US 20230314455A1

(19) **United States**

(12) **Patent Application Publication**

HARA et al.

(10) **Pub. No.: US 2023/0314455 A1**

(43) **Pub. Date: Oct. 5, 2023**

(54) **DISPENSING DEVICE AND METHOD**

(71) Applicant: **Hitachi High-Tech Corporation**, Tokyo (JP)

(72) Inventors: **Daisuke HARA**, Tokyo (JP); **Toshiki YAMAGATA**, Tokyo (JP); **Masashi SHIBAHARA**, Tokyo (JP)

(21) Appl. No.: **18/013,933**

(22) PCT Filed: **Aug. 3, 2020**

(86) PCT No.: **PCT/JP2020/029640**

§ 371 (c)(1),
(2) Date: **Dec. 30, 2022**

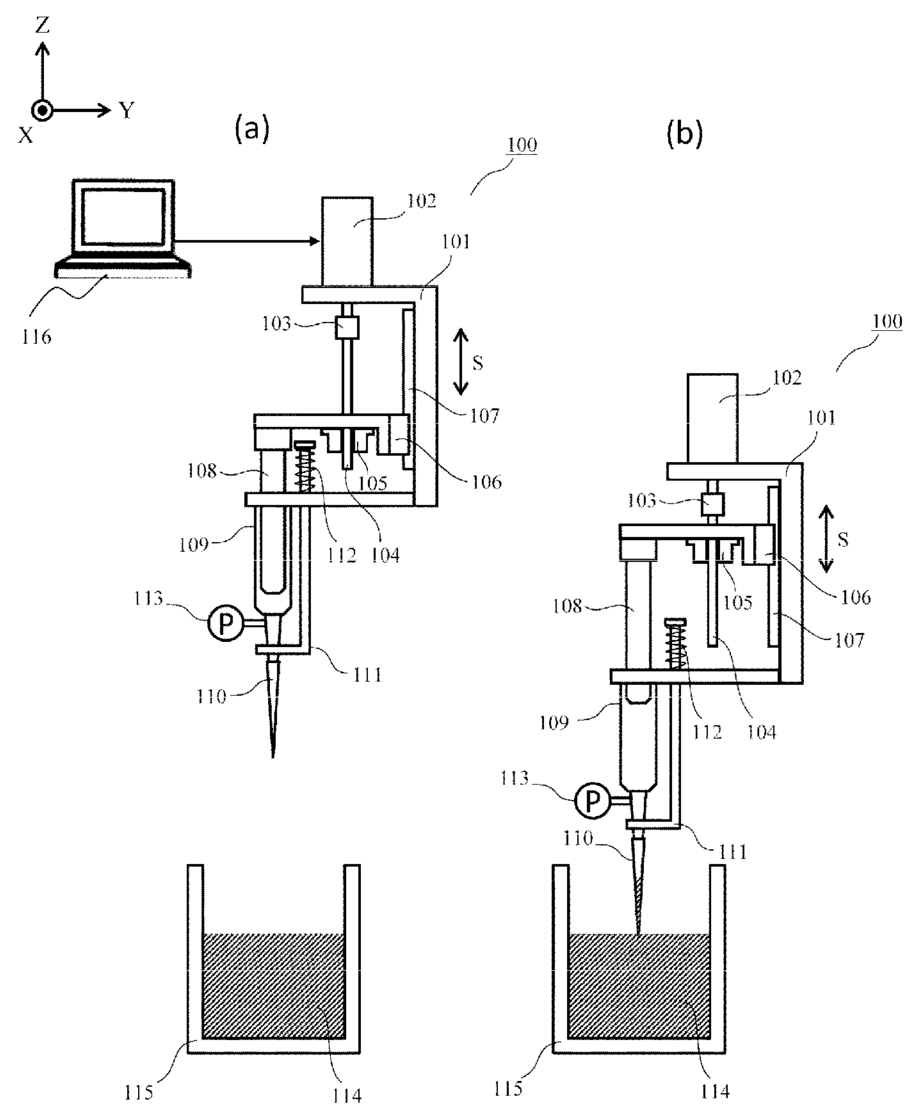
Publication Classification

(51) **Int. Cl.**
G01N 35/00 (2006.01)
G01N 35/10 (2006.01)

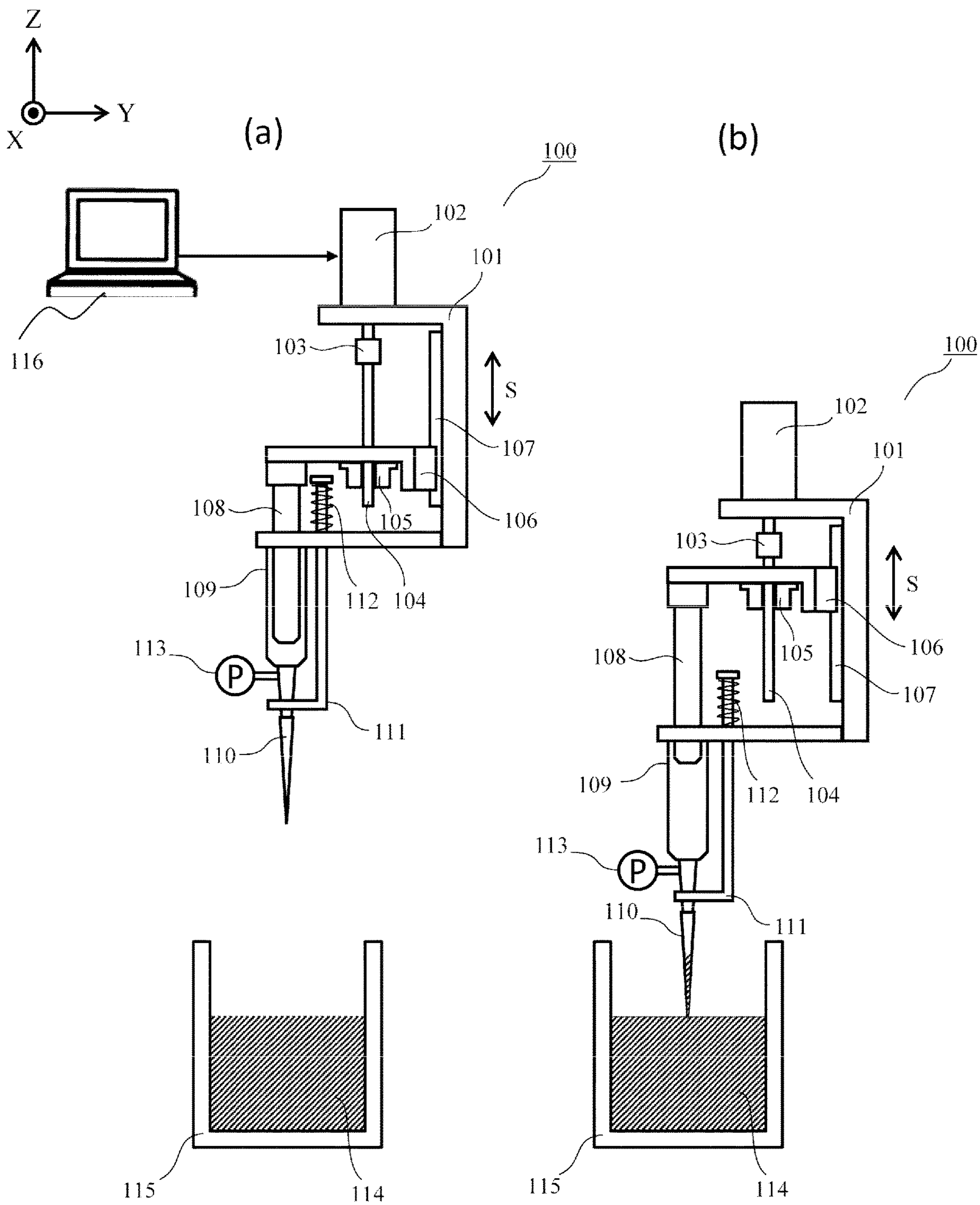
(52) **U.S. Cl.**
CPC ***G01N 35/00623*** (2013.01); *G01N 2035/1013* (2013.01); ***G01N 35/1011*** (2013.01)

