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Microfluidic valve array control system integrating a fluid demultiplexer circuit

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Abstract

This paper proposes an efficient control method for the large-scale integration of microvalves in microfluidic systems. The proposed method can control 2^n individual microvalves with $2n + 2$ control lines (where n is an integer). The on-chip valves are closed by applying pressure to a control line, similar to conventional pneumatic microvalves. Another control line closes gate valves between the control line to the on-chip valves and the on-chip valves themselves, to preserve the state of the on-chip valves. The remaining control lines select an activated gate valve. While the addressed gate valve is selected by the other control lines, the corresponding on-chip valve is actuated by applying input pressure to the control line to the on-chip valves. Using this method would substantially reduce the number of world-to-chip connectors and off-chip valve controllers. Experiments conducted using a fabricated 2^8 microvalve array device, comprising 256 individual on-chip valves controlled with 18 ($2 \times 8 + 2$) control lines, yielded switching speeds for the selected on-chip valve under 90 ms.

Keywords: microvalve, pneumatic valve, hydraulic valve, fluid logic circuit, demultiplexer, valve control system

S Online supplementary data available from stacks.iop.org/JMM/25/065016/mmedia

(Some figures may appear in colour only in the online journal)

1. Introduction

Microwell arrays are used extensively in parallel analysis techniques to analyze large numbers of specimens in chemical synthesis and biological cell analysis. Microfabrication techniques enable the integration of fluid-manipulating components, such as microvalves and micropumps, into microwell array devices in the studies of micro-total analysis systems (μTAS) and lab-on-a-chip systems [1]. The importance of microvalves is increasing as the microchannel and microwell volumes used to manipulate precise reagent flow continue to decrease [2].

Over the last few decades, several microvalve-related structures and methods have been developed. Microvalves, whose role is to manipulate fluid flow inside microdevices, can be broadly categorized into four types: active, passive, mechanical, and non-mechanical. A hydrophobic valve is a non-mechanical, passive microvalve [3, 4]. Microvalves that use physical or chemical properties, such as electrochemical force [5, 6], phase change in hydrogels [6, 7], and photodeformable materials [7, 8], are classified as non-mechanical, active microvalves. Those that utilize check valves and latch valves are classified as mechanical, passive microvalves [9, 10]. Those that utilize magnetic [11], electric [12], thermal forces [13], or external pressure components [14, 15], are classified as mechanical, active microvalves, and are usually equipped with deformable membranes. Of all the types of microvalves, pneumatically driven microvalves are recognized as the most reliable and effective as they afford advantages with no leakage at high input pressures [16]. The device structure is simple and inexpensive to fabricate and can be fabricated with soft and bio-compatible materials such as polydimethylsiloxane (PDMS), which is widely used in biological analysis systems.

However, device miniaturization can be difficult in systems that use pressure driven microvalves because of the requirements of the world-to-chip connector. Because a world-to-chip connector requires approximately 1–10 mm^2 of device area, almost half of the area on a microfluidic device that has a number of world-to-chip connectors will be devoted to the connector area at the expense of the 'microfluidic' area. Another approach is concurrent multi-valve actuation, which involves the piercing of a channel from a connector in exchange for individual valve control [17]. A multiplexed valve control system was proposed to facilitate selection of specific microchannels and microwells in microfluidic, large-scale integration using microvalves with a small number of world-to-chip connectors [18]. However, although this system can control 2^n microchannels with $2n$ control lines, all microchannels except the selected microchannel must be closed while the selected microchannel is open [19].

In this paper, we propose a fluidic logic circuit for a valve control system in microfluidic devices that can control a large number of microvalves individually. The multi-layered PDMS structure of the proposed system actualizes a 3D fluid circuit [20, 21] in a manner analogous to a demultiplexer (DEMUX). The system comprises fluidic logic circuitry to allow for digital signal processing as an electric logic circuit, and to control the opening and closing of arrayed microvalves individually. To evaluate the select valve and the gate valve, which works as a fluidic transistor, we examined pressure leak test against pressure from control lines. The maintanance time of pressure is also observed. To demonstrate the DEMUX valve control system, we fabricated and operated a prototype fluidic chip with 256 (2^8) on-chip valves and 18 ($2 \times 8 + 2$) control lines. This chip valve array demonstrates how the operation of the on-chip valves is kept separate from the fluidic logic circuit of the DEMUX area, for various complex chemical and biological analyses.

