US008168133B2

(12) **United States Patent**
Beebe et al.

(10) **Patent No.: US 8,168,133 B2**
(45) **Date of Patent: May 1, 2012**

(54) **DEVICE FOR PERFORMING A HIGH THROUGHPUT ASSAY**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1672 days.

(21) Appl. No.: **11/124,936**

(22) Filed: **May 9, 2005**

(65) **Prior Publication Data**

US 2006/0263241 A1 Nov. 23, 2006

(51) **Int. Cl.**
G01N 21/75 (2006.01)

(52) **U.S. Cl.** **422/401**; 422/417; 422/68.1; 422/501; 436/180; 73/53.01

(58) **Field of Classification Search** 422/401, 422/417, 68.1, 501; 436/180; 73/53.01
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,695,765	B1 *	2/2004	Beebe et al.	600/33
2002/0182747	A1 *	12/2002	Beebe et al.	436/180
2003/0132112	A1 *	7/2003	Beebe et al.	204/450
2004/0152200	A1 *	8/2004	Deshmukh	436/86

OTHER PUBLICATIONS

"Macro-to-Micro Interfaces for Microfluidic Devices;" Miniaturization for Chemistry, Biology & Bioengineering; vol. 4, pp. 536-533, 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 device and method is provided for performing a high throughput assay. The device includes a plate structure having a plate and a plurality of microfluidic structures positioned thereon. Each microfluidic structure defines a channel having an input and an output. At least one of the input and the output of the channel of each of the plurality of mircofluidic structures includes a first plurality of ports. In operation, the channels are filled with fluid and pressure gradients are generated between the fluids at the inputs and the fluids at the outputs of the channels. As a result, fluid flows through the channels toward the outputs.

13 Claims, 3 Drawing Sheets

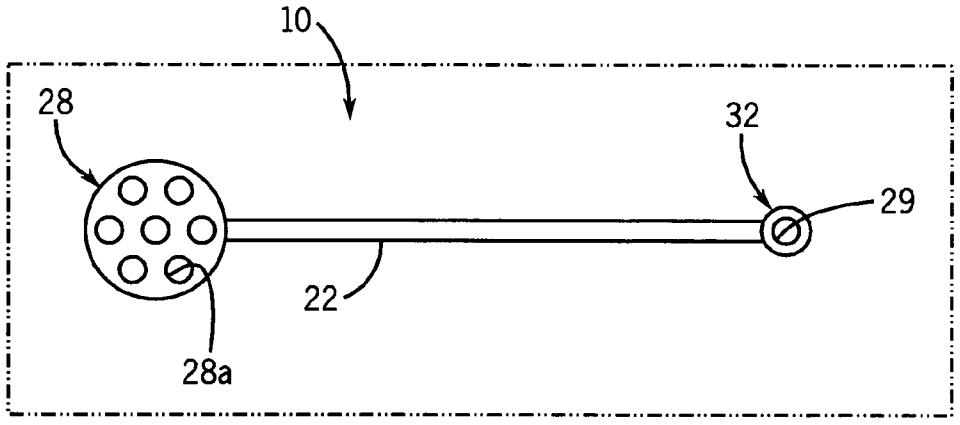
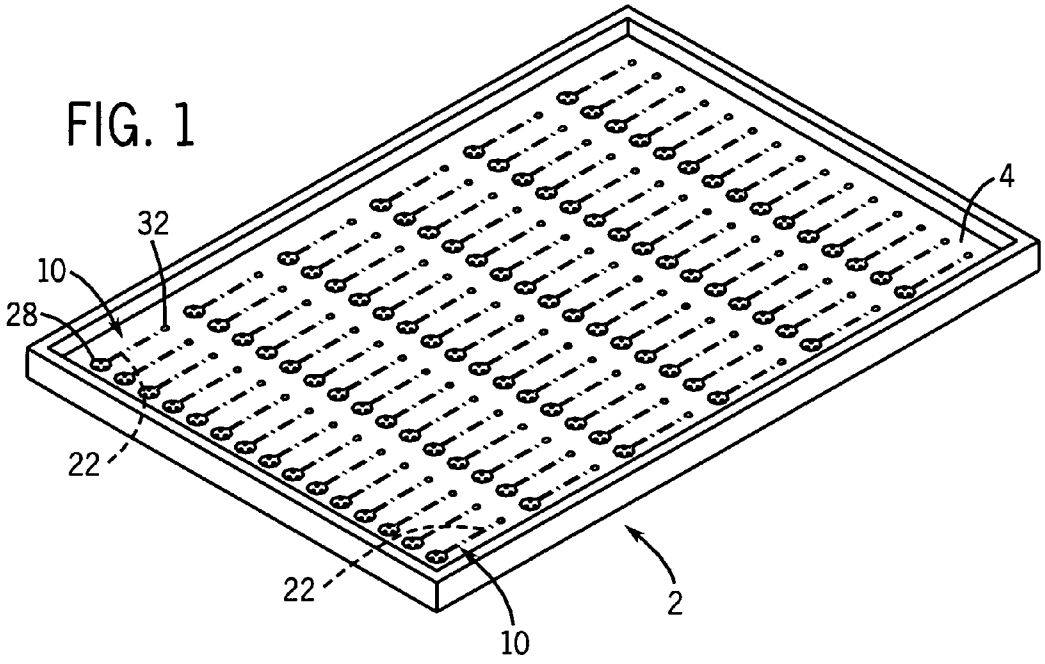