(57) **ABSTRACT**

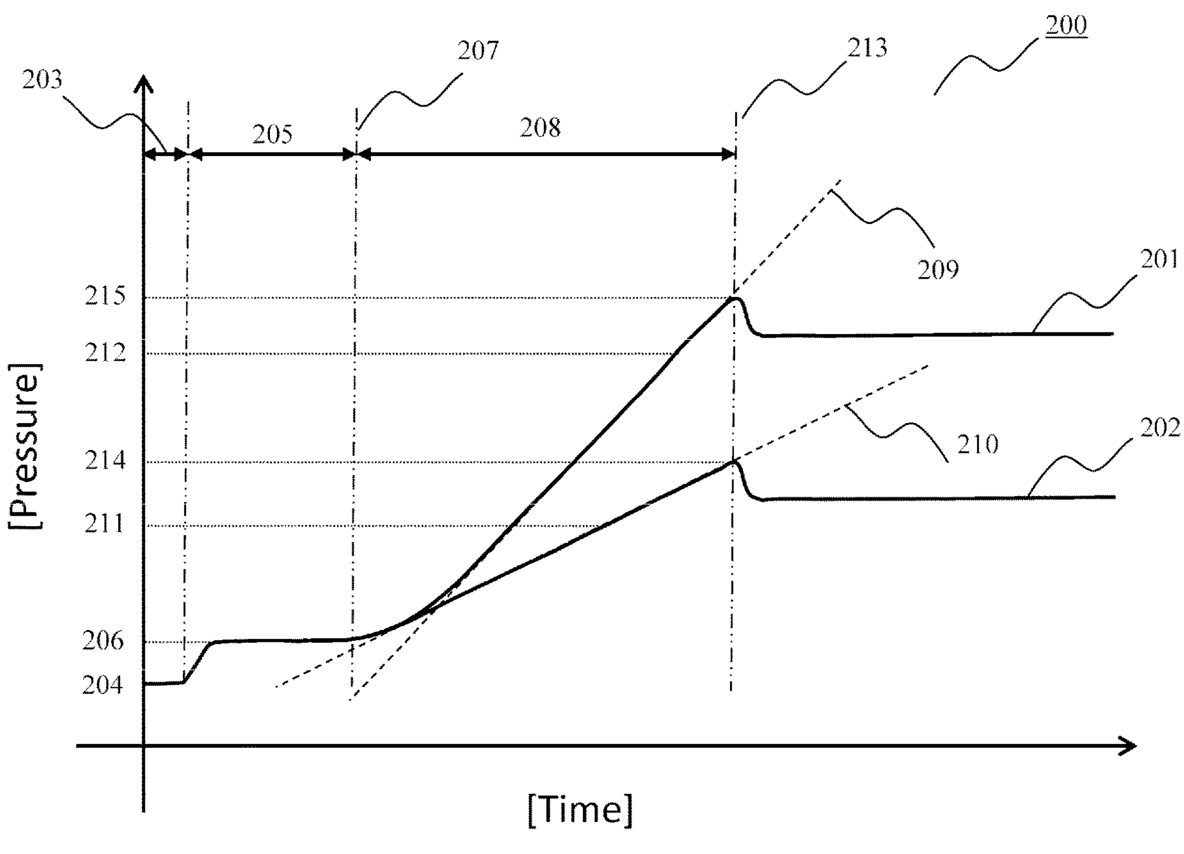
The present invention determines whether or not a mounted tip and a dispensing amount match with each other in order to prevent contamination in a dispensing device. The present invention is provided with a pipette mechanism **108**, **109** that performs suction and discharge, a motor **102** that drives the pipette mechanism, and a pressure sensor **113** that detects a pressure of the pipette mechanism. A dispensing tip **110** is mounted to the pipette mechanism. A control computer **116** controls the motor **102**, drives the pipette mechanism in a suction or discharge direction, and determines a type of the dispensing tip **110** on the basis of a difference in pressure waveform detected by the pressure sensor **113**.



[FIG. 1]

