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(54) **METHOD OF PUMPING FLUID THROUGH A MICROFLUIDIC DEVICE**

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(51) **Int. Cl.**
***G01N 15/06*** (2006.01)

(52) **U.S. Cl.**
USPC ............ **436/180**; 422/50; 422/68.1; 422/503; 422/504; 422/509; 436/43

(58) **Field of Classification Search**
USPC .................. 422/50, 68.1, 502, 503, 504, 509; 436/43, 180
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

| | | | | |
|---|---|---|---|---|
| 6,012,902 | A | 1/2000 | Parce | |
| 6,090,251 | A | 7/2000 | Sundberg et al. | |
| 6,171,067 | B1 | 1/2001 | Parce | |
| 6,174,675 | B1 | 1/2001 | Chow et al. | |
| 6,210,128 | B1 | 4/2001 | Rife et al. | |
| 6,224,728 | B1 | 5/2001 | Oborny et al. | |
| 6,262,519 | B1 | 7/2001 | Furlani et al. | |
| 6,274,089 | B1 | 8/2001 | Chow et al. | |
| 6,296,452 | B1 | 10/2001 | Caren | |
| 6,318,970 | B1 | 11/2001 | Backhouse | |
| 6,368,562 | B1 | 4/2002 | Yao | |
| 6,739,576 | B2 | 5/2004 | O'Connor et al. | |
| 6,767,706 | B2 | 7/2004 | Quake et al. | |
| 6,949,176 | B2 | 9/2005 | Vacca et al. | |
| 7,156,969 | B2 | 1/2007 | Mehta et al. | |
| 7,189,580 | B2 | 3/2007 | Beebe et al. | |
| 7,223,363 | B2 * | 5/2007 | McNeely et al. | 422/417 |
| 7,290,441 | B2 * | 11/2007 | Baek | 73/54.09 |
| 2003/0132112 | A1 * | 7/2003 | Beebe et al. | 204/450 |
| 2003/0203506 | A1 | 10/2003 | Beebe et al. | |
| 2004/0115830 | A1 | 6/2004 | Touzov | |
| 2007/0034270 | A1 | 2/2007 | Yang et al. | |

OTHER PUBLICATIONS

"Macro-to-Micro Interfaces for Microfluidic Devices", Miniaturization for Chemisty, Biology & Bioengineering; vol. 4, pp. 526-533, Jul. 13, 2004, by Carl K. Fredrickson and Z. Hugh Fan.

"Well-Plate Formats and Microfluidics—Applications of Laminar Fluid Diffusion Interfaces to HTP Screening", Micro Total Analysis Systems 2001, pp. 383-384, by Bernard H. Weigl et al.

* cited by examiner

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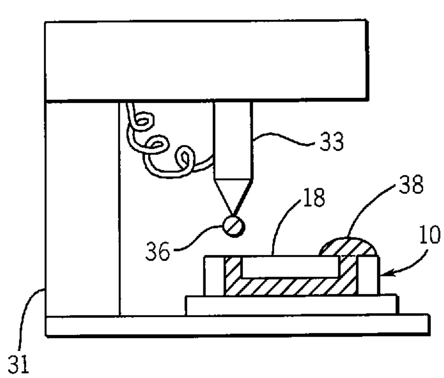
(57) **ABSTRACT**

A method is provided for pumping fluid through a channel of a microfluidic device. The channel has an input port and an output port. The channel is filled with fluid and a pressure gradient is generated between the fluid at the input port and the fluid at the output port. As a result, fluid flows through the channel towards the output port.

