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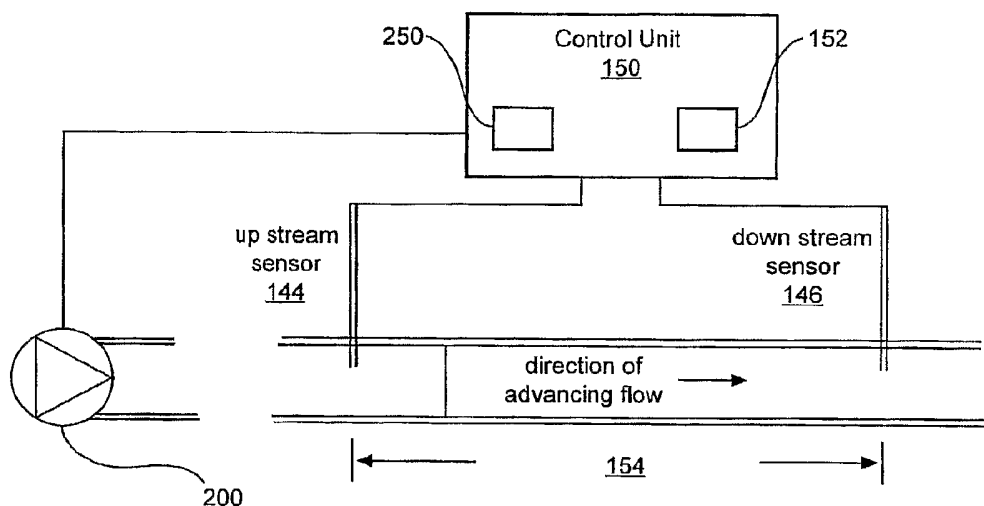
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(54) Title: FLUID DELIVERY DEVICE WITH AUTOCALIBRATION



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(57) Abstract: A micro fluid delivery device is particularly useful in medical applications. The device may be worn or carried by the user and may deliver drugs or other medicaments to the user or patient. The device has a control system that accepts input from the user and controls all aspects of operation of the device. The control system measures the output of the pump and adjusts the output of the pump to achieve the desired dosage rate and size. This eliminates differences from pump to pump that result from inevitable variations in the manufacturing of such small scale affordable devices.

## **FLUID DELIVERY DEVICE WITH AUTOCALIBRATION**

### **FIELD OF THE INVENTION**

[0002] The present invention relates generally to fluid delivery devices such as pumps and relates more specifically to control and use of a small scale pump.

### **BACKGROUND OF THE INVENTION**

[0003] Although the present invention may be used with many different types and sizes of pumps, the present invention is particularly useful with miniature or micro disposable pumps. One application for such a pump is in the delivery of insulin.

[0004] One type of miniature or micro pump utilizes a piston to push a volume of liquid defined by the volume (bore x stroke) of the piston and the volume of an accompanying diaphragm. A dose of the liquid, for example insulin, is said for purposes of discussion, to equal the volume of liquid expelled in one delivery stroke of the piston.

[0005] One characteristic of a miniature pump is that the piston diaphragm assembly requires extremely high manufacturing tolerances in order to generate a reproducible dose volume from one pump to the next. For example, with a typically sized miniature piston type pump the volume of the dose will vary by 0.5% per 1/10000 inch of variation in the stroke length. The stroke length is determined by the linear dimensions of three separate components, the piston, the cylinder, and the diaphragm, each of which has tolerances over 10/10000 inch. A coincidence of maximum variation in each of these components would result in a dose volume variation of  $\pm 15\%$  from the nominal value. Additional tolerances associated with the diaphragm diameter and the piston head diameter further compound the problem.

[0006] Given that some applications of such a pump involve drug delivery, delivering a dose volume that is the same from pump to pump is non trivial. This is especially true in the case of disposable pumps, where a pump is regularly replaced with another pump of the same model. Regardless of the application of the pump, it is desirable to accommodate manufacturing tolerances and produce repeatable pumps with accurate dosage delivery.

## SUMMARY OF INVENTION

[0007] The present invention provides a simple, inexpensive and reliable mechanism and method for determining the dose size produced by a given pump, which is then used to calibrate the pump and thereby normalize manufacturing variations in the volume of the pump. This results in more reliable and repeatable fluid delivery from one pump to the next of a given design.

[0008] Another aspect of the present invention comprises measuring the dose volume of a pump, preferably during the initial priming process, or alternatively anytime thereafter. This volume is then used to calibrate the timing of the dosing period. For example, if the actual measured

volume of a particular pump is determined to be 15 % larger than a basis value, such as the expected nominal value of the volume, then the timing of all subsequent delivery rates is reduced accordingly. The measurement can be made as part of the manufacturing process or can be made by the user as part of a pump initialization process. The measurement can also automatically be made by the pump at any time during operation of the pump. The calibration or adjustment of pump delivery is preferably made before usage of the pump by a user, but may be made any time during the life of the pump.

