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Arndt

(54) **LOW-DEAD VOLUME MICROFLUIDIC COMPONENT AND METHOD**

(76) Inventor: **Heiko Arndt**, Flensborg (DE)

Correspondence Address:
GOODWIN PROCTER LLP
PATENT ADMINISTRATOR
53 STATE STREET, EXCHANGE PLACE
BOSTON, MA 02109-2881 (US)

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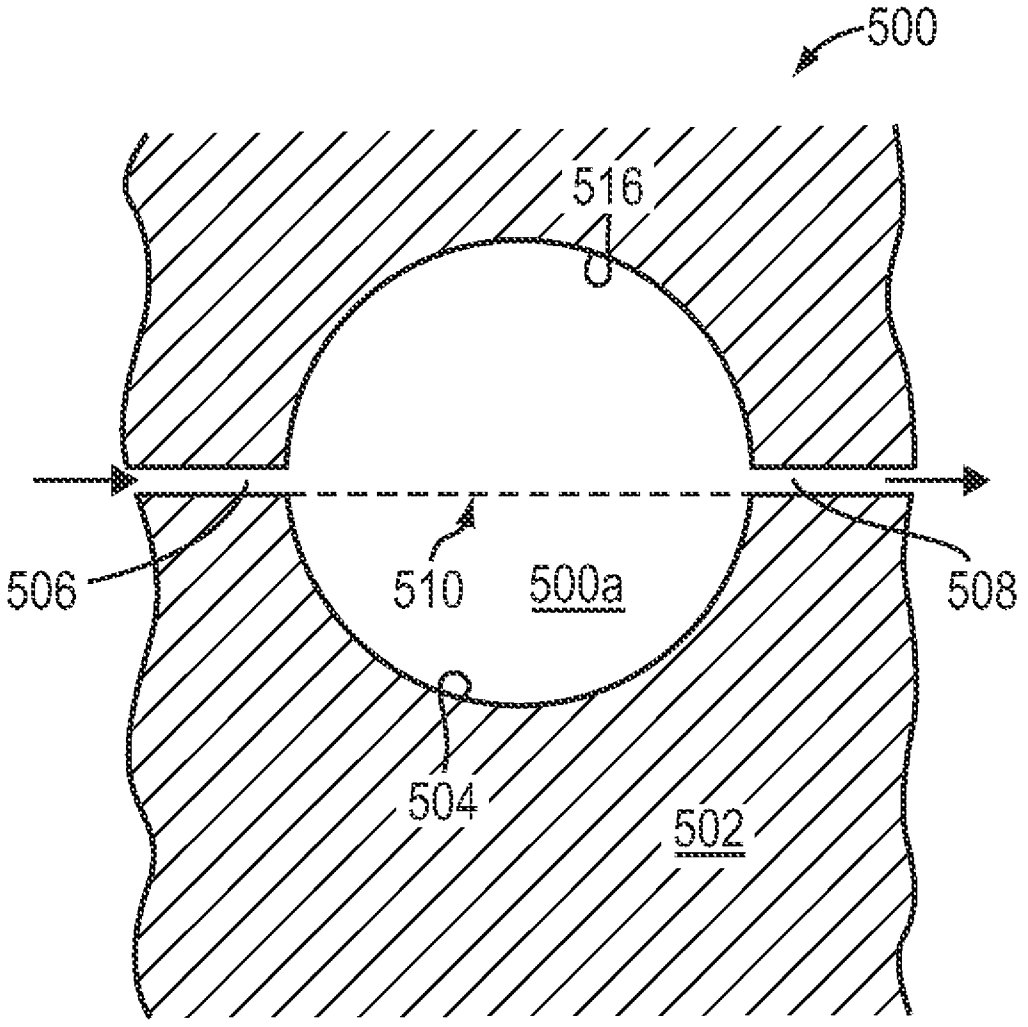
(57) **ABSTRACT**

A method is described for reducing a dead volume of a microfluidic circuit that includes, in one embodiment, a reservoir, an outlet, and a microfluidic flowpath fluidly connecting the reservoir and the outlet. The method includes providing a variable-volume fluid chamber between the reservoir and the outlet for performing a function and in fluidic communication with the microfluidic flowpath, wherein the variable-volume fluid chamber includes a total volume including a working volume and a dead volume. The working volume is a volume necessary for the variable-volume fluid chamber to perform the function and the dead volume is a volume unnecessary for the variable-volume fluid chamber to perform the function. The method includes configuring the variable-volume fluid chamber to reduce the dead volume, such that the working volume of the component is substantially the same as the total volume.



