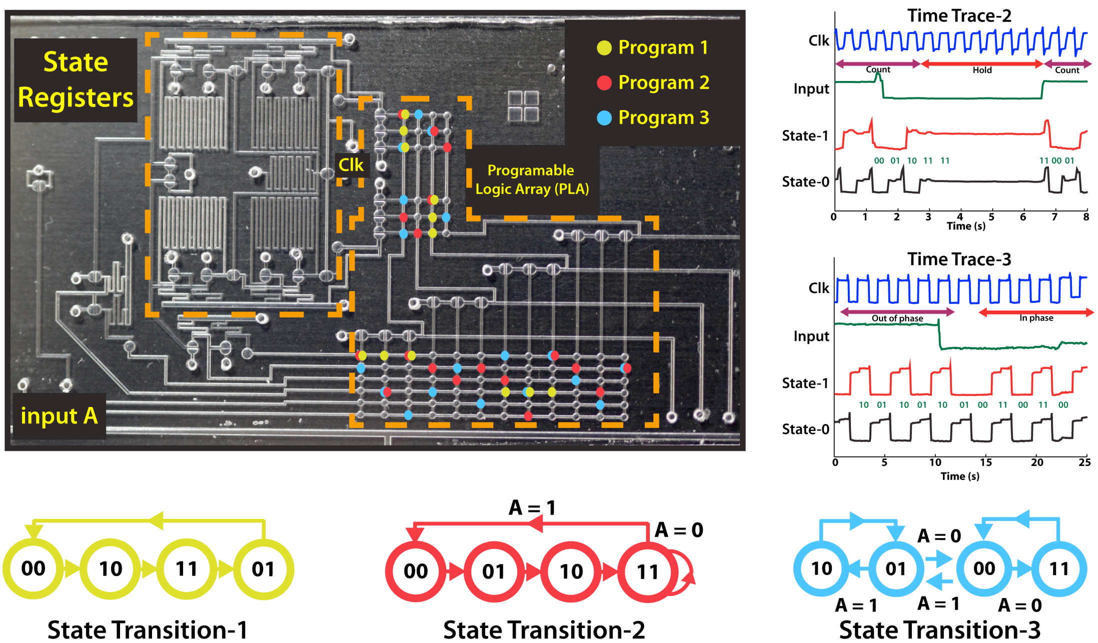

Figure 1: Three different FSM programs were implemented in a single device by boring three different patterns of holes in the programable logic array. The FSM can also take a single bit of user input, A, which enables conditional branching.

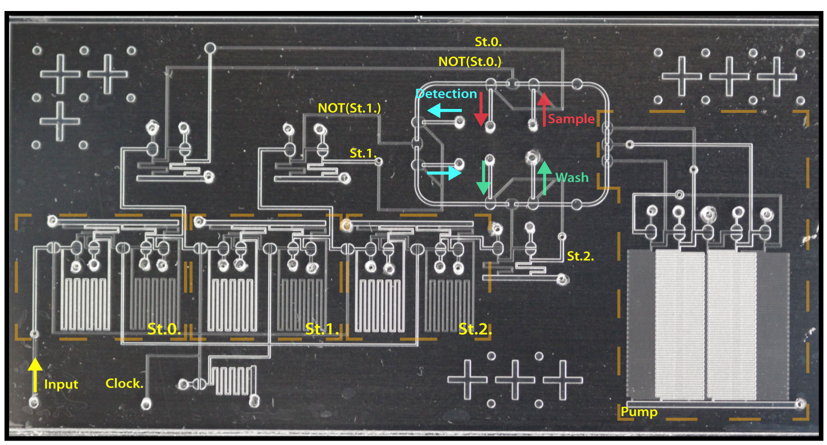

Figure 2: Shift Register based automated liquid network.

To illustrate a diagnostic application, we designed an integrated FSM controller for sequential liquid dispensing, such as required to perform an ELISA assay. This controller was established as three D flip-flops configures as a shift register. Each state of the controller has been verified to trigger pumping and dispensing from a different liquid reservoir, as intended. However, the current design is experiencing leaking issues through liquid bus valve that should be closed, thus additional redesign and optimization is required.

Using the glass etching process, we demonstrated a 6-bit counter circuit, implemented as a series of cascaded T flip-flops. Counter circuits can be used to tally oscillations of a clock reference, for example to provide timing for chemical reactions. The 6-bit counter is a large circuit, occupying a 40 x 80 mm die.

In order to increase circuit density, we examined an alternative fabrication technology based on CNC machining rather than wet etching. One important advantage is the ability to create large differences in channel depth and width, enabling channel resistance to be varied without the need for long serpentine resistor networks. With this CNC process, an 8-bit counter consisting of 64 individual logic gates fit into a 300 mm^2 chip area, achieving more than 10 fold increase in circuit density compared to our glass etching process.

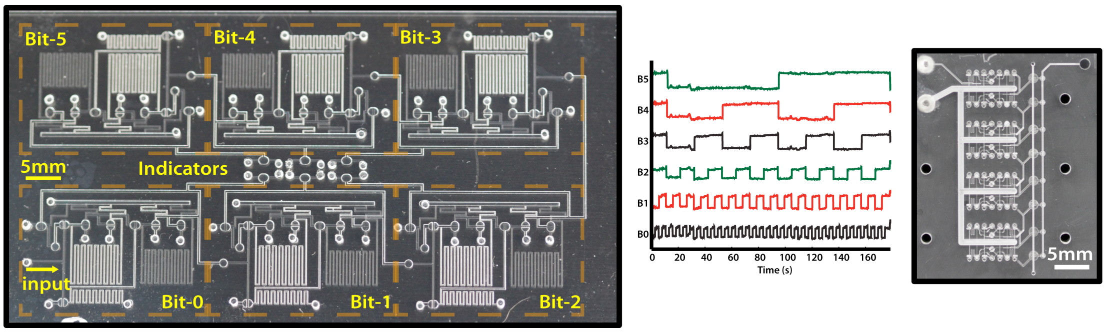

Figure 3: A 6-bit counter circuit in glass-etched process, with the timing diagram of the circuit counting up to 64. 8-bit counter implemented in high-density process shown with the same length scale.

CONCLUSION

We have demonstrated an autonomous and programmable microfluidic controller by integrating a programmable logic array within a finite state machine. This circuit can encode different program sequences by changing the placement of membrane via holes. Integration of pneumatic digital logic with liquid circuits can enable liquid handling control without external controllers. Further redesign and optimization is required before we can completely demonstrate this achievement, however. Finally, we have demonstrated a 10-fold increase in circuit density by utilizing a fabrication process based on CNC machining rather than wet etching.

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