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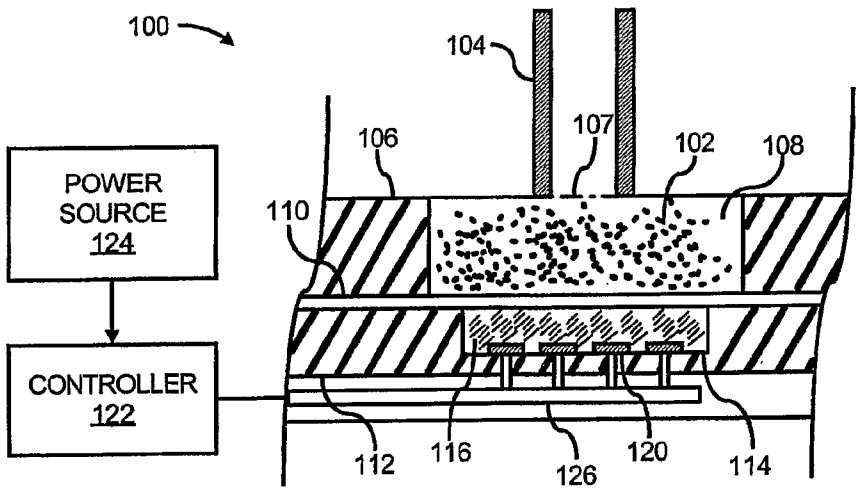
[Continued on next page]

(54) **Title:** A MICROFLUIDIC DEVICE FOR CONTROLLED MOVEMENT OF MATERIAL AND A METHOD FOR DELIVERING A MATERIAL FROM A MICROFLUIDIC DEVICE



(57) **Abstract:** A microfluidic device (100) for controllably moving a material of interest (102) includes a holding cavity (108) configured to hold the material of interest (102) and at least one actuator (120) configured to induce an activation material (116) to expand or contract. Expansion of the activation material (116) decreases the size of the holding cavity (108) to cause the material of interest (102) to be released from the holding cavity (108) and contraction of the activation material (116) increases the size of the holding cavity (108) to cause the material of interest (102) to be received into the holding cavity (108). The at least one actuator (120) is operable at multiple levels between a zero induction level to a maximum induction level on the activation material (116) to thereby controllably expand or contract the holding cavity (108) to release or receive a specified volume of the material of interest (102).

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"A microfluidic device for controlled movement of material and a method for delivering a material from a microfluidic device"

The present invention relates to a microfluidic device for controlled movement of material, and the invention also relates to a method for delivering a material from a microfluidic device.

There has been a growing interest in the use of microfluidic systems in chemical and biological sciences, medical specialities, as well as manufacturing and dispensing operations. This interest has been attributable to the potential increased performance of relatively complicated chemical and biochemical systems which use relatively small volumes of fluids. Microfluidic systems have been employed in these types of applications to introduce the fluids because such systems allow for more easily measured reactions. In addition, minimising sample volumes have resulted in lowered reagent costs, less toxic material-introduction and more easily modelled reactions.

Microfluidic systems for drug delivery have until now used a contacting, but non-penetrating, patch, with or without enhancing agents, to move drugs diffusively through the skin. For those microfluidic systems that use a pump, the actuation unit is typically rather bulky in construction because the actuation units are oftentimes based upon conventional actuating devices, such as piezoelectric and thermoelectric actuators. Many fluids of interest, including drugs, however, are incapable of being delivered in precise extremely low dose amounts through use of these types of actuating devices, necessitating delivery of a larger volume of fluid for reliability and repeatability of the actuation unit. In addition, many drugs may become damaged or otherwise rendered unfit for their intended purposes through use of conventional actuating units.

There is therefore a need for a microfluidic device which addresses at least some of these problems.

The present invention is directed towards providing such a microfluidic device, and the invention is also directed towards providing a method for delivering a material from a microfluidic device.

According to the invention there is provided a microfluidic device for controllably moving a material of interest, said microfluidic device comprising:

a holding cavity configured to hold the material of interest;

at least one actuator configured to induce an activation material to one of expand and contract, wherein expansion of the activation material decreases the size of the holding cavity to thereby cause the material of interest to be released from the holding cavity and wherein contraction of the activation material increases the size of the holding cavity to thereby cause the material of interest to be received into the holding cavity, the at least one actuator being operable at multiple levels between a zero induction level to a maximum induction level on the activation material to thereby controllably one of expand and contract the holding cavity to release or receive a specified volume of the material of interest.

Preferably, the microfluidic device further comprises at least one delivery orifice configured for fluid communication with the holding cavity.

In one embodiment of the invention the at least one delivery orifice comprises a hydrophobic needle.

In another embodiment of the invention the microfluidic device further comprises at least one of a barrier positioned between the at least one delivery orifice and the holding cavity.

In a further embodiment of the invention the material of interest is configured to flow through one or both of the at least one delivery orifice and the barrier when the activation material one of expands and contracts.

In one embodiment of the invention the activation material comprises a gas

configured to remain in a dissolved state at relatively lower temperatures and to evolve back into a gaseous state at relatively higher temperatures. Preferably, the at least one actuator is configured to increase the temperature of the activation material to evolve the activation material back into the gaseous state and thereby cause the material of interest to be released through the at least one delivery orifice.

In another embodiment of the invention the activation material comprises a hydrogel configured to one of expand and contract with at least one of the application of heat and changes in pH. Preferably, the at least one actuator is configured to at least one of increase the temperature and change the pH of the activation material to one of expand and contract the hydrogel and thereby cause the material of interest to be moved through the at least one delivery orifice.

In another embodiment of the invention the activation material comprises a liquid configured to remain in a liquid state at relatively lower temperatures and to transition into a gaseous state at relatively higher temperatures. Preferably, the at least one actuator is configured to increase the temperature of the activation material to vaporise the liquid into the gaseous sate and thereby cause the material of interest to be released through the at least one delivery orifice.

In a further embodiment of the invention the activation material comprises a material configured to one of expand and contract the holding cavity and thereby cause the material of interest to be drawn into the holding cavity after a pre-vacuum treatment.

In another embodiment of the invention the activation material comprises a chemical configured to dissociate through application of a current from the at least one actuator. Preferably, the at least one actuator is configured to supply the current to the activation material. Advantageously, the activation material is configured to expand through the dissociation caused by receipt of the current. Ideally, expansion of the activation material causes the material of interest to be released through the delivery orifice.

In one embodiment of the invention the activation material comprises at least one of water, alcohol and ammonia.

In another embodiment of the invention the microfluidic device further comprises:

a space configured to hold at least one of a solvent and water; and

a membrane separating the holding cavity and the space;

the at least one actuator being configured to induce the activation material to expand, thereby causing the membrane to break and enabling the material of interest and the at least one of the solvent and the water to mix prior to being moved out of the microfluidic device.

In another embodiment of the invention the microfluidic device further comprises an actuation cavity housing the activation material, wherein the actuation cavity is separated from the holding cavity by a flexible membrane.

In an alternative embodiment of the invention the material of interest is interspersed with the activation material. Preferably, expansion of the activation material causes the material of interest and the activation material to be released through the delivery orifice. Advantageously, the material of interest is substantially coated with a substance configured to substantially separate the material of interest from the activation material. Ideally, the substance substantially coating the material of interest is water insoluble and removable by an enzyme.

In one embodiment of the invention the activation material comprises at least one of di-methyl ether and ethyl methyl ether.

Preferably, the microfluidic device further comprises:

a power source for powering the at least one actuator; and

a controller for controlling delivery of power to the at least one actuator.

Advantageously, the power source and the controller are integrally formed with the microfluidic device.

In one embodiment of the invention the at least one actuator comprises a resistive element configured to become heated through application of a potential difference, allowed by the controller.

In another embodiment of the invention the material of interest is provided in a form which is soluble in a suitable solvent.

In a further embodiment of the invention the material of interest is in the form of a reactant. Preferably, the material of interest is in a pure form.

Preferably, the material of interest is reconstituted in the holding cavity. Advantageously, the material of interest is reconstituted by a solvent. Preferably, the material of interest is reconstituted by contact with the solvent. Ideally, the material of interest is reconstituted by mixing with the solvent.