[0009] Another aspect involves a method of dispensing a liquid to a user with a portable dispensing device. The method comprises pumping the liquid, detecting arrival of the liquid at a first sensor, detecting arrival of the liquid at a second sensor, measuring the time elapsed from the arrival of the liquid at the first sensor to the arrival of the liquid at the second sensor, calculating the volumetric flow rate of the dispensing device, and adjusting the volumetric flow rate of the dispensing of the device.

[0010] Yet another aspect involves a method of administering a liquid including a drug to a user with a device worn or carried by a user. The method comprises providing a disposable component comprising a pump element, providing a durable component comprising a microprocessor, the disposable component configured to mate and operate with the durable component, initiating the flow of the liquid through a portion of the device with a known volume, the flow comprising a plurality of doses, determining the time necessary to pump the known volume, and determining the volume of a dose.

[0011] Additional aspects, advantages and features of the present invention are included in the following description of exemplary examples thereof, which description should be taken in conjunction with the accompanying figures, and wherein like (and similar) numerals are used to describe the same feature throughout the figures. All patents, patent applications, articles and other publications referenced herein are hereby incorporated herein by this reference in their entirety for all purposes.

## BRIEF DESCRIPTION OF THE DRAWINGS

[0012] FIG. 1A is a flow chart of operation of an embodiment of the present invention.

[0013] FIG. 1B is a diagram of an embodiment of the present invention referenced in FIG. 1A.

[0014] FIG. 2A illustrates pump 200, an embodiment of one type of pump that may be implemented with the present invention, shown in a first state.

[0015] FIG. 2B illustrates pump 200, an embodiment of one type of pump that may be implemented with the present invention, shown in a second state.

[0016] FIG. 2C is a diagram illustrating an example of a drive circuit for use with pump 200.

[0017] FIG. 3 is a flowchart depicting operation according to one embodiment of the present invention.

[0018] FIG. 4 is a flow chart of operation according to an embodiment of the present invention.

[0019] FIG. 5 is a flow chart of operation according to an embodiment of the present invention.

## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0020] It is important to eliminate the variations from one pump to the next (of the same design) that are a result of manufacturing limitations. The present invention can be used to minimize the effects of these variations and results in accurate delivery in any type of liquid pump.

[0021] As discussed in the background, there is one type of liquid pump with which the present invention is particularly advantageous, the miniature piston type pump. The piston diaphragm assembly of a miniature pump requires extremely high manufacturing tolerances in order to generate a reproducible dose volume from one pump to the next. Even with high precision manufacturing, a not insignificant variation from one pump to the next of a given design may be present. This is less than ideal, especially in applications of the pump involving drug delivery or other medicinal applications.

[0022] The present invention provides a simple, inexpensive and reliable mechanism and method for minimizing, or “zeroing out” the differences from pump to pump. One aspect involves a logic or processor controlled routine that may be thought of as an automatic calibration of the device. In a most general sense, this involves measuring the volume of a of a dosage produced by a given pump, comparing that dosage to a nominal dosage volume expected for that particular type of pump design, and then adjusting the pump output accordingly. This can also be accomplished by measuring the flow rate and then adjusting accordingly. Both volume and flow rate measurement comprise usage of one or more sensors that indicate the presence of liquid at a given point or points. Although there are many ways of adjusting the output of the pump, the preferred way of doing this is by calculating a ratio of a measured versus expected volume and calibrating the delivery based upon the ratio.

[0023] Although the present invention can be used with the delivery of any fluid in any environment, in the medical environment where the present invention is particularly suitable, the types of liquids that can be delivered include, but are not limited to: insulin, antibiotics, anesthetics, nutritional fluids, analgesics, hormones or related drugs, gene therapy drugs, anticoagulants, cardiovascular medications, HIV treatments, cancer treatments, etc. These can be delivered transcutaneously, through a type of patch on the skin, or the liquid may be evaporated and inhaled. The present invention is not limited to the delivery of these liquids or by the means of ingress into the patient’s system, and these are only examples, not an exhaustive list.

[0024] Again, one application where the present invention may be particularly useful is in the delivery of insulin. Specifically, it may be useful in delivery of small quantities of insulin regularly with what is known as a miniature or micro pump. As the name implies, a miniature or micro pump delivers relatively small quantities. In the preferred embodiments described, which are tailored to insulin delivery, each actuation or dose of such a micro or miniature pump is on the order of approximately 0.5 to 5.0 microliters, with a potential total delivery of around 1000 microliters per day. Delivery volumes for other liquids (in the medical arena, that is) may be as high as around 5000 microliters or 5cc’s per day.