2. Experimental methodology

In this section, we explain the underlying concept and design of the DEMUX valve control system to show how manipulation of on-chip valves is performed in a fluidic logic circuit. The fabrication of the system is also explained in detail.

2.1. Concept underlying the DEMUX valve control system

The concept underlying the proposed system is the efficient control of on-chip valves with a small number of world-to-chip connectors by integrating fluidic logic circuitry. The schema of the DEMUX valve control system is shown in figure 1(*a*). In the electric logic circuit, DEMUX relays the signal from the input to one of the outputs that is selected by the signal line according to the select-bit inputs (figure 1(*b*)). Similar to electric DEMUX, fluidic DEMUX outputs the open/closed status of on-chip valves.

The control line that connects to the on-chip valves, the gate valves, and the lines to the DEMUX area, are named drive line, gate line, and select lines, respectively. When $2n$ select lines, a drive line, and a gate line are used, a total of 2^n on-chip valves can be controlled individually. The on-chip valves are driven by pressure or vacuum, from the drive line. Without DEMUX control by the gate and select lines, all of the on-chip valves are actuated simultaneously as a concurrent multi-valve actuation. The gate valves, which are driven by pressure or vacuum from the gate line, maintain the state of the on-chip valves [22, 23]. The gate valves are also actuated simultaneously without DEMUX control by the select lines. The select lines comprise DEMUX and select a gate valve according to the binary input signals.

A three-step procedure for controlling the drive, gate, and select lines performs the essential function of switching the states of the on-chip valves, as shown in figure 2. First, binary signals and pressure input are applied to the select lines and the drive line when all the gate valves are closed, as shown in figures 2(*a*) and (*d*). Second, the gate valve addressed by the select lines is opened, as shown in figures 2(*b*) and (*e*). The on-chip valve addressed, either opens (figure 2(*b*)) or closes (figure 2(*e*)), according to the pressure inputs in the first step. The status of the other on-chip valves is maintained by the gate valves, whose select lines are not activated. The third step is to close the addressed gate valve, as shown in figures 2(*c*) and (*f*). The process is then repeated for all the gate valves. The flow channels are controlled arbitrarily because there is no interference between the statuses of on-chip valves.

2.2. Fabrication of multi-layered PDMS devices

Fabrication of the multi-layered PDMS devices was conducted using a PDMS micromolding and a bonding technique, as shown in figure 3. The DEMUX valve control device comprises three layers of the PDMS microstructure: a top layer for the gate and the select lines; a middle layer for gate and select valves, and connection channels from the drive line; and a bottom layer for flow channels.

In order to close the on-chip valves, gate valves, and select valves without leakage, a portion of the molds (i.e. where the membrane was deformed) for the drive lines, gate lines, and flow channels, was constructed by resist reflow process using positive photoresist (PMER P-LA 900, Tokyo Ohka) after photolithography. The positive photoresist change the cross-sectional profile from rectangle to arc shape at 150 °C 30 min. Because this reheating process of the positive photoresist leads to reflow, any dead-volume in the microchannel can be eliminated when the PDMS membrane is deformed in an arc shape by applying pressure. In order to avoid closing the channels by applying pressure, the molds for the other control lines and through-holes, that were not related to valve operation, were constructed using negative photoresist (SU-8 3000, MicroChem) to attain high aspect microstructures. Molds were then coated with a releasing agent (CYTOP, Asahi grass).