In another embodiment of the invention the at least one actuator is operable to intersperse the solvent with the material of interest for reconstitution thereof. Preferably, the at least one actuator is operable to intersperse the solvent with the material of interest for reconstitution thereof and to subsequently act on the activation material for releasing the reconstituted material of interest from the holding cavity. Advantageously, the at least one actuator is operable to provide a time delay between the time the solvent is interspersed with the material of interest and the activation material is subsequently acted on for releasing the reconstituted material of interest from the holding cavity. Ideally, the time delay is of sufficient duration for facilitating reconstitution of the material of interest.

In one embodiment of the invention the solvent is held in a holding cavity separate from the holding cavity for holding the material of interest.

Preferably, the solvent comprises a reconstituting amount of the activation material.

In another embodiment of the invention the solvent is provided by the activation material.

In one embodiment of the invention the material of interest is freeze dried.

In another embodiment of the invention the activation material comprises carbon dioxide.

In a further embodiment of the invention the holding cavity comprises dimensions ranging between micron to millimetre scales.

The invention also provides a method for delivering a material of interest from a microfluidic device having at least one cavity and a delivery orifice, said method comprising:

dissolving a gaseous activation material at a relatively low temperature;

inserting the dissolved gaseous activation material into the at least one cavity of the microfluidic device;

maintaining the dissolved gaseous activation material at a relatively low temperature; and

heating the dissolved gaseous activation material to cause the dissolved gaseous activation material to evolve into a gaseous state and expand, expansion of the gaseous activation material causing the material of interest to be delivered out of the delivery orifice.

In another embodiment of the invention the microfluidic device includes a holding cavity and an actuation cavity separated by a flexible membrane, and inserting the dissolved gaseous activation material comprises inserting the dissolved gaseous activation material into the actuation cavity.

In an alternative embodiment of the invention the method further comprises:

combining the material of interest and the dissolved gaseous activation material into a mixture; and

inserting the mixture into the at least one cavity.

Preferably, heating the dissolved gaseous activation material further comprises heating the mixture of the material of interest and the dissolved gaseous activation material.

The invention further provides a method for delivering a material of interest from a microfluidic device having a delivery orifice and an actuator, said method comprising:

coating the material of interest with a protective layer that is water insoluble and removable by an enzyme;

combining the coated material of interest into an activation material;

inserting the activation material with the coated material of interest into the microfluidic device; and

initiating an actuation sequence, the actuation sequence causing the activation material to expand and forcing the activation material and the coated material of interest to be delivered from the microfluidic device.

The invention will be more clearly understood from the following description of some preferred embodiments thereof, which are given by way of example only, with reference to the accompanying drawings, in which:

Fig. 1A shows a block diagram of a microfluidic device for controlled release of material, according to an embodiment of the invention,

Fig. 1B shows a schematic diagram, partially in cross-section, of a part of a microfluidic device, according to an embodiment of the invention,

Fig. 1C shows a schematic diagram similar to Fig. 1B, where an activation system in the microfluidic device has expanded,

Fig. 1D shows a schematic diagram, partially in cross-section, of a part of a microfluidic device, according to another embodiment of the invention,

Fig. 1E shows a schematic diagram, partially in cross-section, of a part of a

microfluidic device, according to a further embodiment of the invention,

Fig. 2 illustrates a graph depicting the amount of carbon dioxide gas evolved as a function of temperature,

Figs. 3 and 4 depict flow diagrams of respective methods for delivering a material from a microfluidic device, according to two embodiments of the invention, and

Fig. 5 is a block diagram illustrating a computer system or other smart device operable to perform one or more functions on a microfluidic device, according to an embodiment of the invention.

For simplicity and illustrative purposes, the principles of the embodiments of the invention are described by referring mainly to examples thereof. In the following description, numerous specific details are set forth in order to provide a thorough understanding of the embodiments. It will be apparent, however, to one of ordinary skill in the art that the embodiments may be practised without limitation to these specific details. In other instances, well known methods and structures have not been described in detail so as not to unnecessarily obscure the embodiments.

With reference first to Fig. 1A, a block diagram 10 of a microfluidic device 100 for controlled release of material is depicted, according to an example. It should be understood that the following description of the block diagram is but one manner of a variety of different manners in which such a microfluidic device 100 may be configured. In addition, it should be understood that the microfluidic device 100 may include additional components and that some of the components described herein may be removed and/or modified without departing from a scope of the microfluidic device 100. For instance, the microfluidic device 100 may include any number of sensors, memories, processors, air moving devices, vent tiles, etc., as well as other components, which may be implemented in the operations of the microfluidic device 100.

As shown in the block diagram 10 of Fig. 1A, the microfluidic device 100 includes a dosing mechanism 12, a container 14, and a delivery device 16. The dosing mechanism 12 may include a plunger or other actuation device capable of applying sufficient force on a material of interest contained in the container 14, such that the material of interest is released or received through the delivery device 16. In addition, the dosing mechanism 12 may operate to controllably release the material of interest from or receive the material of interest into the container 14, through the delivery device 16. It should further be noted that the dosing mechanism 12 may, in some instances, be a sampling mechanism configured to apply sufficient negative force to collect a material of interest through the delivery device 16.

The container 14 may include any reasonably suitable container for containing the material of interest and the delivery device 16 may include, for instance, a needle, an orifice, a tube and the like.

A more detailed description of the elements forming the microfluidic device 100 is provided herein below with respect to Figs. 1B to 1E.

With reference first to Fig. 1B, there is shown a schematic diagram, partially in cross-section, of a part of the microfluidic device 100, according to an example. It should be readily apparent that the microfluidic device 100 depicted in Fig. 1B represents a generalised illustration and that other features may be added or existing features may be removed or modified without departing from a scope of the microfluidic device 100. For example, the microfluidic device 100 may include additional features as discussed herein below.

Generally speaking, the microfluidic device 100 may be employed to controllably deliver a material of interest 102, such as a drug, reagent or other type of material. More particularly, for instance, the microfluidic device 100 may be employed to inject or otherwise supply the material of interest 102 onto or through a surface, such as vial membrane or skin. In addition, or alternatively, the microfluidic device 100 may

be employed to collect a sample of a specific volume of the material of interest 102. In any regard, the microfluidic device 100 may include a plurality of delivery orifices 104, which may include, for instance, microneedles, tubes, etc. In Fig. 1B, a single delivery orifice 104 is depicted for purposes of simplicity. It should be understood, however, that the microfluidic device 100 may include any reasonably suitable number of delivery orifices 104.

As shown in Fig. 1B, the delivery orifice 104 is attached to a first spacer layer 106. The first spacer layer 106 may include any reasonably suitable material, such as silicon, glass, polymers, ceramics, etc. The first spacer layer 106 may be formed with a plurality of holding cavities 108 configured to house some or all of the material of interest 102. In addition, the holding cavities 108 may be associated with respective delivery orifices 104, such that the material of interest 102 contained in one of the holding cavities 108 may be delivered through one or more delivery orifices 104. It should be readily understood that a single holding cavity 108 is depicted in Fig. 1B for purposes of simplicity and not of limitation.

The microfluidic device 100 is also depicted as including an optional barrier 107 between the holding cavity 108 and the delivery orifice 104. The optional barrier 107 may generally operate to substantially prevent the material of interest 102 from being prematurely released through the delivery orifice. In addition, the optional barrier 107 may enable the material of interest 102 to flow into the delivery orifice 104 when sufficient pressure is applied on the material of interest 102 contained in the holding cavity 108. As such, the optional barrier 107 may include one or more openings configured to open or otherwise accommodate fluid movement when a sufficient amount of pressure is applied on the material of interest 102. In addition, or alternatively, the optional barrier 107 may be configured to rupture or otherwise create an opening when a sufficient amount of pressure is applied on the material of interest 102.

The barrier 107 is considered optional because the microfluidic device 100 may operate properly in certain instances without the use of the barrier 107. For

instance, the delivery orifice 104 may include a hydrophobic needle capable of preventing delivery of the material of interest 102 until it is desired to do so, which therefore removes the barrier 107 requirement. It should, however, be understood that the barrier 107 may be used in conjunction with the hydrophobic needle without departing from a scope of the microfluidic device 100. In addition, the barrier 107 may be omitted, for instance, when the delivery orifice 104 includes a hydrophobic needle or when the material of interest 102 may otherwise remain within the holding cavity 108 without the use of the barrier 107, when the barrier 107 is not required to shield the material of interest 102, when the microfluidic device 100 is employed to collect samples of the material of interest 102, as shown in Fig. 1D, etc.

