The invention provides for a dispensing assembly (100, 100', 100'', 200, 300, 500, 600, 700, 900) comprising a cartridge holder (102). The cartridge holder is operable for receiving a cartridge (108, 108', 108'') operable for dispensing a fluid (206). The cartridge comprises a reservoir (114, 804, 908) operable for receiving the fluid. The reservoir comprises an outlet (115, 806). The reservoir has an adjustable volume for forcing the fluid through the outlet. The cartridge further comprises a nozzle (116, 912) for dispensing the fluid. The nozzle is connected to the outlet. The dispensing assembly further comprises an actuator (104) for actuating the adjustable volume. The dispensing assembly further comprises an impulse generator (106) for imparting an impulse to the nozzle. The impulse generator comprises an actuator (118) for contacting the nozzle. The dispense assembly further comprises a controller (202, 420) for controlling the actuator and the impulse generator.

Declarations under Rule 4.17:
— as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(H))

Published:
— with international search report (Art. 21(3))
**Description**

**Field of the invention**

The invention relates to the dispensing of fluids.

5 **Background and related art**

In medical laboratories, in vitro diagnostics are commonly performed on biological samples. Such tests may be performed manually using pipettes or maybe performed using an automatic analyzer. Automatic analyzers may automatically add reagents to the biological sample and may measure one or more physical properties.
of the biological sample during analysis. Automatic analyzers are known in the prior art. For example, European patent EP 1 959 257 A2 discloses an automatic analyzer including a reagent cassette holding mechanism for holding a plurality of reagent cassettes.

United States patent US 5,763,278 discloses an automatic pipetting device for small volumes. The device has a pipetting needle and a diluter having a liquid output with a syringe and a valve. The syringe includes a piston and piston drive. Tubing connects the needle and the liquid output of the diluter. An impulse generator is connected to the device and coupled to liquid in the tubing for generating and applying directly to the liquid a mechanical impulse force of at least 0.1 N•s for separating the liquid from the needle.

United States patent application publication 2007/0248498 A1 discloses an apparatus for dispensing small volumes of liquid from a cartridge. An electro-optically sensing meniscus detector is used to detect the position of an emerging meniscus of a nascent drop from a dispensing tip. A pneumatic piston is used to drive the entire cartridge against a stationary mass to detach a micro drop from the dispensing tip.

European patent application EP 1 206 966 A1 discloses an automatic pipetting system for receiving and releasing liquid samples. The system comprises a pump consisting of a cylinder chamber, a plunger and a plunger drive. An impulse generator imparts an impulse to the plunger which causes a pressure wave within a fluid in the cylindrical chamber for releasing the liquid.

Summary
The invention provides for a dispensing assembly and an automatic analyzer in the independent claims. Embodiments are given in the dependent claims.

A controller as used herein encompasses a device, machine, or apparatus for controlling the operation and/or function of one or more other devices. Examples of a controller may include, but are not limited to: a computer, a processor, an imbedded system or controller, a programmable logic controller, and a
A 'computing device' or 'computer' as used herein encompasses to any device comprising a processor. A 'processor' as used herein encompasses an electronic component which is able to execute a program or machine executable instruction.

A 'computer-readable storage medium' as used herein encompasses any tangible storage medium which may store instructions which are executable by a processor of a computing device. The computer-readable storage medium may be referred to as a computer-readable non-transitory storage medium.

'Computer memory' or 'memory' is an example of a computer-readable storage medium. Computer memory is any memory which is directly accessible to a processor or other controller. 'Computer storage' or 'storage' is an example of a computer-readable storage medium. Computer storage is any non-volatile computer-readable storage medium.

A 'user interface' as used herein is an interface which allows a user or operator to interact with a computer or computer system.

A 'hardware interface' as used herein encompasses a interface which enables a processor or other controller to interact with and/or control an external computing device and/or apparatus. A hardware interface may allow a processor to send control signals or instructions to an external computing device and/or apparatus.

In one aspect the invention provides for a dispensing assembly. The dispensing assembly comprises a cartridge holder. The cartridge holder is operable for receiving a cartridge operable for dispensing a fluid. The cartridge comprises a reservoir operable for receiving the fluid. The reservoir comprises an outlet. The reservoir has an adjustable volume for forcing the fluid through the outlet. In some embodiments the volume of the reservoir may be increased to suck fluid into the reservoir. In some embodiments the volume of the reservoir may also be increased to aspirate liquid through the nozzle. This may be used for example to fill the reservoir.
The cartridge further comprises a nozzle for dispensing the fluid. The nozzle is connected to the outlet. The dispensing assembly further comprises an actuator for actuating the adjustable volume. The dispensing assembly further comprises an impulse generator for imparting an impulse to the nozzle. This embodiment may be beneficial because it may provide a means of dispensing the fluid more accurately. The impulse generator may be able to knock droplets or drops out of the nozzle or off of the nozzle to make the dispensing more reliable and more reproducible.