Figures 4(*a*)–(*c*) show the SEM images of the molds for the 256 (2^8) microvalve array. Figure 4(*a*) shows the SEM image of the mold for the select lines in the top layer. Figure 4(*b*) shows the SEM image of the mold for gate valves, select valves, and through-holes in the middle layer. Figure 4(*c*) shows the SEM

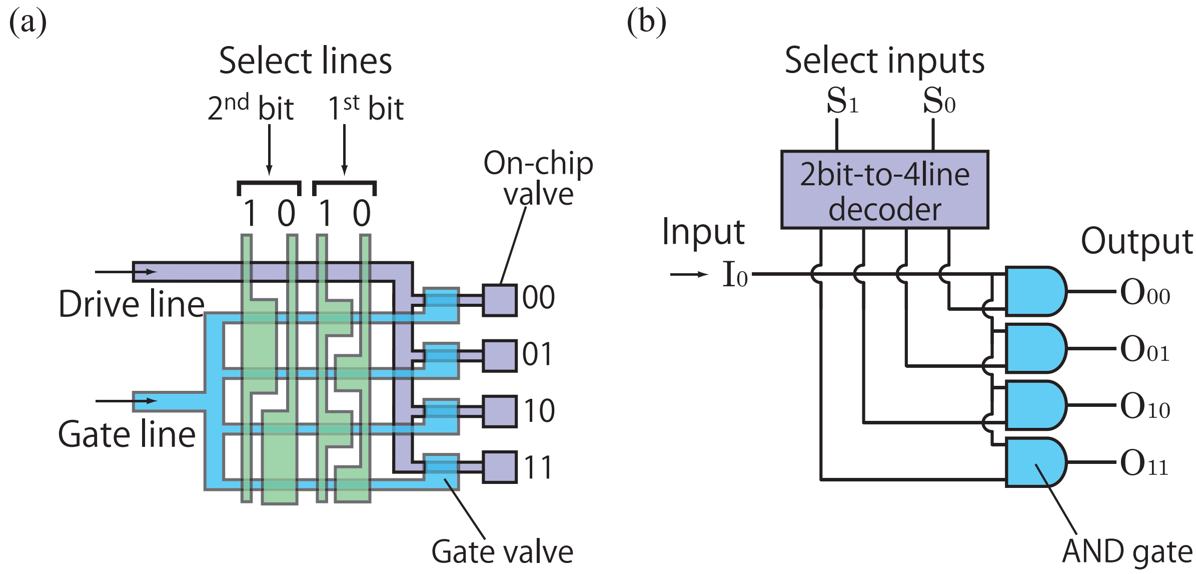

Figure 1. Schemata of a fluidic DEMUX valve control system and electric DEMUX, (*a*) 2 bit DEMUX valve control system for 4 (2^2) microvalves with 6 ($2 \times 2 + 2$) control lines, and (*b*) electric logic circuit of 2 bit DEMUX. Input signal is forwarded to one of the outputs according to the signal of select inputs.