A bottom section of the holding cavity 108 is depicted as being formed by a membrane 110. As discussed in greater detail herein below, the membrane 110 includes a flexible membrane configured to change the size of the holding cavity 108. First, however, a discussion of a second spacer layer 112 is provided. The second spacer layer 112 may include the same material as the first spacer layer 106. Alternatively, however, the second spacer layer 112 may include a different material from the first spacer layer 106, and may include any of the materials listed above with respect to the first spacer layer 106.

According to an example, the first spacer layer 106 and the second spacer layer 112 may include a single component. In this example, the membrane 110 may be formed as part of the first spacer layer 106 and the second spacer layer 112, through, for instance, an etching process. In another example, the first spacer layer 106, the second spacer layer 112 and the membrane 110 may include separate elements that are bonded together.

In any regard, the second spacer layer 112 may include one or more actuation cavities 114 configured to house an activation material 116. The activation material 116 is operable to expand and cause the membrane 110 to deflect, thereby causing the material of interest 102 to be released through the delivery orifice 104. Various examples of suitable activation materials 116 are described herein below. In

addition, although a single actuation cavity 114 is depicted in Fig. 1B, it should be understood that the second spacer layer 112 may include any reasonably suitable number of actuation cavities 114 without departing from a scope of the microfluidic device 100 disclosed herein. The actuation cavity 114 may moreover include multiple compartments.

As shown in Fig. 1B, a top section of the actuation cavity 114 may be formed by the membrane 110. The membrane 110 generally includes a flexible membrane configured to separate the activation material 116 from the material of interest 102 and to increase the size of the actuation cavity 114 as the activation material 116 expands, as shown in greater detail in Fig. 1C. More particularly, and as shown in Fig. 1C, expansion of the activation material 116 causes the membrane 110 above the actuation cavity 114 to deflect in a direction toward the delivery orifice 104. If the deflection of the membrane 110 also reduces the size of the holding cavity 108 for the material of interest 102, the material of interest 102 is then released from the delivery orifice 104, as shown as a released portion 118 of the material of interest 102.

According to another example, and as shown in Fig. 1D, the microfluidic device 100 may operate to draw a material of interest 102 into the holding cavity 108. In Fig. 1D, the activation material 116 is configured to decrease in size, thereby causing the membrane 110 to be deflected away from the delivery orifice 104 and the holding cavity 108 to increase in size. The increase in size of the holding cavity 108 generally causes a negative pressure to be created in the holding cavity 108, which causes the material of interest 102 to be drawn in through the delivery orifice 104, as indicated by the arrow 119.

The activation material 116 may, for instance, include EXPANCEL microspheres available from Expancel, Inc., having an office located in Duluth, Georgia, USA. In this example, the activation material 116 may be in its initial state and may expand when subjected to the appropriate amount of heat, thereby releasing the material of interest 102 through the delivery orifice 104; alternatively, the activation material may

be in a fully expanded state and may shrink when subjected to slightly higher heat, thereby drawing the material of interest 102 through the delivery orifice 104. The activation material 116 may also include hydrogels, which may be engineered to either expand or shrink in volume when heated above a threshold temperature or when subjected to a threshold pH level. Further examples of suitable activation materials 116 may include NH_3-water, $C0_2$-water, etc. The pH levels of these activation materials 116 may change through application of heat. For instance, application of heat on the activation material 116 including the $C0_2$-water will increase the pH of its solution as more and more $C0_2$ escapes from the solution. In addition, application of heat on the activation material 116 including the NH_3-water will decrease the pH of its solution as more and more NH_3 escapes out of the solution. CO_2 and NH_3 are two examples of materials that can change pH with application of temperature. It should be understood, however, that other materials having this property, which may be known to those skilled in the art, may also be employed. Additional examples of suitable activation materials 116 include polyvinylchloride with one or more polyesters configured to shrink with applied heat, such as shrink-wrap, shrink-tubing, etc.

In another example, an external vacuum system may be employed in addition to the activation material 116 to create the negative pressure in the holding cavity 108.

The microfluidic device 100 may be fabricated through any suitable fabrication process. For instance, the microfluidic device 100 may include a silicon or glass substrate and photolithography may be implemented to define the holding and actuation cavities 108 and 114. As another example, the microfluidic device 100 may include silicon, plastic or other polymeric material, and moulding steps may be implemented to fabricate the microfluidic device 100. In addition, various combinations of etching, deposition, lithographic formation, moulding, stamping, imprinting, etc. Processes may be employed to fabricate the microfluidic device 100.

With reference back to Fig. 1B, also shown within the actuation cavity 114 are a plurality of actuators 120. As described in greater detail herein below, the actuators

120 may include various types of actuators and may be operated to controllably expand or contract the activation material 116. Although a plurality of actuators 120 have been illustrated in Fig. 1B, it should be understood that a single actuator 120 may be provided in the actuation cavity 114 without departing from a scope of the microfluidic device 100. In addition, the actuation cavity 114 may contain liquids, gels, solids, vapours, or a combination thereof, which may assist in the expansion or contraction of the activation material 116.

In any regard, the actuators 120 may be controlled on-board, for instance, through a conductive line 126, or remotely by a controller 122, which may include a microprocessor, a microcontroller, an application specific integrated circuit (ASIC), sensors, feedback devices and the like, configured to perform various processing functions. In addition, or alternatively, the controller 122 may include software operating in one or more computing devices. Furthermore, either or both of the controller 122 and a power source 124 may be integrally formed with the microfluidic device 100 or they may include devices that are separate from the microfluidic device 100.

In conjunction with the power source 124, the controller 122 may be configured to activate the actuators 120 according to one or more control schemes. For instance, the controller 122 may be configured to allow actuators 120 to be addressed in response to a local or remote command (for instance, through the push of an activation button or through receipt of a wireless signal). As another example, the controller 122 may be programmed to activate the actuators 120 at a predetermined time, or at predetermined intervals of time, etc. In addition, or alternatively, the controller 122 may be programmed to activate a single actuator, or one or more sets of actuators 120 to deliver the material of interest 102 from a first set of holding cavities 108 at a first time and to activate another set of actuators 120 to deliver the material of interest 102 from a second set of holding cavities 108 at a second time.

In addition, or alternatively, the controller 122 may be programmed to vary operations of the actuators 120 such that the actuators 120 may be operated at

multiple levels between a zero induction level and a maximum induction level on the activation material 116 to thereby controllably expand or contract the holding cavity 108. As such, the controller 122 may control the amounts of the material of interest 102 that are released from or received into the holding cavity 108 at various amounts between a zero amount and a maximum amount.

In one example, the controller 122 may vary the number of actuators 120 that are activated to thereby vary the induction levels applied on the activation material 116. In this example, the controller 122 may be programmed with data indicating the number of actuators 120 required to be activated in order to release a predetermined amount of the material of interest 102. For instance, the controller 122 may be programmed to activate two of the actuators 120 to release 30% of the material of interest 102, to activate three of the actuators 120 to release 50% of the material of interest 102, etc. Likewise, the controller 122 may be programmed to activate two of the actuators 120 to receive an amount of the material of interest 102 that fills 30% of the holding cavity 108, to activate three of the actuators 120 to receive an amount of the material of interest 102 that fills 60% of the holding cavity 108, etc.

In another example, the controller 122 may control the power supplied to the actuators 120. More particularly, for instance, the controller 122 may control the temperatures of the actuators 120 at multiple levels between a zero temperature change to a maximum temperature change, where a maximum temperature change is configured to expand or contract substantially all of the activation material 116. Additionally, the controller 122 may control the temperature changes of the actuators 120 for desired periods of time. For instance, the controller 122 may achieve a first temperature for a first period of time, a second temperature for a second period of time, a third temperature for a third period of time, etc. In this regard, the controller 122 may control the actuators 120 to deliver or receive the material of interest 102 in a multiple dose manner. In this example, the controller 122 may be programmed with data that indicates the amount of time the actuators 120 are required to receive energy to achieve the desired amount of movement of the material of interest 102, the amount of power the actuators 120 are required to receive to achieve the desired

amount of movement, etc.

In any of the above examples, the microfluidic device 100 may include sufficiently small dimensions such that the microfluidic device 100 is capable of substantially accurately releasing or receiving pL, nL and μL volumes. By way of example, the holding cavity 108 may include dimensions ranging between millimetre to micron scales, for instance, 1mm x 1mm x 1mm, 500μm x 500μm x 500μm, etc. In addition, the microfluidic device 100 may be manufactured through, for instance, imprinting, stamping, roll-to-roll processes as well as on discrete substrates and/or with more conventional lithographic processes, etc.