The impulse generator may take different forms depending on how it is constructed. It may be a piezoelectric actuator and may use such things as a piston or ring for actuating the nozzle. The impulse generator may be pneumatically actuated; this may include a concentric nozzle or a fan jet. The actuator may be an electromagnetically actuated piston and plunger, for example a hard magnet inside of a coil. The impulse generator may further be a piston and plunger actuated by a linear drive or a motor of some sort. The impulse generator may further be an acoustic or ultrasonic impulse generator.

The term "actor" as understood herein relates to a mechanical contact element that can be driven to mechanically act upon another element, e.g. the elastomeric fluid conduit, by exercising a mechanical force.

The impulse generator comprises an actor for contacting the nozzle. The actor may be used for imparting the impulse to the nozzle. The impulse is communicated from the impulse generator directly to the nozzle.

In contrast to the present invention, in United States patent application publication US 2007/0248498 A1 a pneumatic piston is used to drive the entire cartridge against a stationary mass to detach a micro drop from the dispensing tip. Also in contrast to the present invention, European patent application EP 1 206 966 A1 discloses transferring an impulse to the plunger. Both of these documents teach the imparting of an impulse indirectly to the nozzle.

Imparting the impulse directly to the nozzle as is done in the present invention, may reduce the amount of force needed to knock a drop from the nozzle in comparison
with the dispensing systems of US 2007/0248498 A 1 or EP 1 206 966 A 1. This may be particularly beneficial when the fluid to be dispensed is sensitive to shear forces.

The actuator may take several different forms. In one embodiment the actuator is a syringe pump. However, other such sorts of pumps such as peristaltic pump, a diaphragm pump or other pressure-generating system may also be used. In some embodiments the cartridge comprises a plunger, however this is not necessary. There could be no plunger at all or the plunger could be part of the actuator.

In another embodiment the nozzle is a flexible nozzle.

In another embodiment the dispensing assembly further comprises a meniscus detector for detecting a meniscus of the fluid.

In another embodiment the cartridge further comprises a piston wherein the piston is operable for changing the volume of the reservoir and for forcing the fluid through the outlet.

In another embodiment the dispensing assembly further comprises a controller for controlling the actuator and the impulse generator.

In another embodiment the dispensing assembly further comprises a meniscus detector for detecting the meniscus of the fluid. The controller is operable or programmed for controlling the actuator to force the fluid through the outlet. The controller is further operable or programmed for detecting the meniscus using the meniscus detector. The controller is further operable or programmed for controlling the actuator to halt the forcing of the fluid through the outlet when the meniscus is in a predetermined location. This embodiment may be beneficial because if the meniscus is in the same place when the fluid dispensing starts then the dispensing of the fluid may be more accurate, more precise and/or more reproducible. The meniscus may be inside or outside the nozzle. For instance the nozzle may be a long tube-like structure and the meniscus may have a particular position within the tube. In other embodiments the meniscus may be formed by a drop of the fluid hanging from the nozzle. So in this case the meniscus may therefore be inside or
outside the flexible nozzle. In many applications, the meniscus is preferably positioned right at the orifice of the nozzle.

In another embodiment the controller is further operable or programmed for controlling the actuator to force a predetermined volume of fluid through the outlet. In some embodiments the actuator may be controlled to force the predetermined volume after the meniscus is in the predetermined location. The controller is further operable or programmed for controlling the impulse generator to impart an impulse to the nozzle after the predetermined volume of fluid is forced through the outlet.

This embodiment may be beneficial because it may be used to knock or remove fluid from the nozzle in a controllable and defined fashion; after dispensing this may make the dispensing of the fluid more accurate and more reproducible.

In another embodiment the impulse generator is controlled to impart a predetermined number of impulses of defined duration and force to the nozzle.

In another embodiment the controller is further operable or programmed for controlling the actuator to force a predetermined volume of fluid through the outlet. In some embodiments the predetermined volume of fluid may be forced through the outlet after the meniscus is in the predetermined location. The controller is further operable or programmed for controlling the impulse generator to impart an impulse to the nozzle during the forcing of the predetermined volume of fluid through the outlet and also after the predetermined volume of fluid is forced through the outlet. In this embodiment an impulse is directed towards the nozzle during and after dispensing of the fluid.

In another embodiment the controller is further operable or programmed for controlling the actuator to force a predetermined volume of fluid through the outlet. In some embodiments the actuator may be controlled to force the predetermined volume of fluid through the outlet after the meniscus is in the predetermined location. The controller is further operable or programmed for controlling the impulse generator to impart an impulse to the nozzle during the forcing of the predetermined volume of fluid through the outlet.
In another embodiment the controller is further operable or programmed to control the actuator to withdraw a second predetermined volume of fluid through the outlet from the nozzle after controlling the impulse generator to impart the impulse. This embodiment may be beneficial because it may be used to withdraw fluid from the nozzle further into the nozzle or even back into the reservoir.