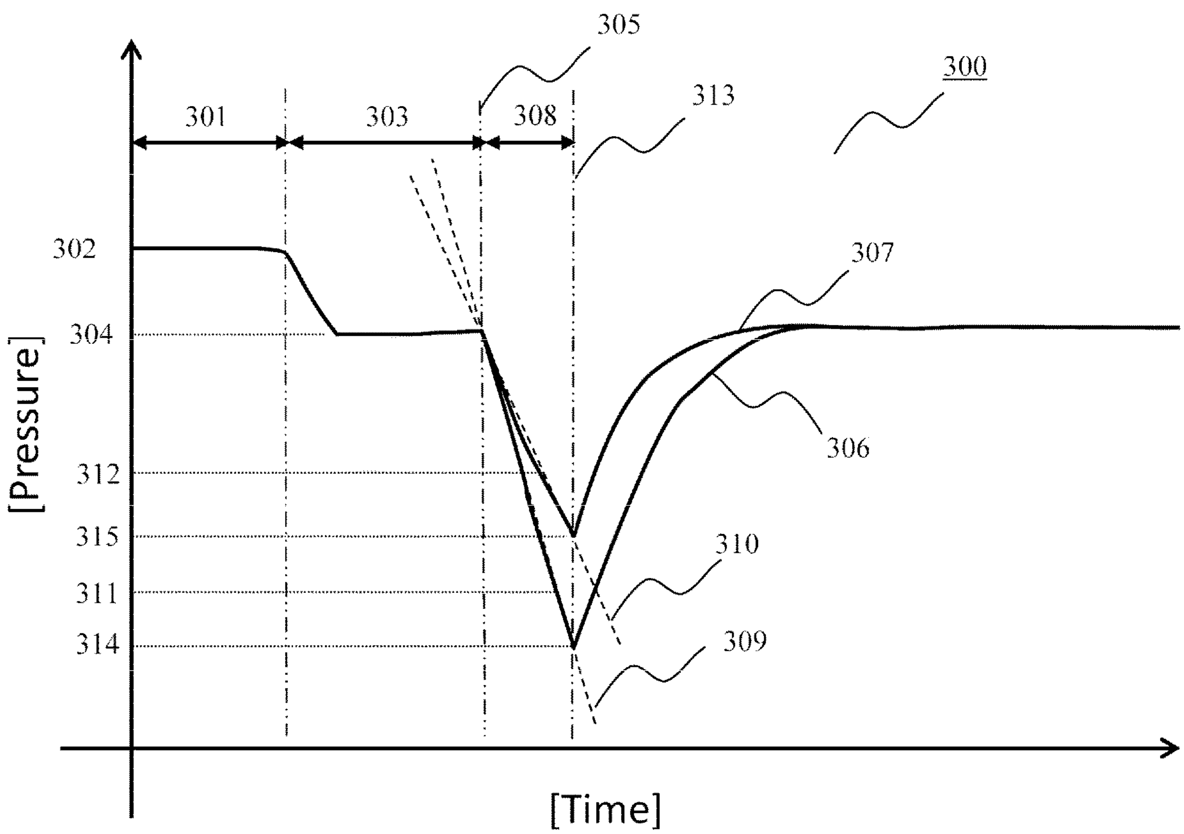

Z
Y
X
(a)
(b)
100
102
101
103
S
107
106
105
108
112
104
109
113
P
111
110
116
115
114

[FIG. 2]

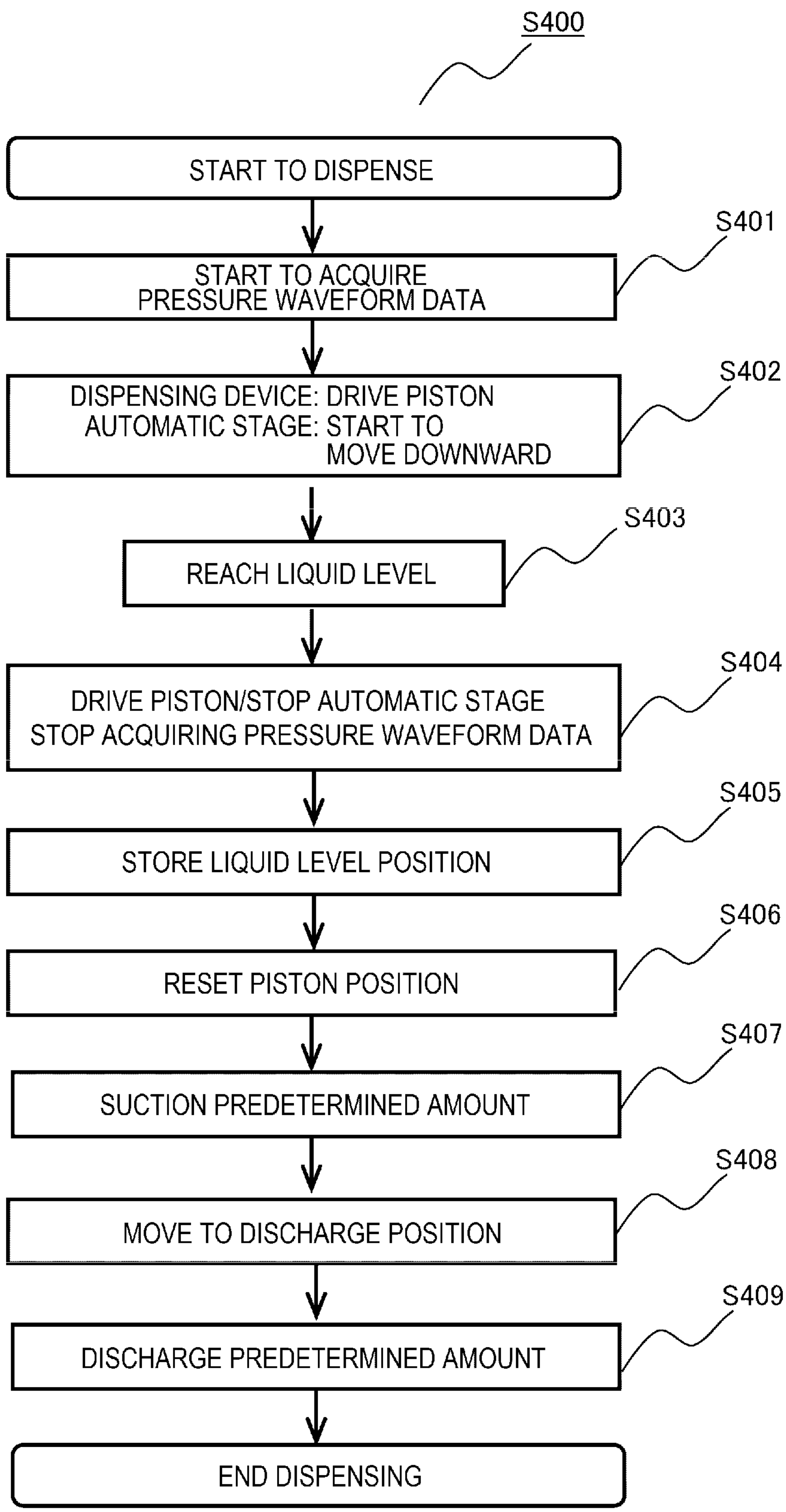


200
203
205
207
208
213
209
210
201
202
215
212
214
211
206
204
[Pressure]
[Time]

