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(54) METHOD FOR CONTROLLING COMMUNICATION BETWEEN MULTIPLE ACCESS PORTS IN A MICROFLUIDIC DEVICE

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(51) **Int. Cl.**
B01L 3/00 (2006.01)

(52) **U.S. Cl.** **436/180**; 422/504; 422/507

(58) **Field of Classification Search** 436/180; 422/504, 507

See application file for complete search history.

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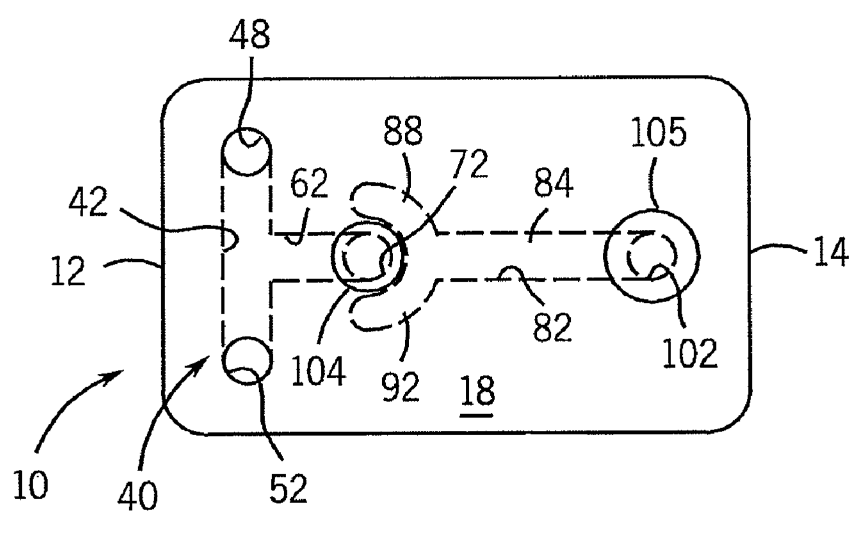
(57) **ABSTRACT**

A method is provided of controlling communication between multiple ports in a microfluidic device. The method includes the step of providing a channel network in a microfluidic device. The channel network including a first channel having a first input port and an output port. The first channel is filled with a fluid and a first output droplet is deposited on the output port. The first output droplet has a radius of curvature. The first output droplet flows toward the first input port in response to placement of a first input droplet having a radius of curvature greater than the radius of curvature of the first output droplet on the first input port. The first input droplet flows toward the output port in response to the first input droplet having a radius of curvature less than the radius of curvature of first output droplet.