**4 Claims, 3 Drawing Sheets**



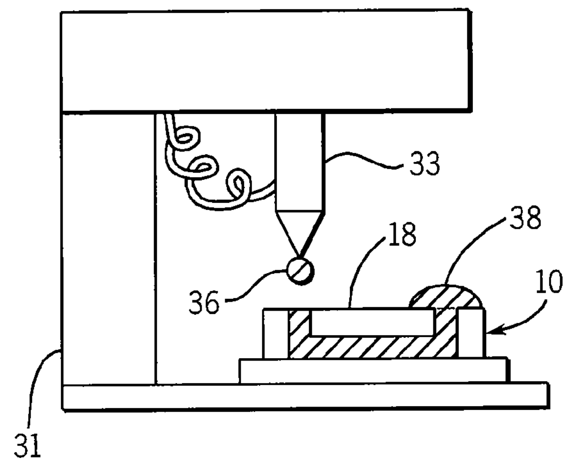



FIG. 1

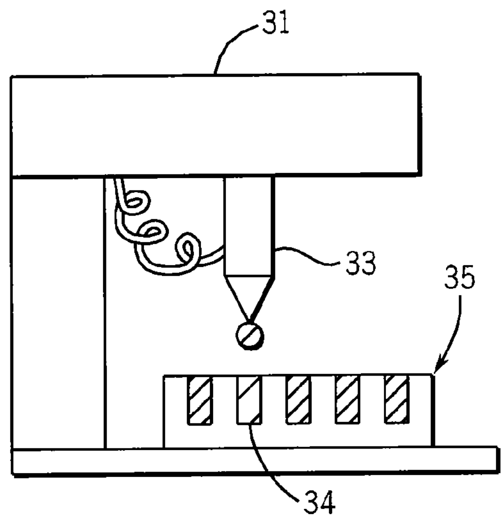



FIG. 2

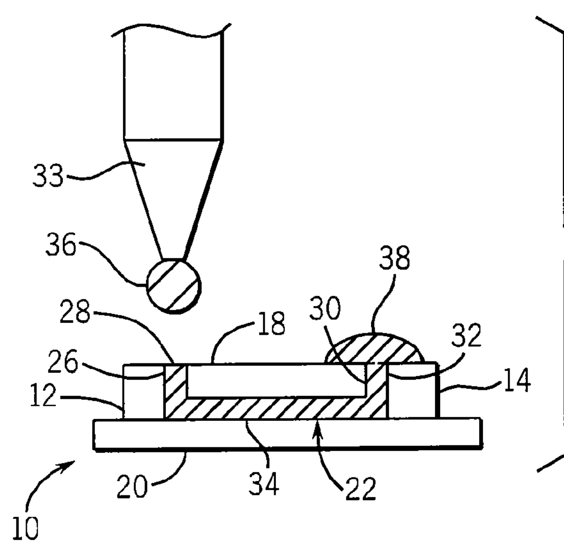



FIG. 3

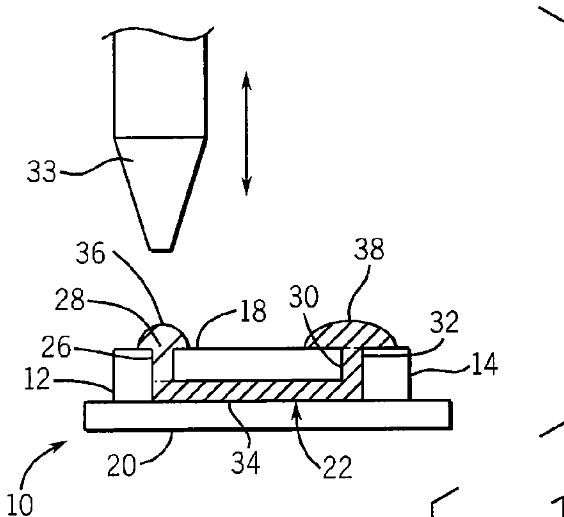
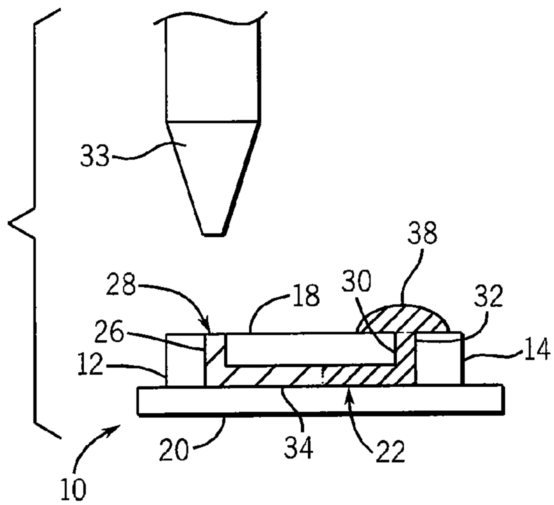