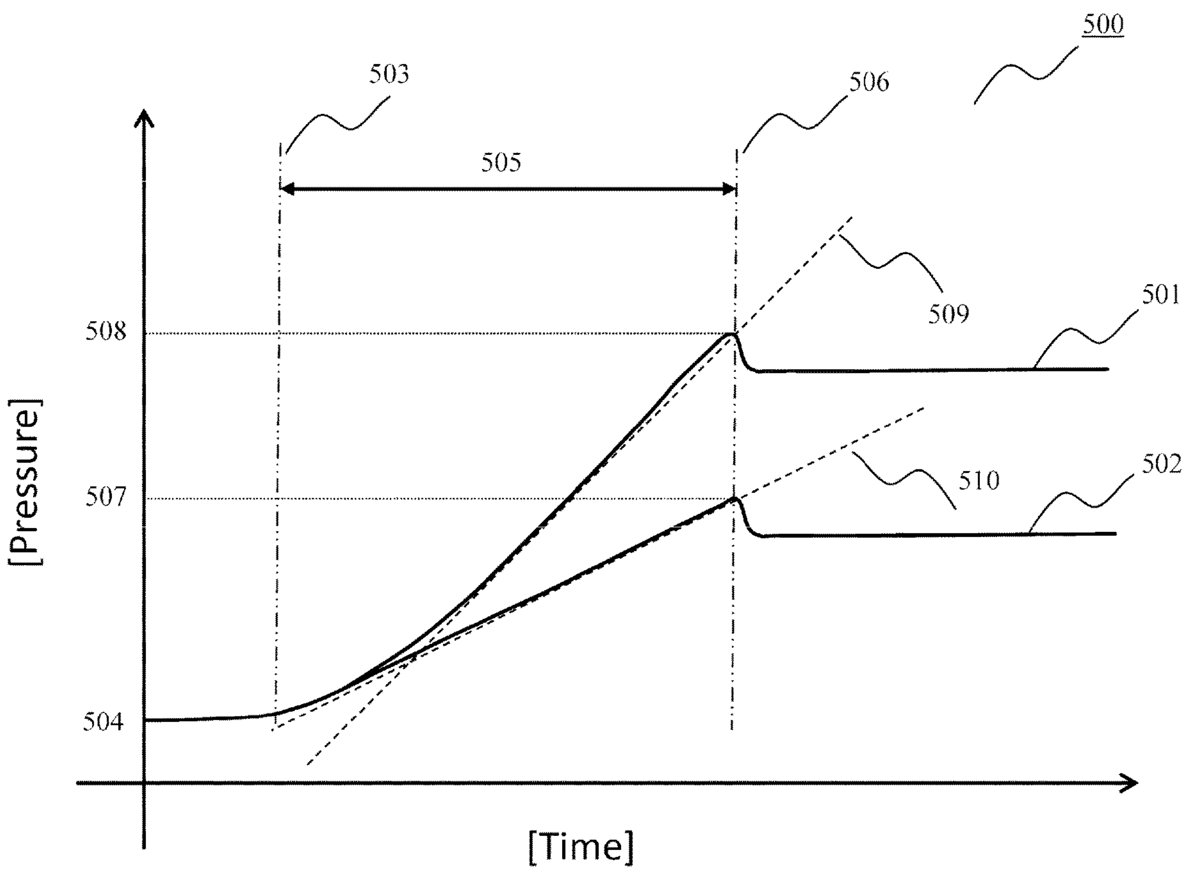
[FIG. 3]


305
300
301
303
308
313
302
307
304
306
312
315
310
311
314
309
[Pressure]
[Time]

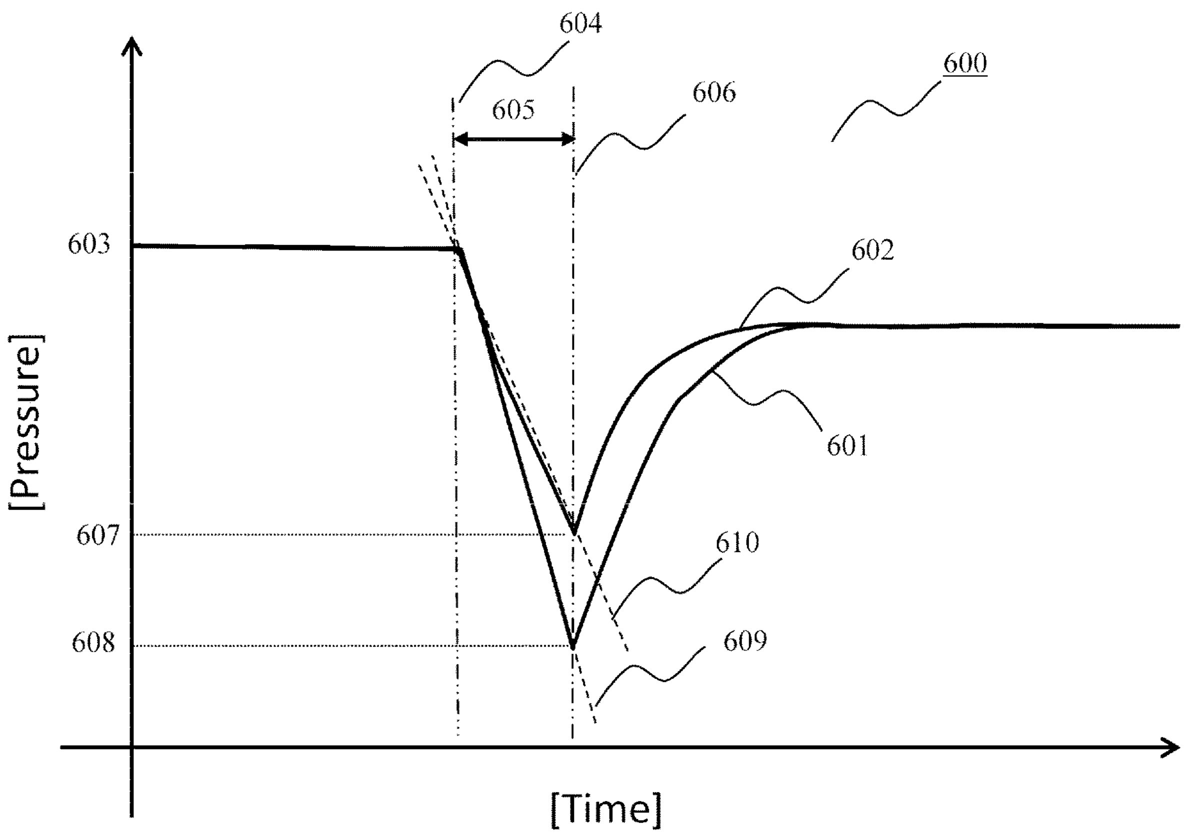
[FIG. 4]