5 Claims, 7 Drawing Sheets



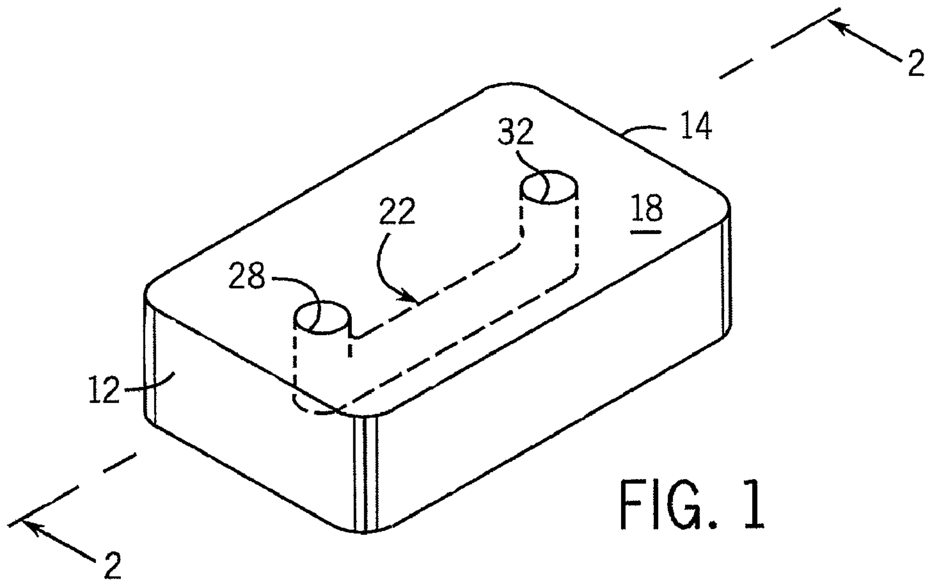


FIG. 1

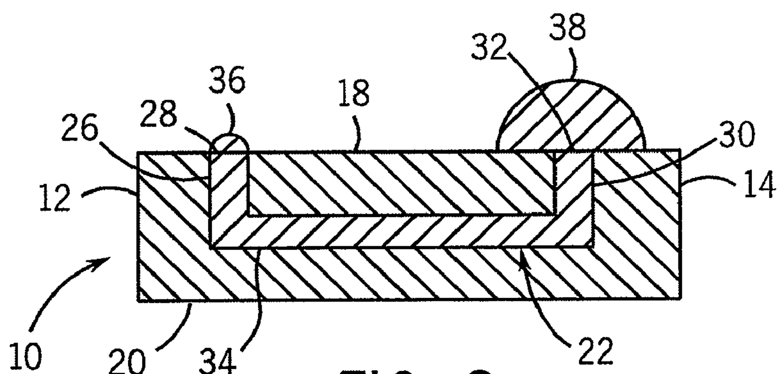


FIG. 2

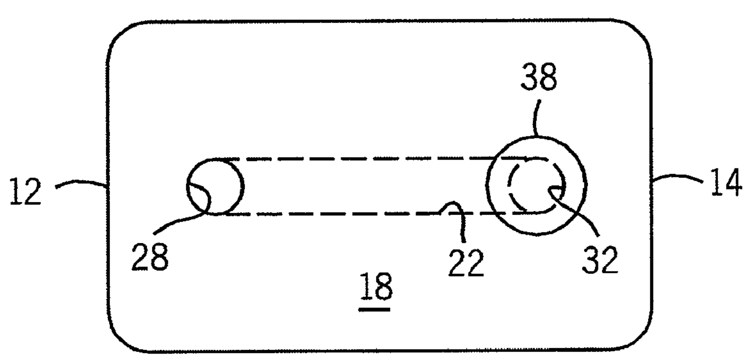


FIG. 3

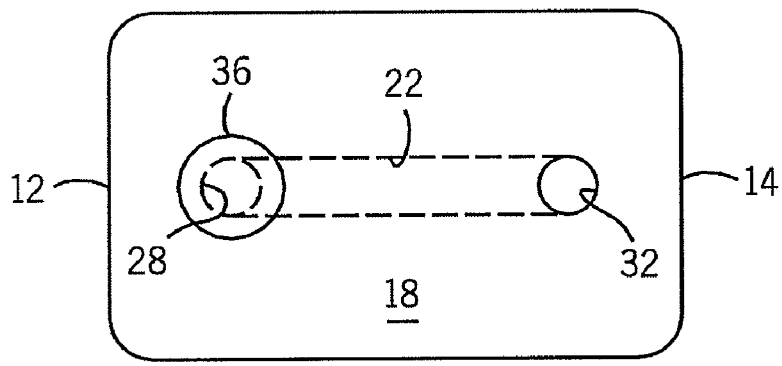


FIG. 4

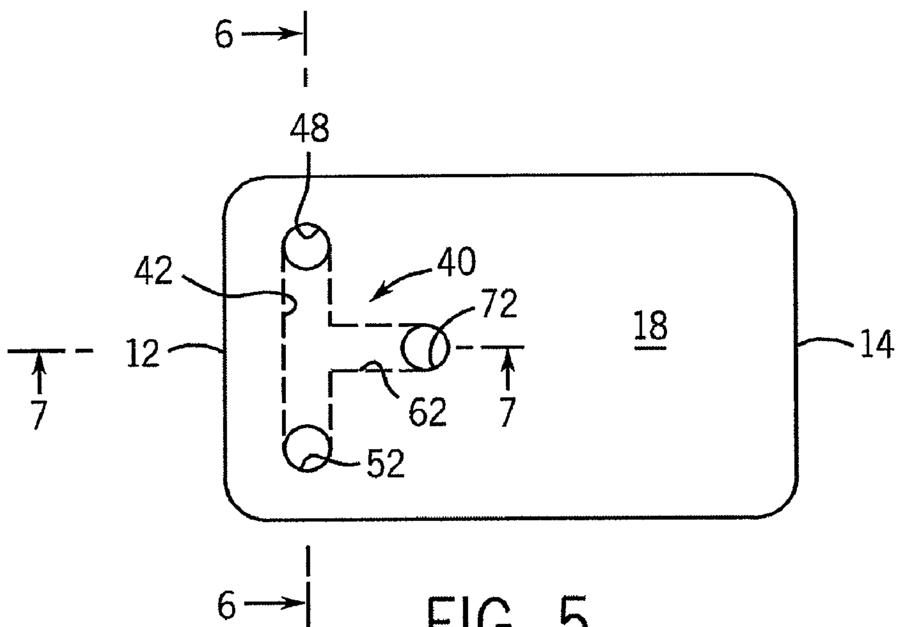


FIG. 5

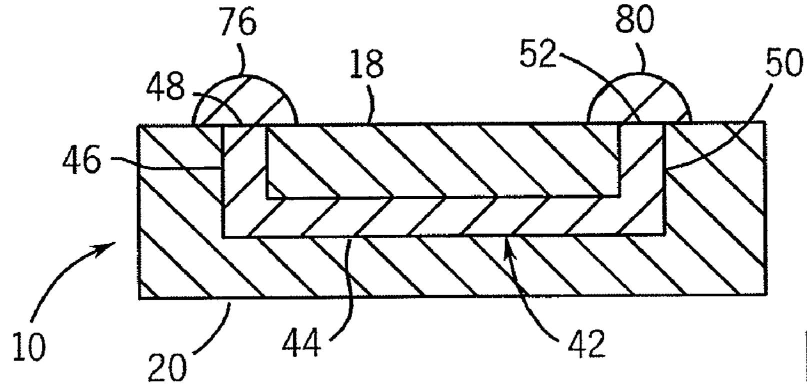


FIG. 6

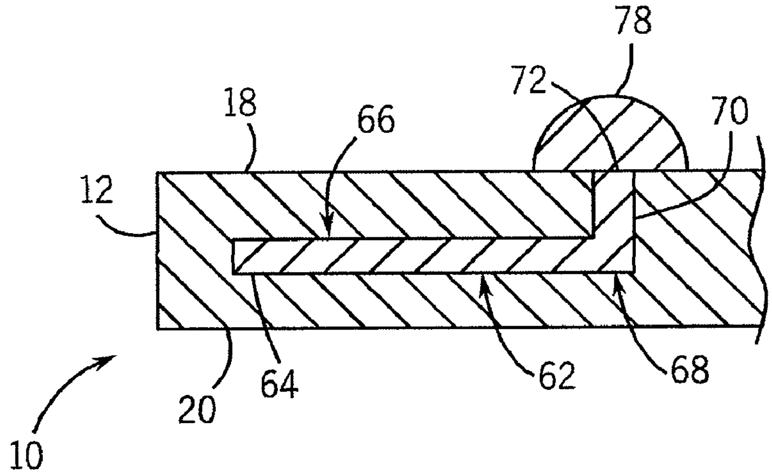


FIG. 7

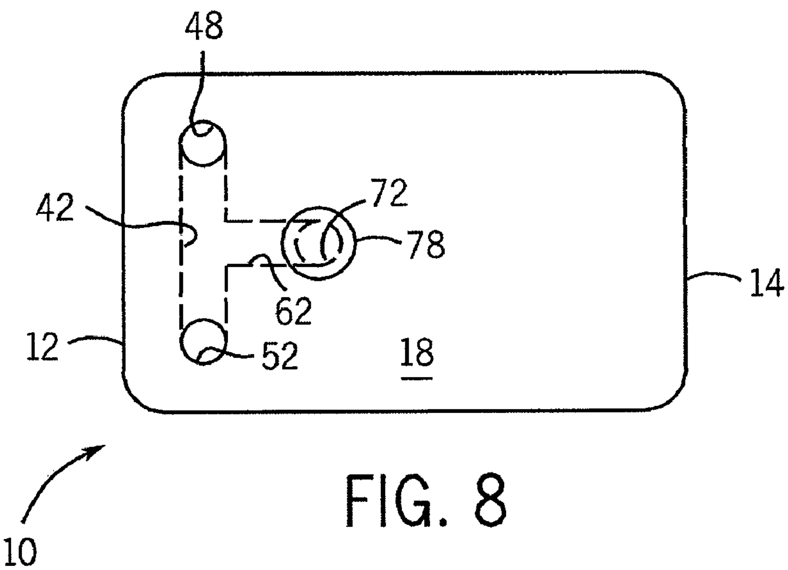


FIG. 8

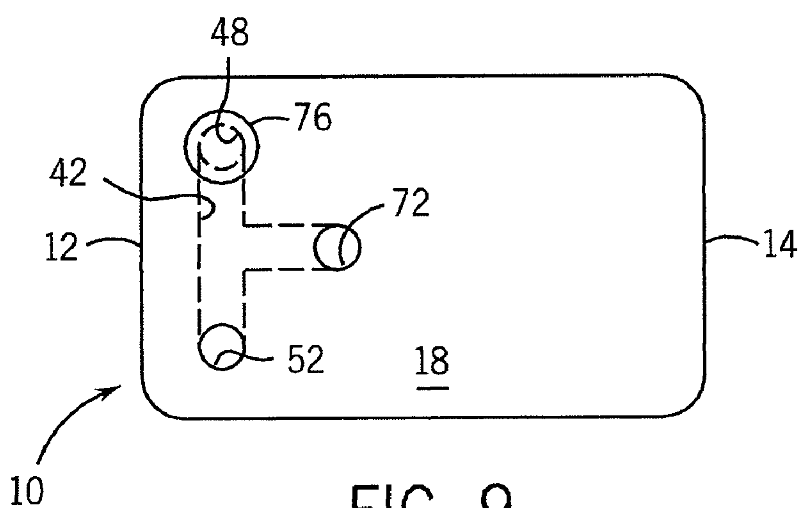


FIG. 9

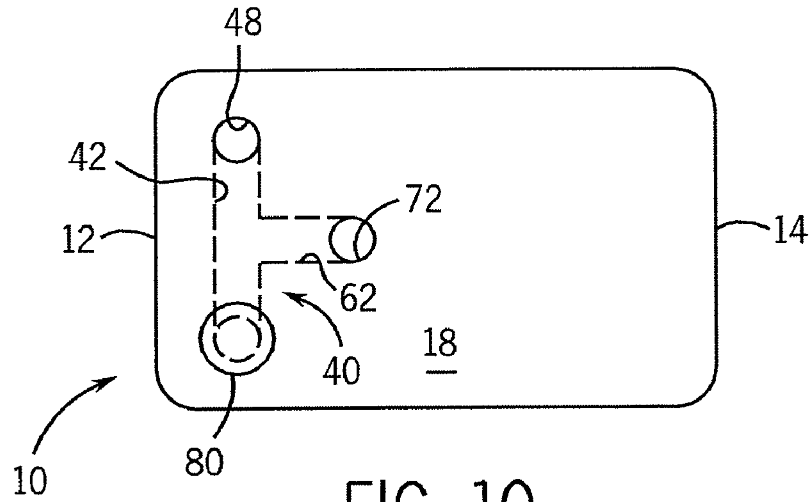


FIG. 10

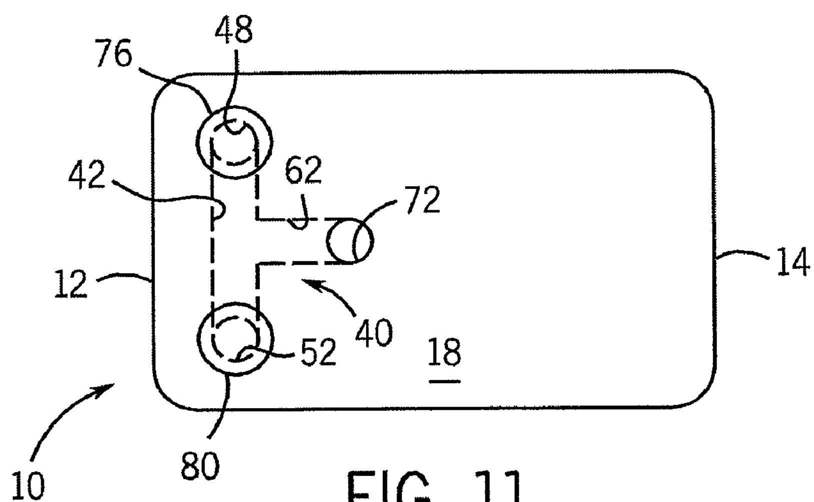


FIG. 11

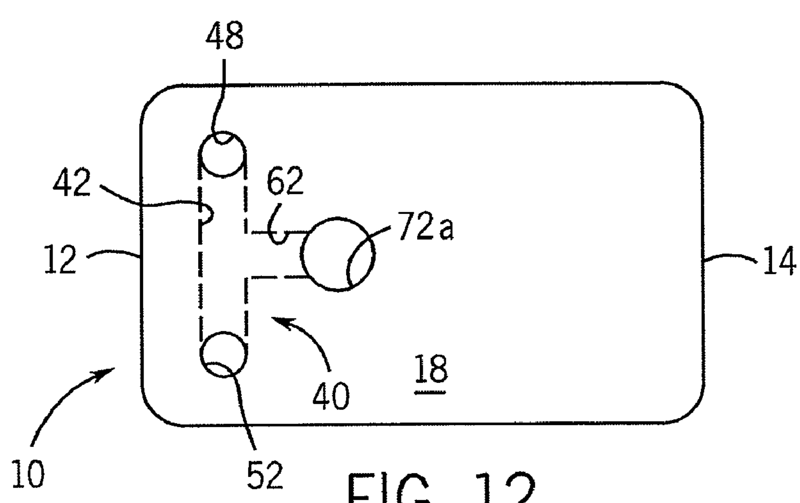


FIG. 12

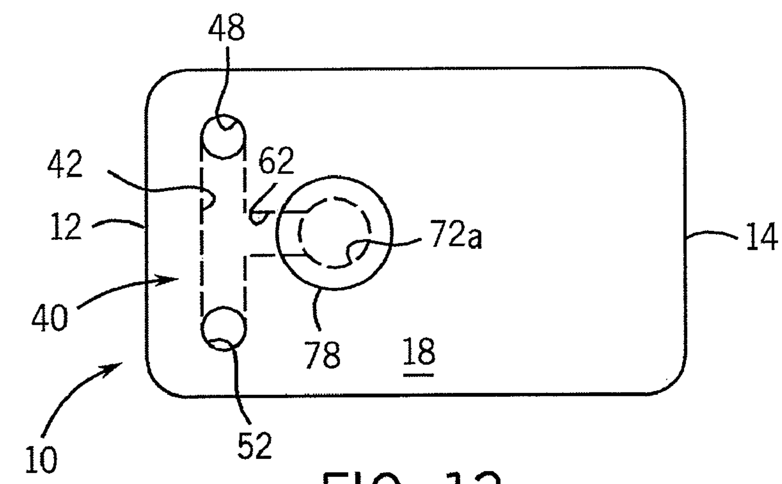


FIG. 13

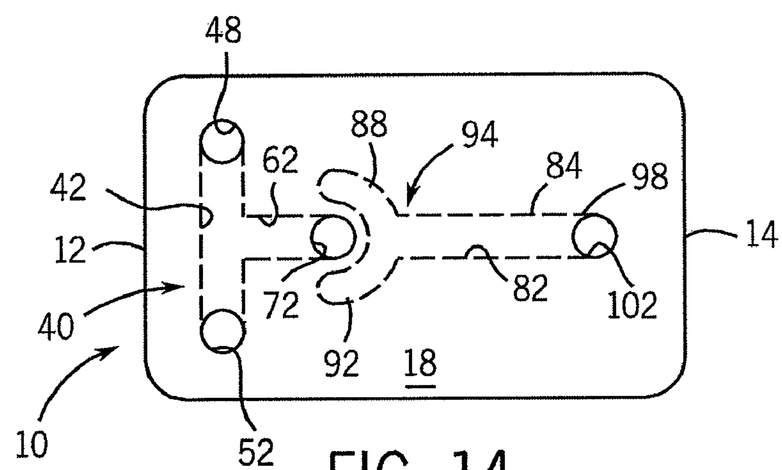


FIG. 14

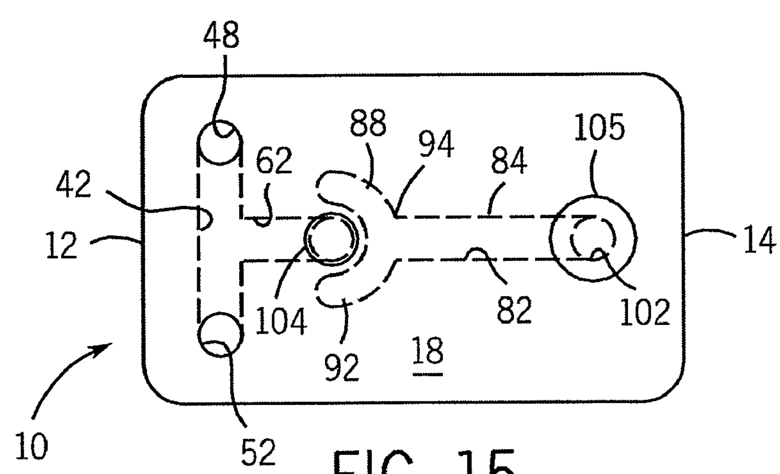


FIG. 15

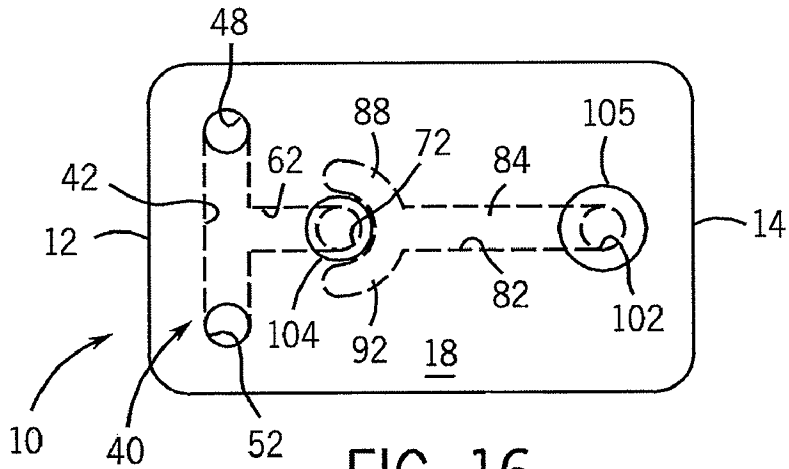


FIG. 16