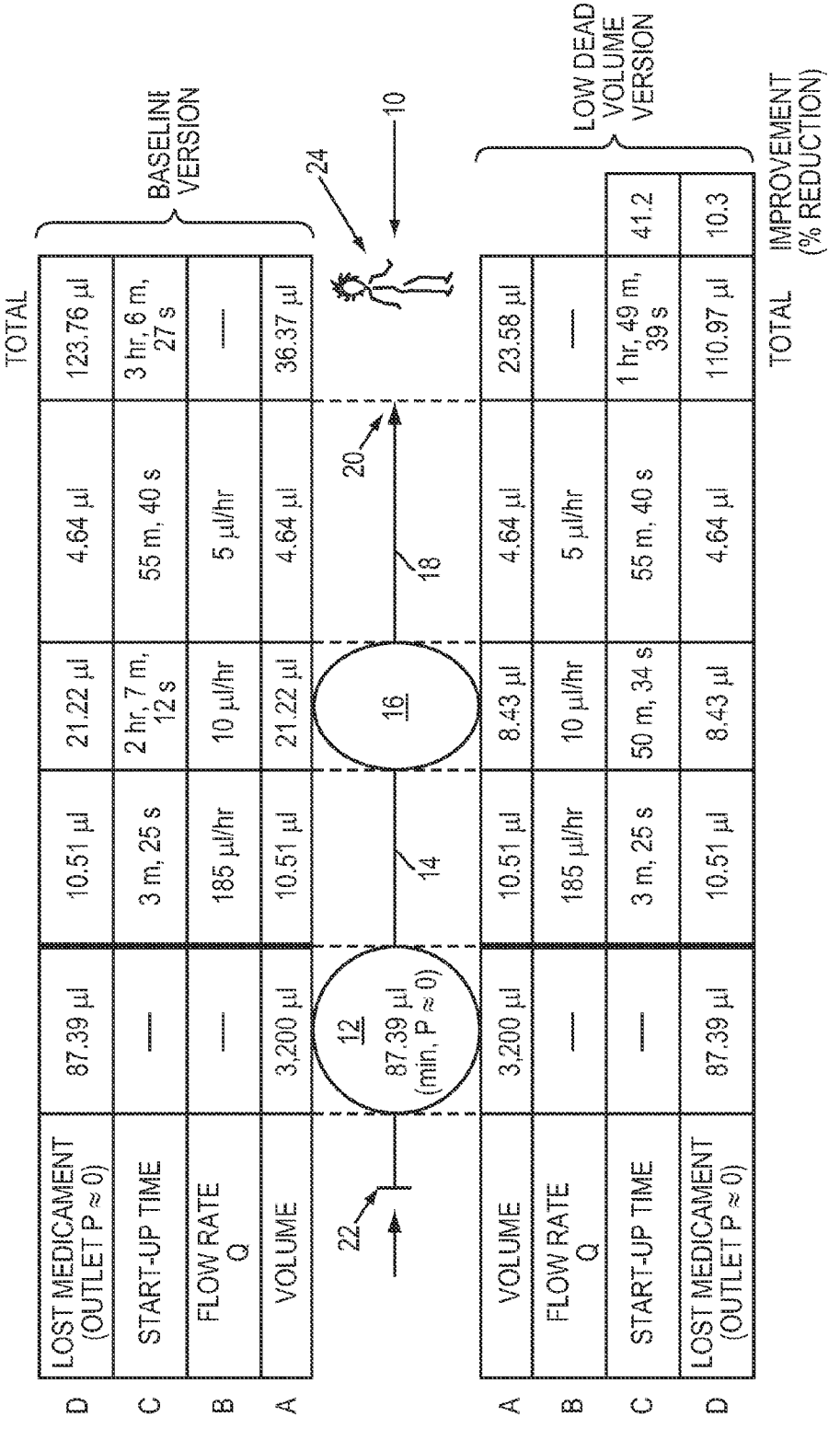

BASELINE VERSION
LOW DEAD VOLUME VERSION
TOTAL
TOTAL
IMPROVEMENT (% REDUCTION)
A
B
C
D
VOLUME
FLOW RATE Q
START-UP TIME
LOST MEDICAMENT (OUTLET P ≈ 0)
3,200 µl
—
—
87.39 µl
10.51 µl
3 m, 25 s
185 µl/hr
10.51 µl
21.22 µl
2 hr, 7 m, 12 s
10 µl/hr
21.22 µl
4.64 µl
55 m, 40 s
5 µl/hr
4.64 µl
123.76 µl
3 hr, 6 m, 27 s
—
36.37 µl
3,200 µl
—
—
87.39 µl
10.51 µl
3 m, 25 s
185 µl/hr
10.51 µl
8.43 µl
50 m, 34 s
10 µl/hr
8.43 µl
4.64 µl
55 m, 40 s
5 µl/hr
4.64 µl
23.58 µl
1 hr, 49 m, 39 s
—
110.97 µl
41.2
10.3
12
87.39 µl (min, P ≈ 0)
14
16
18
20
22
24
10