S400
START TO DISPENSE
S401
START TO ACQUIRE PRESSURE WAVEFORM DATA
S402
DISPENSING DEVICE: DRIVE PISTON
AUTOMATIC STAGE: START TO MOVE DOWNWARD
S403
REACH LIQUID LEVEL
S404
DRIVE PISTON/STOP AUTOMATIC STAGE
STOP ACQUIRING PRESSURE WAVEFORM DATA
S405
STORE LIQUID LEVEL POSITION
S406
RESET PISTON POSITION
S407
SUCTION PREDETERMINED AMOUNT
S408
MOVE TO DISCHARGE POSITION
S409
DISCHARGE PREDETERMINED AMOUNT
END DISPENSING

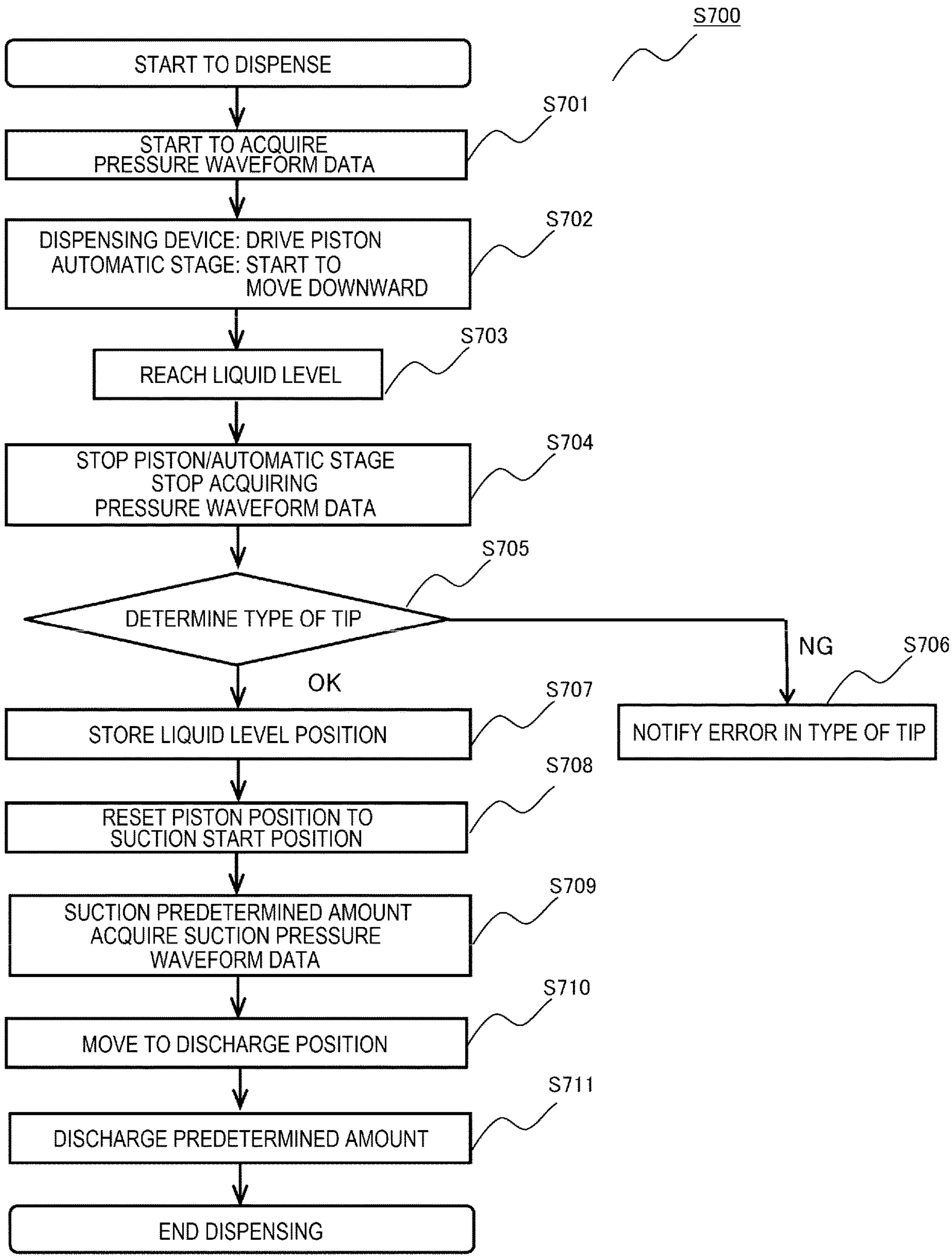
[FIG. 5]



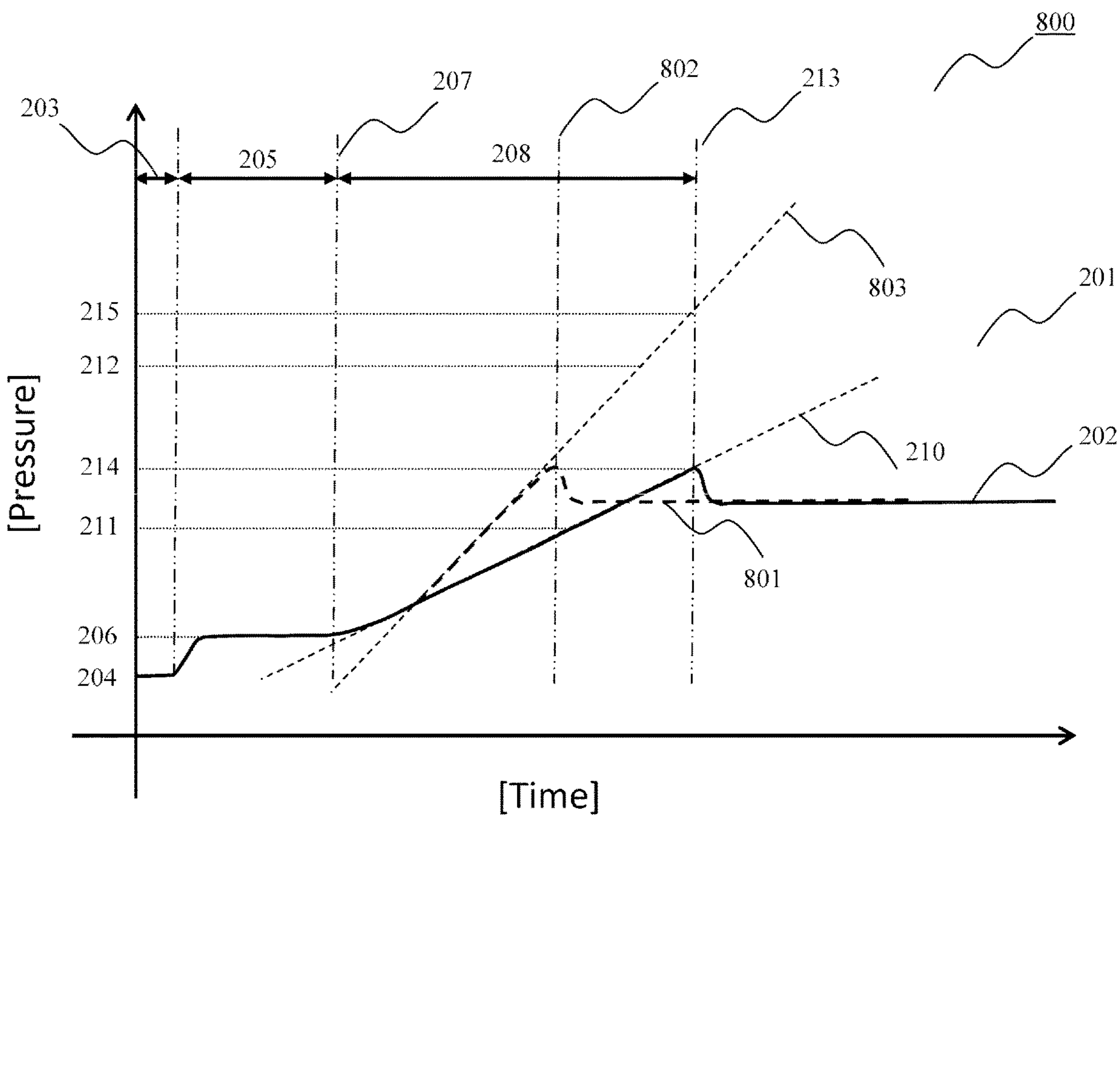
[FIG. 6]