[0025] FIG. 1A is a flow chart describing operation according to an embodiment of the present invention seen in the schematic diagram of FIG. 1B. The process depicted in FIG. 1A can be performed at any time. It may also be done in conjunction with priming of the pump. In FIG. 1B there are two sensors, up-stream sensor 144, and down stream sensor 146, with a known volume between the two sensors. In this embodiment the known volume, or calibration region 154, has a cylindrical shape, but any geometric (regular or irregular) shape may be employed, so long as the volume is known or can be ascertained. The geometry of the calibration region should be such that it can be manufactured with sufficiently high reproducibility, and the volume of the calibration region is preferably much greater than the volume of an individual dose of insulin solution. This ensures good resolution and accuracy in the measurement. The sensors are connected to control unit 150, which is also connected to pump 200. Control unit 150 comprises drive circuitry 250 and logic unit 152, which is preferably in the form of a microprocessor. Each sensor comprises a pair of conductive electrodes, and when current passes between the electrodes of the pair, it indicates the presence of a liquid by the establishment of electrical continuity between the pair of electrodes. As long as the liquid has some measure of electrical conductivity, the presence of the liquid can be measured. As is appreciated in the art, the material of the electrodes may be tailored for the particular application. In the case of insulin, gold electrodes work well. As mentioned previously, pump 200 may be any type of liquid pump. In applications where cost is a driving factor, it is often preferable to utilize a pump that is driven by a shape memory actuator. This is particularly the case in the medical field, where devices are disposed of and replaced relatively frequently for various reasons.

[0026] The control unit 150 controls operation of the pump 200 and of the fluid delivery device generally, which may also comprise a user interface (not shown) for setting various operating parameters such as the delivery rate and for starting and stopping the device. The control unit also initiates and controls calibration of the device. For more information on the construction and operation of such a device, please refer to U.S. Application No. 10/683,659 filed on 10/09/2003, published as U.S. Patent Application Publication No. 2004/0115067 A1, and hereby incorporated by this reference in its entirety.

[0027] Returning to the flowchart of FIG. 1A, in step 105 the control unit initiates liquid flow. Then, in step 110, the control unit detects the arrival of the liquid at point A, which is a first point. This corresponds to up-stream sensor 144 in FIG. 1B. This can be done either when the liquid first advances or by placing an interruption in the flow stream before it reaches up-stream sensor 144. For instance, one way of interrupting the flow is to interject a gas bubble into the flow stream. In step 120, the control unit detects the arrival of the advancing liquid at point B, which corresponds to down-stream sensor 146 in FIG. 1B. In the case of a cylindrical calibration region 154 with a known diameter, the volume of the region is known if the distance between the two sensors is known.

[0028] In step 130, control unit 150 measures the time it takes for the liquid to travel from point A to point B. The volumetric flow rate is also calculated in step 135 based upon the time measured and the known volume between the points. This information is then used to adjust the delivery of the pump, as is seen in step 140. This process can take place at any time. It can be used initially to calibrate the pump, or during any time during operation of the device. Even if a discrete break is not inserted into the flow stream, the sensors may also indicate the flow rate of the device. The signal produced by the electrodes will increase as the rate of conduction of the liquid increases. Thus, given that the liquid is uniformly mixed, the signal will increase as the flow rate increases. For a given electrode/liquid combination, a profile of the output versus flow rate can be determined for given concentrations. The controller can then reference this data stored in memory to determine the flow rate. For more information on this, please refer to a co-pending U.S. Application No. --/---,--- of Benjamin M. Rush, entitled Devices And Methods For Use in Assessing a Flow Condition of a Fluid in a Flow Path, which is hereby incorporated by this reference in its entirety.

[0029] FIGS. 2A and 2B illustrate pump 200, an embodiment of one type of pump particularly suited for use in the present invention. This pump is driven by a shape memory element 206 and employs feedback including that from switch 209, switch 210, and linear feedback system 211, all of which indicate the position of piston 204.



[0030] Pump 200 is shown in the inactive state in FIG 2A, and the active state in FIG 1B. Switch 209 indicates that the plunger or pump is in the open position, and switch 210 indicates it is in the closed position. The pump body comprises a case 201, a top cap 202, and a plunger cap 203. Within the pump is a plunger 204 that is normally (in the inactive state) held against the plunger cap 203 by a plunger bias spring 205. The plunger 204 is connected to shape memory element 206 which contracts when heated by a pulse or pulses of current flowing from the V+ 207 contact to the V- 208 contact through the shape memory element 206 (where the V- 208 contact may be the system ground reference). The power in each pulse is determined by the voltage applied to the shaped memory element through the contacts. It is worth noting that the case is made of an insulating material while the plunger is either made of a conductive material (e.g. metal) or is coated with an appropriately conductive material.

[0031] FIG 2A depicts the pump in the inactive state where the shape memory element 206 is not contracted, and the plunger 204 is held against the plunger cap 203 by the plunger bias spring 205. This is the state to which the pump returns after each activation or pumping cycle.

[0032] FIG 2B shows the pump in the active state where the shaped memory element 206 has contracted enough to pull the plunger 204 up against a stop built into the case 201.

[0033] FIG. 2C illustrates drive circuit 250, an embodiment of a circuit that may be used with pump 200. Drive circuit 250 includes input and feedback to/from logic unit 152, which preferably comprises a microprocessor, as mentioned previously. For more information on this and other aspects of a shape memory actuated pump, please refer to co-pending U.S. Application No. --/--,---, of Christopher V. Reggiardo *et al.*, entitled "Variable Volume, Shape Memory Actuated Insulin Dispensing Pump," which is hereby incorporated by this reference in its entirety.