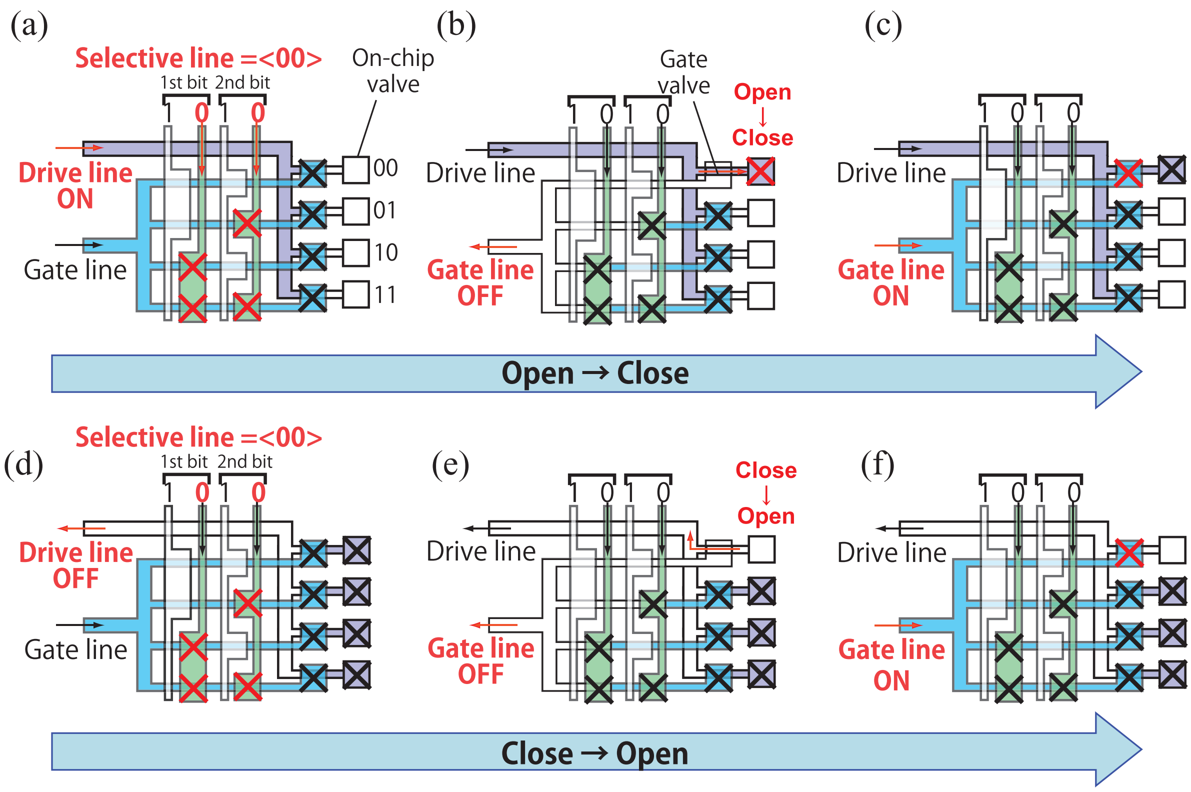

Figure 2. Schemata of valve actuations in a fluidic DEMUX circuit, (*a*)–(*c*) open-to-closed, and (*d*)–(*f*) closed-to-open. The first step is applying the input 00 to select lines and (*a*) pressure application to the drive line (open valve), or (*b*) air-venting of the drive line (closed valve) for on-chip valve 00. (*b*)–(*d*) The second step is air-venting of the gate line. Only gate valve 00 is switched open, and the on-chip valve is also switched due to pressure from drive line. The third step is pressure application to the gate line which maintains the status of the on-chip valves.

image of the mold for on-chip valve and connection channels in the middle layer. The gate valves were connected to the gate line of the top layer via the through-hole of the middle layer.

PDMS pre-polymer components (in a 10:1 base: curing agent) were then poured over the molds for soft lithography to fabricate the top layer. The middle layer, including the through-holes, was molded by sandwiching PDMS between Polyethyleneterephthalate (PET) sheet and the mold under pressure, to fabricate the membrane with through-holes. The flow channel in the bottom layer was fabricated from PDMS

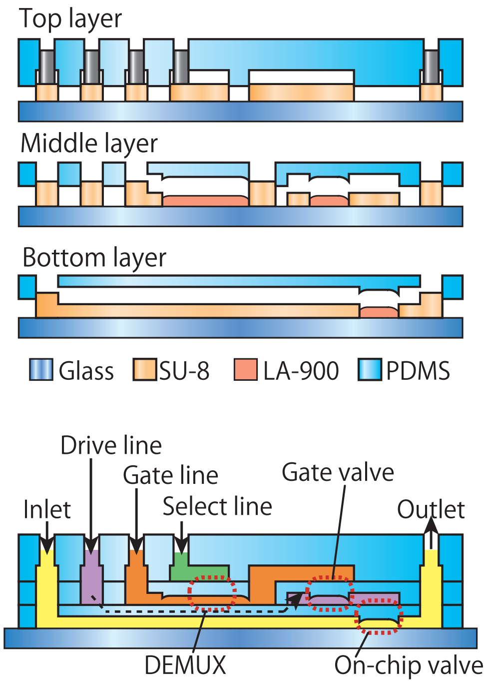

Figure 3. Fabrication of multi-layered PDMS device in which three molded PDMS layers were aligned and bonded after O_2 plasma treatment.

membranes formed by spin coating. After curing, the PDMS layers were peeled off the molds. Finally, the layers were aligned and bonded via oxygen plasma treatment. The fabricated DEMUX valve control system with 256 (2^8) on-chip valves is shown in figures 4(*d*)–(*f*).