In another embodiment the meniscus detector is any one of the following: a capacitive sensor, an optical sensor and a camera. When the meniscus is inside of the nozzle a capacitive sensor may be used to detect the location of the meniscus. In case the nozzle is optically transparent an optical sensor may also be used to determine the location of the meniscus within the nozzle. If the meniscus extends beyond the nozzle then a capacitive sensor, an optical sensor or a camera may each be used to determine the location of the meniscus.

In another embodiment the nozzle is a flexible nozzle and the dispensing assembly further comprises a valve for compressing the flexible nozzle at a compression location. This embodiment may be beneficial because it enables the flexible nozzle to be sealed. This may prolong the lifetime of the fluid within the reservoir. In some embodiments the valve is a pinch valve.

In another embodiment the nozzle may be operable for receiving a cap for sealing it.

In another embodiment withdrawing the second predetermined volume of the fluid causes the meniscus to withdraw to a withdrawal location within the flexible nozzle. The flexible nozzle has an orifice. The compression location is between the withdrawal location and the orifice. This embodiment may be beneficial because all of the fluid has been withdrawn such that it will be sealed by the valve.

In another embodiment the impulse generator comprises an actor for contacting the nozzle. The actor may be used for imparting the impulse to the nozzle or may be considered to attach or detach the impulse generator to the nozzle.

In another embodiment, the impulse generator is in contact or permanent contact with the nozzle. When impulse generator generates an impulse it causes the actor
to move which in turn imparts an impulse to the nozzie. This impulse causes the nozzle to move also. In this embodiment the actor causes a brief momentary displacement of the nozzle. Since the actor is already in contact with the nozzle there is no impact. The imparting of the impulse without an impact may be beneficial if the fluid has a delicate component such as stem cells. In some embodiments, the impulse generator causes the actor to move approximately 30 µm.

In another embodiment the dispensing assembly further comprises a linear translator for placing the actor in contact with the nozzle. For example the linear translator may move the entire impulse generator and the actor such that the actor is in contact with the nozzle. A translation table could for example have a range of movement of 20 mm.

In another example, the linear translator is a part which expands or contracts between the impulse generator and the actor such that the impulse generator remains in a fixed position as the actor is positioned to be in contact with the nozzle.

In another embodiment the meniscus detector is located between the orifice and the actor.

In another embodiment there is a first distance between the meniscus detector and the orifice to prevent contamination of the meniscus detector when dispensing the fluid.

In another embodiment there is a second distance between the meniscus detector and the actor to prevent motion of the actor from affecting operation of the meniscus detector.

In another embodiment the meniscus detector is operable for measuring the meniscus location within the nozzle. For example the side walls of the nozzle can be transparent and the meniscus detector may be optical. In other embodiments the meniscus detector may be a capacitive detector.
In another embodiment the actor is operable for moving approximately 30 micrometers when receiving an impulse from the impulse generator. For example when the actor is already in contact with the nozzle, it may receive an impulse which causes the actor and the nozzle to move 30 micrometers.

In another embodiment the nozzle forms a channel or is a tube. In one example, the reservoir has an inner diameter of approximately 500 micrometers, 200 micrometers, or 1 mm in diameter. The cross section of the nozzle need not be circular.

In another embodiment the nozzle has a side wall. The actor is operable for transferring the impulse of the impulse generator to the side wall. This embodiment may be beneficial because it would require a low force to knock any droplets off of the nozzle. In some cases the fluid may contain fragile structures which could be damaged by large impacts. If the actor and the side wall are in contact before the impulse is generated, then the nozzle is moved without an impact from the actor.

In another embodiment the impulse generator is operable for imparting an impulse to the nozzle by impacting the nozzle with the actor.

In another embodiment the nozzle is formed from a plastic. This embodiment may be beneficial because the nozzle is extremely light and therefore requires less force to knock a droplet off than other materials such as metal or glass.

In another embodiment the nozzle is operable for dispensing the fluid in a first direction. The actor is operable for contacting the nozzle with motion in a second direction. The first direction is transverse or almost transverse to the second direction. This embodiment may be beneficial because applying the impulse transverse to the direction of dispensing may reduce the shear forces necessary to knock a droplet free.

In one example the first direction is vertical or mostly vertical in an operating position of the dispensing assembly. In this case the second direction is horizontal or mostly horizontal.
In another embodiment the dispenser is a micro-fluidic dispensing assembly.

In another embodiment the dispensing assembly is operable for dispensing any one of the following volumes: less than 10 ml, less than 5 mL, less than 1 mL, less than 10 µL, less than 500 nL, less than 200 nL, less than 100 nL, and less than 20 nL.