[0034] FIG. 3 is a flowchart depicting operation according to one embodiment of the present invention. In step 310, the control unit measures the flow rate, as discussed earlier. Next in step 320, the system determines the desired dosage volume. This may be done automatically or may be entered by the user. In step 330, the system determines the calibration factor based upon the measured flow rate. The calibration factor preferably comprises a ratio of the expected volume

of a dose versus the actual volume of a dose. In the case of the piston type pump earlier described, the calibration factor comprises a ratio of the nominal volume of the cylinder versus the actual volume of the cylinder. The nominal volume is either the value of the volume expected from the design specifications or the value expected based upon the nominal value of a large sample of production pieces. Once it has been determined, the calibration factor is applied in step 340 and will be applied to subsequent operation of the system, including when a desired dosage is delivered in step 350.

[0035] FIG. 4 is a flowchart depicting operation according to another embodiment of the present invention. In step 410, the volume delivered in one pump stroke is determined. In step 420, the system determines the desired dosage volume, which may be done automatically or entered by the user. Next in step 430 the system determines the number of required strokes corresponding to a desired dosage volume. Because of the linear feedback of the present invention, the system may deliver fractions of a stroke, and the number of strokes may include any number and fraction of strokes. Next, in step 440, the system delivers the desired dosage volume by moving the piston the proper number of strokes.

[0036] FIG. 5 is a flowchart depicting usage of two embodiments of the system. One embodiment comprises two units, a disposable unit and a re-usable unit, whereas the other embodiment incorporates all the components into one disposable unit. Some or all of the parts of the system shown in FIG. 1B may be reusable, but in the case where there exists a reusable component, it comprises control unit 150. The term disposable refers to the ordinary meaning of the word, and is involves intended usage on the order of days to months. The term reusable also refers to the ordinary meaning and describes a durable component with an intended usage on the order of months to years.

[0037] In step 510, the user unpackages the disposable component that has a selected liquid or drug in a reservoir. Next, in step 520, the user mates the disposable component with the re-usable component.

[0038] Alternatively, the user simply unpackages the system (pre-loaded with the liquid in the reservoir), which is entirely disposable, in step 525.

[0037] In step 510, the user unpackages the disposable component that has a selected liquid or drug in a reservoir. Next, in step 520, the user mates the disposable component with the reusable component.

[0038] Alternatively, the user simply unpackages the system (pre-loaded with the liquid in the reservoir), which is entirely disposable, in step 525.

[0039] Thereafter, the controller initiates priming and calibration of the pump in step 530. In step 540, the pump then drives the liquid from the reservoir through the internal volume of the pump, including through calibration region 154. Next in step 550, calibration parameters, such as the calibration factor are determined. Thereafter, in step 560, the controller modifies the subsequent pump timing based upon the calibration parameters. For instance, if the calibration parameters indicate the measured volume of a particular pump is less than the expected nominal volume of production units, the dosage frequency will be increased. In step 570, the user installs the disposable component (including the controller in one embodiment) and programs the desired delivery rate through the controller user interface. Step 560 may occur before or after step 570, and there is no particular order of the steps unless explicitly stated.

## EXPERIMENTAL RESULTS

[0040] An embodiment of the present invention was tested in three trials. The dose volume was determined with the embodiment and compared to a gravimetric determination of the dose volume. The results confirm the accuracy of measurements made with the embodiment. The results of three measurements are shown below.

[0041] A functional model of the calibration device of the present invention was constructed of a length of tubing with an outer diameter of 0.125 inches and an inner diameter of 0.0625 inches. The sensors were pairs of copper wire and electrical continuity between the two wires of a given pair was measured as an indication of wetting by insulin. A small voltage was applied between each of the sensor electrode pairs. At the point at which the leading edge of the advancing insulin contacted either of the sensor electrode pairs, a circuit was completed resulting in the flow of current through the circuit. This current flow was detected by monitoring the voltage across a current sensing resistor placed in each sensor circuit. The time required for the leading

edge of the advancing insulin to traverse the distance between the two sensors was monitored with a timing device.

[0042] As can be seen below, three trial measurements were consistent to within 1% and agreed with the two gravimetric measurements to within 1%. The two gravimetric measurements agreed to within 2%. The measurement made with the functional model is approximately the average of the two gravimetric measurements. This confirms the accuracy of the present invention.

#### Test Calibration Region

ID:	1.588 mm (0.0625")
Cross sectional area:	1.979 mm <sup>2</sup>
Electrode spacing:	76.20 mm (3.00 ")
Volume:	150.80 mm <sup>3</sup>

#### Trial 1

Dose period:	14.92 seconds
Time to traverse electrodes:	1003 seconds
Doses to traverse electrodes:	67 (rounded to nearest whole)
Dose volume:	2.251 mm <sup>3</sup>
Measured dose volume (gravimetric)	188.47 mg/83 doses = 2.271 mg/dose
Ratio:	0.99

#### Trial 2

Dose period:	14.92 seconds
Time to traverse electrodes:	996 seconds
Doses to traverse electrodes:	67 (rounded to nearest whole)
Dose volume:	2.251 mm <sup>3</sup>
Measured dose volume (gravimetric)	N/A
Ratio:	N/A

#### Trial 3

Dose period	14.92 seconds
Time to traverse electrodes	995 seconds
Doses to traverse electrodes	67 (rounded to nearest whole)
Dose volume:	2.251 mm <sup>3</sup>

Measured dose volume (gravimetric)	184.64 mg/83 doses = 2.225 mg/dose
Ratio:	0.99

[0043] Although the various aspects of the present invention have been described with respect to exemplary embodiments thereof, it will be understood that the present invention is entitled to protection within the full scope of the appended claims.