The controller 122 may be configured to instruct specific reservoirs to deliver one or more different types of materials at one or more different times. In one example, the controller 122 may be configured to control the delivery of a plurality of drugs based upon different delivery schedules and doses. In this example, the amount of material of interest 102 delivered may be controlled through control of the individual or sets of actuators 120 positioned in the various reservoirs as described above.

According to another example, the actuators 120 may be controllably activated to thereby create a desired level of expansion or contraction of the activation material 116 in a specific reservoir. In this example, the controller 122 may substantially accurately regulate the amount of the material of interest 102 released from or received by the specific reservoir by controlling the expansion or contraction of the activation material 116 in the specific reservoirs.

In one example, the actuators 120 may include resistive elements which experience a temperature rise in response to applied voltage. The resistive elements comprising the actuators 120 may differ from resistive elements employed in conventional thermal inkjet systems. For instance, in conventional thermal inkjet systems, the resistive elements are configured to heat up very rapidly and thereby cause a substance, such as ink, to vaporise and form a bubble. As the bubble expands, some of the substance/ink is expelled from a holding chamber. Once the

bubble collapses, a vacuum is created which draws more of the substance/ink into the holding chamber from a reservoir. The holding chamber is refilled with the substance and this process is repeated, but it is repeated under a single set of parameters. Any total fluid expelled is a quantised multiple of the number of times the system is fired. As such, simply holding the system at temperature longer does not expel more fluid.

The operating conditions useful for thermal inkjet typically induce damaging cavitation, creating spots of very high temperature and shock. In contrast, the resistive elements comprising the actuators 120 are configured to heat up relatively slower or in multiple stages. It should be noted that boiling is not the same as cavitation. The microfluidic device 100 disclosed herein is designed to operate without cavitational effects and to operate in an analogue fashion (different predetermined amount of the material of interest 102 may be expelled from or received through the delivery orifice 104 at one initiation). In this regard, the amounts of the material of interest 102 that are released or received may be controlled with relatively greater degrees of accuracy and control as compared with the use of thermal inkjet systems.

In this example, the activation material 116 may include a material configured to expand or contract when heated. For instance, the activation material 116 may include a liquid having a sufficiently low boiling point temperature such that the activation material 116 is vaporised through application of heat from the actuators 120. In addition, or alternatively, the activation material 116 may include a solid or a gel configured to expand through application of heat, such as the EXPANCEL microspheres discussed above. The activation material 116 may also include hydrogels engineered to expand or contract after reaching a threshold temperature or when subjected to a threshold pH level.

According to an example, the material of interest 102 contained in the holding cavity 108 may be processed to be highly water soluble to enable two-stage delivery of the material of interest 102. For instance, a reactant material may be kept in a separate

holding cavity and maintained in solid form and just prior to release, or as part of the release, the reactant material may be mixed with a solvent/water to liquefy it or to place it in solution. By way of example, the reactant material may include a freeze-dried material in an extremely pure form, which may be made into a water-free powder that instantaneously goes into solution when brought in contact with the solvent/water. In this example, the freeze-dried material and the solvent/water may be housed in holding cavities 108 that are separated by a membrane configured to break when the activation material 116 is activated.

As another example, the freeze-dried material may be adhered or otherwise contained in the delivery orifice 104, such that the freeze-dried material may be mixed with the solvent/water as the solvent/water is expelled from the holding cavity 108.

The actuators 120 may be operable to initially intersperse the solvent with the reactant material for reconstitution thereof, and then subsequently act on the activation material to expel the reconstituted material from the holding cavity 108. Further, the actuators 120 may be operated with a time delay so that the actuators 120 are initially operated to intersperse the solvent with the reactant material, and after a time period sufficient to allow reconstitution of the reactant material, the actuators 120 are operated to act on the activation material to expel the reconstituted material from the holding cavity 108.

The reactant material, the solvent and the activation material may be held in separate holding cavities. Alternatively, the activation material may be provided in the form of the solvent, and in which case, the reactant material and the activation material would be held in separate holding cavities. Where the activation material is provided in the form of the solvent, the actuators 120 would be initially operated to intersperse some of the activation material with the reactant material to produce the reconstituted material, and the amount of the activation material interspersed with the reactant material would be a reconstituting amount of the activation material. In these cases, where the reactant material and the solvent and/or the activation

material are held in separate holding cavities, the holding cavities would be selectively communicable, and in general, would be communicable in response to operation of the actuators 120. Depending on the type of actuators 120, only some of the actuators 120 may be initially operable to intersperse the solvent or the activation material with the reactant material, as the case may be, and then others of the actuators 120 would be operable to act on the activation material to expel the reconstituted material from the holding cavity 108.

The activation material 116 may additionally, or alternatively, include a chemical configured to expand by evolving into a gas through receipt of a current. In this example, the actuators 120 may include devices configured to apply a current through the activation material 116 to thereby cause dissociation of the activation material 116 and expansion of the actuation cavity 114. By way of example, the activation material 116 may include a material configured to expand when heated. Examples of suitable activation materials 116 include ethyl alcohol, isopropyl alcohol, etc. In addition, the activation material 116 may include carbon dioxide in water or ammonia in water.

In another example, the microfluidic device 100 may be configured to deliver a mixture 130 of the activation material 116 and the material of interest 102. In this example, expansion of the activation material 116 may cause both the material of interest 102 and the activation material 116 to be released from the microfluidic device 100. In one regard, therefore, the activation material 116 may include a relatively inert material that does not substantially affect the material of interest 102 nor the target into which the mixture 130 is delivered.

An example of a microfluidic device 100' configured to deliver the mixture 130 of the activation material 116 and the material of interest 102 is shown in Fig. 1E. Many of the elements depicted in Fig. 1E have the same reference numerals as those depicted in Figs. 1B and 1C. It should be understood that those elements that those elements that share the same reference numerals are the same in all of the figures and thus a detailed discussion of those elements is omitted with respect to Fig. 1E.

Instead, those elements in Fig. 1E that differ from the elements shown in Figs. 1B and 1C are described with respect to Fig. 1E.

As shown, the microfluidic device 100' includes a single chamber 132 that houses the mixture 130. The single chamber 132 may be formed in a layer 134 of silicon, glass, plastic, polymeric material, etc. In addition, as the activation material 116 expands, the mixture 130 is forced out of the delivery orifice 104. In one regard, therefore, the mixture 130 may contain a sufficient amount of activation material 116 to generally cause a sufficient amount of pressure inside the chamber 132 to cause a desired amount of the material of interest 102 to be released through the delivery orifice 104.

In one example, the activation material 116 may include a dissolved gas configured to remain in the dissolved state at a relatively lower temperature and is configured to return to the gaseous state around a relatively higher temperature. An example of a suitable activation material 116 includes carbon dioxide. More particularly, for instance, carbon dioxide may be dissolved in water within a pH range of around 4 to 9 and at a relatively lower temperature, and the dissolved carbon dioxide may be distributed with a material of interest 102 to form the mixture 130. The gas capture is illustrated in the following examples:

$$CO_2 + H_2O \Rightarrow H_2CO_3$$

$$NH_3 + H_2O \Rightarrow NH_4{}^{+}OH$$

Moreover, the mixture 130 may be expanded through application of heat through the actuators 120 as described above. A graphical representation of how carbon dioxide may be employed as the activation material 116 is depicted in Fig. 2. More particularly, depicted in Fig. 2 is a graph 200 illustrating the amount of carbon dioxide gas evolved as a function of temperature, assuming a water volume of 1pl. Horizontal axis 202 of the graph 200 shows the temperature in degrees Celsius. Vertical axis 204 shows litres of gas evolved per µg of water (H_2O). Vertical axis 206 shows the solubility of carbon dioxide (CO_2) per 100g of water (H_2O). In addition, the thinner line 208 indicates the grams of carbon dioxide dissolved per 100 grams of

water at various temperatures and the thicker line 210 indicates the litres of gas evolved over a temperature of 20°C.

As shown in Fig. 2, a relatively large amount of gas may be evolved from a relatively small amount of dissolved carbon dioxide. In this regard, carbon dioxide may be suitable for use as the activation material 116 in the microfluidic device 100'. In addition, the dissolved carbon dioxide may be employed as the activation material 116 in the microfluidic device 100 depicted in Figs. 1B and 1C.