FIG. 4

FIG. 5



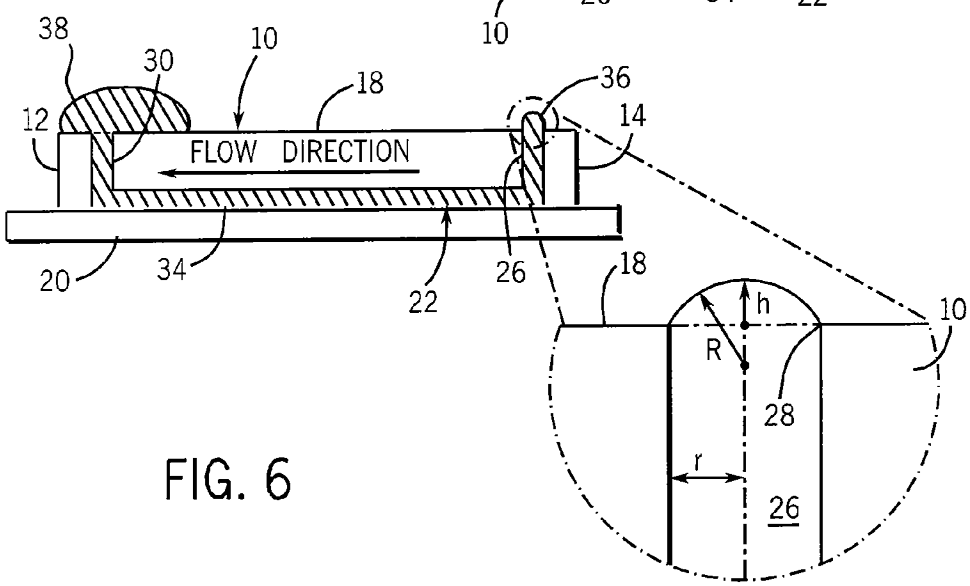




FIG. 6

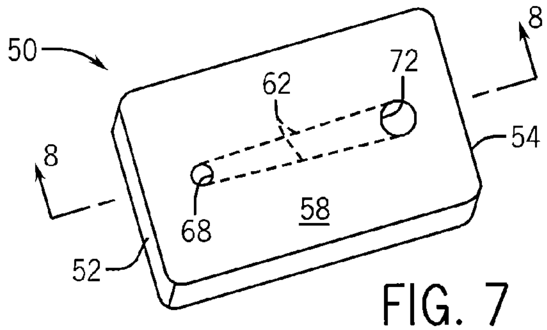



FIG. 7

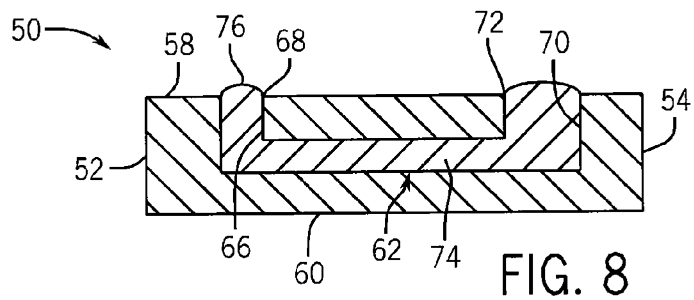



FIG. 8

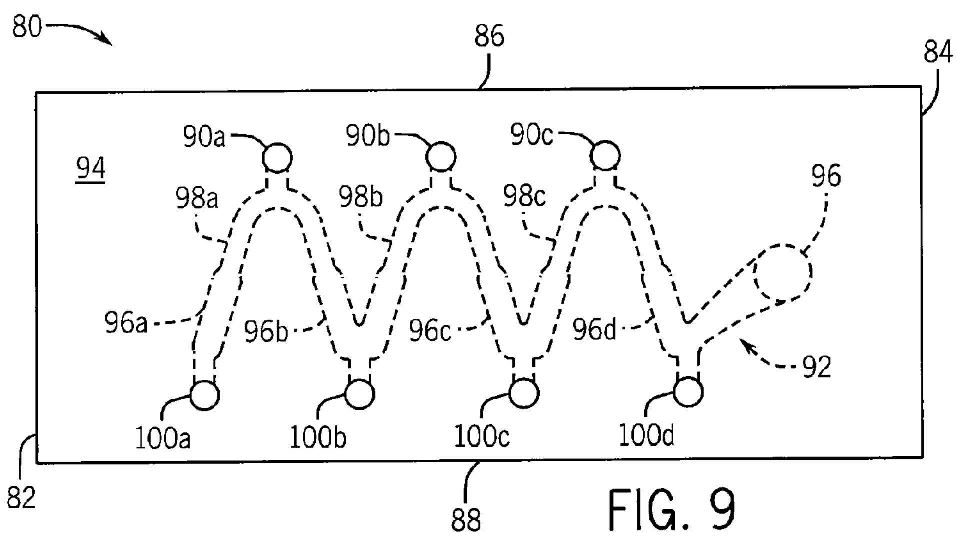



FIG. 9

# METHOD OF PUMPING FLUID THROUGH A MICROFLUIDIC DEVICE

## CROSS-REFERENCE TO RELATED APPLICATION

This application is a divisional of Ser. No. 11/684,949, filed Mar. 12, 2007 now U.S. Pat. No. 8,053,249.

## REFERENCE TO GOVERNMENT GRANT

This invention was made with government support under W81XWH-04-1-0572 awarded by the ARMY/MRMC, F30602-00-2-0570 awarded by the DOD/DARPA, and CA104162 awarded by the National Institutes of Heath. The government has certain rights in the invention.

## FIELD OF THE INVENTION

This invention relates generally to microfluidic devices, and in particular, to a method of pumping fluid through a channel of a microfluidic device.

## BACKGROUND AND SUMMARY OF THE INVENTION

As is known, microfluidic devices are being used in an increasing number of applications. However, further expansion of the uses for such microfluidic devices has been limited due to the difficulty and expense of utilization and fabrication. It can be appreciated that an efficient and simple method for producing pressure-based flow within such microfluidic devices is mandatory for making microfluidic devices a ubiquitous commodity.

Several non-traditional pumping methods have been developed for pumping fluid through a channel of a microfluidic device, including some which have displayed promising results. However, the one drawback to almost all pumping methods is the requirement for expensive or complicated external equipment, be it the actual pumping mechanism (e.g., syringe pumps), or the energy to drive the pumping mechanism (e.g., power amplifiers). The ideal device for pumping fluid through a channel of a microfluidic device would be semi-autonomous and would be incorporated totally at the microscale.