FIG. 1



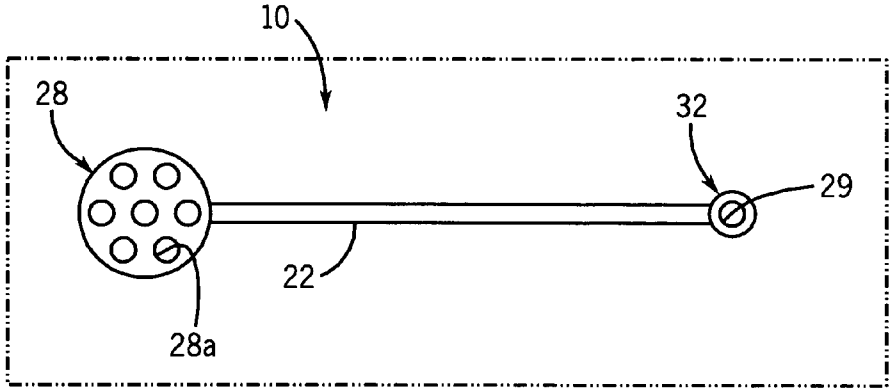


FIG. 2

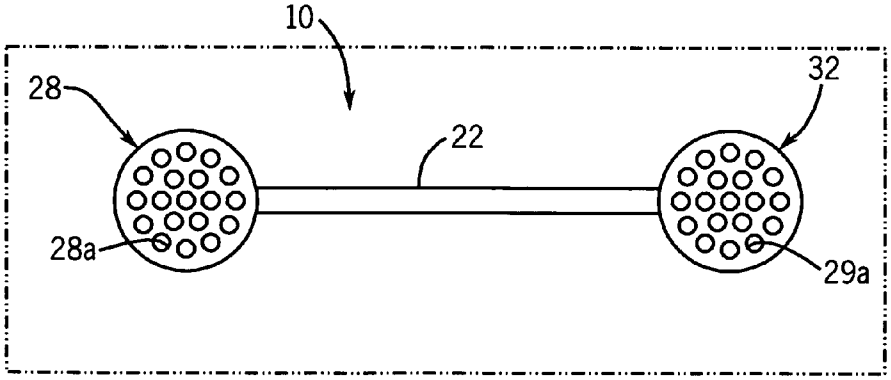


FIG. 9

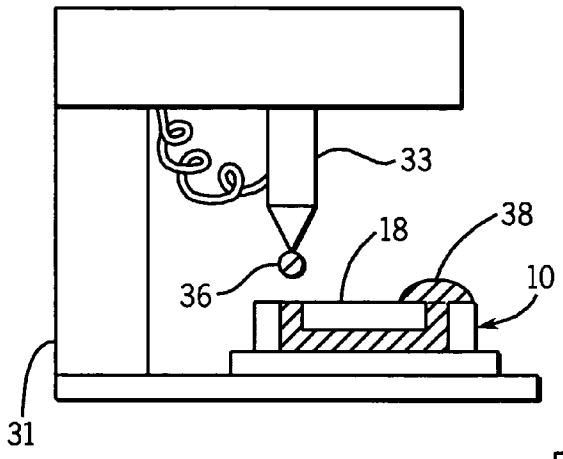


FIG. 3

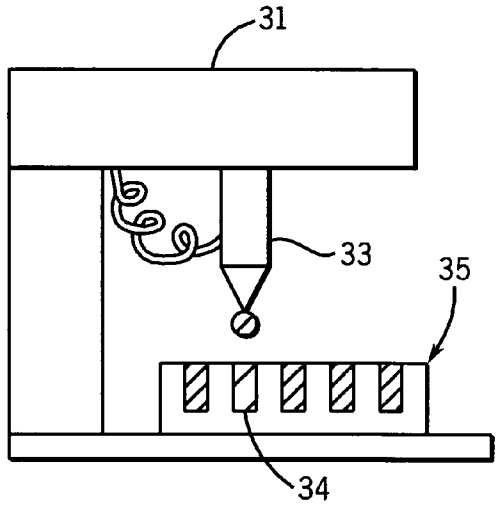


FIG. 4

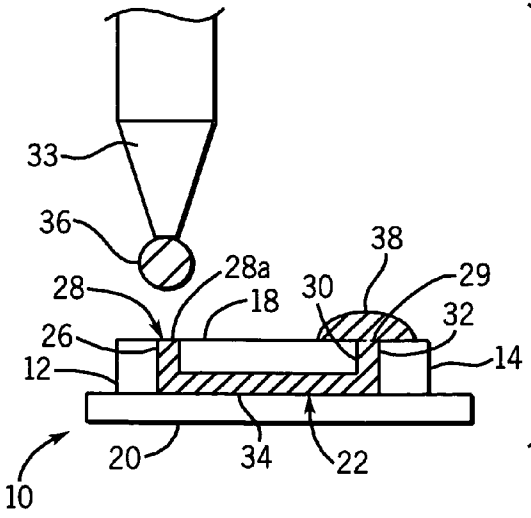


FIG. 5

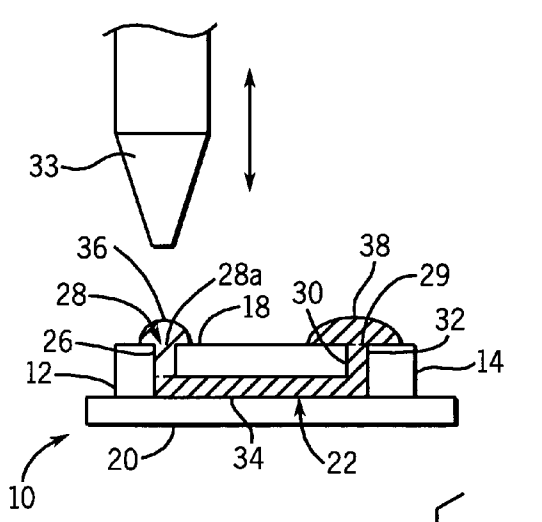


FIG. 6

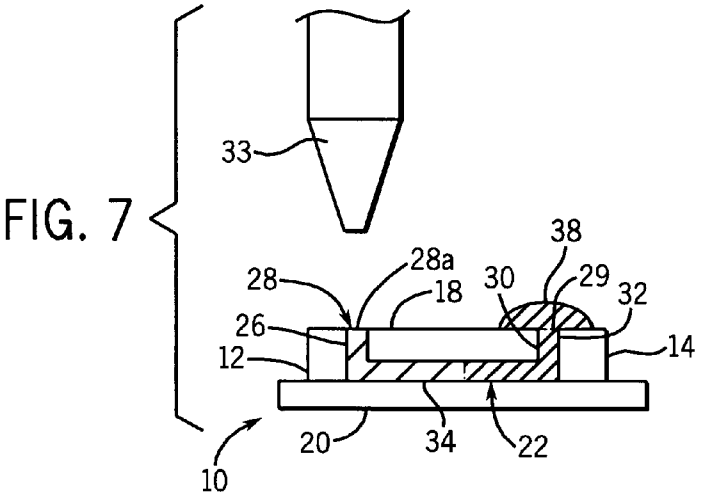


FIG. 7

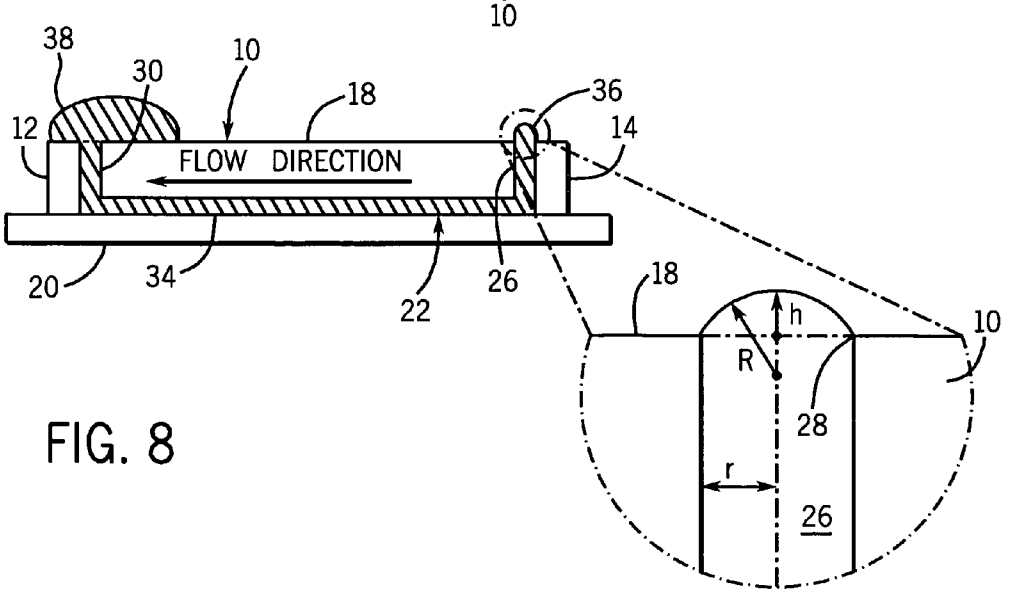


FIG. 8

DEVICE FOR PERFORMING A HIGH THROUGHPUT ASSAY

REFERENCE TO GOVERNMENT GRANT

This invention was made with United States government support awarded by the following agencies: Army, MQ-96. 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 microfluidic device and method for performing high throughput assays utilizing commercially available liquid handling robotics.

BACKGROUND AND SUMMARY OF THE INVENTION

One of the central paradigms of modern drug discovery is high throughput screening (HTS), which is the heart of lead discovery programs in the pharmaceutical industry. HTS involves the execution of a large number of assays where hypothetical drug targets are exposed to a library of small molecules. As these programs have developed, the number of