According to another example, the material of interest 102 may be combined in the activation material 116 and may be coated with a material (not shown) configured to protect the material of interest 102 from the activation material 116. In this example, the coating material may include a water insoluble, but enzyme removable material, such as polypeptides, gelatine, starch, etc. Following injection/insertion of the material of interest 102, the coating may be stripped away by a reagent, bodily fluids, etc., which would make the material of interest 102 available for use in the system into which it was introduced.

Figs. 3 and 4 show flow diagrams of respective methods 300 and 400 for delivering a material of interest from a microfluidic device, according to two examples. It is to be understood that the following description of the methods 300 and 400 are but two manners of a variety of different manners in which examples of the invention may be practised. It should also be apparent to those of ordinary skill in the art that the methods 300 and 400 represent generalised illustrations and that other steps may be added or existing steps may be removed, modified or rearranged without departing from the scopes of the methods 300 and 400.

The descriptions of the methods 300 and 400 are made with reference to the microfluidic devices 100, 100' illustrated in Figs. 1A to 1E, and thus makes reference to the elements cited therein. It should, however, be understood that the methods 300 and 400 are not limited to the elements set forth in the microfluidic devices 100, 100'. Instead, it should be understood that the methods 300 and 400 may be

practised by a microfluidic device having a different configuration than that set forth in the microfluidic devices 100, 100' depicted in figs. 1A to 1E.

With particular reference first to Fig. 3, a gaseous activation material 116 is dissolved at a relatively low temperature at step 310. The gaseous activation material 116 may include carbon dioxide, ammonia, di-methyl ether, methyl ether or any water soluble or partial soluble gaseous chemicals, etc. For instance, carbon dioxide may be dissolved at a temperature according to the graph 200 depicted in Fig. 2.

At step 320, the dissolved gaseous activation material 116 may be inserted into at least one of the holding and actuation cavities 108, 114 of the microfluidic device 100, 100'. In a first example, the dissolved gaseous activation material 116 may be inserted into the actuation cavity 114 as illustrated in Fig. 1B to thereby maintain a separation between the dissolved gaseous activation material 116 and the holding cavity 108. In a second example, the dissolved gaseous activation material 116 may be combined with the material of interest 102 to form a mixture 130 and the mixture 130 may be housed in single chamber 132 of the microfluidic device 100' depicted in Fig. 1E.

In either example, the dissolved gaseous activation material 116 housed in the microfluidic device 100, 100' may be maintained at a relatively low temperature as indicated at step 330. Again, the relatively low temperature may be selected according to the correlations depicted in the graph 200, or any other temperature below the threshold of harm to the material of interest 102 or the maximum temperature of any part or subject in the delivery path.

In addition, at step 340, the dissolved gaseous activation material 116 may be heated to thereby evolve the gaseous activation material 116 back into a gaseous state and expand, where expansion of the gaseous activation material 116 causes the material of interest 102 to be released from the microfluidic device 100, 100'.

With reference now to Fig. 4, the material of interest 102 is coated with a protective layer comprising a substance that is water insoluble and removable by an enzyme at step 410. In addition, the coated material 102 may be immersed into an activation material 116 to form a mixture 130 at step 420. At step 430, the mixture 130 may be placed into a cavity 132 of the microfluidic device 100', as shown in Fig. 1E.

At step 440, an actuation sequence may be initiated to cause delivery of the coated material of interest 102. In the actuation sequence, an actuator 120 may be activated to cause the activation material 116 to expand, where expansion of the activation material 116 forces the activation material 116 and the coated material of interest 102 to be delivered from the microfluidic device 100'.

Referring to Fig. 5, a schematic diagram of a computer system 500 is shown in accordance with an embodiment. The computer system or other smart device 500 shown may be used as the controller 122 in the microfluidic devices 100, 100' shown in Fig. 1A to 1E. In one regard, computer system or other smart device 500 may be configured to receive various inputs and to control operations of the actuators 120 to thereby control delivery of the material 102 from the microfluidic devices 100, 100'. By way of example, system 500 may include software, internal or external storage media and a timing circuit to activate one or more of the actuators 120 after a predetermined time period or time intervals to cause a local increase in the temperature which causes the activation material 116 to expand and which then causes material of interest 102, such as a drug, to be delivered from the microfluidic device 100, 100'.

The system 500 may include a processor 510, which generally provides an execution platform for executing software for controlling the actuators 120. The system 500 also includes memory 520, which may include internal, external, fixed, removable or programmable storage.

A user may interface with the system 500 with one or more input devices 530, such as a keyboard, a mouse, a stylus and the like. The user may also interface with the

system 500 with a display 540. A network interface 550, such as telephone, IR or other bus types, may be provided for communicating with other data storage, retrieval and analysis systems. One or more components of the system 500 may be considered optional, such as the display and input device, and other types of components may be used or substituted without departing from a scope of the system 500.

It will be appreciated that the microfluidic devices described may be provided with the power source 124 and the controller 122 integrally formed with the microfluidic devices, or the microfluidic devices may be provided for use with a remote power source 124 and/or a remote controller 122, and in cases where the microfluidic devices are supplied for use with a remote controller 122, a suitable interface would be provided on the microfluidic device for interfacing with the remote controller 122.

What has been described and illustrated herein are embodiments along with some of their variations. The terms, descriptions and figures used herein are set forth by way of illustration only and are not meant as limitations. Those skilled in the art will recognise that many variations are possible within the spirit and scope of the subject matter, which is intended to be defined by the following claims – and their equivalents – in which all terms are meant in their broadest reasonable sense unless otherwise indicated.

Claims

1. A microfluidic device for controllably moving a material of interest, said microfluidic device comprising:

a holding cavity configured to hold the material of interest;

at least one actuator configured to induce an activation material to one of expand and contract, wherein expansion of the activation material decreases the size of the holding cavity to thereby cause the material of interest to be released from the holding cavity and wherein contraction of the activation material increases the size of the holding cavity to thereby cause the material of interest to be received into the holding cavity, the at least one actuator being operable at multiple levels between a zero induction level to a maximum induction level on the activation material to thereby controllably one of expand and contract the holding cavity to release or receive a specified volume of the material of interest.

2. A microfluidic device as claimed in Claim 1 further comprising at least one delivery orifice configured for fluid communication with the holding cavity.

3. A microfluidic device as claimed in Claim 2 in which the at least one delivery orifice comprises a hydrophobic needle.

4. A microfluidic device as claimed in Claim 2 or 3 further comprising at least one of a barrier positioned between the at least one delivery orifice and the holding cavity.

5. A microfluidic device as claimed in Claim 4 in which the material of interest is configured to flow through one or both of the at least one delivery orifice and the barrier when the activation material one of expands and contracts.

6. A microfluidic device as claimed in any of Claims 2 to 5 in which the activation material comprises a gas configured to remain in a dissolved state at relatively lower temperatures and to evolve back into a gaseous state at relatively higher temperatures.

7. A microfluidic device as claimed in Claim 6 in which the at least one actuator is configured to increase the temperature of the activation material to evolve the activation material back into the gaseous state and thereby cause the material of interest to be released through the at least one delivery orifice.

8. A microfluidic device as claimed in any of Claims 2 to 5 in which the activation material comprises a hydrogel configured to one of expand and contract with at least one of the application of heat and changes in pH.

9. A microfluidic device as claimed in Claim 8 in which the at least one actuator is configured to at least one of increase the temperature and change the pH of the activation material to one of expand and contract the hydrogel and thereby cause the material of interest to be moved through the at least one delivery orifice.

10. A microfluidic device as claimed in any of Claims 2 to 5 in which the activation material comprises a liquid configured to remain in a liquid state at relatively lower temperatures and to transition into a gaseous state at relatively higher temperatures.

11. A microfluidic device as claimed in Claim 10 in which the at least one actuator is configured to increase the temperature of the activation material to vaporise the liquid into the gaseous sate and thereby cause the material of interest to be released through the at least one delivery orifice.

12. A microfluidic device as claimed in any of Claims 2 to 5 in which the activation material comprises a material configured to one of expand and contract the holding cavity and thereby cause the material of interest to be drawn into the holding cavity after a pre-vacuum treatment.

13. A microfluidic device as claimed in any of Claims 2 to 5 in which the activation material comprises a chemical configured to dissociate through application

of a current from the at least one actuator.

14. A microfluidic device as claimed in Claim 13 in which the at least one actuator is configured to supply the current to the activation material.