The most popular method of moving a fluid through a channel of a microfluidic device is known as electrokinetic flow. Electrokinetic flow is accomplished by conducting electricity through the channel of the microfluidic device in which pumping is desired. While functional in certain applications, electrokinetic flow is not a viable option for moving biological samples through a channel of a microfluidic device. The reason is twofold: first, the electricity in the channels alters the biological molecules, rendering the molecules either dead or useless; and second, the biological molecules tend to coat the channels of the microfluidic device rendering the pumping method useless. Heretofore, the only reliable way to perform biological functions within a microfluidic device is by using pressure-driven flow. Therefore, it is highly desirable to provide a more elegant and efficient method of pumping fluid through a channel of a microfluidic device.

In addition, as biological experiments become more complex, an unavoidable fact necessitated by the now apparent complexity of genome-decoded organisms, is that more complex tools will be required. Presently, in order to simultaneously conduct multiple biological experiments, plates having a large number (e.g. either 96 or 384) of wells are often used. The wells in these plates are nothing more than holes that hold liquid. While functional for their intended purpose, it can be appreciated that these multi-well plates may be used in conjunction with or may even be replaced by microfluidic devices.

To take advantage of existing hardware, "sipper" chips have been developed. Sipper chips are microfluidic devices that are held above a traditional 96 or 384 well plate and sip sample fluid from each well through a capillary tube. While compatible with existing hardware, sipper chips add to the overall complexity, and hence, to the cost of production of the microfluidic devices. Therefore, it would be highly desirable to provide a simple, less expensive alternative to devices and methods heretofore available for pumping fluid through a channel of a microfluidic device.

Therefore, it is a primary object and feature of the present invention to provide a method of pumping fluid through a channel of a microfluidic device which is simple and inexpensive.

It is a further object and feature of the present invention to provide a method of pumping fluid through a channel of a microfluidic device which is semi-autonomous and requires only minimal additional hardware.

It is a still further object and feature of the present invention to provide a method of pumping fluid through a channel of a microfluidic device which is compatible with preexisting robotic high throughput equipment.

In accordance with the present invention, a method of pumping sample fluid through a channel of a microfluidic device is provided. The method includes the step of providing the channel with an input and an output. The channel is filled with a channel fluid. A first pumping drop of the sample fluid is deposited at the input of the channel such that the first pumping drop flows into the channel through the input.

A second pumping drop of the sample fluid may be deposited at the input of the channel after the first pumping drop flows into the channel. The input of the channel has a predetermined radius and the first pumping drop has a radius generally equal to the predetermined radius of the input of the channel. The first pumping drop has an effective radius of curvature and the fluid at the output has an effective radius of curvature. The effective radius of curvature of the fluid output is greater than the effective radius of curvature of the first pumping drop.

The first pumping drop has a user selected volume and projects a height above the microfluidic device when deposited at the input of the channel. The radius of the first pumping drop is calculated according to the expression:

$$R = \left[\frac{3V}{\pi} + h^3\right]\frac{1}{3h^2}$$

wherein: R is the radius of the first pumping drop; V is the user selected volume of the first pumping drop; and h is the height of the first pumping drop above the microfluidic device.

The method may include the additional step of sequentially depositing a plurality of pumping drops at the input of the channel after the first pumping drop flows into the channel. Each of the plurality of pumping drops is sequentially deposited at the input of the channel as the previously deposited pumping drop flows into the channel. The first pumping drop has a volume and the plurality of pumping drops have volumes generally equal to the volume of the first pumping drop.

It is contemplated for the channel fluid to be the sample fluid.

The method may also include the additional step of varying the flow rate of first pumping drop through the channel. The channel has a cross-sectional area and the step of varying the flow rate of first pumping drop through the channel includes the step of reducing the cross-sectional area of at least a portion of the channel.

In accordance with a still further aspect of the present invention, a method of pumping fluid is provided. The method includes the step of providing a microfluidic device having a channel therethough. The channel includes a first input port and a first output port. The channel is filled with fluid and a pressure gradient is generated between the fluid at the input port and the fluid at the output port such that the fluid flows through the channel towards the output port.

The step of generating the pressure gradient includes the step of sequentially depositing pumping drops of fluid at the input port of the channel. Each of the pumping drops has a radius generally equally to the predetermined radius of the input port of the channel. Each of the pumping drops has an effective radius of curvature and the fluid at the first output port has an effective radius of curvature. The effective radius of curvature of the fluid at the output port is greater than the effective radius of curvature of each pumping drop.