## IT IS CLAIMED:

1. A method of calibrating the flow rate of a fluid pumping device, the method comprising:
  - pumping the liquid;
  - detecting arrival of the liquid at a first sensor;
  - detecting arrival of the liquid at a second sensor;
  - measuring the time elapsed from the arrival of the liquid at the first sensor to the arrival of the liquid at the second sensor; and
  - adjusting the volumetric flow rate of the dispensing of the device.
2. The method of claim 1 wherein the dispensing device comprises a disposable portion, and wherein the method further comprises attaching the disposable portion to a re-usable portion of the device.
3. The method of claim 2, wherein after a disposable portion is attached the volumetric flow rate of the dispensing device is adjusted.
4. A portable drug delivery system comprising:
  - a disposable component comprising:
    - a shape memory actuated pump;
    - a drug reservoir; and
  - a calibration region, the calibration region having a first sensor at a first part of the region and a second sensor at a second part of the region; and
  - a reusable component comprising a processor, wherein the processor monitors the time it takes for the liquid to pass from the first sensor to the second sensor.
5. The drug delivery system of claim 4 wherein the processor monitors a number of pump actuations during the time it takes for the liquid to pass from the first sensor to the second sensor.

6. The drug delivery system of claim 5 wherein the processor of the reusable component calibrates drug delivery for each disposable component used with the system.
7. A method of delivering a dosage of liquid with a piston actuated pump, the piston having a stroke length, the method comprising:
  - measuring a flow rate of the pump;
  - determining a desired dosage;
  - determining a number of strokes corresponding to the desired dosage; and
  - delivering the desired dosage by moving the piston the corresponding number of strokes.
8. The method of claim 7 wherein moving the piston comprises altering the shape of a shape memory actuator by applying a potential to the actuator.
9. The method of claim 7 wherein measuring the flow rate comprises:
  - actuating the pump;
  - noting when liquid moved by the pump passes a first sensor; and
  - noting when liquid moved by the pump passes a second sensor.
10. The method of claim 9 wherein the volume of a portion of the pump between the first and second sensor is known and measuring the flow rate further comprises calculating the number of times the piston is actuated in order to produce the known volume.
11. The method of claim 7 wherein measuring the flow rate comprises detecting a constituent in a liquid with one or more electrodes.
12. The method of claim 8 further comprising altering the potential based upon feedback from a signal from one or more sensors indicative of the position of the piston.

13. A method of administering a liquid including a drug to a user with a device worn or carried by a user, the method comprising:
- providing a disposable component comprising a pump element;
  - providing a durable component comprising a microprocessor, the disposable component configured to mate and operate with the durable component;
  - Initiating the flow of the liquid through a portion of the device with a known volume, the flow comprising a plurality of doses;
  - determining the time necessary to pump the known volume; and
  - determining the volume of a dose.
14. The method of claim 13 further comprising creating a ratio of the determined dose volume to an expected dose volume.
15. The method of claim 14 further comprising modifying a frequency of dosage delivery based upon the ratio.
16. The method of claim 13 further comprising mating the durable component and the disposable component.
17. A method of administering a liquid including a drug to a user with a device worn or carried by a user, the method comprising:
- providing a pump element;
  - providing a control unit including a processor;
  - initiating pumping of a plurality of doses;
  - measuring the plurality of doses; and
  - comparing one or more of the measured doses to an expected value of one or more doses.
18. The method of claim 17, further comprising calculating a ratio based upon the comparison, and applying the ratio in delivering subsequent doses.



19. The method of claim 17 further comprising modifying a frequency of dosage delivery based upon the comparison.
20. A micro pump for delivering liquid, comprising:  
a pump element;  
means for measuring the quantity of a unit volume provided by the pump element;  
means for detecting the difference of the measured unit volume from an expected unit volume; and  
means for modifying the delivery based upon the difference.
21. A method of dispensing a liquid including a drug to user with a portable dispensing device, the method comprising:  
pumping the liquid;  
detecting arrival of the liquid at a first sensor;  
detecting arrival of the liquid at a second sensor;  
measuring the time elapsed from the arrival of the liquid at the first sensor to the arrival of the liquid at the second sensor;  
calculating the volumetric flow rate of the dispensing device; and  
adjusting the volumetric flow rate of the dispensing of the device.