15. A microfluidic device as claimed in Claim 13 or 14 in which the activation material is configured to expand through the dissociation caused by receipt of the current.

16. A microfluidic device as claimed in Claim 15 in which expansion of the activation material causes the material of interest to be released through the delivery orifice.

17. A microfluidic device as claimed in any of Claims 13 to 16 in which the activation material comprises at least one of water, alcohol and ammonia.

18. A microfluidic device as claimed in any of Claims 2 to 17 further comprising:
a space configured to hold at least one of a solvent and water; and
a membrane separating the holding cavity and the space;
the at least one actuator being configured to induce the activation material to expand, thereby causing the membrane to break and enabling the material of interest and the at least one of the solvent and the water to mix prior to being moved out of the microfluidic device.

19. A microfluidic device as claimed in any of Claims 2 to 18 further comprising an actuation cavity housing the activation material, wherein the actuation cavity is separated from the holding cavity by a flexible membrane.

20. A microfluidic device as claimed in any of Claims 2 to 18 in which the material of interest is interspersed with the activation material.

21. A microfluidic device as claimed in Claim 20 in which expansion of the

activation material causes the material of interest and the activation material to be released through the delivery orifice.

22. A microfluidic device as claimed in Claim 20 or 21 in which the material of interest is substantially coated with a substance configured to substantially separate the material of interest from the activation material.

23. A microfluidic device as claimed in Claim 22 in which the substance substantially coating the material of interest is water insoluble and removable by an enzyme.

24. A microfluidic device as claimed in Claim 22 or 23 in which the activation material comprises at least one of di-methyl ether and ethyl methyl ether.

25. A microfluidic device as claimed in any preceding claim further comprising:
a power source for powering the at least one actuator; and
a controller for controlling delivery of power to the at least one actuator.

26. A microfluidic device as claimed in Claim 25 in which the power source and the controller are integrally formed with the microfluidic device.

27. A microfluidic device as claimed in Claim 25 or 26 in which the at least one actuator comprises a resistive element configured to become heated through application of a potential difference, allowed by the controller.

28. A microfluidic device as claimed in any of Claims 2 to 5 in which the material of interest is provided in a form which is soluble in a suitable solvent.

29. A microfluidic device as claimed in Claim 28 in which the material of interest is in the form of a reactant.

30. A microfluidic device as claimed in Claim 28 or 29 in which the material of interest is in a pure form.

31. A microfluidic device as claimed in any of Claims 28 to 30 in which the material of interest is reconstituted in the holding cavity.

32. A microfluidic device as claimed in any of Claims 28 to 31 in which the material of interest is reconstituted by a solvent.

33. A microfluidic device as claimed in Claim 32 in which the material of interest is reconstituted by contact with the solvent.

34. A microfluidic device as claimed in Claim 32 or 33 in which the material of interest is reconstituted by mixing with the solvent.

35. A microfluidic device as claimed in any of Claims 32 to 34 in which the at least one actuator is operable to intersperse the solvent with the material of interest for reconstitution thereof.

36. A microfluidic device as claimed in Claim 35 in which the at least one actuator is operable to intersperse the solvent with the material of interest for reconstitution thereof and to subsequently act on the activation material for releasing the reconstituted material of interest from the holding cavity.

37. A microfluidic device as claimed in Claim 36 in which the at least one actuator is operable to provide a time delay between the time the solvent is interspersed with the material of interest and the activation material is subsequently acted on for releasing the reconstituted material of interest from the holding cavity.

38. A microfluidic device as claimed in Claim 36 in which the time delay is of sufficient duration for facilitating reconstitution of the material of interest.

39. A microfluidic device as claimed in any of Claims 32 to 38 in which the solvent is held in a holding cavity separate from the holding cavity for holding the material of interest.

40. A microfluidic device as claimed in any of Claims 32 to 39 in which the solvent comprises a reconstituting amount of the activation material.

41. A microfluidic device as claimed in any of Claims 31 to 36 in which the solvent is provided by the activation material.

42. A microfluidic device as claimed in any of Claims 28 to 41 in which the material of interest is freeze-dried.

43. A microfluidic device as claimed in any preceding claim in which the activation material comprises carbon dioxide.

44. A microfluidic device as claimed in any preceding claim in which the holding cavity comprises dimensions ranging between micron to millimetre scales.

45. A method for delivering a material of interest from a microfluidic device having at least one cavity and a delivery orifice, said method comprising:

dissolving a gaseous activation material at a relatively low temperature;

inserting the dissolved gaseous activation material into the at least one cavity of the microfluidic device;

maintaining the dissolved gaseous activation material at a relatively low temperature; and

heating the dissolved gaseous activation material to cause the dissolved gaseous activation material to evolve into a gaseous state and expand, expansion of the gaseous activation material causing the material of interest to be delivered out of the delivery orifice.

46. A method as claimed in Claim 45 in which the microfluidic device includes a holding cavity and an actuation cavity separated by a flexible membrane, and inserting the dissolved gaseous activation material comprises inserting the dissolved gaseous activation material into the actuation cavity.

47. A method as claimed in Claim 45 further comprising:

combining the material of interest and the dissolved gaseous activation material into a mixture; and

inserting the mixture into the at least one cavity.

48. A method as claimed in Claim 47 in which heating the dissolved gaseous activation material further comprises heating the mixture of the material of interest and the dissolved gaseous activation material.

49. A method for delivering a material of interest from a microfluidic device having a delivery orifice and an actuator, said method comprising:

coating the material of interest with a protective layer that is water insoluble and removable by an enzyme;

combining the coated material of interest into an activation material;

inserting the activation material with the coated material of interest into the microfluidic device; and

initiating an actuation sequence, the actuation sequence causing the activation material to expand and forcing the activation material and the coated material of interest to be delivered from the microfluidic device.