The channel has a resistance and each of the pumping drops has a radius and a surface free energy. The fluid at the first output port has a height and a density such that the fluid flows through the channel at a rate according to the expression:

$$\frac{dV}{dt} = \frac{1}{Z}\left(\rho gh - \frac{2\gamma}{R}\right)$$

wherein: dV/dt is the rate of fluid flowing through the channel; Z is the resistance of the channel; $\rho$ is the density of the fluid at the first output port; g is gravity; h is the height of the fluid at the output port; $\gamma$ is the surface free energy of the pumping drops; and R is the radius of the pumping drops.

In accordance with a still further aspect of the present invention, a method of pumping fluid through a channel of a microfluidic device is provided. The channel has a first input port and an output port. The channel is filled with fluid and pumping drops of fluid are sequentially deposited at the first input port of the channel to generate a pressure gradient between fluid at the input port and fluid at the output port. As a result, the fluid in the channel flows toward the output port.

Each of the pumping drops has an effective radius of curvature and the fluid at the first output port has an effective radius of curvature. The effective radius of curvature of the fluid at the output port is greater than the effective radius of curvature of each pumping drop. In addition, each of the pumping drops has a radius generally equally to the predetermined radius of the input port of the channel.

The method may also include the additional step of varying the flow rate of first pumping drop through the channel. The channel has a cross-sectional area and the step of varying the flow rate of first pumping drop through the channel includes the step of reducing the cross-sectional area of at least a portion of the 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 a schematic view of a robotic micropipetting station for depositing drops of liquid on the upper surface of a microfluidic device;

FIG. **2** is a schematic view of the robotic micropipetting station of FIG. **1** depositing drops of liquid in a well of a multi-well plate;

FIG. **3** is an enlarged, schematic view of the robotic micropipetting station of FIG. **1** showing the depositing of a drop of liquid on the upper surface of a microfluidic device by a micropipette;

FIG. **4** is a schematic view, similar to FIG. **3**, showing the drop of liquid deposited on the upper surface of the microfluidic device by the micropipette;

FIG. **5** is a schematic view, similar to FIGS. **3** and **4**, showing the drop of liquid flowing into a channel of the microfluidic device by the micropipette;

FIG. **6** is an enlarged, schematic view showing the dimensions of the drop of liquid deposited on the upper surface of the microfluidic device by the micropipette;

FIG. **7** is an isometric view of an alternate embodiment of a microfluidic device for use in the methodology of the present invention;

FIG. **8** is a cross sectional view of the microfluidic device taken along line **8-8** of FIG. **7**; and

FIG. **9** is a top plan view of a still further embodiment of a microfluidic device for use in the methodology of the present invention.

## DETAILED DESCRIPTION OF THE DRAWINGS

Referring to FIGS. **1** and **3-6**, 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), for reasons hereinafter described, 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** are arbitrary.

A robotic micropipetting station **31** is provided and includes micropipette **33** for depositing drops of liquid, such as pumping drop **36** and reservoir drop **38**, on upper surface **18** of microfluidic device **10**, for reasons hereinafter described. Modern high-throughput systems, such as robotic micropipetting station **31**, are robotic systems designed solely to position a tray (i.e. multiwell plate **35**, FIG. **2**, or microfluidic device **10**, FIG. **1**) and to dispense or withdraw microliter drops into or out of that tray at user desired locations (i.e. well **34** of multiwell plate **35** or the input and output ports **28** and **32**, respectively, of channel **22** of microfluidic device **10**) with a high degree of speed, precision, and repeatability.

The amount of pressure present within a pumping drop **36** 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 $\gamma$ is the surface free energy of the liquid; and R1 and R2 are the radii of curvature for two axes normal to each other that describe the curvature of the surface of pumping drop **36**.

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

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

wherein: R is the radius of the spherical pumping drop **36**, FIG. **6**.

From Equation (2), it can be seen that smaller drops have a higher internal pressure than larger drops. Therefore, if two drops of different size are connected via a fluid-filled tube (i.e. channel **22**), the smaller drop 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. In view of the foregoing, it can be appreciated that fluid can be pumped through channel **22** by using the surface tension in pumping drop **36**, as well as, input port **28** and output port **32** of channel **22**.

In accordance with the pumping method of the present invention, fluid is provided in channel **22** of microfluidic device **10**. Thereafter, a large reservoir drop **38** (e.g., 100 µL), is deposited by micropipette **33** over output port **32** of channel **22**, FIG. **3**. The radius of reservoir drop **38** is greater than the radius of output port **32** and is of sufficient dimension that the pressure at output port **32** of channel **22** is essentially zero. A pumping drop **36**, of significantly smaller dimension than reservoir drop **38**, (e.g., 0.5-5 µL), is deposited on input port **28** of channel **22**, FIGS. **4** and **6**, by micropipette **33** of robotic micropipetting station **31**, FIG. **1**. Pumping drop **36** may be hemispherical in shape or may be other shapes. As such, it is contemplated that the shape and the volume of pumping drop **36** be defined by the hydrophobic/hydrophilic patterning of the surface surrounding input port **28** in order to extend the pumping time of the method of the present invention. As heretofore described, microfluidic device **10** is formed from PDMS which has a high hydrophobicity and has a tendency to maintain the hemispherical shapes of pumping drop **36** and reservoir drop **38** on input and output ports **28** and **32**, respectively. It is contemplated as being within the scope of the present invention that the fluid in channel **22**, pumping drops **36** and reservoir drop **38** be the same liquid or different liquids.