2.3. Design of 8 bit DEMUX valve control system

For this system, we designed and constructed an array of 256 (2^8) on-chip valves covering an $8 \times 8\,mm^2$ area, and fabricated onto a $45 \times 55\,mm^2$ device. The width and height of the control lines were 100 and 20 μm, respectively. The area of the on-chip valves was $200 \times 200\,\mu m^2$. The area of the gate and the select valves was $300 \times 300\,\mu m^2$. The dimension of the through-holes was $200 \times 200 \times 60\,\mu m$ (figure 3(*f*)). The thickness of the top layer for connecting pneumatic tubes was approximately 5 mm. The select lines were comprised of 16 (2×8) control lines, and 8 bit operation was attained by 8 pairs of control lines for ‘0’ and ‘1’. The DEMUX area surrounded the on-chip valve area. On-chip valves could be set at any arbitrary point separate from the DEMUX area through the connection channels. The select lines on each side of the device controlled 64 on-chip valves. The width and height of the connection channels between the on-chip valves and the control area were 20 and 20 μm, respectively. The width and height of the flow channels were 100 and 10 μm, respectively. The on-chip valves and the gate valves were denoted using double hexadecimal digits from ‘00’ to ‘FF’.

3. Operation of DEMUX valve control system

To verify the function of the gate valves and select valves, we performed preliminary valve switching experiments. Throughout the experiments, the overall system was controlled by LabVIEW software. Pressure from compressed air was first applied to the control lines via pressure regulators and solenoid valves, which were external components used to control the drive and gate lines according to the signal from the LabVIEW software. In the proposed design of the fluidic chip, the effectiveness of the DEMUX control system is shown in terms of the fluidic logic circuit with drive, gate, and select lines.

3.1. Pressure leak test at gate valves and select valves

The response time of pneumatic valve actuation depends on the time delay in the connecting tubes of the external components. Using air, which is compressible, as the driving fluid for control lines, the valve was closed within 50 ms, and opened within 100 ms. To eliminate the compression of the fluid itself, the driving fluid was changed to water, an incompressible fluid. This change improved the switching speed to 25 ms from the open to the closed state; however, the switching time from the closed to the open state increased to 200 ms. This is because the actuation of the valve opening is due to the elastic power of the valve membrane. The viscosity of water is higher than that of air. Applying evacuation from the port to the atmosphere reduced the switching time from the closed to the open state to 30 ms. The switching speed of the addressed on-chip valves with the three-step control procedure was under 90 ms. Consequently, the length of time that the open/closed state was maintained with inert liquid or water as the driving fluid was over 24 h, whereas for air, it was a maximum of 60 s.

The permissible pressure from the drive line to keep closed at the gate valve, was examined as shown in figure 5(*a*). Pressure leakage at gate valve was originated under approximately 50 kPa pressure difference between drive line and gate line. The permissible pressure from the gate line to keep closed at the select valve was examined as shown in figure 5(*b*). Pressure leakage at gate valve was originated under approximately 60 kPa pressure difference between gate line and select line.