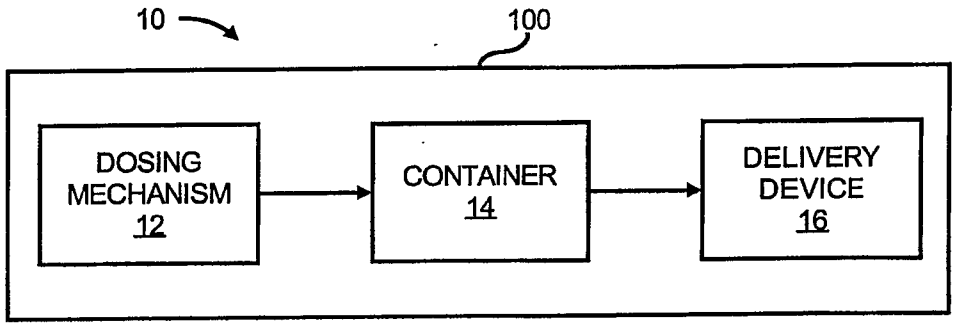

10
100
DOSING MECHANISM 12
CONTAINER 14
DELIVERY DEVICE 16

FIG. 1A

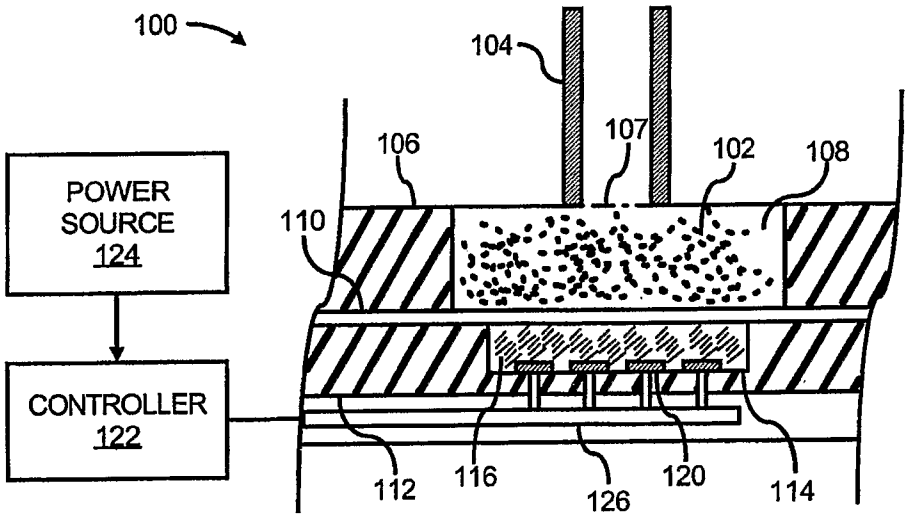
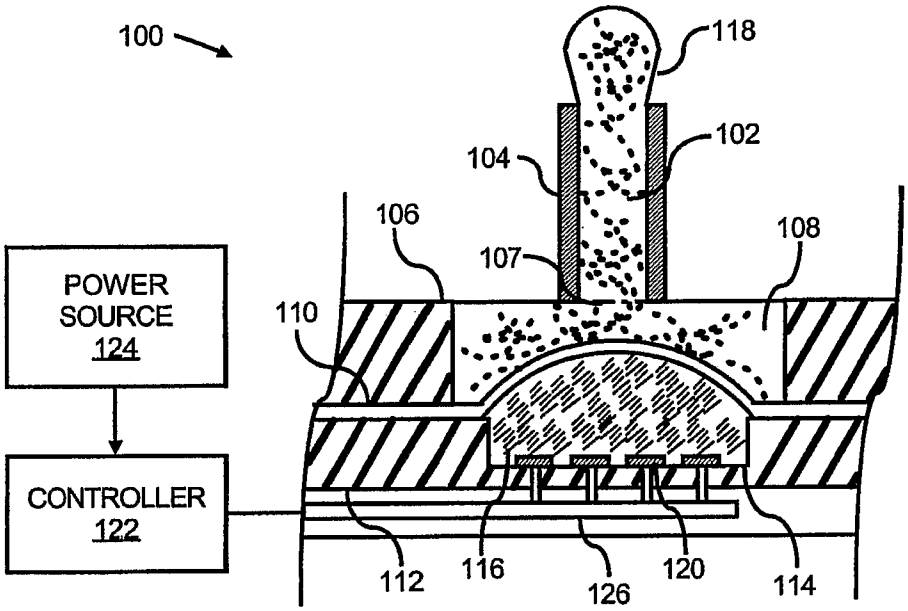

100
104
106
107
102
108
110
POWER SOURCE 124
CONTROLLER 122
112
116
126
120
114

FIG. 1B


100
118
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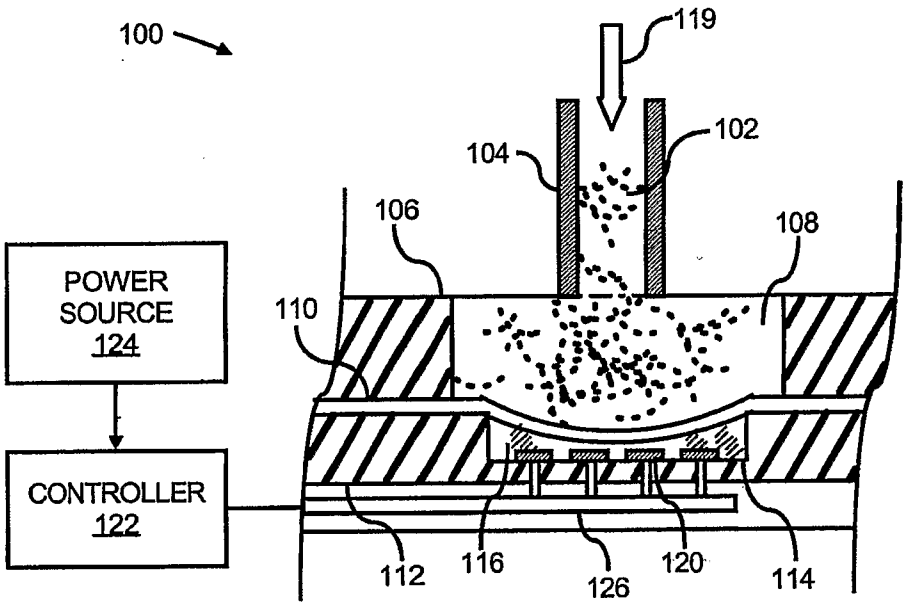
106
107
108
110
POWER SOURCE 124
CONTROLLER 122
112
116
126
120
114

FIG. 1C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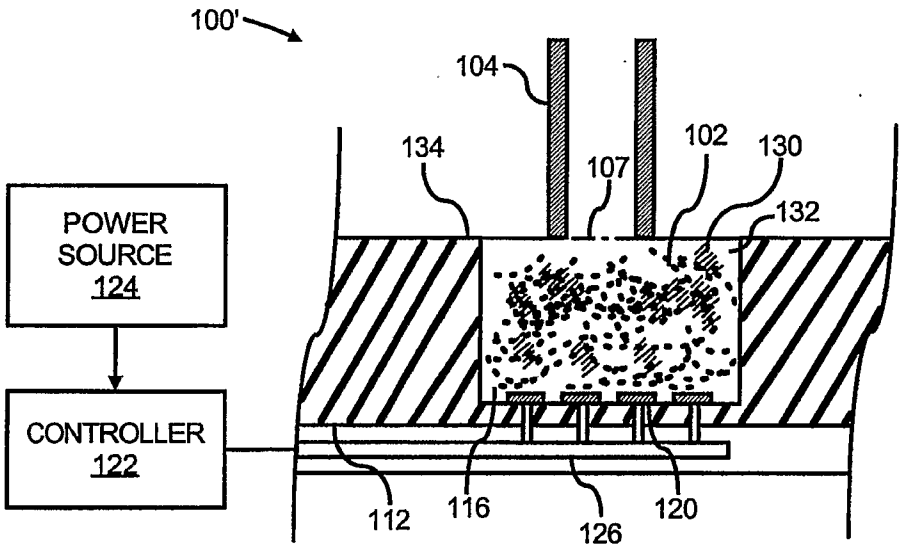
102
104
106
108
110
POWER SOURCE 124
CONTROLLER 122
112
116
126
120
114

FIG. 1D


100'
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134
107
102
130
132
POWER SOURCE 124
CONTROLLER 122
112
116
126
120

FIG. 1E

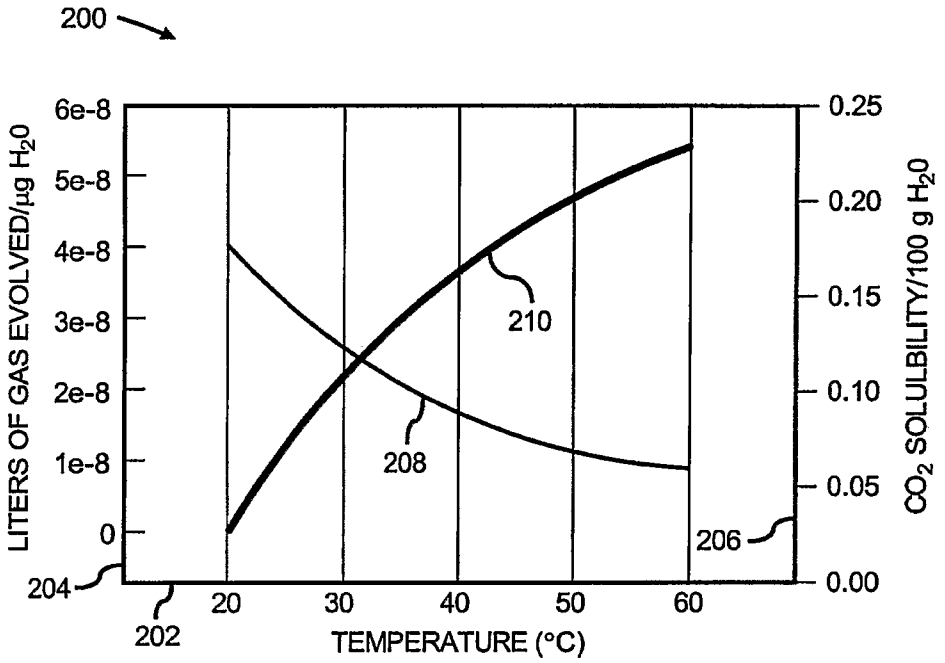
200
6e-8
5e-8
4e-8
3e-8
2e-8
1e-8
0
LITERS OF GAS EVOLVED/μg H_2O
0.25
0.20
0.15
0.10
0.05
0.00
CO_2 SOLULBILITY/100 g H_2O
210
208
206
204
202
20
30
40
50
60
TEMPERATURE (°C)