Because pumping drop **36** has a smaller radius than reservoir drop **38**, a larger pressure exists on the input port **28** of channel **22**. The resulting pressure gradient causes the pumping drop **36** to flow from input port **28** through channel **22** towards reservoir drop **38** over output port **32** of channel **22**, FIG. **5**. It can be understood that by sequentially depositing additional pumping drops **36** on input port **28** of channel **22** by micropipette **33** of robotic micropipetting station **31**, the resulting pressure gradient will cause the pumping drops **36** deposited on input port **28** to flow through channel **22** towards reservoir drop **38** over output port **32** of channel **22**. As a result, fluid flows through channel **22** from input port **28** to output port **32**.

Referring back to FIG. **6**, the highest pressure attainable for a given radius, R, of input port **28** of channel **22** is a hemispherical drop whose radius is equal to the radius, r, of input port **28** of channel **22**. Any deviation from this size, either larger or smaller, results in a lower pressure. As such, it is preferred that the radius of each pumping drop **36** be generally equal to the radius of input port **28**. The radius (i.e., the radius which determines the pressure) of pumping drop **36** can be determined by first solving for the height, h, that pumping drop **36** rises above a corresponding port, i.e. input port **28** of channel **22**. The pumping drop **36** radius can be calculated according to the expression:

$$R = \left[\frac{3V}{\pi} + h^3\right]\frac{1}{3h^2} \quad \text{Equation (3)}$$

wherein: R is the radius of pumping drop **36**; V is the user selected volume of the first pumping drop; and h is the height of pumping drop **36** above upper surface **18** of microfluidic device **10**.

The height of pumping drop **36** of volume V can be found if the radius of the spherical cap is also known. In the present application, radius of the input port **28** is the spherical cap radius. As such, the height of pumping drop **36** may be calculated according to the expression:

$$h = \frac{1}{6}\left[108b + 12(12a^3 + 81b^2)^{\frac{1}{2}}\right]^{\frac{1}{3}} - \frac{2a}{\left[108b + 12(12a^3 + 81b^2)^{\frac{1}{2}}\right]^{\frac{1}{3}}} \quad \text{Equation (4)}$$

wherein: $a=3r^2$ (r is the radius of input port **28**); and $b=6\,V/\pi$ (V is the volume of pumping drop **36** placed on input port **28**).

The volumetric flow rate of the fluid flowing from input port **28** of channel **22** to output port **32** of channel **22** will change with respect to the volume of pumping drop **36**. Therefore, the volumetric flow rate or change in volume with respect to time can be calculated using the equation:

$$\frac{dV}{dt} = \frac{1}{Z}\left(\rho g h - \frac{2\gamma}{R}\right) \quad \text{Equation (5)}$$

wherein: dV/dt is the rate of fluid flowing through channel **22**; Z is the flow resistance of channel **22**; $\rho$ is the density of pumping drop **36**; g is gravity; h is the height of reservoir drop **38**; $\gamma$ is the surface free energy of pumping drop **36**; and R is the radius of the pumping drops **36**.

It is contemplated that various applications of the method of the present invention are possible without deviating from the present invention. By way of example, multiple input ports could be formed along the length of channel **22**. By designating one of such ports as the output port, different flow rates could be achieved by depositing pumping drops on different input ports along length of channel **22** (due to the difference in channel resistance). In addition, temporary output ports **32** may be used to cause fluid to flow into them, mix, and then, in turn, be pumped to other output ports **32**. It can be appreciated that the pumping method of the present invention works with various types of fluids including water and biological fluids. As such fluid media containing cells and fetal bovine serum may be used to repeatedly flow cells down channel **22** without harming them.

Further, it is contemplated to etch patterns in upper surface **18** of microfluidic device **10** about the outer peripheries of input port **28** and/or output port **32**, respectively, in order to alter the corresponding configurations of pumping drop **36** and reservoir drop **38** deposited thereon. By altering the configurations of pumping and reservoir drops **36** and **38**, respectively, it can be appreciated that the volumetric flow rate of fluid through channel **22** of microfluidic device **10** may be modified. In addition, by etching the patterns in upper surface **18** of microfludic device **10**, it can be appreciated that the time period during which the pumping of the fluid through channel **22** of microfluidic device **10** takes place may be increased or decreased to a user desired time period.

As described, there are several benefits to use of the pumping method of the present invention. By way of example, the pumping method of the present invention allows high-throughput robotic assaying systems to directly interface with microfluidic device **10** and pump liquid using only micropipette **33**. In a lab setting manual pipettes can also be used, eliminating the need for expensive pumping equipment. Because the method of the present invention relies on surface tension effects, it is robust enough to allow fluid to be pumped in microfluidic device **10** in environments where physical or electrical noise is present. The pumping rates are determined by the volume of pumping drop **36** present on input port **28** of the channel **22**, which is controllable to a high degree of precision with modern robotic micropipetting stations **31**. The combination of these factors allows for a pumping method suitable for use in a variety of situations and applications.