In another embodiment the dispensing assembly comprises the cartridge.

In another embodiment the cartridge comprises the fluid.

In another embodiment the fluid comprises a reagent.

In another embodiment the fluid comprises a blood grouping reagent.

In another embodiment the fluid comprises a solvent.

In another embodiment the fluid comprises a diluent.

In another embodiment the fluid comprises a catalyst.

In another embodiment the fluid comprises an antibody.

In another embodiment the fluid comprises an enzyme.

In another embodiment the fluid comprises a recombinant protein.

In another embodiment the fluid comprises a virus isolate.

In another embodiment the fluid comprises a vims.

In another embodiment the fluid comprises a biological reagent.

In another embodiment the fluid comprises a protein.
In another embodiment the fluid comprises a salt.

In another embodiment the fluid comprises a detergent.

In another embodiment the fluid comprises a nucleic acid.

In another embodiment the fluid comprises an acid.

In another embodiment the fluid comprises a base.

In another embodiment the fluid comprises a dispersion such as a dispersion of particles within the fluid.

In another embodiment the fluid comprises latex particles.

In another embodiment the fluid comprises nanoparticles.

In another embodiment the fluid comprises magnetic particles.

In another embodiment the fluid comprises stem cells.

In another embodiment the fluid comprises cells.

In another embodiment the fluid comprises biological structures.

In another embodiment the fluid comprises microorganisms.

In another embodiment the cartridge comprises a syringe. For instance the syringe may be connected to a nozzle and a syringe pump may be used as the actuator for actuating the syringe.

In another embodiment the actuator is a syringe pump.
In another aspect the invention provides for an automatic analyzer for analyzing the biological sample comprising a dispensing assembly according to an embodiment of the invention.

It is understood that one or more of the aforementioned embodiments of the invention may be combined as long as the combined embodiments are not mutually exclusive.

**Brief description of the drawings**

In the following embodiments of the invention are explained in greater detail, by way of example only, making reference to the drawings in which:

- Fig. 1 illustrates a dispenser assembly according to an embodiment of the invention.
- Fig. 2 illustrates a dispenser assembly according to a further embodiment of the invention;
- Fig. 3 illustrates a dispenser assembly according to a further embodiment of the invention;
- Fig. 4 illustrates an automatic analyzer according to an embodiment of the invention;
- Fig. 5 illustrates a dispenser assembly according to a further embodiment of the invention;
- Fig. 6 illustrates a dispenser assembly according to a further embodiment of the invention;
- Fig. 7 illustrates a dispenser assembly according to a further embodiment of the invention;
- Fig. 8 illustrates an example of a tube and a piston which are used to form a reservoir;
- Fig. 9 illustrates a dispenser assembly according to a further embodiment of the invention;
- Fig. 10 illustrates a dispenser assembly 1000 which is similar to the dispenser assembly shown in Fig. 2; and
- Fig. 11 shows a plot of the viscosity versus surface tension for several different fluids used as test liquids.
Detailed description

Like numbered elements in these figures are either equivalent elements or perform the same function. Elements which have been discussed previously will not necessarily be discussed in later figures if the function is equivalent.

Fig. 1 illustrates a dispenser assembly 100 according to an embodiment of the invention. The dispensing assembly 100 comprises a cartridge holder 102, an actuator 104 and an impulse generator 106. The cartridge holder 102 is shown as being attached to a cartridge 108. The actuator 104 in this example is shown as having a plunger 110 in contact with a piston 112. The plunger 110 and piston 112 may not be present in all embodiments. Depending upon the implementation the plunger 110 and/or the piston 112 could be components of the dispenser assembly 100 or the cartridge 108. The cartridge 108 in this embodiment has a reservoir 114 whose size is controlled by the piston 112. Moving the piston 112 makes the reservoir 114 larger or smaller. The reservoir 114 has an outlet 115 into a nozzle 116. The impulse generator 106 has an actor 118 which is able to come in physical contact with the nozzle 116. The piston 112 is able to be depressed to force fluid from the reservoir 114 through the nozzle 116. This enables fluid to be forced out of an orifice 120 in the nozzle 116. The impulse generator 106 is able to use the actor 118 to physically contact the nozzle 116 to knock droplets out of the nozzle 116.