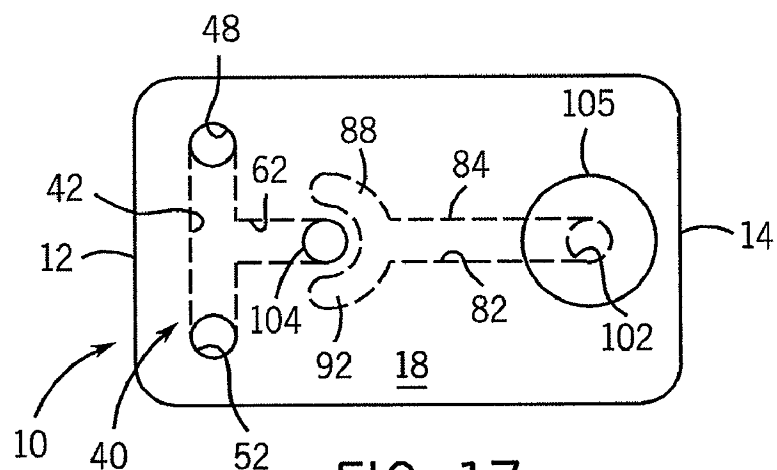


FIG. 17

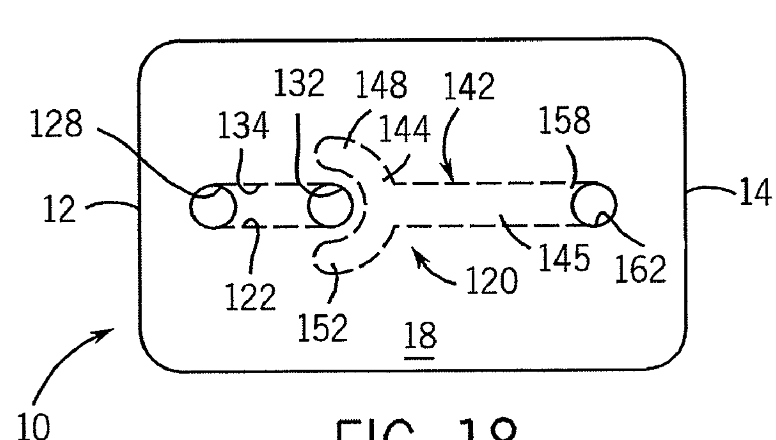


FIG. 18

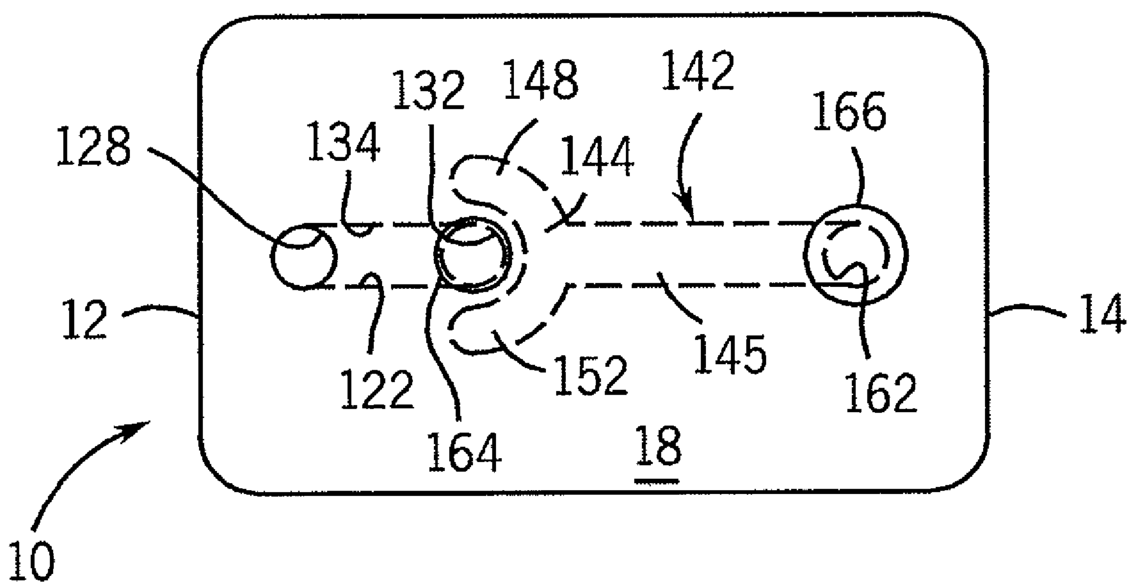


FIG. 19

METHOD FOR CONTROLLING COMMUNICATION BETWEEN MULTIPLE ACCESS PORTS IN A MICROFLUIDIC DEVICE

REFERENCE TO GOVERNMENT GRANT

This invention was made with United States government support awarded by the following agencies: ARMY/MRMC W81XWH-04-1-0572; and NIH CA104162. The United States has certain rights in this invention

FIELD OF THE INVENTION

This invention relates generally to microfluidic devices, and in particular, to a method for controlling communication between multiple access ports in a microfluidic device in order to create a plurality of digital microfluidic circuit components.

BACKGROUND AND SUMMARY OF THE INVENTION

Microfluidic devices have been used to explore a variety of biological problems of interest, ranging from fundamental research in protein crystallization to diagnostic assays. A number of these applications require the integration of valves, mixers, and other components into the devices in order to successfully carry out various steps. The incorporation of actively controlled functionalities, either directly in the device or via fixed interface with external components, often leads to more complex fabrication and the need for ancillary equipment. The use of passive and autonomous microfluidic components, while sometimes requiring more complex fabrication, can help to reduce or eliminate the need for additional equipment. Eliminating external components makes point-of-care devices more portable and facilitates operation of many devices in parallel, which is of particular interest for large parametric screening applications.