Referring to FIGS. **7** and **8**, an alternate embodiment of a microfluidic device for use in the methodology of the present invention is generally designated by the reference numeral **50**. Microfluidic device **50** may be formed from polydimethylsiloxane (PDMS), for reasons hereinafter described, and has first and second ends **52** and **54**, respectively, and upper and lower surfaces **58** and **60**, respectively. Channel **62** extends through microfluidic device **50** and includes first vertical portion **66** terminating at input port **68** that communicates with upper surface **58** of microfluidic device **50** and second vertical portion **70** terminating at output port **72** that also communicates with upper surface **58** of microfluidic device **50**. First and second vertical portions **66** and **70**, respectively, of channel **62** are interconnected by and communicate with horizontal portion **74** of channel **62**.

In accordance with the pumping method of the present invention, fluid is provided in channel **62** of microfluidic device **50**. Pumping drop **76** of substantially the same dimension as input port **68** of channel **62** is deposited thereon by micropipette **33** of robotic micropipetting station **31**, FIG. **1**. Pumping drop **76** may be hemispherical in shape or may be other shapes. As such, it is contemplated that the shape and the volume of pumping drop **76** be defined by the hydrophobic/hydrophilic patterning of the surface surrounding input port **68** in order to extend the pumping time of the method of the present invention. As heretofore described, microfluidic device **60** is formed from PDMS which has a high hydrophobicity and has a tendency to maintain the hemispherical shape of pumping drop **76** on input port **68**.

It is contemplated for pumping drop **76** deposited on input port **68** to have a predetermined effective radius of curvature that is less than the effective radius of the curvature of the fluid at output port **72** of channel **62**, for reasons hereinafter described. As is known, the effective radius of curvature of a drop can be calculated according to the equation:

$$RC=(R1\times R2)/(R1+R2) \qquad \text{Equation (6)}$$

wherein RC is the radius of curvature; and R**1** and R**2** are the radii of the drop on orthogonal axes. In the case of a circle, R**1** and R**2** are equal. For an ellipse, R**1** and R**2** would be the radii of the major and minor axes respectively.

Referring to Equations (1) and (2), supra., it can be appreciated that drops having a smaller radius of curvature have a higher internal pressure. Therefore, if pumping drop **76** is connected to output port **72** via a fluid-filled tube (i.e. channel **62**), the pumping drop **76** will shrink and the fluid at output port **72** will grow if pumping drop **76** at input port **68** has a smaller radius of curvature than the meniscus of the fluid at output port **72**. As previously noted, the highest pressure attainable for a given radius, R, of pressure drop **76** at input port **68** of channel **62** is a hemispherical drop whose radius is equal to the radius, r, of input port **68** of channel **62**. As such, by depositing pumping drop **76** on input port **68**, the internal pressure of pumping drop **76** generates a pressure gradient that causes pumping drop **76** to flow from input port **68** through channel **62** towards reservoir output port **72** of channel **62**. It can be understood that by sequentially depositing additional pumping drops **76** on input port **68** of channel **62** by micropipette **33** of robotic micropipetting station **31**, the resulting pressure gradient will cause pumping drops **76** deposited on input port **68** to flow through channel **62** towards output port **72** of channel **62**. As a result, fluid flows through channel **62** from input port **68** to output port **72**.

As heretofore described, the volumetric flow rate of the fluid flowing from input port **68** of channel **62** to output port **72** of channel **62** will change with respect to the volume of pumping drop **76**. Therefore, the volumetric flow rate or change in volume with respect to time can be calculated using the equation:

$$\frac{dV}{dt} = \frac{1}{Z}\left(\rho gh - \frac{2\gamma}{R}\right) \qquad \text{Equation (7)}$$

wherein: dV/dt is the rate of fluid flowing through channel **62**; Z is the flow resistance of channel **62**; ρ is the density of the fluid at output port **72**; g is gravity; h is the height of the fluid (the meniscus) at output port **72**; γ is the surface free energy of pumping drop **76**; and R is the radius of the pumping drops **76**.

It is contemplated to vary the volumetric flow rate of the fluid flowing from an input port of a channel though a microfluidic device to an output port of the channel by varying the flow resistance of the channel. Referring to FIG. **9**, a still further embodiment of a microfluidic device for effectuating a method in accordance with the present invention is generally designated by the reference numeral **80**. Microfluidic device **80** includes first and second ends **82** and **84**, respectively, and first and second sides **86** and **88**, respectively. By way of example, a generally sinusoidal-shaped channel **92** extends through microfluidic device **80**. It can be appreciated that channel **92** may have other configurations without deviating from the scope of the present invention. Channel **92** terminates at output port **96** that communicates with upper surface **94** of microfluidic device **80**. Channel **92** further includes a plurality of enlarged diameter portions **96***a*-**96***d* and a plurality of reduced diameter portions **98***a*-**98***c*. Enlarged diameter portions **96***a*-**96***d* alternate with corresponding reduced diameter portions **98***a*-**98***c*, for reasons hereinafter described.