FIG. 1

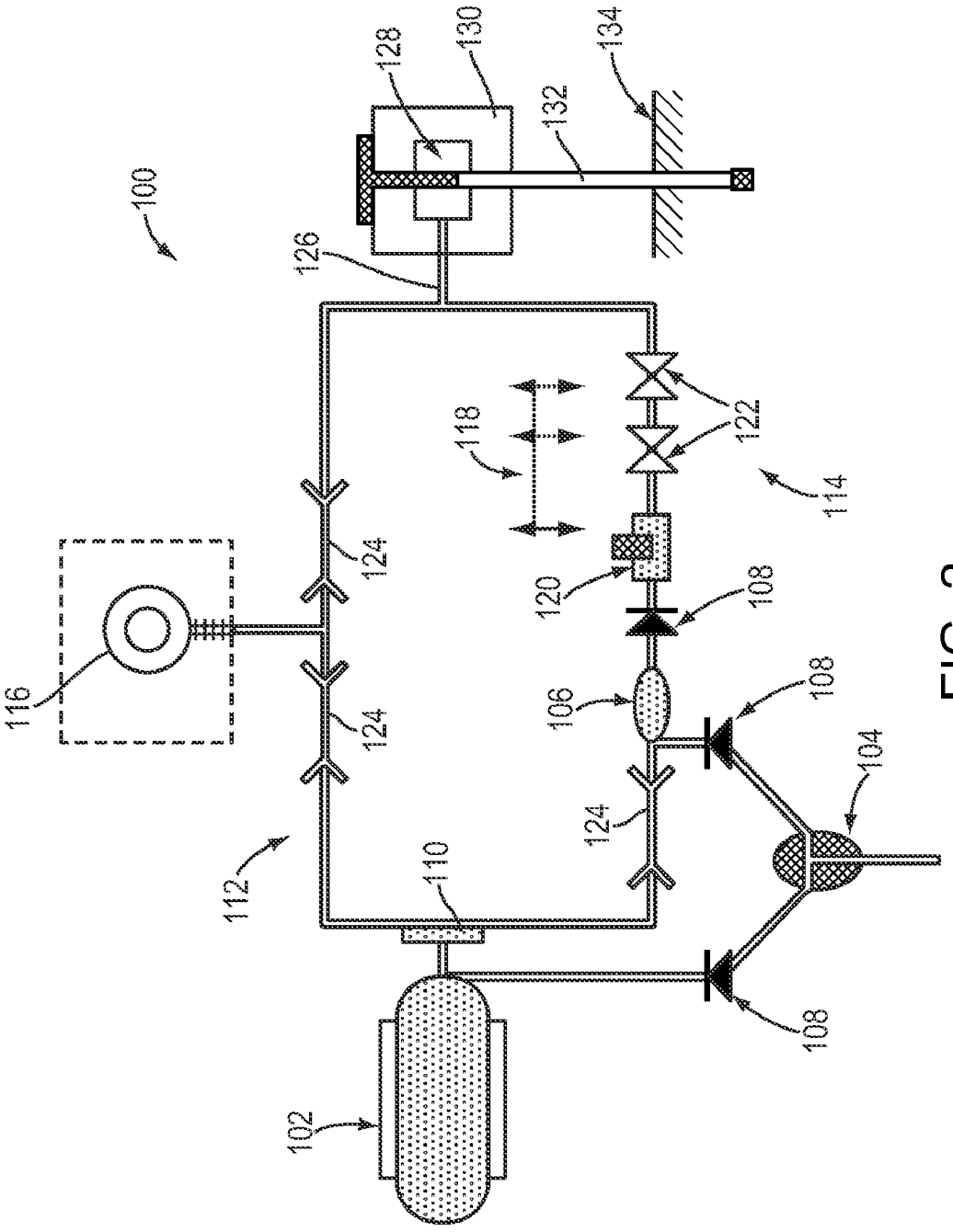

100
102
104
106
108
110
112
114
116
118
120
122
124
126
128
130
132
134

FIG. 2

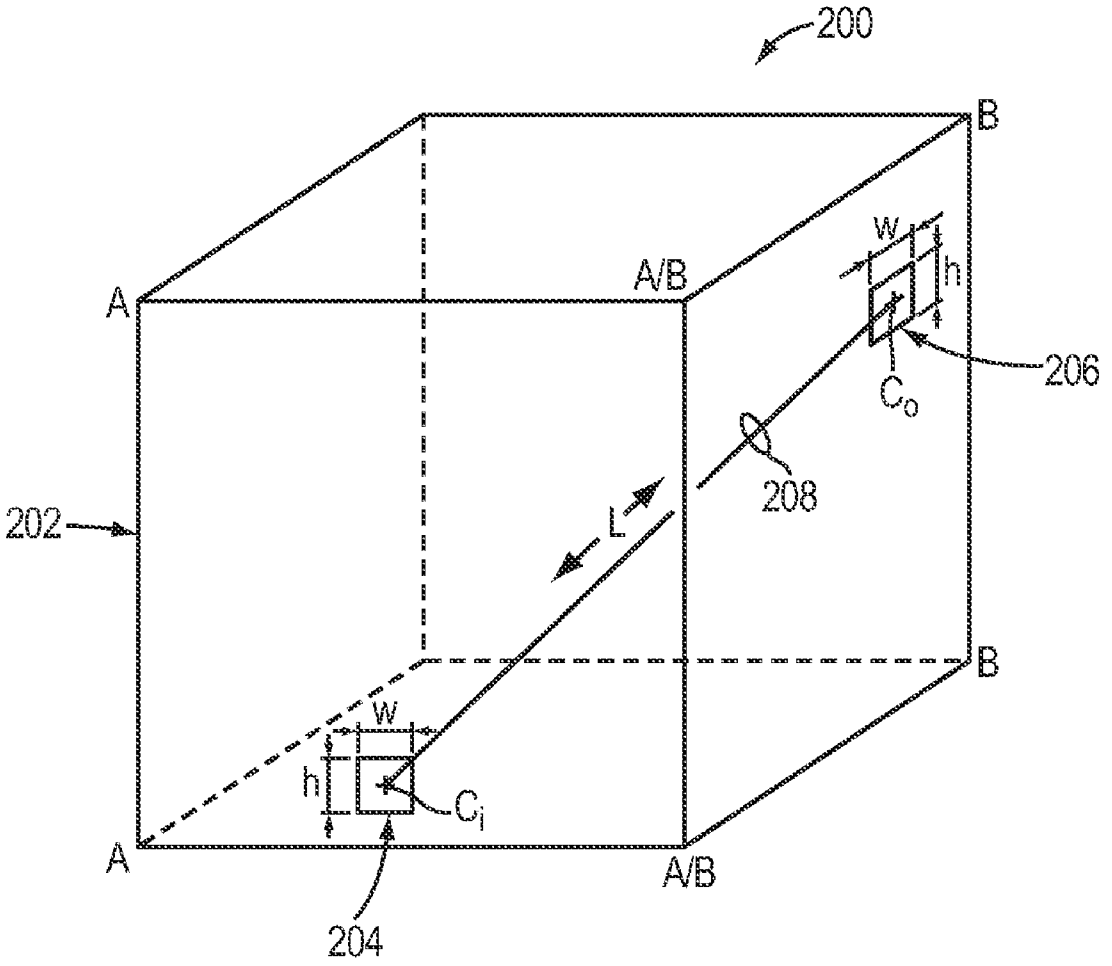


FIG. 3

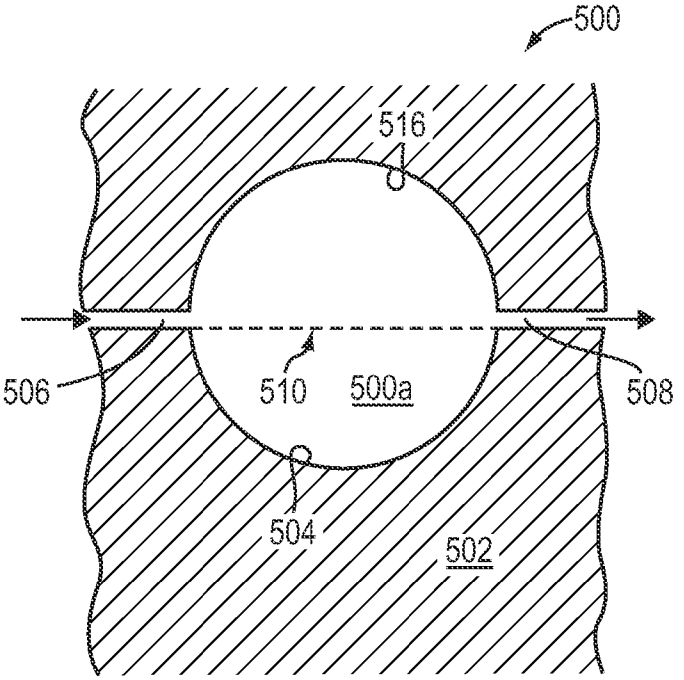


FIG. 4A

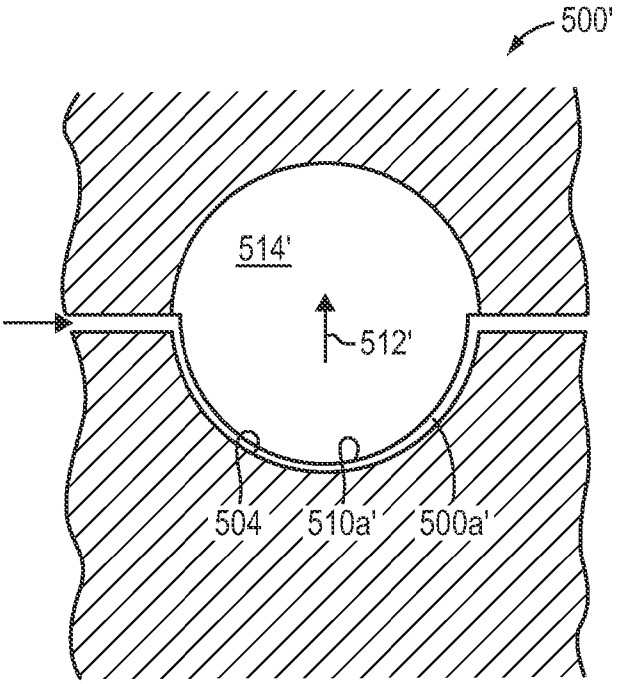


FIG. 4B

LOW-DEAD VOLUME MICROFLUIDIC COMPONENT AND METHOD

FIELD OF THE INVENTION

[0001] This invention relates generally to a system and method of reducing dead volume in a microfluidic circuit and, more specifically, to a system and method of reducing the dead volume in a component utilized within microfluidic circuits.