Many of the fabrication methods used to create microfluidic devices were first developed for microelectronics, so it is fitting that a number of parallels can be drawn between the two fields. Resistance, driving forces (pressure/voltage), and current (fluid/electrons) analogies are commonly used to compare electronic components and fluid networks. The analogy has been further extended in microfluidics to include diodes, rectifiers, memory elements, and capacitors. Two-phase flow has recently been used to encode and decode data sets using droplets. As with electronics, microfluidic components can be combined to form more complex devices and a microfluidic breadboard has already been demonstrated. Microfluidics can also be used to address problems that are not easily solved using standard computational methods. Regulatory systems can also be implemented in microfluidic devices. Responsive hydrogels have been used in microfluidic devices to regulate the pH or temperature of a solution. The use of pneumatic control in three dimensional channel structures has been shown as a means of self-regulation flow. Hence, it is highly desirable to couple a conditional action to more than one input, thereby enabling the creation of logic gates, which can be combined to perform computation and more complex functions.

Fluidic logic elements can be traced back to the 1950's; however, most of the early constructs depended on turbulent and multistable flow states, which are not scalable due to the low Reynolds numbers that are typically observed in microfluidic channels. More recent efforts using microfluidics have employed fluidic resistance, electrochemistry, pneumatics, channel geometry, multiphase flow, and chemistry to create logic elements. Many of these approaches rely on continuous flow and are unable to create more integrated constructs due to different input/output (e.g. pressure/dye). Additionally, the electronic components used to input and read out signals are more complex than the devices themselves. Ideally, fluidic logic elements would use consistent signal input/output and require minimal supporting equipment.

Therefore, it is a primary object and feature of the present invention to provide a method for controlling communication between multiple access ports in a microfluidic system in order to create a plurality of digital microfluidic circuit components.

It is a further object and feature of the present invention to provide a method for controlling communication between multiple access ports in a microfluidic system to create fluidic logic gates in the microfluidic system.

It is a still further object and feature of the present invention to provide a method for controlling communication between multiple access ports in a microfluidic system in order to allow various computations and complex functions to be performed with the system.

In accordance with the present invention, a method is provided of controlling communication between multiple ports in a microfluidic device. The method includes the step of providing a channel network in a microfluidic device. The channel network includes a first channel having a first input port and an output port. The first channel is filled with a fluid and a first output droplet is deposited on the output port. The first output droplet has a radius of curvature. The first output droplet flows toward the first input port in response to placement of a first input droplet having a radius of curvature greater than the radius of curvature of the first output droplet on the first input port.

The first channel includes a second input port. The first output droplet flows toward the second input port in response to placement of a second input droplet having a radius of curvature greater than the radius of curvature of the first output droplet on the second input port. The method also includes the additional step of depositing a first input droplet on the first input port. The first input droplet flows toward the output port in response to the first input droplet having a radius of curvature less than the radius of curvature of the first output droplet. A second input port is provided for the first channel. A second input droplet is deposited on the second input port. The second input droplet flows toward the output port in response to the second input droplet having a radius of curvature less than the radius of curvature of the first output droplet.

The channel network may include a second channel. The second channel has an input port and an output port. The input port of the second channel is placed in proximity to the output port of the first channel. The first output droplet communicates with the input port of the second channel when the first output droplet exceeds a predetermined volume. A second output droplet is deposited on the output port of the second channel. The second output droplet has a radius of curvature wherein the first output droplet flows toward the output port of the second channel in response to the first output droplet communicating with the input port of the second channel and having a radius of curvature less than the radius of curvature of the second output droplet on the output port of the second channel.

In accordance with a further aspect of the present invention, a method is provided of controlling communication between multiple ports in a microfluidic device. The method includes the step of providing a channel network in a microfluidic device. The channel network includes a first channel having first and second input ports and an output port. The first channel is filled with a fluid. A first output droplet is deposited on the output port. The first output droplet has a radius of curvature. A first input droplet is deposited on the first input port. The first input droplet flows toward the output port in response to the first input droplet having a radius of curvature less than the radius of curvature of the first output droplet. The first output droplet flows toward the first input port when the first input droplet has a radius of curvature greater than the radius of curvature of the first output droplet.

A second input droplet may be deposited on the second input port. The second input droplet flows toward the output port in response to the second input droplet having a radius of curvature less than the radius of curvature of the first output droplet. The first output droplet flows toward the second input port in response the second input droplet having a radius of curvature greater than the radius of curvature of the first output droplet.

The channel network may include a second channel. The second channel has an input port and an output port. The input port of the second channel is positioned in proximity to the output port of the first channel. The first output droplet communicates with the input port of the second channel when the first output droplet exceeds a predetermined volume. A second output droplet may be deposited on the output port of the second channel. The second output droplet has a radius of curvature wherein the first output droplet flows toward the output port of the second channel in response to the first output droplet communicating with the input port of the second channel and having a radius of curvature less than the radius of curvature of the second output droplet on the output port of the second channel.

In accordance with a further aspect of the present invention, a method is provided of controlling communication between multiple ports in a microfluidic device. The method includes the step of providing a channel network in a microfluidic device. The channel network includes a first channel having a first input port and an output port. The first channel is filled with a fluid. A first output droplet is deposited on the output port. The first output droplet has a radius of curvature. A first input droplet is deposited on the first input port. The first input droplet has a radius of curvature. The first output droplet flows toward the first input port when the first input droplet has a radius of curvature greater than the radius of curvature of the first output droplet. The first input droplet flows toward the output port in response to the first input droplet having a radius of curvature less than the radius of curvature of the first output droplet.

The method may include the additional steps of providing a second input port for the first channel and depositing a second input droplet on the second input port. The second input droplet flows toward the output port in response the second input droplet having a radius of curvature less than the radius of curvature of the first output droplet. The first output droplet flows toward the second input port in response the second input droplet having a radius of curvature greater than the radius of curvature of the first output droplet.

The channel network may include a second channel. The second channel has an input port and an output port. The input port of the second channel is positioned in proximity to the output port of the first channel. The first output droplet communicates with the input port of the second channel when the first output droplet exceeds a predetermined volume. A second output droplet is deposited on the output port of the second channel. The second output droplet has a radius of curvature wherein the first output droplet flows toward the output port of the second channel in response to the first output droplet communicating with the input port of the second channel and having a radius of curvature less than the radius of curvature of the second output droplet on the output port of the second channel.

BRIEF DESCRIPTION OF THE DRAWINGS

The drawings furnished herewith illustrate a preferred construction of the present invention in which the above advantages and features are clearly disclosed as well as others which will be readily understood from the following description of the illustrated embodiment.

In the drawings:

FIG. **1** is an isometric view of a microfluidic device for use in performing the methodology of the present invention;

FIG. **2** is a cross-sectional view of the microfluidic device taken along line **2-2** of FIG. **1**;

FIG. **3** schematic, top plan view of the microfluidic device of FIG. **1**;

FIG. **4** schematic, top plan view of the microfluidic device of FIG. **1**;

FIG. **5** schematic, top plan view of a further embodiment of a microfluidic device for use in performing the methodology of the present invention;

FIG. **6** is a cross-sectional view of the microfluidic device taken along line **6-6** of FIG. **5**;

FIG. **7** is a cross-sectional view of the microfluidic device taken along line **7-7** of FIG. **5**;

FIG. **8** schematic, top plan view of the microfluidic device of FIG. **5**;

FIG. **9** schematic, top plan view of the microfluidic device of FIG. **5**;

FIG. **10** schematic, top plan view of the microfluidic device of FIG. **5**;

FIG. **11** schematic, top plan view of the microfluidic device of FIG. **5**;

FIG. **12** schematic, top plan view of a still further embodiment of a microfluidic device for use in performing the methodology of the present invention;

FIG. **13** schematic, top plan view of the microfluidic device of FIG. **12**;

FIG. **14** schematic, top plan view of a still further embodiment of a microfluidic device for use in performing the methodology of the present invention;

FIG. **15** schematic, top plan view of the microfluidic device of FIG. **14**;

FIG. **16** schematic, top plan view of the microfluidic device of FIG. **14**;

FIG. **17** schematic, top plan view of the microfluidic device of FIG. **14**;

FIG. **18** schematic, top plan view of a still further embodiment of a microfluidic device for use in performing the methodology of the present invention; and

FIG. **19** schematic, top plan view of the microfluidic device of FIG. **19**.