3.2. Individual on-chip valve control by DEMUX fluid circuit

We tested the operation of the on-chip valve using the prototype device with 2^8 on-chip valves. Video 1 (stacks.iop.org/JMM/25/065016/mmedia) shows the addressing of a gate valve by DEMUX for select lines. Video 2 (stacks.iop.org/JMM/25/065016/mmedia) shows the on-chip valve operation without DEMUX control. Video 3 (stacks.iop.org/JMM/25/065016/mmedia) shows the individual on-chip valve operation with DEMUX control. The valve operations of the 256 on-chip valves are shown in figures 6. Figure 6(*a*) shows the initial state of on-chip valve array. All of the on-chip valves were opened. Figure 6(*b*) shows the switching of on-chip valves without DEMUX control. All of the on-chip valves were closed according to the pressure input from drive line. Figures 5(*c*) and (*d*) show the switching of the on-chip valve 00. The 8 bit pressure inputs 00000000 to the select lines chose the gate valve 00 (figure 6(*c*)), and the consequent pressure

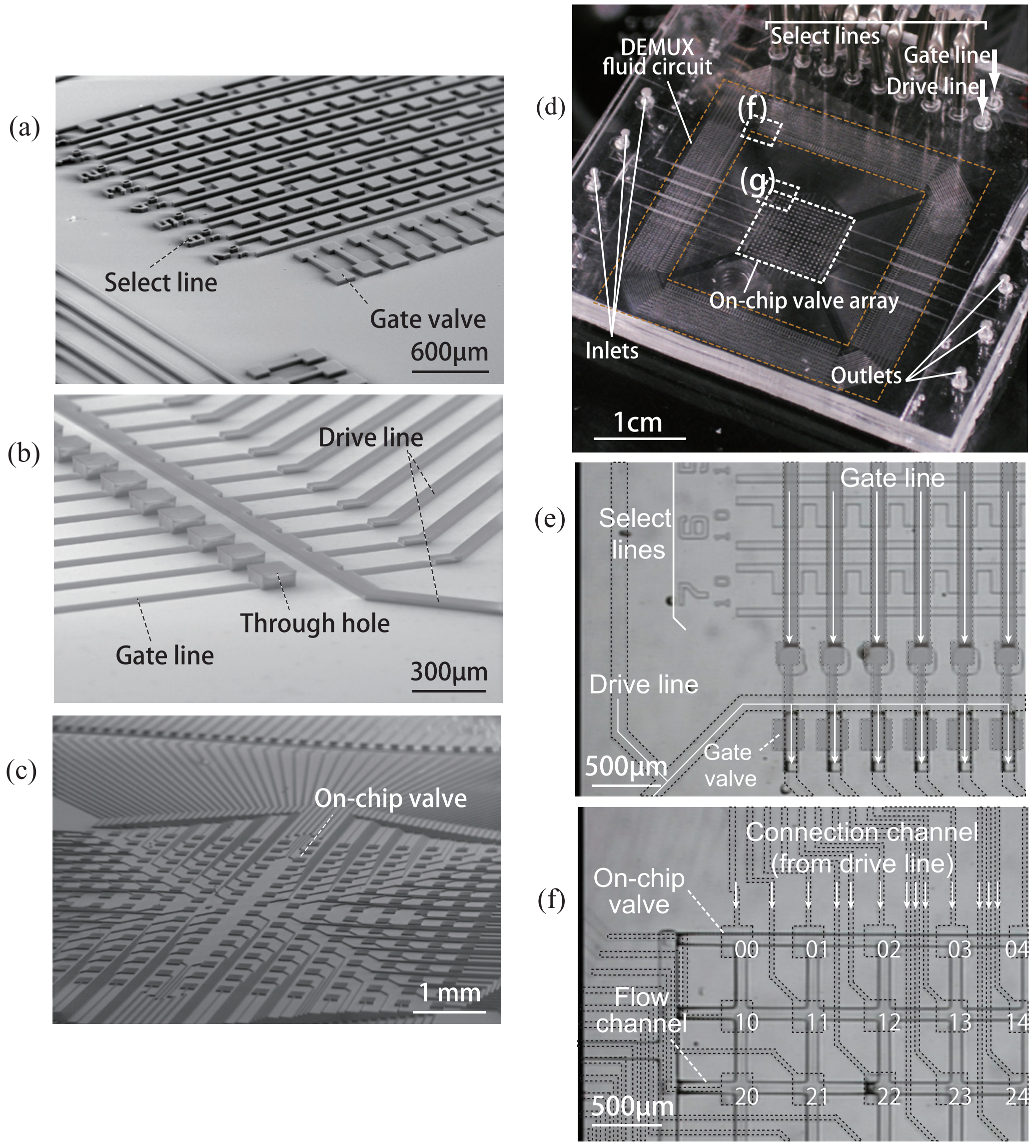

Figure 4. (*a*) SEM image of the select lines and gate valve in the top layer, (*b*) SEM image of the gate valve, gate line, through-hole, and connection channels in the middle layer, (*c*) SEM image of the on-chip valves and connection channels in the middle layer, (*d*) overview of prototype device with 256 (2^8) on-chip valves for the DEMUX valve control system, (*e*) enlarged view of the DEMUX area, and (*f*) enlarged view of the on-chip valve area.

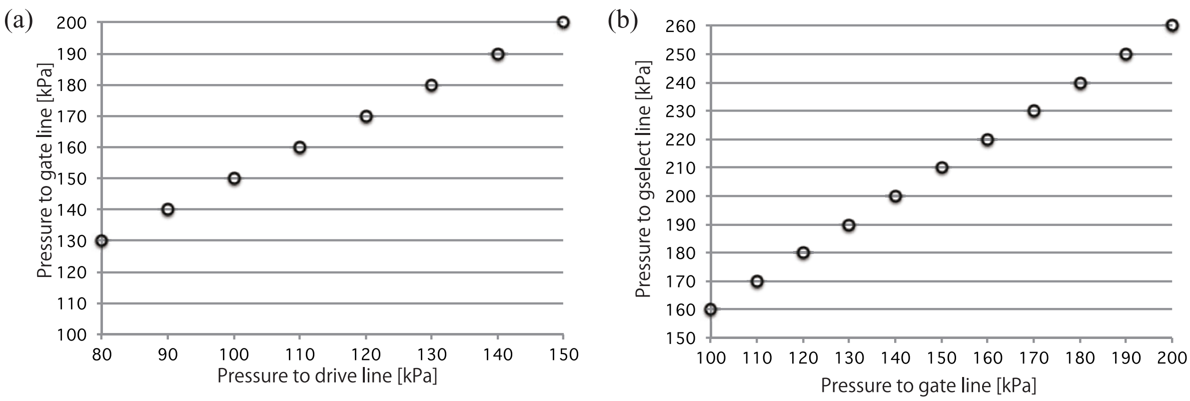

Figure 5. Graphs of pressure imperviousness (pressure leak) at gate valve and select valve against pressure from drive line and gate line respectively, (*a*) pressure to drive line versus to gate valve, and (*b*) pressure to gate line versus to select valve.