assays that need to be performed has increased dramatically. Combinatorial chemistry has been applied to make an extraordinary variety of small molecule themes, and numerous potential targets have emerged from functional genomics.

In view of the foregoing, an ongoing need for improved screening technology has developed in order to hold back the cost and time consumption requirements of prior HTS systems. The introduction of high-density, low volume formats addresses both issues. The industry has gradually been incorporating miniaturized microtiter plate based technology. The necessary liquid handling and readout devices for 384, 1536 and 3456-well plates are commercially available. The first choice tends to be 1536 well plates, but 3456 and 384 well plates are also used, the latter often being preferred for cellular assays. Assay volumes in 384 well plates range down to 10 microliters and for 1536 well plates down to 1 microliter. Applications of 9600 well plates with assay volumes down to 0.2 microliters have been reported.

The assays employed in HTS fall into two categories: homogeneous and heterogeneous assays. The former involve only fluidic additions, incubations and reading. In addition to these operations, heterogeneous assays may require washing, filtering or centrifugation. Each category of HTS has its own pros and cons. While heterogeneous assays take more time to perform and require more complex robotics to automate, they generally provide higher quality data and are easier to develop. Heterogeneous assays can be developed for any analyte for which either a binding protein or an antibody exists. This is very important considering that assay development is often the rate limiting step in the lead discovery process.

An alternative approach towards further assay miniaturization is microfluidics. There have been numerous attempts to provide the valving and the mixing functionality necessary to enable an entire assay to be performed within a microfluidic system. Practically all of these prior attempts at providing a functional microfluidic system require the continuous flow of a fluid through a channel of a microfluidic device. Consequently, 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 and/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 was 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.