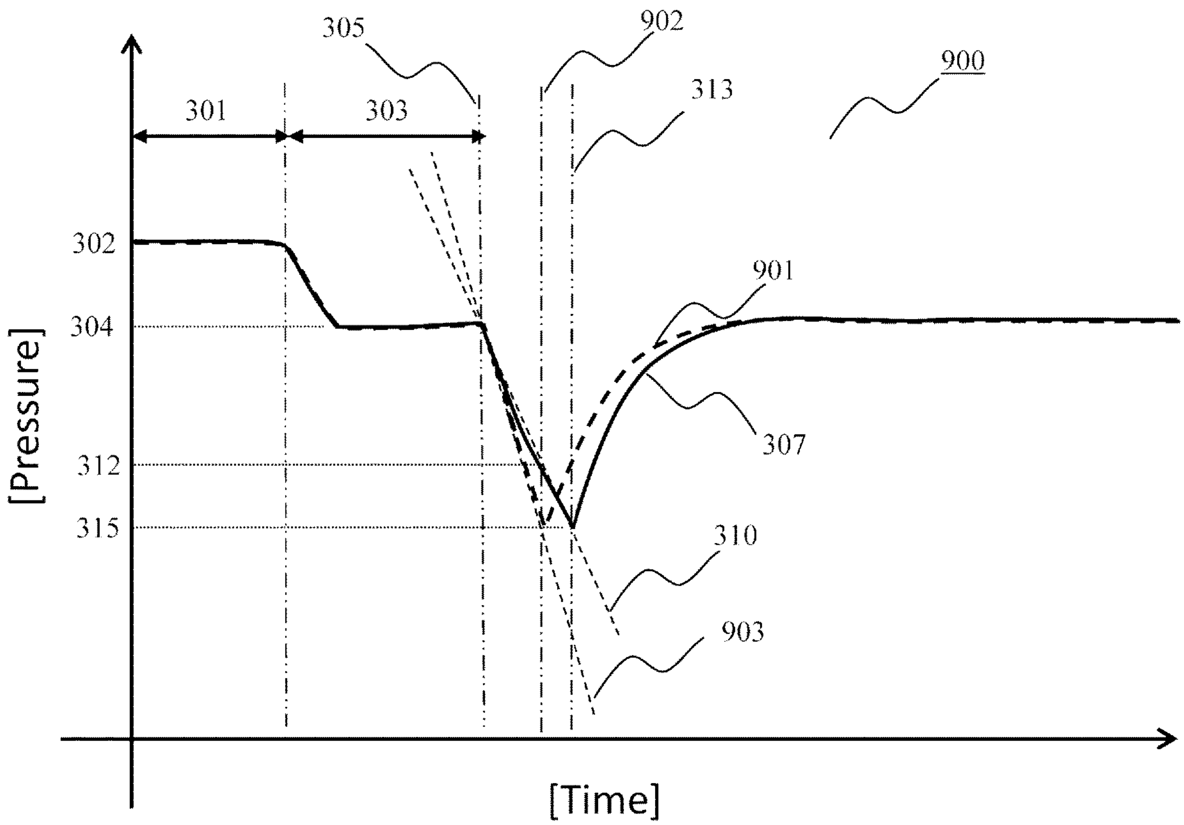
[FIG. 7]


S700
START TO DISPENSE
S701
START TO ACQUIRE PRESSURE WAVEFORM DATA
S702
DISPENSING DEVICE: DRIVE PISTON
AUTOMATIC STAGE: START TO MOVE DOWNWARD
S703
REACH LIQUID LEVEL
S704
STOP PISTON/AUTOMATIC STAGE
STOP ACQUIRING PRESSURE WAVEFORM DATA
S705
DETERMINE TYPE OF TIP
NG
S706
NOTIFY ERROR IN TYPE OF TIP
OK
S707
STORE LIQUID LEVEL POSITION
S708
RESET PISTON POSITION TO SUCTION START POSITION
S709
SUCTION PREDETERMINED AMOUNT
ACQUIRE SUCTION PRESSURE WAVEFORM DATA
S710
MOVE TO DISCHARGE POSITION
S711
DISCHARGE PREDETERMINED AMOUNT
END DISPENSING

[FIG. 8]