BACKGROUND

[0002] Microfluidic circuits are utilized in various personal medical devices (e.g., insulin infusion devices) to control delivery of medications or other fluids. In general, the volumetric flow rates within these circuits are very low, due to low dosing schedules, and to allow for accurate control of the medication being delivered. The low flow rates, however, can prevent the circuit from being quickly filled prior to utilizing the device, which can pose a significant inconvenience to the user. Additionally, any excess volume within the circuit results in medication that remains undelivered once a pressure source for the medication is terminated.

[0003] Lengthy fill times and undelivered medication are related to total volume within a microfluidic system. Each component (e.g., reservoirs or other chambers, valves, conduits or channels, pressure sensors, flow restrictors, etc.) of a system has an internal capacity for a volume of fluid. This capacity is defined, in part, by the internal dimensions, function, and configuration of the component, including moving components within the flowpath. Manufacturing methods and tolerances may affect the capacity, as well. While a particular component may only require a relatively small portion of the total internal volume to perform its function (this volume may be referred to as the "working volume"), access required for manufacturing the component may prevent minimizing the total volume. This excess volume (or "dead volume") over that of the working volume increases the total volume of the flow component and, subsequently, of the fluidic circuit of the delivery system.

SUMMARY OF THE INVENTION

[0004] In one aspect, the invention relates to a method for reducing a dead volume of a microfluidic circuit having a reservoir, an outlet, and a microfluidic flowpath fluidly connecting the reservoir and the outlet, the method including providing a variable-volume fluid chamber located between the reservoir and the outlet for performing a function and in fluidic communication with the microfluidic flowpath. The variable-volume fluid chamber includes a total volume having a working volume and a dead volume, wherein the working volume is a volume necessary for the variable-volume fluid chamber to perform the function and the dead volume is a volume unnecessary for the variable-volume fluid chamber to perform the function. The method includes configuring the variable-volume fluid chamber to reduce the dead volume, such that the working volume is substantially the same as the total volume. In an embodiment, the configuring step results in the total volume being substantially the same as the working volume.

[0005] In yet another embodiment, the variable-volume fluid chamber includes a base surface, an inlet, and a separate outlet. The configuring step includes providing a flexible membrane, wherein the base surface and the membrane define a first volume when the membrane is proximate the base surface, and the base surface and the membrane define a second volume when the membrane is displaced by a fluid pressure away from the base surface. The membrane can be biased towards the base surface. In another aspect, the invention relates to a low-dead volume variable-volume fluid chamber manufactured in accordance with the method of the above embodiment. In an embodiment of the above aspect, the working volume is about 5% of the total volume.

BRIEF DESCRIPTION OF THE FIGURES

[0006] Other features and advantages of the present invention, as well as the invention itself, can be more fully understood from the following description of the various embodiments, when read together with the accompanying drawings, in which:

[0007] FIG. **1** is a schematic diagram and related time/volume tables of an exemplary infusion device microfluidic circuit;

[0008] FIG. **2** is a schematic diagram of another exemplary infusion device microfluidic circuit in accordance with one embodiment of the invention;

[0009] FIG. **3** is a schematic diagram of a theoretical microfluidic circuit flow component; and

[0010] FIGS. **4**A and **4**B are schematic sectional views of an exemplary variable-volume chamber and a low-dead volume version of the same variable-volume chamber in accordance with one embodiment of the invention.

DETAILED DESCRIPTION

[0011] Consider one embodiment of a microfluidic circuit **10** for delivering a fluid medication to a patient, as depicted in FIG. **1**. The fluid delivery or flow components of this circuit **10** include, in series, an elastomer reservoir or bladder **12**, a first channel **14**, a flow component **16**, a second channel **18**, and an outlet **20**. The flow component **16** may function, e.g., as a storage chamber for doses of medicament to be delivered on an infrequent basis to a human user or patient **24**. The reservoir **12** is filled with medication via a one-way inlet valve **22**. In this example, the microfluidic circuit **10** is utilized in an insulin infusion delivery device used to deliver insulin to the patient **24** via a subcutaneous cannula in fluidic communication with the outlet **20**. The lower table included in FIG. **1** depicts information relevant to a low-dead volume version of the microfluidic circuit **10**. The upper table depicts information relevant to a baseline version of the microfluidic circuit **10** upon which no volume reduction modifications have been made. The total volume of each flow component is depicted in FIG. **1** in Row A of both the upper and lower tables. The elastomer reservoir **12** supplies the downstream microfluidic circuit flow components with insulin until the elastomer no longer exerts sufficient pressure to overcome the flow resistance in the circuit **10**. At that point, in this example, 87.39 μl of insulin remains in the reservoir **12**. See Row D.