Fig. 2 shows a further example of a dispenser assembly 200 according to an embodiment of the invention. This embodiment is similar to that shown in Fig. 1 except in this case the dispenser assembly 200 further comprises a controller 202 and a meniscus detector 204. The controller 202 is a controller or other control apparatus which is adapted for controlling the actuator 104, the impulse generator 106 and the meniscus detector 204. The meniscus detector 204 is adapted for detecting a meniscus 208 in the nozzle 116. The reservoir 114 and the nozzle 116 are shown as containing a fluid 206. With the meniscus detector 204 the controller 202 is able to control the actuator 104 such that the piston 112 is depressed the right amount to position the meniscus 208 in a precise location. Doing this before beginning the dispensing process the dispenser apparatus 200 is able to more accurately dispense the proper amount of fluid 206.
In Fig. 2 the meniscus detector 204 is illustrated by a small box to one side of the nozzle 116. This representation of the meniscus detector 204 is intended to be representative. For example if the meniscus detector is a capacitive detector, the meniscus detector 204 may surround all or a portion of the nozzle 116.

Fig. 3 shows a dispenser assembly 300 according to a further embodiment of the invention. The embodiment shown in Fig. 3 is similar to that shown in Figs. 1 and 2. In this embodiment the dispenser assembly 300 comprises a pinch valve 302 and the nozzle 116 is flexible. The pinch valve 302 is adapted for squeezing and pinching closed the flexible nozzle 116 at a compression location 304. This location at which the pinch valve closes the flexible nozzle 116 is marked by the dashed line. In this example it can be seen that the compression location 304 is between the orifice 120 and the fluid meniscus 208. When the pinch valve 302 closes the entire volume of the fluid 206 will be sealed from the atmosphere.

In Fig. 3 the representation of the pinch valve 302 by 2 rectangles is intended to be representative. Different sorts of mechanisms could be used to function as a pinch valve 302. For instance the pinch valve 302 may be a single movable piece which presses or compresses the flexible nozzle 116 against a stationary object.

Fig. 4 illustrates an automatic analyzer 400 according to an embodiment of the invention. This automatic analyzer is shown as having three cartridges 108, 108' and 108". There is a dispenser assembly 100 connected to cartridge 108. There is an dispenser assembly 100' attached to cartridge 108'. There is an dispenser assembly 100" attached to cartridge 108". The dispenser assemblies 100, 100', and 100" are equivalent to the dispenser assembly 100 shown in Fig. 1. However not all components of the dispenser assembly are detailed in Fig. 4.

The automatic analyzer 400 is shown as having a relative movement means 410 which provides relative movement 412 between a sample holder 406 and the cartridges 108, 108' and 108". The sample holder 406 is shown as containing a biological sample 408. The cartridges 108, 108', 108" may be used to add one or more fluids to the biological sample 408. The automatic analyzer 400 is shown as further containing a sensor system 414. The sensor system comprises one or more
sensors for measuring a physical quantity or physical property of the biological sample 408. For example the sensor system 414 may comprise an NMR system, an optical transmission or reflectance measurement system, a spectrometric measurement system, an electrochemical or optical sensor, a pH meter, a camera system, and a chromatography system. The relative movement means 410 is also operable for moving the sample holder 406 to the sensor system 414.

The arrangement of the cartridges 108, 108', 108'' and the sensor system 414 is representative. In some embodiments the sample holder 406 may remain in a fixed position and the cartridges 108, 108', 108'' may move. Each cartridge 108, 108', 108'' is shown as being installed in a dispenser assembly 100, 100', 100''.

The dispenser assemblies 100, 100', 100'' each comprise an impulse generator 106, 106', 106'' and an actuator 104, 104', 104''. The impulse generators 106, 106', 106'', the actuators 104, 104', 104'', and the sensor system 414 are shown as being connected to a hardware interface 422 of a computer system 420. The computer system 420 functions as a controller for the automatic analyzer 400. The computer 420 is further shown as containing a processor 424 which is able to control the operation and function of the automatic analyzer 400 using the hardware interface 422. The processor 424 is shown as further being connected to a user interface 426, computer storage 428 and computer memory 430. The computer storage 428 is shown as containing an analysis request 432. The analysis request 432 contains a request to analyze the biological sample 408.

The computer storage 428 is shown as further containing sensor data 434 received from the sensor system 414. The computer storage 428 is shown as further containing an analysis result 436 which was determined using the sensor data 434. The computer memory 430 contains a control module 440. The control module 440 contains computer executable code which enables the processor 424 to control the operation and function of the automatic analyzer 400. For instance the control module 440 may use the analysis request 432 to generate commands to generate and send to the dispenser assemblies 100, 100', 100'', the sensor system 414 and the relative movement system 410. The control module 440 may also generate the analysis result 436 using the sensor data 434.
Fig. 5 shows a functional diagram of a dispenser assembly 500 according to a further embodiment of the invention. The embodiment shown in Fig. 5 is similar to that shown in Figs. 1, 2 and 3. In this example a syringe pump 502 is used as the actuator. In this example an optical detector is used as the meniscus detector 204, it may also be used to measure droplets of fluid 206 exiting from the nozzle 116.

Fig. 6 shows a dispenser assembly 600 according to an alternative embodiment of the invention. In this embodiment there is a reservoir 114 that is bag-like and the actuator 104 exerts pressure directly on the reservoir 114 to force liquid out of the orifice 120. The bag-like reservoir 114 is squeezed between the actuator 104 and the cartridge holder 102.