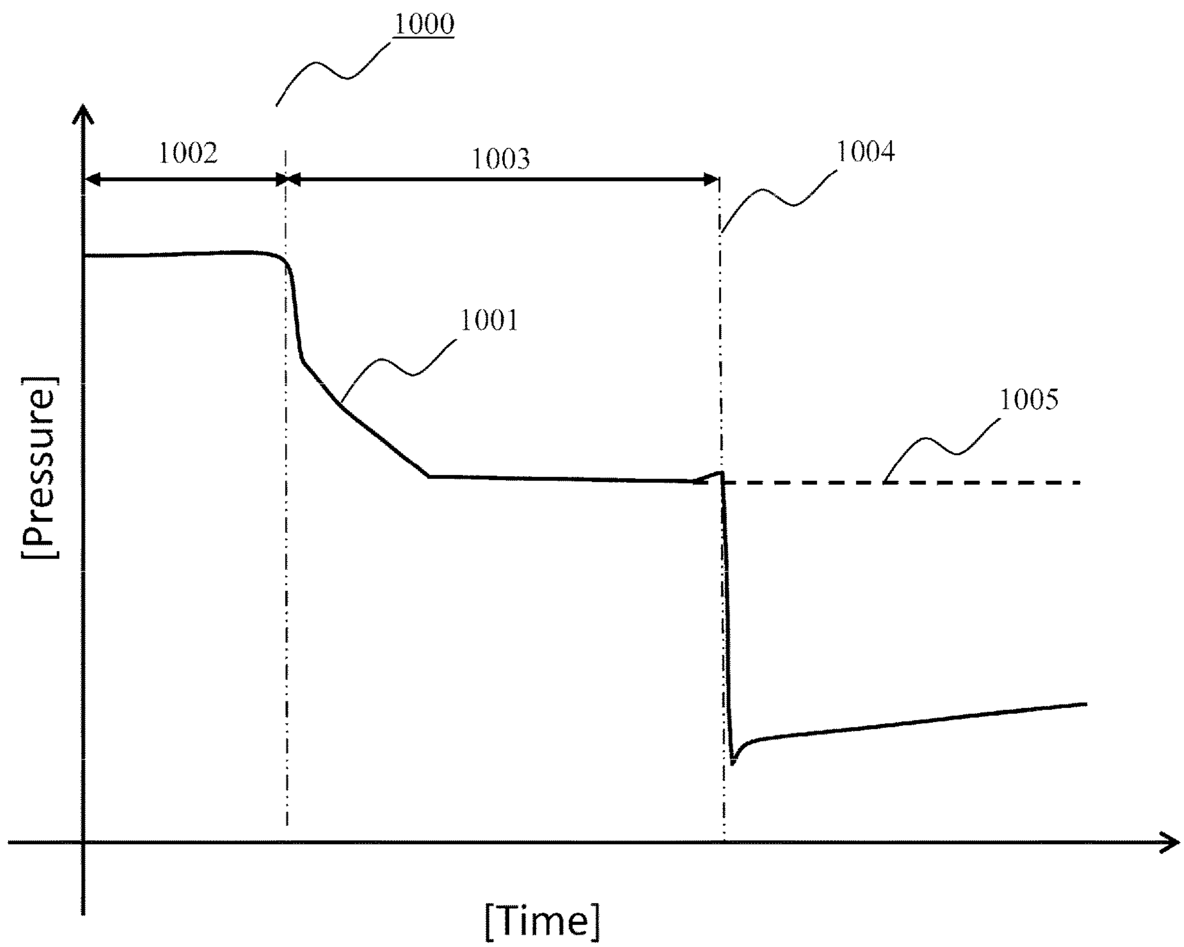

800
203
205
207
208
802
213
803
201
215
212
214
211
206
204
210
202
801
[Pressure]
[Time]

[FIG. 9]

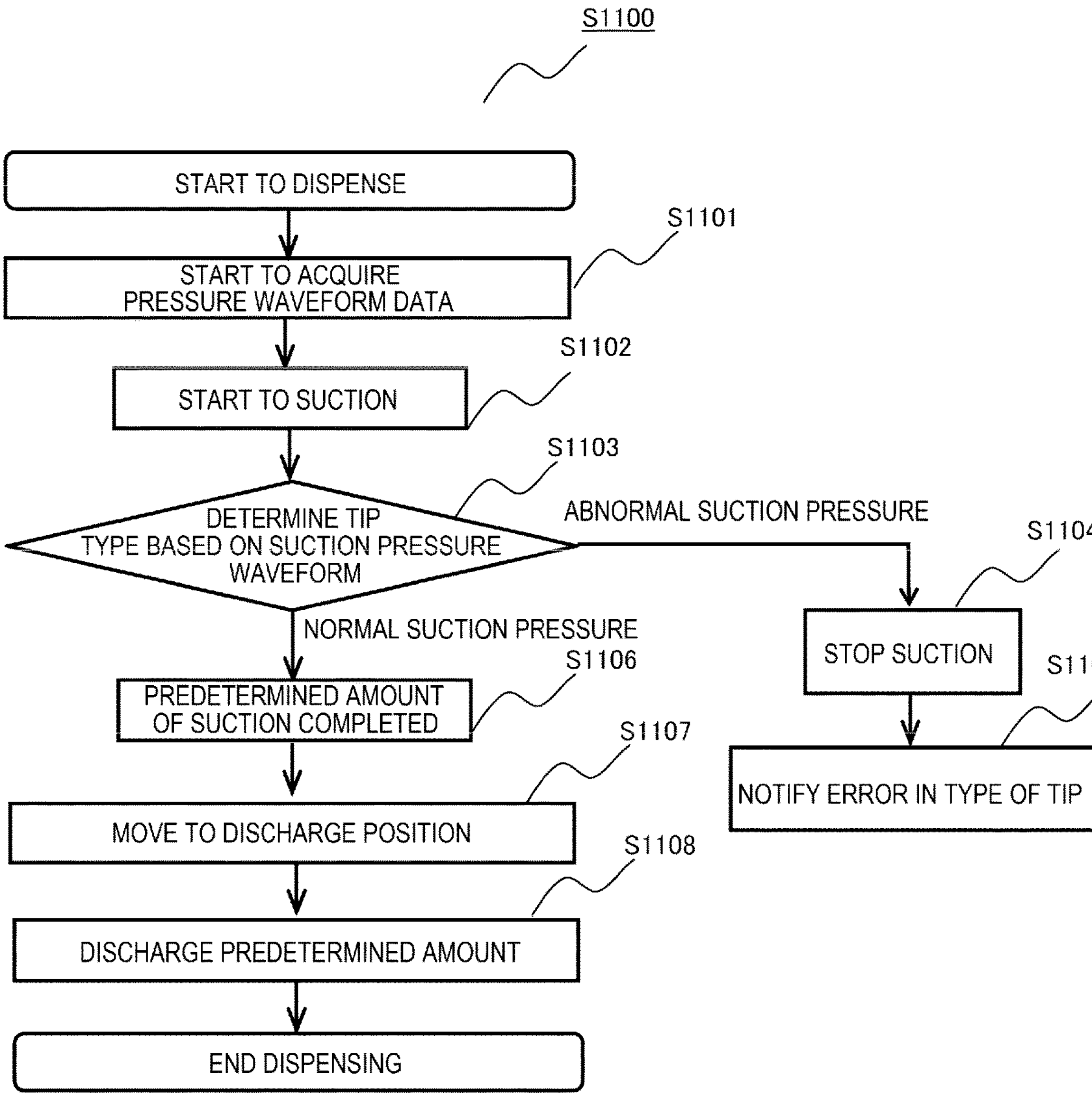


305
902
900
313
301
303
302
304
312
315
901
307
310
903
[Pressure]
[Time]