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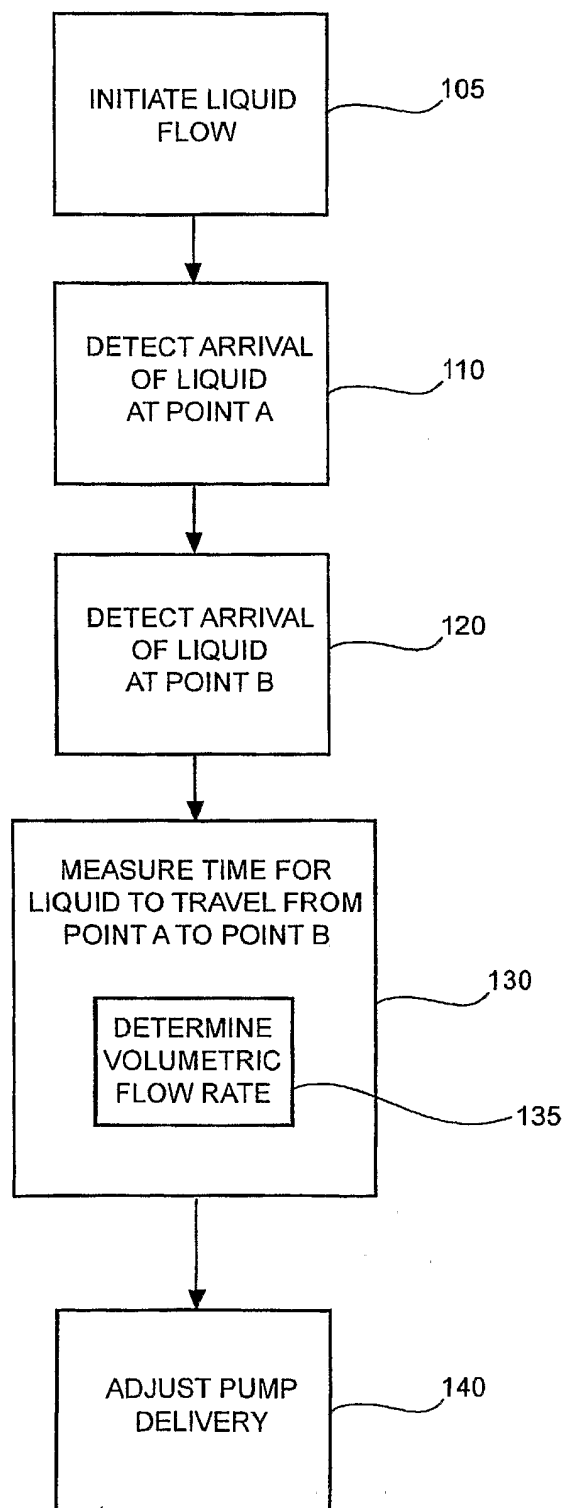


FIG. 1A

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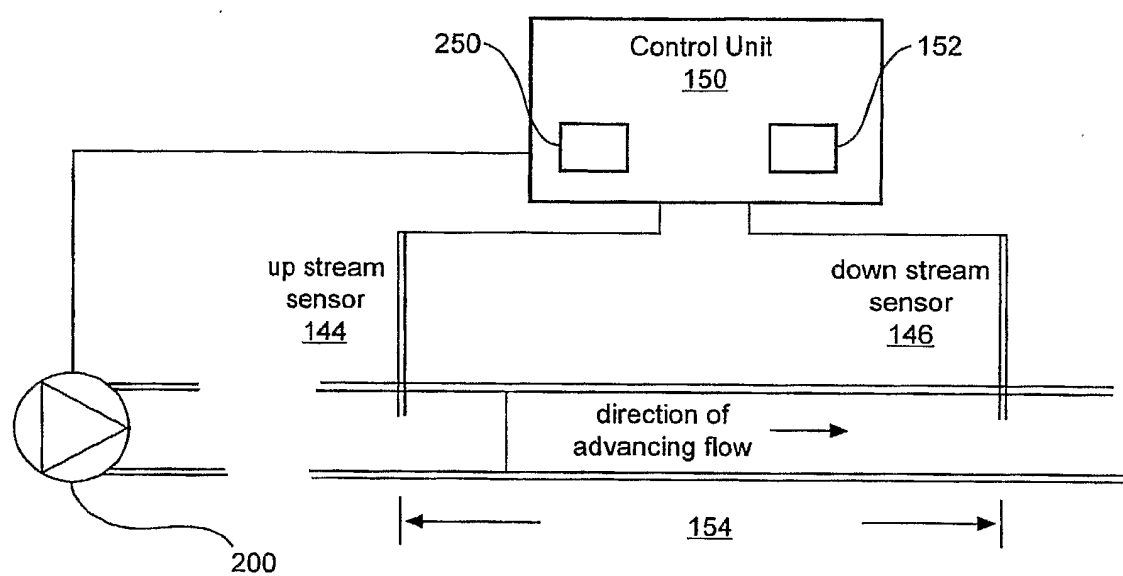