Fig. 7 shows a dispenser assembly 700 according to a further embodiment of the invention. This embodiment is similar to the embodiments shown in Figs. 1, 2, 3 and 5. In this case the reservoir 114 is formed by a bag 702 which is contained within a bag support 704. The plunger 112 is used to compress the bag 702 and force fluid out of the orifice 120.

Fig. 8 shows an example of a tube 800 and a piston 802 which are used to form a reservoir 804. The reservoir 804 has an outlet 806. In this embodiment the piston 802 could be actuated by a plunger attached to an actuator. In this embodiment the outlet 806 is shown as have an Luer-Lock connection.

Fig. 9 illustrates a further example of a dispenser assembly 900 according to an embodiment of the invention. In this embodiment there is a syringe pump 902 which functions as the actuator 104. There is a plunger 904 which is actuated by the syringe pump 902. The inflatable gripper 905 on the end of the plunger 904 is able to grab pistons 906 each of which are mounted at the end of the reservoirs 908. The plunger 904 is then able to move a piston back and forth to change the volume of the reservoir 908. At the bottom of the reservoir 908 is a nozzle 910 with an orifice 912 through which fluid is forced out of. As an alternative to the inflatable gripper 905, other types of grippers; e.g., holding the piston by vacuum, electromagnetic holding systems, and etc.; could be used.
In another embodiment a robotic arm could move the cartridge from a parking to a dispensing position and vice versa.

In another embodiment a contact or distance sensor could be integrated into the plunger to detect the distance to the piston when the piston is to be contacted by the plunger. If the plunger is part of the cartridge, a finger gripper with a contact sensor could be added to contact the plunger.

In another embodiment the impulse generator may be put in contact with the nozzle before an impulse is generated by the impulse generator. After the dispensing process, the impulse generator may be removed to a sufficient distance in order to be able to remove the cartridge without touching the impulse generator with the orifice or the reagent. This may help to eliminate or reduce cross contamination. For this automation purpose an additional actor may be beneficial. For example, a pneumatic linear actuator may be used.

Fig. 10 shows a dispenser assembly 1000 which is similar to the dispenser assembly shown in Fig. 2. The dispenser assembly 1000 may also have a controller, but it is not shown in this figure. For example the dispense assembly may have a controller 202 as is shown in Fig. 2 or a controller 420 as is shown in Fig. 4.

The meniscus detector 204 is shown as surrounding the nozzle 116. The dispenser assembly 1000 is operable for dispensing the fluid in a first direction 1002. For instance the dispenser may dispense the fluid in a downward vertical direction. The actor 118 is operable for moving in the direction 1004. The direction 1002 and the direction 1004 are shown as being transverse or approximately transverse to each other. The meniscus detector 204 is a first distance 1006 from the orifice 120. Placing the meniscus detector 204 at the first distance 1006 prevents fluid 114 which is been dispensed from contacting the meniscus detector 204.

In some examples the actor 118 may be in contact with a sidewall 1010 of the nozzle 116 before the impulse generator 106 generates the impulse.
The meniscus detector 204 is placed at a second distance 1008 from the actor 118. This is done so that when the actor 118 is contacting the sidewall 1010 of the nozzle 116 the motion of the actor does not interfere with the operation of the meniscus detector 204. The arrangement shown in figure 10 may be particularly beneficial if the nozzle 116 is constructed of a material such as plastic. The actor 118 contacts the nozzle 116 directly. This means that not much force needs to be transferred to the nozzle 116 in order to knock droplets off the orifice 120. If the fluid 114 contains a component which may be damaged due to high shear forces, for example stem cells, this arrangement may help reduce the risk of damaging those components. If for instance forces were applied to the entire assembly 1000 or to the plunger 110 a larger amount of force would need to be transferred in order to knock a droplet off the orifice 120.

Figure 11 shows a plot of the viscosity versus surface tension for several different fluids used as test liquids. Table 1 lists these fluids along with the viscosity, the surface tension, and the density for each of the fluids.