DETAILED DESCRIPTION OF THE DRAWINGS

Referring to FIGS. **1-2**, a microfluidic device for use in the method of the present invention is generally designated by the reference numeral **10**. Microfluidic device **10** may be formed from polydimethylsiloxane (PDMS) or other suitable material and has first and second ends **12** and **14**, respectively, and upper and lower surfaces **18** and **20**, respectively. Channel **22** extends through microfluidic device **10** and includes a first vertical portion **26** terminating at an input port **28** that communicates with upper surface **18** of microfluidic device **10** and a second vertical portion **30** terminating at an output port **32** also communicating with upper surface **18** of microfluidic device **10**. First and second vertical portions **26** and **30**, respectively, of channel **22** are interconnected by and communicate with horizontal portion **34** of channel **22**. The dimension of channel **22** connecting input port **28** and output port **32** is arbitrary. In the depicted embodiment, the input ports and output ports of microfluidic device **10** have generally circular configurations. However, alternate configurations, such as slit-shaped and oval ports, are possible without deviating from the scope of the present invention. It has been found the oval ports are better for directing drop growth, as hereinafter described, in a particular direction. In addition, it has been found that drops are more thoroughly pumped away, as hereinafter described, from slit-shaped ports.

The amount of pressure present within a drop of liquid at an air-liquid interface is given by the Young-LaPlace equation:

$$\Delta P=\gamma(1/R1+1/R2) \qquad \text{Equation (1)}$$

wherein γ is the surface free energy of the liquid; and R**1** and R**2** are the radii of curvature for two axes normal to each other that describe the curvature of the surface of first drop **36**.

For spherical drops, Equation (1) may be rewritten as:

$$\Delta P=2\gamma/R \qquad \text{Equation (2)}$$

wherein: R is the radius of the spherical first drop **36**.

From Equation (2), it can be seen that smaller drops have a higher internal pressure than larger drops. Therefore, if two drops having different radii of curvature are connected via a fluid-filled tube (i.e. channel **22**), the drop with the smaller radius of curvature will shrink while the larger one grows in size. One manifestation of this effect is the pulmonary phenomenon called "instability of the alveoli" which is a condition in which large alveoli continue to grow while smaller ones shrink. As described, fluid can be pumped through channel **22** by using the surface tension in first and second drops **36** and **38**, respectively, on input port **28** and output port **32** of channel **22**.

It can be appreciated that the embodiment disclosed in FIGS. **1-2** may be used as an inverter. More specifically, referring to FIGS. **3-4**, channel **22** may be filed with a fluid and second drop **38** may be placed on output port **32** of channel **22**. If no drop is placed on input port **28** of channel **32** (in other words, there is an input of 0 at input port **28**), second drop **38** placed on output port **32** of channel **22** remains. Hence, the "value" of channel **22** at output port **32** would be 1, while the value of the channel at input port **28** would remain 0. Thereafter, first drop **36** may be placed on input port **28** of channel **22**. If first drop **36** on input port **28** is larger than second drop **38** on output port **32**, second drop **28** will be pumped from the output port **32** to the input port **28**. As a result, the value of channel **22** at output port **32** would be 0, while the value of the input port **28** would be 1.

Referring to FIGS. **5-7**, a further embodiment of a channel network for microfluidic device **10** is generally designated by the reference numeral **40**. Channel network **40** includes first channel **42** that extends through microfluidic device **10** and includes a first vertical portion **46** terminating at first input port **48** that communicates with upper surface **18** of microfluidic device **10** and a second vertical portion **50** terminating at a second input port **52** also communicating with upper surface **18** of microfluidic device **10**. First and second vertical portions **46** and **50**, respectively, of channel **42** are interconnected by and communicate with horizontal portion **44** of channel **42**. The dimension of channel **42** connecting input ports **48** and **52** is arbitrary.

Channel network **40** further includes second channel **62** that extends through microfluidic device **10** and includes a horizontal portion **64** having a first end **66** communicating with first channel **42** and a second end **68** communicating with vertical portion **70**. Vertical portion **70** of second channel **62** terminates at output port **72** that communicates with upper surface **18** of microfluidic device **10**. The dimension of second channel **62** connecting first channel **42** and output port **72** is arbitrary.

It can be appreciated that the embodiment disclosed in FIGS. **5-7** may be used as a NOR gate. More specifically, referring to FIGS. **8-11**, channel network **40** is filled with a fluid and output drop **78** is placed on output port **72** of second channel **62**. If no drop is placed on input ports **48** and **52** of first channel **42** (in other words, there are inputs of 0 at input ports **48** and **52**), output drop **78** placed on output port **72** of second channel **62** remains. Hence, the "value" at output port **72** of second channel **42** would be 1, while the values at input ports **48** and **52** would remain 0, FIG. **8**. Thereafter, if a first drop **76** is placed on input port **48** of first channel **42** that is larger than output drop **78** on output port **72**, output drop **78** will be pumped from the output port **72** to the input port **48**. As a result, the value at output port **72** would be 0, while the value of the input port **48** would be 1, FIG. **9**. Similarly, if a second drop **80** is placed on input port **52** of first channel **42** that is larger than output drop **78** on output port **72**, output drop **78** will be pumped from the output port **72** to the input port **52**. Hence, the value at output port **72** would be 0, while the value of the input port **52** would be 1, FIG. **10**. Finally, if first and second drops **76** and **80**, respectively, are placed on input ports **48** and **52**, respectively, of first channel **42** that are larger than output drop **78** on output port **72**, output drop **78** will be pumped from the output port **72** to the input ports **48** and **52**. Hence, the value at output port **72** would be 0, while the values of input ports **48** and **52** would be 1, FIG. **11**.

As hereinafter described, it can be appreciated that same design can be used as an OR gate or an AND gate by simply changing the size or number of drops that are used to define an input of 1. In other words, the size of the drops can be varied to change the type of gate that is created with a given channel geometry. As is known, OR/AND gates require an output of 1 only if at least one of the inputs is 1. As such, fluid must be pumped to a port originally without a drop deposited thereon. While a larger droplet has heretofore been used as a low-pressure sink in the passive pumping method, it is not a necessity. For the OR/AND gates, output port **72***a* is formed with a radius larger than that of the radius of input ports **48** and **52**. As a result, the curvature of the meniscus in the output port is large enough to drive fluid flow to output port **72***a* from input ports **48** and **52**, provided sufficiently small drops are used on input ports **48** and **52**.