FIG. 1B

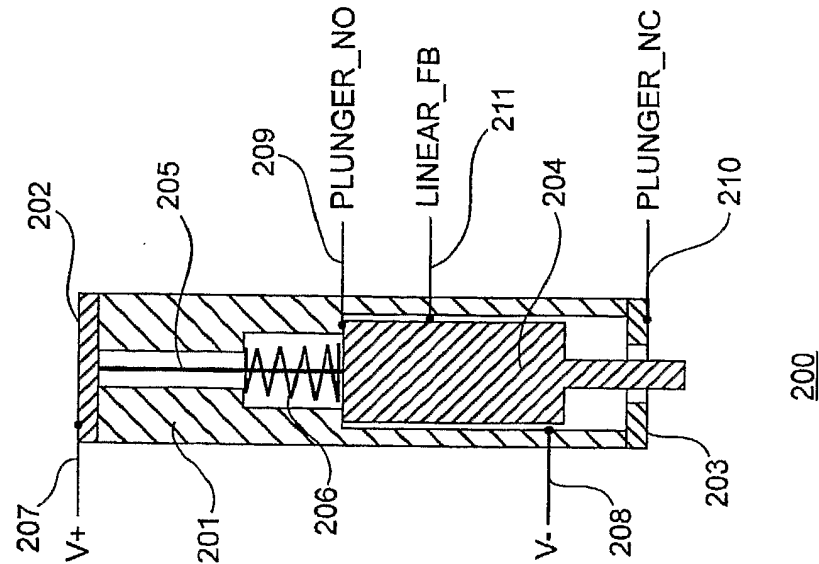


FIG. 2A

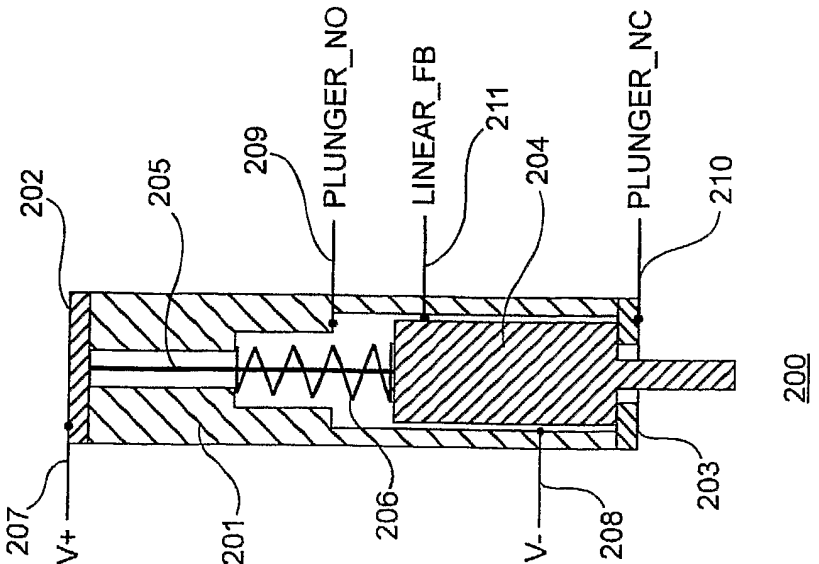


FIG. 2B

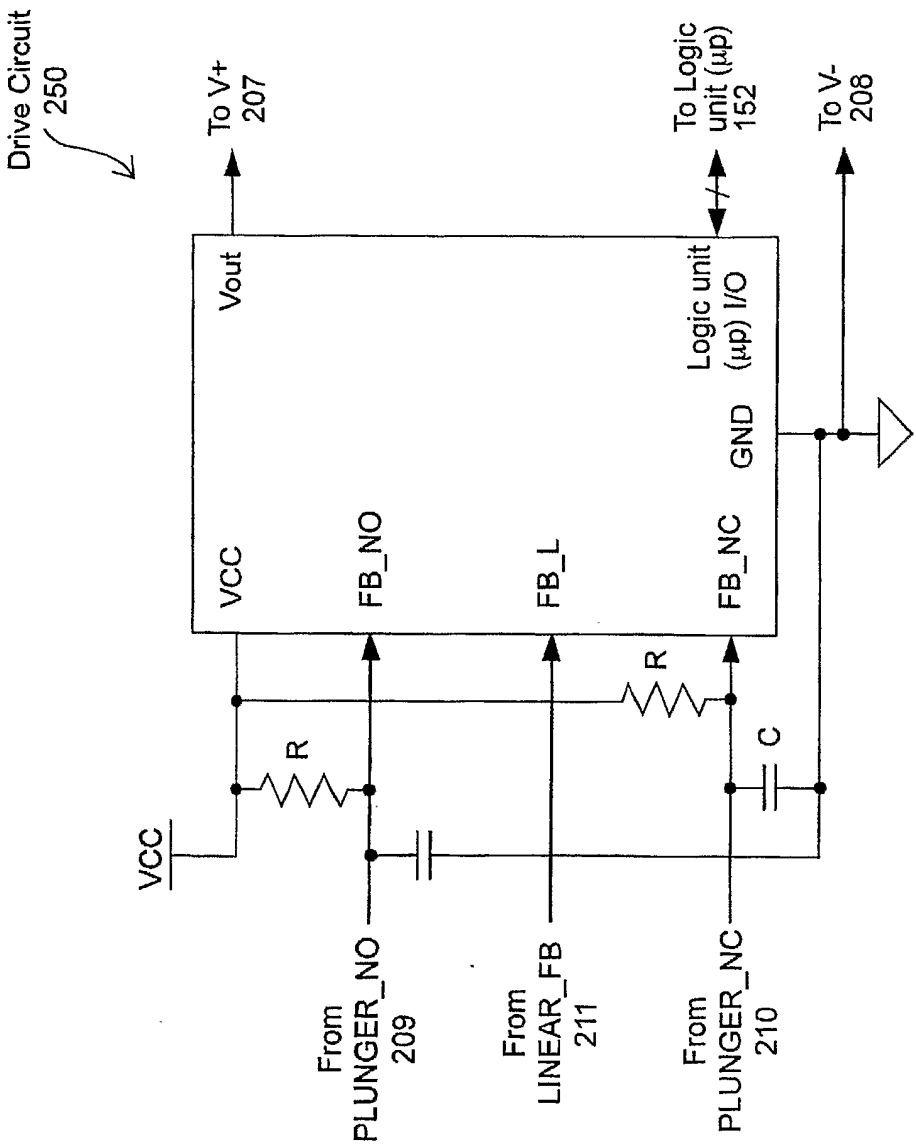


FIG. 2C