[0012] Row B in both the upper and lower tables depicts the flow rate Q through the various components. The flow rate Q is defined, at least in part, by flow restrictors and other components present within the circuit. Row C in both the upper and lower tables depicts the amount of time required for insulin to completely fill each dry flow component once flow from the reservoir **12** is initiated, as the sum of which is the total start-up time for the entire microfluidic circuit **10** to fill. This total start-up time reflects the time required to deliver a

first dose of insulin to the user **24**. Notably, the difference in volume between a standard flow component **16** (21.22 μl) and a low-dead volume flow component **16** (8.34 μl) contributes directly to the significant reduction in total start-up time of the circuit **10**. Note that the fill time for the standard flow component **16** is over twice that of the low-dead volume fill time, while the total fill time of the standard circuit is over 1 hour and 15 minutes greater than the microfluidic circuit using a low-dead volume component. This significant delay inherent in the baseline version of the circuit **10** is both an inconvenience and could be a risk to the user's health.

[0013] Row D in both the upper and lower tables depicts the amount of insulin that is effectively trapped within the microfluidic circuit **10** once the elastomer reservoir **12** can no longer induce flow at the outlet **20**. Note that a significant portion of the trapped insulin, other than that remaining in the reservoir **12**, is contained within the flow component **16**. Accordingly, use of a low-dead volume flow component, for example, a variable-volume chamber, is advantageous to reduce the total amount of lost insulin within the microfluidic circuit **10**.

[0014] FIG. **2** is a schematic diagram of an exemplary infusion device microfluidic circuit **100** that benefits from the low-dead volume technology described herein. Other infusion device microfluidic circuits benefit as well, such as those described, for example, in U.S. Patent Application Publication No. 2005/0165384 A1, published Jul. 28, 2005, the disclosure of which is hereby incorporated by reference herein in its entirety. Microfluidic circuits having other configurations or utilizing any number of other components also may benefit from inclusion of the low-dead volume variable-volume fluid chamber described herein. The microfluidic circuit **100** includes a reservoir **102** that is, in this case, comprised of an elastomer bladder. A fill port **104** is used to introduce insulin to the microfluidic circuit **100**. In this microfluidic circuit **100**, introducing insulin via the fill port **104** fills both the reservoir **102** and a variable-volume bolus reservoir **106**. Check valves **108** in the circuit **100** prevent backflow of insulin in a number of locations.

[0015] During use, insulin is forced from the reservoir **102** due to contraction of the elastomer bladder, through a filter **110**, and into two parallel flowpaths: a basal flowpath **112** and a bolus flowpath **114**. The basal flowpath **112** delivers a constant dose of insulin to a user; the bolus flowpath **114** delivers a bolus dose of insulin to the user as needed or desired by the user, upon actuation of a bolus button **118**. The basal flowpath **112** includes a pressure sensor **116** or other flow sensor in communication with the flowpath **112**. To deliver a bolus via the bolus flowpath **114**, the user presses the bolus button **118** that drives a single stroke (delivering a single dose) of a bolus displacement chamber **120** and opens two valves **122**. The valves **122** are in series providing failsafe redundancy for safety purposes. Flow restrictors **124** limit the rate of fluid flow through the flowpaths **112**, **114**. The parallel flowpaths **112**, **114** join at a common channel **126**, upstream of an internal chamber or a cannula void **128**. The cannula void **128** is formed in a cannula base **130**, that provides a fluidic connection to a cannula **132**. The cannula **132** extends below the skin **134** of the user, thus delivering the insulin subcutaneously. In the depicted microfluidic circuit **100**, reducing the dead volume in the variable-volume bolus reservoir **106** decreases the dead volume throughout the entire microfluidic circuit **100**.

[0016] FIG. **3** depicts a theoretical flow component **200**. While most flow components utilized in a microfluidic circuit serve specific purposes, each generally share several common elements, as depicted in FIG. **3**. First, the flow component includes a housing or some other inner physical boundary that is in contact with the fluid passing therethrough. In FIG. **3**, this inner physical boundary **202** is depicted as a hollow cube. Second, the flow component includes an inlet, through which fluid flows into the component. In FIG. **3**, the inlet **204** penetrates a wall of the physical boundary **202** defined by corners bearing the letter "A"; the dimensions of the inlet **204** are defined by a height h, and a width w, although the inlet **204** could be circular or any other shape. Third, the flow component includes an outlet, through which fluid flows out of the component. In FIG. **3**, the outlet **206** penetrates a wall of the physical boundary **202** defined by the corners bearing the letter "B"; the dimensions of the outlet **206** are defined by a height h, and a width w, in this case, matching the dimensions of the inlet **204**, although the outlet **206** could be any shape or size and disposed at any location along the boundary **202**.