Referring to FIGS. **12-13**, to operate as an AND gate, channel network **40** is filled with a fluid. If no drop is placed on input ports **48** and **52** of first channel **42** or output port **72***a* (in other words, there are inputs of 0 at input ports **48** and **52**), the "value" of second channel **62** at output port **72***a* would be 0. Thereafter, if a first drop **76** is placed on input port **48** of first channel **42**, that drop **76** will be pumped to output port **72***a*. However, while the value at input port **48** goes to 0, the value at output port **72***a* remains 0, since the volume of first drop **76** is small as compared to the size of output port **72***a*, FIG. **12**. Similarly, if a second drop **80** is placed on input port **52** of first channel **42**, that drop is pumped to the output port **72***a*. However, while the value at input port **52** goes to 0, the value at output port **72***a* remains 0, since the volume of second drop **80** is small as compared to the size of output port **72***a*, FIG. **12**. Finally, if first and second drops **76** and **80**, respectively, are placed on input ports **48** and **52** of first channel **42**, first and second drops **76** and **80**, respectively, are pumped to output port **72***a*. The resulting fluid flow of the first and second drops **76** and **80**, respectively, displaces the air/liquid interface from within output port **72***a* to form output drop **78** at output port **72***a*. Hence, the value at output port **72***a* would be 1, while the values of input ports **48** and **52** would be 0, FIG. **13**.

Referring specifically to FIG. **13**, in order to operate as an OR gate, channel network **40** is filled with a fluid. If no drop is placed on input ports **48** and **52** of first channel **42** or output port **72***a* (in other words, there are inputs of 0 at input ports **48** and **52**), the "value" of second channel **42** at output port **72***a* would be 0. Thereafter, if a first drop **76** having an enlarged volume is placed on input port **48** of first channel **42**, that drop **76** will be pumped to output port **72***a*. As the value at input port **48** goes to 0, first drop **76** displaces the air/liquid interface from within output port **72***a* to form output drop **78** at output port **72**. The value at output port **72***a* would be 1, while the values of input ports **48** and **52** would be 0. Similarly, if an enlarged second drop **80** is placed on input port **52** of first channel **42**, second drop **80** is pumped to the output port **72***a*. As the value at input port **52** goes to 0, second drop **80** displaces the air/liquid interface from within output port **72***a* to form output drop **78** at output port **72**. Hence, the value at output port **72***a* would be 1, while the values of input ports **48** and **52** would be 0. Finally, if first and second drops **76** and **80**, respectively, are placed on first and second input ports **48** and **52**, respectively, of first channel **42**, first and second drops **76** and **80**, respectively, are pumped to output port **72***a*. The resulting fluid flow of the first and second drops **76** and **80**, respectively, displaces the air/liquid interface from within output port **72***a* to form output drop **78** at output port **72***a*. Hence, the value at output port **72***a* would be 1, while the values of input ports **48** and **52** would be 0.

Referring to FIG. **14**, a NAND gate can be constructed by incorporating a third channel **82** into channel network **40**. More specifically, third channel **82** extends through microfluidic device **10** and includes a first vertical portion terminating at first input port **88** that communicates with upper surface **18** of microfluidic device **10** and a second vertical portion terminating at a second input port **92** also communicating with upper surface **18** of microfluidic device **10**. First and second input ports **88** and **92**, respectively, are positioned in close proximity to output port **72** of second channel **62**, for reasons hereinafter described. In addition, first and second input ports **88** and **92**, respectively, of channel **82** are interconnected by and communicate with first end **94** of horizontal portion **84** of channel **82**. Horizontal portion **84** of third channel **82** further includes a second end **98** communicating with output port **102** that communicates with upper surface **18** of microfluidic device **10**.

In operation, first, second and third channels **42**, **62** and **82**, respectively, of channel network **40** are filled with a fluid. Referring to FIG. **15**, drop **104** is placed on output port **72** of second channel **62**. Drop **104** is of sufficient size to overlap output port **72**, but does not communicate with first and second input ports **88** and **92**, respectively, of third channel **82**. In addition, drop **105** is positioned on output port **102** of third channel **82**. Drop **105** has a radius of curvature greater than the radius of curvature of drop **104**. Thereafter, if first drop **76** is placed on input port **48** of first channel **42**, that drop **76** will be pumped to output port **72**, thereby increasing the size of drop **104**, FIG. **16**. However, drop **104** will not grow to such size as to overlap and communicate with first and second input ports **88** and **92**, respectively, of third channel **82**. As such, the value at output port **72** would be 1, while the values of input ports **48** and **52** would be 0. Similarly, if second drop **80** is placed on input port **52** of first channel **42**, second drop **80** is pumped to the output port **72**, thereby increasing the size of drop **104**, FIG. **16**. However, drop **104** will not grow to such a size as to overlap and communicate with first and second input ports **88** and **92**, respectively, of third channel **82**. As such, the value at output port **72** would be 1, while the values of input ports **48** and **52**, respectively, would be 0. Finally, if first and second drops **76** and **80**, respectively, are placed on input ports **48** and **52** of first channel **42**, first and second drops **76** and **80**, respectively, are pumped to output port **72**. The resulting fluid flow of the first and second drops **76** and **80**, respectively, increases the size of drop **104** such that drop **104** communicates with first and second input ports **88** and **92**, respectively, of third channel **82**. Drop **104** is then be pumped away through third channel **82** to output port **102**, leaving an output of 0 at output port **72** of second channel **62**, FIG. **17**.

It can be appreciated that the NAND gate, heretofore described, can be operated as a NOR gate by increasing the size of drop **104** on output port **72** or the size of drops **76** and **80** on first and second input ports **48** and **52**, respectively, of first channel **42**. More specifically, if first drop **76** is placed on input port **48** of first channel **42**, that drop **76** will increase the size of drop **104** to a sufficient dimension so as to overlap and communicate with first and second input ports **88** and **92**, respectively, of third channel **82**. Drop **104** is then pumped away through third channel **82** to output port **102**, leaving an output of 0 at output port **72** of second channel **62**, FIG. **17**. Similarly, if second drop **80** is placed on input port **52** of first channel **42**, second drop **80** is pumped to output port **72**, thereby increasing the size of drop **104**. Drop **104** is then pumped away through third channel **82** to output port **102**, leaving an output of 0 at output port **72** of second channel **62**, FIG. **17**. Finally, if first and second drops **76** and **80**, respectively, are placed on input ports **48** and **52**, respectively, of first channel **42**, first and second drops **76** and **80**, respectively, are pumped to output port **72**. The resulting fluid flow of the first and second drops **76** and **80**, respectively, increases the size of drop **104** such that drop **104** communicates with first and second input ports **88** and **92**, respectively, of third channel **82**. Drop **104** is then pumped away through third channel **82** to output port **102**, leaving an output of 0 at output port **72** of second channel **62**, FIG. **17**.