FIG. 2

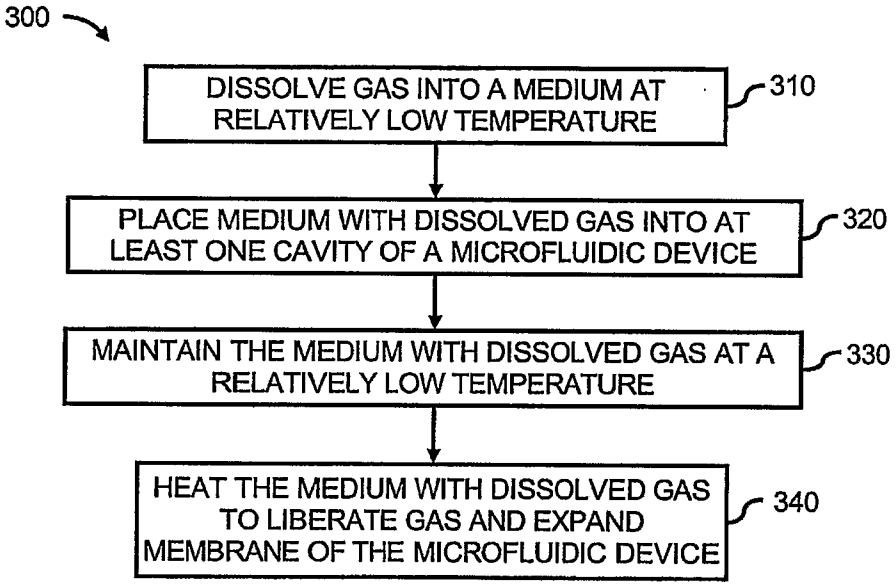
300
DISSOLVE GAS INTO A MEDIUM AT RELATIVELY LOW TEMPERATURE
310
PLACE MEDIUM WITH DISSOLVED GAS INTO AT LEAST ONE CAVITY OF A MICROFLUIDIC DEVICE
320
MAINTAIN THE MEDIUM WITH DISSOLVED GAS AT A RELATIVELY LOW TEMPERATURE
330
HEAT THE MEDIUM WITH DISSOLVED GAS TO LIBERATE GAS AND EXPAND MEMBRANE OF THE MICROFLUIDIC DEVICE
340

FIG. 3

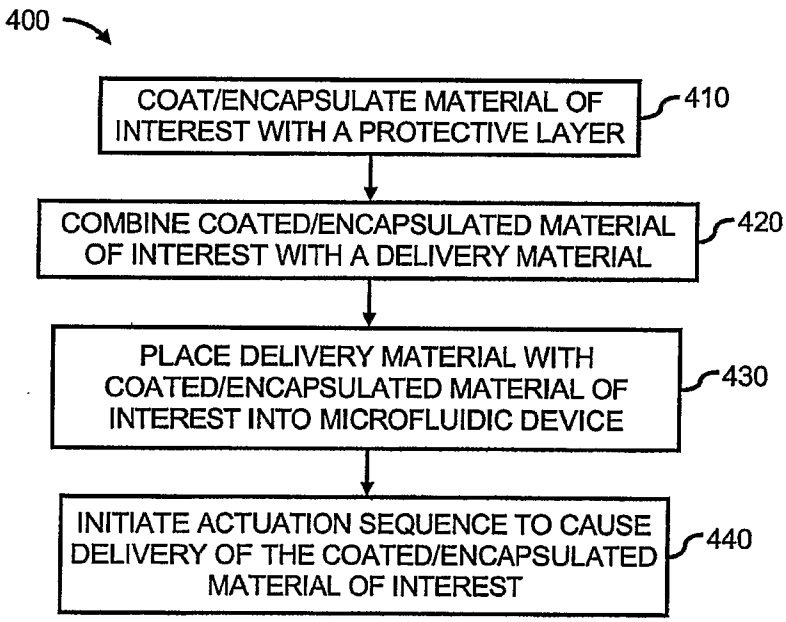
400
COAT/ENCAPSULATE MATERIAL OF INTEREST WITH A PROTECTIVE LAYER
410
COMBINE COATED/ENCAPSULATED MATERIAL OF INTEREST WITH A DELIVERY MATERIAL
420
PLACE DELIVERY MATERIAL WITH COATED/ENCAPSULATED MATERIAL OF INTEREST INTO MICROFLUIDIC DEVICE
430
INITIATE ACTUATION SEQUENCE TO CAUSE DELIVERY OF THE COATED/ENCAPSULATED MATERIAL OF INTEREST
440

FIG. 4

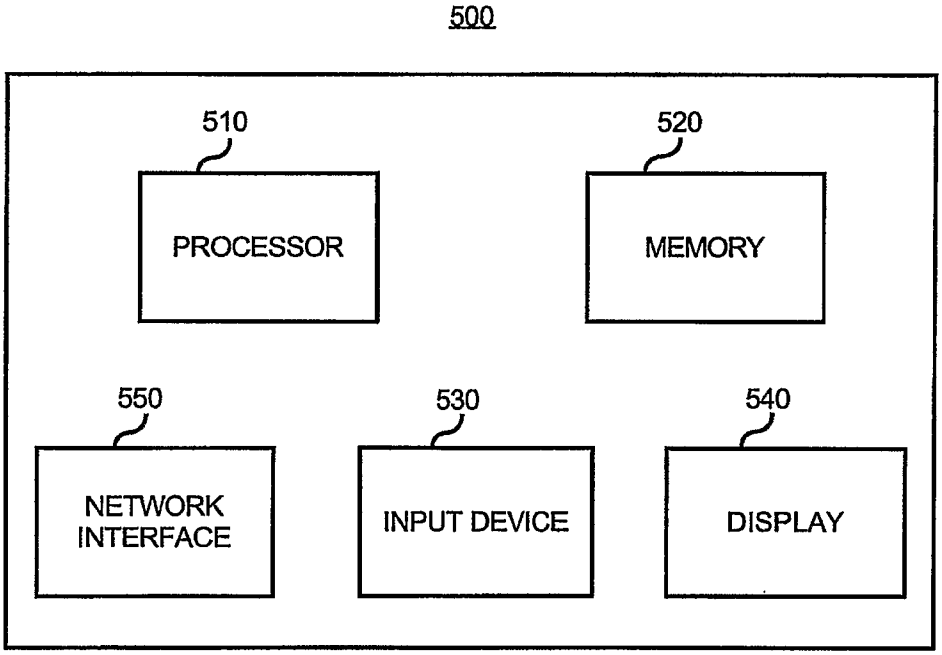
500
510
PROCESSOR
520
MEMORY
550
NETWORK INTERFACE
530
INPUT DEVICE
540
DISPLAY

FIG. 5

INTERNATIONAL SEARCH REPORT

International application No
PCT/IE2007/000074

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01L3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/016558 A (COPPETA JONATHAN, R [US] ET AL) 24 February 2005 (2005-02-24) page 10, lines 5-13; figure 4 page 13, line 27 - page 14, line 4 page 22, lines 4-7 page 22, line 24 - page 23, line 11 page 24, lines 3-26 page 25, lines 29-31	1-5, 10-44,49
Y		8,9

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
9 November 2007	20/11/2007

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hoyal, Barnaby

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	HILT ET AL: "Microfabricated drug delivery devices" INTERNATIONAL JOURNAL OF PHARMACEUTICS, AMSTERDAM, NL, vol. 306, no. 1-2, 8 December 2005 (2005-12-08), pages 15-23, XP005173572 ISSN: 0378-5173 page 18, column 2, line 14 - page 19, column 1, line 24 page 19, column 2, line 1 - page 20, column 2, line 9	1,3,8,9, 44
Y	US 2005/038379 A1 (BEEBE DAVID J [US] ET AL) 17 February 2005 (2005-02-17) paragraphs [0012], [0014], [0016]; figures 12,13	8,9
A	US 2004/248326 A1 (ZIAIE BABAK [US] ET AL) 9 December 2004 (2004-12-09) paragraphs [0028], [0029], [0068], [0083]; figures 9-12	1,8,9
P,X	US 2007/104023 A1 (HOOD LEROY E [US] ET AL) 10 May 2007 (2007-05-10) paragraphs [0113], [0114], [0138]	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/IE2007/000074

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2005016558 A	24-02-2005	NONE	
US 2005038379 A1	17-02-2005	NONE	
US 2004248326 A1	09-12-2004	NONE	
US 2007104023 A1	10-05-2007	US 2007147170 A1	28-06-2007
		US 2007149954 A1	28-06-2007
		WO 2007056473 A2	18-05-2007