Input ports **90***a*-**90***c* communicate with upper surface **94** of microfluidic device **80** and with corresponding reduced diameter portions **98***a*-**98***c*, respectively, of channel **92**. Input ports **100***a*-**100***d* communicate with upper surface **94** of microfluidic device **80** and with corresponding enlarged diameter portions **96***a*-**96***d*, respectively, of channel **92**. Input ports **90***a*-**90***c* and **100***a*-**100***d* have generally identical dimensions. As depicted in FIG. **9**, input ports **90***a*-**90***c* and **100***a*-**100***d* are spaced along the sinusoidal path of channel **92** such that each input port **90***a*-**90***c* and **100***a*-**100***d* is a corresponding, predetermined distance from output port **96**.

In operation, fluid is provided in channel **92** of microfluidic device **80**. A pumping drop of substantially the same dimension as input ports **90***a*-**90***c* and **100***a*-**100***d* of channel **92** is deposited on one of the input ports **90***a*-**90***c* and **100***a*-**100***d* by micropipette **33** of robotic micropipetting station **31**, FIG. **1**. As heretofore described, the pumping drop may be hemispherical in shape or may be other shapes. As such, it is contemplated that the shape and the volume of pumping drop be defined by the hydrophobic/hydrophilic patterning of the surface surrounding the input port on which the pumping drop is deposited in order to extend the pumping time of the method of the present invention. As previously noted, microfluidic device **80** is formed from PDMS which has a high hydrophobicity and has a tendency to maintain the hemispherical shape of the pumping drop on its corresponding input port.

It is contemplated for the pumping drop deposited on a selected input port **90***a*-**90***c* and **100***a*-**100***d* to have a predetermined effective radius of curvature that is less than the effective radius of the curvature of the fluid at output port **96** of channel **92**. As previously noted, the highest pressure attainable for a given radius, R, of the pressure drop at the selected input port **90***a*-**90***c* and **100***a*-**100***d* of channel **92** is a hemispherical drop whose radius is equal to the radius, r, of the selected input port of channel **92**. By depositing the pumping drop on the selected input port, the internal pressure of the pumping drop on the selected input port generates a pressure gradient that causes the pumping drop to flow from the selected input port through channel **92** towards output port **96** of channel **92**. Since the input ports **90***a*-**90***c* and **100***a*-**100***d* have identical dimensions, fluid does not flow to the non-selected input ports. It can be understood that by sequentially depositing additional pumping drops on the selected input port of channel **92** by micropipette **33** of robotic micropipetting station **31**, the fluid flows through channel **92** from the selected input port to output port **96**.

It is contemplated to vary the volumetric flow rate of the fluid flowing from the selected input port of channel **92** though a microfluidic device to output port **96** of channel **92** by varying the flow resistance of channel **92**. It can be appreciated that the flow resistance of channel **92** is dependent upon on the input port **90***a*-**90***c* and **100***a*-**100***d* selected. More specifically, the flow resistance of channel **92** is greater in reduced diameter portions **98***a*-**98***c*. As a result, the fastest volumetric flow rate of the fluid flowing through channel **92** occurs when the pumping drops are deposited on input port **100***d*. On the other hand, the slowest volumetric flow rate of the fluid flowing through channel **92** occurs when the pumping drops are deposited on input port **100***d* wherein the fluid must pass through reduced diameter portions **98***a*-**98***c*. It can be appreciated that by depositing the pumping drops on input ports **90***a*-**90***c* and **100***b*-**100***c*, the volumetric flow rate of the fluid flowing through channel **92** can be adjusted between the fastest and slowest flow rate.

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 pumping fluid through a channel of a microfluidic device, the channel having a first input port having a cross-sectional area and an output port having a cross-sectional area greater than the cross-sectional area of the first input port, comprising the steps of:

filling the channel with fluid; and

sequentially depositing pumping drops of fluid at the first input port of the channel to generate a pressure gradient between fluid at the input port and fluid at the output port, each of the pumping drops having an effective radius of curvature and the fluid at the first output port having an effective radius of curvature greater than the effective radius of curvature of each pumping drop;

whereby the fluid in the channel flows toward the output port without use of an external device to facilitate the flow of fluid in the channel.

**2**. The method of claim **1** wherein each of the pumping drops has a radius generally equally to the predetermined radius of the input port of the channel.

**3**. The method of claim **1** comprising the additional step of varying the flow rate of first pumping drop through the channel.

**4**. The method of claim **1** wherein the channel has a cross-sectional area and wherein step of the flow rate of first pumping drop through the channel includes the step of reducing the cross-sectional area of at least a portion of the channel.

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