It can be appreciated that one of the benefits of using microfluidic channels to perform assays is that only a small fraction of the liquid surface is exposed to the atmosphere. This reduces evaporation, which is a serious problem associated with low-volume microtitre plate assays. A few microfluidics-based HTS solutions are commercially available, but all require investment in specialized hardware for reagent introduction and readout. As such, it is highly desirable to provide a microfluidic system that is compatible with conventional microplate pipetting workstations.

Therefore, it is a primary object and feature of the present invention to provide a device and method for performing high throughput assays that utilize commercially available liquid handling robotics.

It is a further object and feature of the present invention to provide a device and method for performing high throughput assays that are simple and inexpensive.

It is a still further object and feature of the present invention to provide a method for performing a high throughput assay the may be performed more quickly than and with a fraction the fluids required in prior methods.

In accordance with the present invention, a device is provided for performing an assay. The device includes a plate structure having a channel therein. The channel has an input and an output. A plurality of ports are provided in the input of the channel.

The plate structure includes a plate having an upper surface. The channel is provided in a first microfluidic structure positioned on the upper surface of the plate. The first microfluidic structure includes an upper surface that is hydrophobic. The plate structure includes a second microfludic structure positioned on the upper surface of the plate. The second microfluidic structure defines a channel having an input and an output. The input of the channel of the second microfluidic structure has a plurality of ports. In addition, the output of the channel of the second microfluidic structure may include a plurality of output ports. The device may include a liquid dispensing instrument that extends along an axis. It is contemplated for the input of the channel to be axially aligned with the liquid dispensing instrument.

In accordance with a further aspect of the present invention, a device is provided for performing a high throughput assay. The device includes a plate and a plurality of microfluidic structures thereon. Each microfluidic structure defines

a channel having an input and an output. At least one of the inputs and the outputs of the channels of the plurality of mircofluidic structures includes a first plurality of ports.

Each of the plurality of microfluidic structures includes an upper surface that is hydrophobic. It is contemplated for the plurality of microfluidic structures to be removable from the plate. Further, each of the outputs of the channels of the plurality of microfluidic structures may include a plurality of output ports. A liquid dispensing instrument deposits drops along a plurality of generally parallel axis. Each axis extends through a corresponding input of the channels of the plurality of microfluidic structures.

In accordance with a still further aspect of the present invention, a method of pumping fluid is provided. The method includes providing a microfluidic device having a channel therethough. The channel has a plurality of input ports and an output. The channel is filled with fluid and a pressure gradient is generated between the fluid at the input ports and the fluid at the output port such that the fluid flows through the channel towards the output. It is contemplated for the output of channel to include a plurality of output ports.

The pressure gradient is generated by depositing a reservoir drop of fluid over the output of the channel of sufficient dimension to overlap the output and by sequentially depositing pumping drops of fluid at the input ports of the channel. Each of the pumping drops has a predetermined radius. The reservoir drop has a radius greater than the radii of the pumping drops and greater than the predetermined radius of the output of the channel. The channel through the microfluidic device has a resistance and each of the pumping drops has a radius and a surface free energy. The reservoir drop has a height and a density such that fluid flows through the channel at a rate according to the expression:

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

wherein: dV/dt is the rate of fluid flowing through the channel; Z is the resistance of the channel; ρ is the density of the reservoir drop; g is gravity; h is the height of the reservoir drop; γ is the surface free energy of the pumping drops; and R is the radius of the pumping drops.

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 isometric view of a plate incorporating a plurality of microfluidic devices in accordance with the present invention;

FIG. **2** is a top plan view of a first embodiment of the microfluidic device of the present invention;

FIG. **3**. is a schematic view of a robotic micropipetting station for depositing drops of liquid on the upper surface of the microfluidic device of FIG. **2**;

FIG. **4** is a schematic view of the robotic micropipetting station of FIG. **3** depositing drops of liquid in a well of a multi-well plate;

FIG. **5** is an enlarged, schematic view of the robotic micropipetting station of FIG. **3** showing the depositing of a drop of liquid on the upper surface of the microfluidic device of the present invention by a micropipette;

FIG. **6** is a schematic view, similar to FIG. **5**, showing the drop of liquid deposited on the upper surface of the microfluidic device by the micropipette;

FIG. **7** is a schematic view, similar to FIGS. **5** and **6**, showing the drop of liquid flowing into a channel of the microfluidic device by the micropipette;

FIG. **8** 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; and

FIG. **9** is a top plan view of an alternate embodiment of the microfluidic device of the present invention.