[0017] The inner physical boundary of a flow component defines three volumes: a total volume V, a working volume W, and a dead volume D. The total volume V is the volume bounded by the inner physical boundary; accordingly, in FIG. **3**, the total volume V is defined by the walls of the cube (i.e., the inner physical boundary **202**). The working volume W is the minimum volume required to perform the function of the flow component, including connecting fluidicly the inlet and the outlet. In FIG. **3**, assume that the theoretical flow component **200** functions as a constant-volume chamber through which fluid passes (where the entire cube must be filled with fluid via the inlet **204** prior to any fluid exiting the cube via the outlet **206**). The working volume W is the volume defined around a straight line **208** from a center C_i of the inlet **204** to a center C_o of the outlet **206**, the straight line having a length L. The actual volume of this working volume W may be defined, in part, by the total length of straight line L and the height h and width w of the inlet **204** and the outlet **206**, assuming the working volume has outer dimensions substantially similar to height h and width w. Therefore the working volume W may be defined approximately by equation (i) below.

$$W=h\times w\times L \tag{i}$$

The dead volume D is the volume of the flow component **200** unnecessary to perform the function, and may be defined as the difference between the total volume V and the working volume W (in this case, the remainder of the volume contained within the inner physical boundary **202**, not including the working volume W), as shown in equation (ii) below.

$$D=V-W \tag{ii}$$

By reducing the dead volume D of a flow component, the dead volume of a microfluidic circuit may be decreased, approaching, ideally, a condition where the total volume of the low-dead volume component V_{LD} equals the working volume W of a standard-dead volume flow component, i.e., $V_{LD}=W$.

[0018] Different implementations may be utilized to decrease the dead volume of a flow component. In general, however, the dead volume-reduction example described herein may effectively configure the flow component to reduce the dead volume, such that the working volume is substantially the same as the total volume or as close to the total volume as reasonably achievable, under the circumstances. Regardless of the configuration change imple-

mented, a number of factors may be considered. For example, the function and operational performance of the flow component should not be affected adversely by the dead volume-reduction configuration change. The dead volume-reduction change should consider the potential impact on pressure losses associated with the flow component. Care should be taken when reducing dead volume of a flow component, to ensure the component can still be manufactured at acceptable cost. An example of the use of dead volume-reduction configuration change to reduce the dead volume of a flow component is described below.

EXAMPLE

[0019] FIG. **4**A is a schematic sectional view of a variable-volume chamber **500**. The chamber **500** is formed within a solid housing **502** and has a rigid base surface **504**, as well as an inlet **506**, and an outlet **508**. A rigid top surface **516** defines the upper surface of the chamber **500**. As can be seen in FIG. **4**A, the entire volume of an internal chamber **500***a* below a line **510***a* must be filled before any fluid may pass out of the outlet **508**.

[0020] Depicted in FIG. **4**B is a variable-volume chamber **500'** according to one embodiment of the present invention with reduced dead volume. In this case, membrane **510'** is biased or disposed against the rigid base **504** of the internal chamber **500***a'* to define a first small volume approaching zero, as depicted here. As fluid enters the internal chamber **500***a'*, the membrane **510***a'* expands **512'**. The pressure contained within expansion volume **514'** is immediately exerted against the membrane **510***a'* and the fluid contained within the internal chamber **500***a'*. Pressure within the expansion volume **514'** may be relieved by a suitable vent, not shown. Due to the initial location of the membrane **510***a'*, once filling begins, pressure is essentially immediately exerted against the fluid, without requiring filling of an excessive dead volume of the internal chamber **500***a'*.

[0021] In one embodiment, the variable-volume chamber **500** depicted in FIG. **4**A includes a total volume V of 230 μl. Of this amount, 218.5 μl was determined to be dead volume D and was subsequently reduced by membrane **510***a'*, leaving a working volume W of 11.5 μl. For this embodiment, then, reducing the dead volume D results in a working volume W that is about 5% of the total volume V for the variable-volume chamber **500'** of FIG. **6**B, thus achieving a 95% reduction in the volume of the variable-volume chamber **500**. Other reductions are also contemplated.

[0022] Application of the low-dead volume technique described herein can significantly reduce dead volume of a microcircuit **100** such as that depicted in FIG. **2**. As depicted in FIG. **2**, the basal circuit **112** includes a pressure sensor **116** and a cannula void **128**. The bolus circuit **114** includes a variable-volume chamber **106** and two valves **122**. The total volume of all conduits in the microcircuit **100** is about 7 μl, of which nearly none is dead volume. TABLE 1, below, depicts relevant properties of a low-dead volume variable-volume chamber, in an exemplary microcircuit, as that component is described in the Example. Other flow components in an exemplary microcircuit, as depicted in TABLE 1, may include at least a cannula void **128**, valves **122**, and a pressure sensor **116**. Assuming a microcircuit **100**, such as that depicted in FIG. **2**, the difference in volume of a standard microcircuit (having a baseline-volume fluid chamber) versus the volume of a low-dead volume circuit (having a low-dead volume variable-volume chamber) is depicted.