<table>
<thead>
<tr>
<th>Model Fluid</th>
<th>Viscosity / mPas</th>
<th>Surface Tension / mN/m</th>
<th>Density / kg/m³</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.0</td>
<td>31.9</td>
<td>998</td>
</tr>
<tr>
<td>B</td>
<td>16.9</td>
<td>65.9</td>
<td>1169</td>
</tr>
<tr>
<td>C</td>
<td>10.5</td>
<td>47.3</td>
<td>1139</td>
</tr>
<tr>
<td>Water</td>
<td>1.0</td>
<td>70.8</td>
<td>998</td>
</tr>
<tr>
<td>D</td>
<td>16.9</td>
<td>30.5</td>
<td>1169</td>
</tr>
</tbody>
</table>

The tests liquids in table 1 cover the typical range of viscosities, surface tensions and densities of reagents that are typically used for in-vitro diagnostics. To evaluate the dispensing performance for liquids of different viscosities and surface tensions the fluids shown in Fig. 11 and Table 1 were characterized using an example of a dispensing assembly as described herein. The actuation parameters of the syringe and the impulse generator were not changed for any of the liquids. This means that no specific calibration of the system was performed for each individual fluid.
Table 2 shows the coefficient of variation (CV) and the accuracy (Acc) obtained with the test liquids for 2 different target volumes (1 µL and 25 µL).

<table>
<thead>
<tr>
<th>Fluid →</th>
<th>Water</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV</td>
<td>1 µL</td>
<td>0.9%</td>
<td>-1.9%</td>
<td>1.8%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Acc</td>
<td>1 µL</td>
<td>-3.4%</td>
<td>-8.8%</td>
<td>-1.0%</td>
<td>0.3%</td>
</tr>
<tr>
<td>CV</td>
<td>25 µL</td>
<td>2.1%</td>
<td>3.7%</td>
<td>0.7%</td>
<td>3.4%</td>
</tr>
<tr>
<td>Acc</td>
<td>25 µL</td>
<td>0.5%</td>
<td>-0.9%</td>
<td>0.6%</td>
<td>-1.2%</td>
</tr>
</tbody>
</table>

As can be seen in Table 2, the dispensing performance was as precise for the test liquids as it was for water. The CV was below 4% for all liquids. The accuracy ranged in between 0.3% at 1 µL for liquid C to 8.8% at 1 µL for liquid A. Table 2 illustrates a potential benefit of examples of the dispensing assembly when dispensing micro fluidic quantities of fluid. The variation and accuracy in the dispensing of the fluid is essentially independent of the rheological properties of the respective fluid. Such a dispensing assembly would therefore be useful when a variety of different fluids showing different rheological properties needs to be dispensed in very small micro fluidic quantities. For example in an automatic analyzer there may be different cartridges which dispense a variety of reagents. It may be beneficial to use an example of a dispensing assembly as described herein because it may not be necessary to calibrate for each particular reagent.
List of reference numerals

100 dispenser assembly
100' dispenser assembly
100" dispenser assembly
102 cartridge holder
104 actuator
106 impulse generator
108 cartridge
110 plunger
112 piston
114 reservoir
115 outlet
116 nozzle
118 actor
120 orifice
200 dispenser assembly
202 controller
204 meniscus detector
206 fluid
208 meniscus
300 dispenser assembly
302 pinch valve
304 compression location
400 automatic analyzer
402 cartridge
402' cartridge
402" cartridge
406 sample holder
408 biological sample
410 relative movement means
412 relative movement
414 sensor system
420 computer
422 hardware interface
424 processor
426 user interface
428 computer storage
430 computer memory
432 analysis request
434 sensor data
436 analysis result
440 control module
500 dispenser assembly
502 syringe pump
600 dispenser assembly
700 dispenser assembly
702 bag
704 bag support
800 tube
802 piston
804 reservoir
806 outlet
900 dispenser assembly
902 syringe pump
904 plunger
905 inflatable gripper
906 piston
908 reservoir
910 nozzle
912 orifice
1000 dispenser assembly
1002 first direction
1004 second direction
1006 first distance
1008 second distance
1010 side wall
Claims

1. A dispensing assembly (100, 100', 100", 200, 300, 500, 600, 700, 900) comprising:
   - a cartridge holder (102), wherein the cartridge holder is operable for receiving a cartridge (108, 108', 108") operable for dispensing a fluid (206), wherein the cartridge comprises a reservoir (114, 804, 908) operable for receiving the fluid, wherein the reservoir comprises an outlet (115, 806), wherein the reservoir has an adjustable volume for forcing the fluid through the outlet, wherein the cartridge further comprises a nozzle (116, 912) having an orifice (120) for dispensing the fluid, wherein the nozzle is connected to the outlet;
   - an actuator (104) for actuating the adjustable volume;
   - an impulse generator (106) for imparting an impulse to the nozzle, wherein the impulse generator comprises an actor (118) for contacting the nozzle;
   - a controller (202, 420) for controlling the actuator and the impulse generator.

2. The dispensing assembly of claim 1, wherein the dispensing assembly further comprises a meniscus detector (204) for detecting a meniscus (208) of the fluid.

3. The dispensing assembly of claim 2, wherein the meniscus detector is located between the orifice and the actor.

4. The dispensing assembly of claim 2 or 3, wherein the controller is programmed for:
   - controlling the actuator to force fluid through the outlet;
   - detecting the meniscus using the meniscus detector; and
   - controlling the actuator to halt the forcing of fluid through the outlet when the meniscus is in a predetermined location.