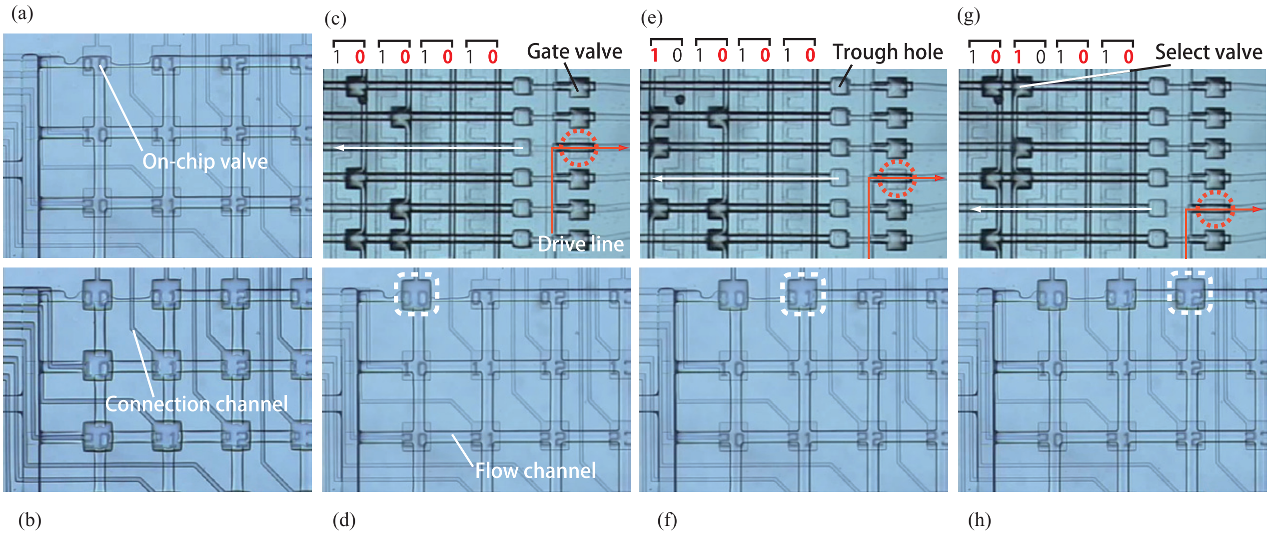

Figure 6. 256 on-chip valve operation in 256 (2^8) DEMUX valve control system, (*a*) before control (initial state), (*b*) actuation of on-chip valves without DEMUX control, (*c*) (*d*) actuation of on-chip valve 00, (*e*) (*f*) actuation of on-chip valve 01, and (*g*) (*h*) actuation of on-chip valve 02.

input to the drive line actuated the closure of the on-chip valve 00 (figure 6(*d*)). The other on-chip valves were maintained open by DEMUX. Figures 6(*e*) and (*f*) show the switching of the on-chip valve 01. The 8 bit pressure inputs 00000001 to the select lines chose the gate valve 01 (figure 6(*e*)), and the consequent pressure input to the drive line actuated the closure of the on-chip valve 01 (figure 6(*f*)). The on-chip valve 00 was maintained closed, and the other on-chip valves open by DEMUX. Figures 5(*g*) and (*h*) show the switching of the on-chip valve 02. The 8 bit pressure inputs 00000010 to the select lines chose the gate valve 02 (figure 6(*g*)), and the consequent pressure input to the drive line actuated the closure of the on-chip valve 02 (figure 6(*h*)). The on-chip valves 00 and 01 were maintained closed, and the other on-chip valves open by DEMUX. Each on-chip valve from 00 to FF can be controlled within 90 ms, and the individual 256 valves were controlled by 18 off-chip control valves.

4. Conclusion

This paper proposed a DEMUX valve control system that can control a large number of arrayed valves using only a small number of world-to-chip connectors. The proposed system comprises a fluidic logic circuit with drive, gate, and select lines. The use of water as a working fluid for the control lines, and application of evacuation for pressure venting, provided rapid valve switching performance. Using hydraulic valve control, response times of 25 ms for the open-to-closed state and 30 ms for the closed-to-open state were achieved. We confirmed that the state of the on-chip valve was maintained over 24 h. 8 bit DEMUX allowed for control of 256 (2^8) individual on-chip valves with 18 ($2 \times 8 + 2$) control lines. 2^n individual microvalve control with $2n + 2$ control lines using the fluidic logic circuit of DEMUX was proposed and confirmed.

In conventional pneumatic valve control system, valve integration and arbitrary control are incompatible. DEMUX valve control system is useful for such microfluidic device which has a numerous arbitrary-controlled microvalves. On the contrary, when the n is smaller than four, the required number of control lines and world-to-chip connectors is almost same or large to the number of arbitrary-controllable microvalve, and rather should be used for direct control. However, as the n is larger, the number of arbitrary-controllable microvalve is exponentially increased. Over one thousand (1024) microvalves can be controlled arbitrary using only 22 control lines ($n = 10$) and over 1 million (1048576) microvalves can be controlled by only 42 control lines ($n = 20$). Considering its advantages, such as the fact that the system can be controlled using arbitrary on-chip valves without limitations from the other on-chip valves, our system has the potential to be incorporated in a variety of applications for various types of chemical and biological analyses [24]. We plan to control complex chemical synthesis and high throughput screening in future work.

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