An XNOR gate can be formed by modifying the third channel **82** of the NAND/NOR design to have a high fluidic resistance. Output port **72** of second channel **62** of the XNOR gate is primed with drop **104**, as with the NAND/NOR configuration. A single drop either **76** or **80** on either first or second input ports **48** and **52**, respectively, of first channel **42**, is sufficient to increase the size of drop **104** such that drop **104** communicates with first and second input ports **88** and **92**, respectively, of third channel **82**. Drop **104** is then be pumped away through third channel **82** to output port **102**, though at a slower rate than in the case of the NOR gate, leaving an output of 0 at output port **72** of second channel **62**. The addition of a second drop **76** or **80** on the other of the first or second input ports **48** and **52**, respectively, of first channel **42**, can then be used to increase the volume of drop **104** such that drop **104** is larger than drop **105** positioned on output port **102** of third channel **82**, provided that drop **104** grows at a much faster rate than drop **105**. Thus, the drop **104** remains only if the values at first and second input ports **48** and **52**, respectively, are either 0/0 or 1/1.

In view of the foregoing, it can be appreciated that multi-channel designs can also be used to merge and split individual drop. For example, channels may be used to either split an individual drop or merge two separate drops. The output drops of a central channel can be split between two side channels if the radius of curvature of the drop is smaller than both of the outer channels. Alternatively, a central drop can be used to mix the two drops from corresponding feeder channels if the radius of curvature of the central drop is larger than the radius of curvature of the drops from the feeder channels. Further, a number of channels can be connected in series by using the output of a preceding channel as the input for next channel. In addition to potentially enabling several gates to be connected in series, the cascading nature of some of the gates confers a degree of temporal control over subsequent pumping steps. That is, a set amount of time may be required for the initial input drop(s) to be pumped through a given channel before the output drop will reach a critical size to carry out the next pumping step.

Referring to FIG. **18**, a passive timer may be constructed with a two-channel design similar to the NAND gate. More specifically, microfluidic device **10** may include a channel network **120** having a first channel **122** extending through microfluidic device **10**. First channel **122** includes a first vertical portion terminating at an input port **128** that communicates with upper surface **18** of microfluidic device **10** and a second vertical portion terminating at an output port **132** also communicating with upper surface **18** of microfluidic device **10**. First and second input ports **128** and **132**, respectively, of channel **122** are interconnected by and communicate with horizontal portion **134** of channel **122**. First channel **122** is made with a high fluidic resistance that acts like an hourglass of sorts, with fluid moving from one end of the channel to the other.

Channel network **120** further includes a second channel **142**. Second channel **142** extends through microfluidic device **10** and includes a first vertical portion terminating at first input port **148** that communicates with upper surface **18** of microfluidic device **10** and a second vertical portion terminating at a second input port **152** also communicating with upper surface **18** of microfluidic device **10**. First and second input ports **148** and **152**, respectively, are positioned in close proximity to output port **132** of first channel **122**, for reasons hereinafter described. First and second input ports **148** and **152**, respectively, of second channel **142** are interconnected by and communicate with first end **144** of horizontal portion **145** of second channel **142**. Horizontal portion **145** of second channel **142** further includes a second end **158** communicating with output port **162** that, in turn, communicates with upper surface **18** of microfluidic device **10**.

In operation, output drops **164** and **166** are placed on corresponding output ports **132** and **162**, respectively, of first and second channels **122** and **142**, respectively, FIG. **19**. Thereafter, a first input drop is deposited on input port **128** of first channel **122** such that fluid is pumped through the high-resistance first channel **122** to output port **132**. The output drop **164** eventually grows large enough to overlap inlet ports **148** and **152** of second channel **142**, creating a fluid connection between the first and second channels **122** and **142**, respectively. If the pressure in output drop **164** is greater than the pressure at output port **162** of second channel **142**, the fluid connecting the two channels will be pumped through second channel **142**. Output drop **164** may be completely pumped away or a portion of the liquid can be left behind to maintain the connection, depending on the design of output port **132**. The time required to achieve fluidic connection is determined by the fluid resistance of first channel **122**, i.e., the dimensions of first channel **122**, and by the size of the inlet drop and output drops **164** and **166**.

It can be appreciated that a central channel with multiple input ports can be used to provide variable fluidic resistance, thereby allowing for a wide range of times to be set using a single device. Time delays ranging from a few seconds to a number of hours can be achieved by varying the channel resistance and initial pressure differential. Further, multiple timing channels can be used to carry out a series of treatments on an individual channel. In addition, the multi-inlet design used for the variable timer structure can also be used to generate continuous slow perfusion by connecting each input port directly to a central channel having portions of both high and low fluidic resistance. The flow rate varies over the course of the pumping due to the changing volume of the source (input port) and sink (output port) drop; however, the variation is gradual because the volumetric flow rate is small relative to the overall drop size for a significant portion of the process. The variation in flow rate can be partially compensated for by using several drops along a multi-inlet path. Drops furthest away from the sink (output port) will not add significantly to the flow into the central channel, but will slowly replenish source drops closer to the central channel. Transient flows can be observed when a small drop is placed between two relatively larger droplets with different volumes and resistance paths. Such an approach could be used to achieve timed dosing of samples, provided reactive components are appropriately isolated.

It can be appreciated that the present method provides a simple way to integrate functionalities into microfluidic devices without adding complexity to the fabrication process and to limit the dependence on external equipment. The method can be implemented in a high throughput manner with the use of multi-channel pipettes and robotic dispensers. While the current designs use the active placement of drops, platforms could also be constructed using responsive hydrogels to initiate fluid movement without deviating from the scope of the present invention. For example, the input ports could be isolated from the output drop by a hydrogel wall. If a certain condition is met in the solution, such as a pH, the wall could shrink to fluidly connect the input to the output.

Various modes of carrying out the invention are contemplated as being within the scope of the following claims particularly pointing out and distinctly claiming the subject matter, which is regarded as the invention.

We claim:

1. A method of controlling communication between multiple ports in a microfluidic device, comprising:

providing a first channel network in the microfluidic device, the first channel network including a first channel having a first input port, a second channel having a second input port, and an output port communicating with the first and second channels;

providing a second channel network in the microfluidic device, the second channel network including a channel input port in proximity to the output port of the first channel network and an output port;

filling the first and second channel networks with a fluid;

providing air-liquid interfaces at the output ports of the first and second channel networks, the air-liquid interfaces having radii of curvatures;

depositing a first input droplet having a radius of curvature on the first input port, the first input droplet flowing toward the output port of the first channel network in response to the first input droplet having a radius of curvature less than the radius of curvature of the air-liquid interface and forming a first output droplet having a dimension on the output port of the first channel network;

depositing a second input droplet having a radius of curvature on the second input port, the second input droplet flowing toward the output port of the first channel network in response to the second input droplet having a radius of curvature less than the radius of curvature of the air-liquid interface and increasing the dimension of the first output droplet on the output port of the first channel network; and

wherein the first output droplet flows into the input port of the second channel network towards the output port of the second channel network in response to the dimension of the first outlet droplet exceeding a threshold.

2. The method of claim **1** wherein the first output droplet flows toward the first input port when the first input droplet has a radius of curvature greater than the radius of curvature of the first output droplet.

3. The method of claim **2** wherein the first output droplet flows toward the second input port in response to the radius of curvature of the second input droplet being greater than the radius of curvature of the first output droplet.

4. The method of claim **1** wherein the threshold is a predetermined volume.

5. The method of claim **1** comprising the additional step of depositing a second output droplet on the output port of the second channel network , the second output droplet having a radius of curvature wherein the first output droplet flows toward the output port of the second channel network in response to the first output droplet communicating with the input port of the second channel network and having a radius of curvature less than the radius of curvature of the second output droplet on the output port of the second channel network.

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