DETAILED DESCRIPTION OF THE DRAWINGS

Referring to FIG. **1**, a microtiter plate for use in the methodology of the present invention is generally designated by the reference numeral **2**. Plate **2** includes upper surface **4** adapted for receiving a plurality of microfluidic devices **10** thereon. Microfluidic devices **10** may be fabricated collectively on upper surface **4** of plate **2** or individually. Further, a sheet of microfluidic devices **10** may be fabricated and positioned on plate **2** without deviating from the scope of the present invention or integrally molded with plate **2**. It is intended for microfluidic devices **10** to be used in the performance of high throughput screening (HTS). It is preferred that plate **2** include a predetermined number of microfluidic devices **10** thereon corresponding to the number of wells in a standard microtiter well plate. By way of example, plate **2** may include any number of microfluidic devices **10** thereon, such as 384, 1546 or 3456, without deviating from the scope of the present invention.

As best seen in FIG. **1**, each microfluidic device **10** is identical in structure, and as such, the description hereinafter of microfluidic device **10** is understood to described all of the microfluidic devices depicted in FIG. **1** as if fully described herein. Referring to FIGS. **2-8**, 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 **28** that communicates with upper surface **18** of microfluidic device **10** and a second vertical portion **30** terminating at an output **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 **28** and output **32** is arbitrary.

Referring to FIG. **2**, input **28** is defined by a plurality of pores or input ports **28***a*. Input ports **28***a* of input **28** communicate with the interior of channel **22** for reasons hereinafter described. Output **32** of channel **22** may comprise a single opening **29** communicating with the interior of channel **22**, FIG. **2**. Alternatively, output **32** may includes a plurality of pores or output ports **29***a*, FIG. **9**.

A robotic micropipetting station **31** is provided and includes a liquid dispensing instrument such as 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 to position micropipette **33** at a predetermined location above a microtiter well plate. In the present embodiment, it is intended for micropipetting

station **31** to position micropipette **33** over input **28** and/or output **32** of a predetermined microfluidic device **10**, FIGS. **3-4**, and to dispense or withdraw a drop into one of the input ports **28***a* of input **28** or out of output **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:

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

wherein γ 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. **8**.

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 ports **28***a* of input **28** and opening **29** of output **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, micropipette **33** is axially aligned with output **32**. Reservoir drop **38** (e.g., 100 μL), is deposited by micropipette **33** over output **32** of channel **22**, FIG. **5**. The radius of reservoir drop **38** is greater than the radius of opening **29** in output **32** and is of sufficient dimension that the pressure at output **32** of channel **22** is essentially zero. In order to perform the methodology of the present invention with smaller volumes of fluid, it is contemplated to provide a plurality of output ports **29***a* in output **32**. Output ports **29***a* of output **32**, FIG. **9**, have smaller radii than opening **29** in output **32**, FIG. **2**, thereby allowing the use of a smaller reservoir drop. Further, by providing multiple output ports **29***a* in output **32**, the margin of error associated the depositing of reservoir drop **38** on one of the output ports **29***a* of output **32** by micropipette **33** is increased.

Micropipette **33** is axially aligned with input **28**. Pumping drop **36**, of significantly smaller dimension than reservoir drop **38**, is deposited on one of the input ports **28***a* of input **28** of channel **22**, FIGS. **6** and **8**, by micropipette **33** of robotic micropipetting station **31**, FIG. **5**. It can be appreciated by providing multiple input ports **28***a* in input **28**, the margin of error associated the depositing of pumping drop **36** on one of the input ports **28***a* of input **28** by micropipette **33** is increased. 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***a* of input **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 **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** deposited on one of the input ports **28***a* of input **28** has a smaller radius than reservoir drop **38**, a larger pressure exists on the one of the input ports **28***a* of input **28** of channel **22**. The resulting pressure gradient causes the pumping drop **36** to flow from the one of the input ports **28***a* of input **28** through channel **22** towards reservoir drop **38** over opening **29** of output **32** of channel **22**, FIG. **7**. It can be understood that by sequentially depositing additional pumping drops **36** on an input port **28***a* of input **28** of channel **22** by micropipette **33** of robotic micropipetting station **31**, the resulting pressure gradient will cause the pumping drops **36** deposited on the input ports **28***a* of input **28** to flow through channel **22** towards reservoir drop **38** over opening **29** of output **32** of channel **22**. As a result, fluid flows through channel **22** from input **28** to output **32**.