5. The dispensing assembly of claims 2, 3, or 4, wherein the meniscus detector is any one of the following: a capacitive sensor, an optical sensor, and a camera.
6. The dispensing assembly of any one of the preceding claims, wherein the controller is further programmed for:
- controlling the actuator to force a predetermined volume of fluid through the outlet;
- controlling the impulse generator to impart an impulse to the nozzle after the predetermined volume of fluid is forced through the outlet and/or controlling the impulse generator to impart an impulse to the nozzle during the forcing of the predetermined volume fluid through the outlet.

7. The dispensing assembly of any one of any one of the preceding claims, wherein the controller is programmed to control the actuator to withdraw a second predetermined volume of fluid through the outlet from the nozzle after controlling the impulse generator to impart the impulse.

8. The dispensing assembly of any one of the preceding claims, wherein the actor is contact with the nozzle.

9. The dispensing assembly of any one of the preceding claims, wherein the nozzle is formed from a plastic.

10. The dispensing assembly of any one of the preceding claims, wherein the nozzle is operable for dispensing the fluid in a first direction (1002), wherein the actor is operable for contacting the nozzle with motion in a second direction (1004), wherein the first direction is transverse to the second direction.

11. The dispensing assembly of any one of the preceding claims, wherein the dispenser is a micro-fluidic dispensing assembly.

12. The dispensing assembly of any one of the preceding claims, wherein the dispensing assembly further comprises a valve (302) for sealing the nozzle at a sealing location (304).

13. The dispensing assembly of claim 12, wherein withdrawing the second predetermined volume of fluid causes a meniscus of the fluid within nozzle to
withdraw to a withdrawal location, and wherein the sealing location is between the withdrawal location and the orifice.

14. The dispensing assembly of any one of the preceding claims, wherein the dispensing assembly comprises the cartridge.

15. The dispensing assembly of any one of the preceding claims, wherein the fluid comprises any one of the following: a reagent, a blood grouping reagent, a solvent, a diluent, a catalyst, an antibody, an enzyme, a recombinant protein, a virus isolate, a virus, a biological reagent, a protein, a salt, a detergent, a nucleic acid, an acid, a base, a dispersion, latex particles, nano particles, magnetic particles, stem cells, cells, a biological structure, a microorganism, and combinations thereof.

16. The dispensing assembly of any one of the preceding claims, wherein the cartridge comprises a syringe.

17. An automatic analyzer (400) for analyzing a biological sample (408) comprising a dispensing assembly according to any one of the preceding claims.
Fig. 9
FIG. 11
INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/059492

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01L3/Q2 G01N35/1Q ... Office, P.B. 5818 Patentlaan 2
N L - 2280 H V Rijswijk
Tel. (+31-70) 340-2040,
Fax: (+31-70) 340-3016

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.)
BOIL G01N B05C B05B

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 practicable, search terms used)
EPO-Internal , WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>EP 1 099 484 A1 (TRINITY COLLEGE DUBLIN [IE]) 16 May 2001 (2001-05-16) paragraph [0061] - paragraph [0074]; figures 2-6 paragraph [0094] - paragraph [0099]; figures 20-22</td>
<td>1-17</td>
</tr>
</tbody>
</table>

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 application or patent 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)
  "Q" 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
  "A" document member of the same patent family

Date of the actual completion of the international search
29 July 2013

Date of mailing of the international search report
06/08/2013

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

Authorized officer
Daintith, Edward

Form PCT/ISA/210 (second sheet) (April 2009)
<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>JP 2010 175291 A (HITACHI HIGH TECH CORP) 12 August 2010 (2010-08-12) figures</td>
<td>1-17</td>
</tr>
<tr>
<td>Patent document cited in search report</td>
<td>Publication date</td>
<td>Patent family member(s)</td>
</tr>
<tr>
<td>----------------------------------------</td>
<td>-----------------</td>
<td>-------------------------</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wo 2007124346 A2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AU 1204002 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AU 9536301 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CA 2363301 AI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>CH 695544 A5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 50100406 DI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 50104853 DI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 1206966 AI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 1333925 AI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 4084034 B2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 2002214244 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>JP 2004512951 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2002131903 AI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2005244303 AI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wo 0240162 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wo 0240163 A</td>
</tr>
<tr>
<td></td>
<td></td>
<td>AT 422399 T</td>
</tr>
<tr>
<td></td>
<td></td>
<td>DE 69931787 T2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>EP 1099484 AI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IE 20000696 AI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IE 20000912 AI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 6713021 Bl</td>
</tr>
<tr>
<td></td>
<td></td>
<td>US 2004101445 AI</td>
</tr>
<tr>
<td></td>
<td></td>
<td>J P 2010175291 A</td>
</tr>
</tbody>
</table>