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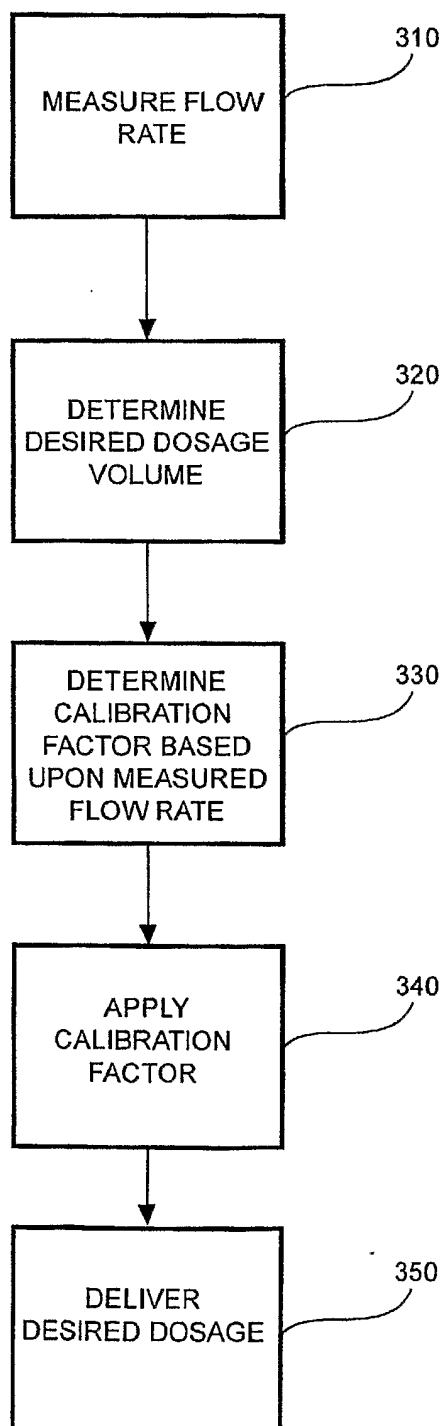


FIG. 3

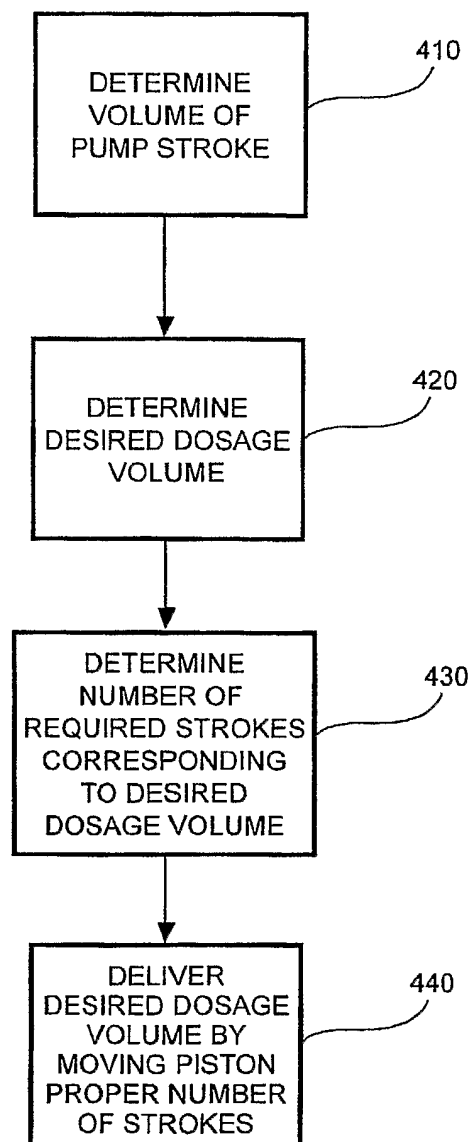


FIG. 4

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FIG. 5