TABLE 1

Reduction in Dead Volume for Microcircuit Utilizing Low-Dead Volume Variable-Volume Chamber

Component	V (μl)	D (μl)	W (μl)	Improvement (% Reduction In V)
Bolus Reservoir 106	230	218.5	11.5	95
Other Flow Components	25.26	0	25.26	0
All Conduits	7	0	7	0
Total	262.26	218.5	43.76	83.3

[0023] TABLE 2, below, depicts other relevant properties of a low-dead volume variable-volume chamber, in an exemplary microcircuit, as that component is described in the Example. The total volume V and dead volume D of a standard flow component is provided. Other flow components in an exemplary microcircuit, as depicted in TABLE 2, may include at least a cannula void **128**, valves **122**, and a pressure sensor **116**. In TABLE 2, the cannula void **128** flow component is set aside separately, because its flow rate is different than the other flow components. After utilizing the low-dead volume structure described herein, dead volume D of the variable-volume chamber was essentially eliminated, to achieve the significantly smaller, essentially idealized, working volume W. Also provided is the cumulative volume for all conduits within the microcircuit.

[0024] Flow rates Q through each component are also provided. The flow rates Q are used to calculate the fill time for each component. Initially, the fill time for the exemplary fluid chamber is calculated before any dead-volume reduction structure is utilized. In that case, total volume V is divided by the flow rate Q to obtain the fill time for that component. Next, the fill time for the variable-volume chamber is calculated after the dead-volume reduction structure is utilized. In that case, working volume W is divided by the flow rate Q to obtain the fill time for the low-dead volume variable-volume chamber. It should be noted that the working volume is, as defined above, the minimum volume required to perform the function of the flow component. Since the function of the chamber is to hold liquid medicine, it has been assumed here for the purposes of illustration of the concept that a minimum of 11.5 μl is required for the functional working volume. Indeed, the working volume and dead volume of the variable-volume chamber may change as the chamber is made to hold different amounts of liquid medicine.

[0025] Reduction in fill times from that of the standard baseline component to that of the low-dead volume component are also provided. As noted above, while the reduction in fill time for the Example is quite large, this reduction varies depending on the working volume W selected and results in a significant reduction in fill time for the complete circuit.

TABLE 2

Reduction in Fill Time for Microcircuit Utilizing Low-Dead Volume Variable-Volume Chamber

Component	V (μl)	D (μl)	W (μl)	Flow Rate Q (μl/hr)	Fill Time V at Q (hr)	Fill Time W at Q (hr)	Fill Time Reduc. (hr)	Improvement (% Reduc.)
Cannula Void 128	1.74	0	1.74	5	0.348	0.348	0	0
Bolus Reservoir 106	230	218.5	11.5	10	23	1.15	21.85	95
Other Flow Components	23.52	0	23.52	10	2.352	2.352	0	0
All Conduits	7	0	7	185	0.038	0.038	0	0
Total	262.26	218.5	43.76	N/A	25.738	3.888	21.85	84.9

[0026] The various materials utilized in the flow components described herein, as well as the microfluidic circuits in which those flow components are utilized, may be metal, glass, and/or any type of polymer suitable for sterilization and useful for delivering insulin or other medicaments subcutaneously. Polyurethane, polypropylene, PVC, PVDC, EVA, and others are contemplated for use. More specifically, medical-grade plastics may be utilized for the cannula itself, as well as other components that contact or otherwise penetrate the body of the patient. Needles made from medical-grade stainless steel are also desirable, to prevent failure associated with use. Accordingly, the components utilized to reduce the dead volume within the various components should be the same as, similar to, or at least compatible with the existing materials utilized.

[0027] While there have been described herein what are to be considered exemplary and preferred embodiments of the present invention, other modifications of the invention will become apparent to those skilled in the art from the teachings herein. The particular methods of manufacture and geometries disclosed herein are exemplary in nature and are not to be considered limiting. It is therefore desired to be secured in the appended claims all such modifications as fall within the spirit and scope of the invention. Accordingly, what is desired to be secured by Letters Patent is the invention as defined and differentiated in the following claims, and all equivalents.

What is claimed is:

1. A method for reducing a dead volume of a microfluidic circuit comprising a reservoir, an outlet, and a microfluidic flowpath fluidly connecting the reservoir and the outlet, the method comprising:

providing a variable-volume fluid chamber located between the reservoir and the outlet for performing a function and in fluidic communication with the microfluidic flowpath,

wherein the variable-volume fluid chamber comprises a total volume comprising a working volume and a dead volume, wherein the working volume comprises a volume necessary for the variable-volume fluid chamber to perform the function and the dead volume comprises a volume unnecessary for the variable-volume fluid chamber to perform the function; and

configuring the variable-volume fluid chamber to reduce the dead volume, such that the working volume is substantially the same as the total volume.

2. The method of claim **1**, wherein the configuring step results in the total volume being substantially the same as the working volume.

3. The method of claim **1**, wherein the variable-volume fluid chamber comprises a base surface, an inlet, and a separate outlet, and wherein the configuring step comprises:

providing a flexible membrane wherein the base surface and the membrane define a first volume when the membrane is proximate the base surface, wherein the base surface and the membrane define a second volume when the membrane is displaced by a fluid pressure away from the base surface, and wherein the membrane is biased towards the base surface.

4. A low-dead volume variable-volume fluid chamber manufactured in accordance with the method of claim **3**.

5. The low-dead volume variable-volume fluid chamber of claim **4**, wherein the working volume comprises about 5% of the total volume.

* * * * *