Referring back to FIG. **8**, the highest pressure attainable for a given radius, R, of an input port **28***a* of input **28** of channel **22** is a hemispherical drop whose radius is equal to the radius, r, of an input port **28***a* of input **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 an input port **28***a* of input **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., an input port **28***a* of input **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, the radius of an input port **28***a* of input **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***a*); and $b=6V/\pi$ (V is the volume of pumping drop **36** placed on input port **28***a*).

The volumetric flow rate of the fluid flowing from input **28** of channel **22** to output **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**; ρ is the density of pumping drop **36**; g is gravity; h is the height of reservoir drop **38**; γ 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 inputs could be formed along the length of channel **22**. By designating one of such inputs as the output, different flow rates could be achieved by depositing pumping drops on different inputs along length of channel **22** (due to the difference in channel resistance). In addition, temporary outputs **32** may be used to cause fluid to flow into them, mix, and then, in turn, be pumped to other outputs **32**. It can be appreciated that the pumping method of the present invention works with various types of fluids including water and biological fluids.

Further, it is contemplated to etch patterns in upper surface **18** of microfluidic device **10** about the outer peripheries of input **28** and/or output **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 **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.

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 device for performing an assay, comprising:

a plate structure having a channel therein, the channel having an input end, an output end, and a diameter;

an input plate at the input end of the channel, the input plate having a diameter generally equally to the diameter of the channel at the input end thereof, an inner surface communicating with the channel and an outer surface; and

a plurality of ports extending between the inner and outer surfaces of the input plate and communicating with the channel, each port having a diameter less than the diameter of the channel at the input end and being axially aligned with the input end of channel.

2. The device of claim **1** wherein the plate structure includes a plate having an upper surface and wherein the channel is provided in a first microfluidic structure positioned on the upper surface of the plate.

3. The device of claim **2** wherein the first microfluidic structure includes an upper surface, the upper surface being hydrophobic.

4. The device of claim **2** wherein the plate structure includes a second microfludic structure positioned on the upper surface of the plate.

5. The device of claim **4** wherein the second microfluidic structure defines:

a channel having an input end and an output end;

an input at the input end of the channel, the input of the second microfluidic structure having an inner surface communicating with the channel, an outer surface, and a plurality of ports extending between the inner and outer surfaces of the second microfluidic structure.

6. The device of claim **5** wherein the second microfluidic structure further includes an output at the output end of the channel of second microfluidic structure, the output of the second microfluidic structure having a plurality of output ports therethrough.

7. The device of claim **1** further comprising an output at the output end of the channel, the output including a plurality of output ports therethrough.

8. The device of claim **1** further comprising a liquid dispensing instrument extending along an axis and wherein the input of the channel is axially aligned with the pipette.

9. A device for performing an assay, comprising:

a plate; and

a plurality of microfluidic structures positioned on the plate, each microfluidic structure defining:

a channel having an input end, an output end and a diameter;

an input plate at the input end of the channel, the input plate having a diameter generally equally to the diameter of the channel at the input end thereof, an inner surface communicating with the channel and an outer surface; and

an output plate at the output end of the channel, the output plate having a diameter generally equally to the diameter of the channel at the output end

thereof, an inner surface communicating with the channel and an outer surface;

wherein at least one of the of the input plates and the of the output plates of the channels of the plurality of mircofluidic structures includes a first plurality of ports therethrough.

10. The device of claim **9** wherein the each of the plurality of microfluidic structures includes an upper surface, each upper surface being hydrophobic.

11. The device of claim **9** wherein the plurality of microfluidic structures are removable from plate.

12. The device of claim **9** wherein the other of the inputs and the outputs of the channels of the plurality of microfluidic structures include a second plurality of ports therethough.

13. The device of claim **9** further comprising a liquid dispensing instrument for depositing drops along a plurality of generally parallel axis, each axis extending through a corresponding input of the channels of the plurality of microfluidic structures.

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