[FIG. 10]



[FIG. 11]


S1100
START TO DISPENSE
START TO ACQUIRE PRESSURE WAVEFORM DATA
S1101
START TO SUCTION
S1102
DETERMINE TIP TYPE BASED ON SUCTION PRESSURE WAVEFORM
S1103
ABNORMAL SUCTION PRESSURE
NORMAL SUCTION PRESSURE
STOP SUCTION
S1104
NOTIFY ERROR IN TYPE OF TIP
S1105
PREDETERMINED AMOUNT OF SUCTION COMPLETED
S1106
MOVE TO DISCHARGE POSITION
S1107
DISCHARGE PREDETERMINED AMOUNT
S1108
END DISPENSING

DISPENSING DEVICE AND METHOD

TECHNICAL FIELD

[0001] The present invention relates to a dispensing device and method, and particularly to a technique for determining a type of a tip of a dispensing mechanism for examination.

BACKGROUND ART

[0002] A dispensing device is used as a method for distributing a liquid such as a specimen and a reagent to another container in medical and biomedical fields. In an examination using a polymerase chain reaction (hereinafter, referred to as PCR) method in such as a gene examination device, since even slight contamination affects an examination result, it is important to prevent contamination in order to obtain a correct examination result.

[0003] As an example, PTL 1 discloses an invention for monitoring a pressure in the dispensing device and effectively reducing the occurrence of liquid dripping from a nozzle and an air gap. If the liquid dripping occurs, the dropped liquid droplets may contaminate other containers, and if an air gap occurs, liquid pools may occur at a tip of the nozzle via the air gap. When the liquid is discharged, contamination may occur due to the generation of bubbles or flipping of the bubbles.

[0004] In order to cope with these problems, in PTL 1, air suction setting information is information in which air suction conditions defined in advance for each of various dispensing conditions (a shape of the nozzle, a type of the liquid, a target suction amount, and the like), more specifically, an air suction speed va, an air amount upper limit value Va, and the like are recorded, and the air suction setting information is defined based on previous experimental results and the like. In addition, PTL 1 discloses that the liquid dripping can be more reliably prevented or reduced by performing the air suction based on the air suction conditions defined in advance. In the related art, it is intended to prevent contamination by reducing liquid dripping or an air gap generated after the suction of a liquid.

CITATION LIST

Patent Literature

[0005] PTL 1: JP2010-256200A

SUMMARY OF INVENTION

Technical Problem

[0006] In the related art, there is a device configuration in which the nozzle is washed each time and used repeatedly, but in the examination using the PCR method in such as a gene examination device, even the slight contamination affects the examination result. Therefore, it is common to use a disposable tip for the nozzle. Since the required dispensing amount is different for each examination item, a plurality of types of tips suitable for the dispensing amounts are used. In particular, in a dispensing device having a wide dispensing range, since a large volume dispensing tip or a small volume dispensing tip may be used, there are a wide variety of types of tips. In a case where the plurality of types of tips are used, when suction is performed beyond a tip volume, the inside of the dispensing device may be contaminated. Therefore, it is necessary to determine whether the dispensing amount and the mounted tip match with each other.

[0007] For example, a human error such as an installation error in a type of a tip can be considered as a factor. By making a case dedicated such that only a specific tip can be housed, the relation between the tip and a tip case can be uniquely determined, but it cannot be determined whether a tip suitable for the dispensing amount is installed. Although an installation error can be prevented, it is still necessary to determine whether a tip suitable for the dispensing amount is installed.

[0008] From the viewpoint of dispensing accuracy, it is important to determine a type of a tip. The larger a tip volume, the larger an air volume inside the tip. Therefore, when the air volume is excessively large relative to the dispensing amount, there is a possibility that no dispensing accuracy can be satisfied.

[0009] An object of the invention is to provide a dispensing device and method capable of solving the above problems and preventing contamination in the dispensing device caused by a mismatch between a tip and a dispensing amount at the time of dispensing.

Solution to Problem

[0010] In order to achieve the above object, the invention provides a dispensing device for suctioning a liquid sample with a dispensing tip and discharging a predetermined amount of the suctioned liquid sample to perform dispensing. The dispensing device includes a pressure sensor configured to measure an internal pressure of the dispensing device, and a type of the dispensing tip is determined based on a pressure waveform measured by the pressure sensor.

[0011] In order to achieve the above object, the invention further provides a dispensing method for a dispensing device for suctioning a liquid sample with a dispensing tip and discharging a predetermined amount of the suctioned liquid sample to perform dispensing. The dispensing method includes: measuring an internal pressure of the dispensing device; and determining a type of the dispensing tip based on a measured pressure waveform.

Advantageous Effects of Invention

[0012] According to the invention, it is possible to determine a type of a tip, that is being used, based on characteristics of the pressure waveform.

BRIEF DESCRIPTION OF DRAWINGS

[0013] FIG. **1** is a diagram showing an example of a configuration of a dispensing device and a liquid level detection operation according to the present disclosure.

[0014] FIG. **2** is a diagram showing a pressure waveform obtained when a piston is operated in a discharge direction to detect a liquid level according to the present disclosure.

[0015] FIG. **3** is a diagram showing a pressure waveform obtained when the piston is operated in a suction direction to detect a liquid level according to the present disclosure.

[0016] FIG. **4** is a diagram showing a processing flow of a normal dispensing method.

[0017] FIG. **5** is a diagram showing a pressure waveform obtained when a predetermined minute amount of air is discharged in a liquid according to a first embodiment.

[0018] FIG. **6** is a diagram showing a pressure waveform obtained when a predetermined minute amount of liquid is suctioned in the liquid according to the first embodiment.

[0019] FIG. **7** is a diagram showing a dispensing processing flow according to a second embodiment.

[0020] FIG. **8** is a diagram showing a pressure waveform obtained when a liquid level detection parameter is freely set and the piston is operated in the discharge direction to detect a liquid level according to the second embodiment.

[0021] FIG. **9** is a diagram showing a pressure waveform obtained when the liquid level detection parameter is freely set and the piston is operated in the suction direction to detect a liquid level according to the second embodiment.

[0022] FIG. **10** is a diagram showing a pressure waveform obtained when suction is performed beyond a tip volume according to a third embodiment.

[0023] FIG. **11** is a diagram showing a dispensing processing flow according to the third embodiment.

DESCRIPTION OF EMBODIMENTS

[0024] Hereinafter, embodiments of the present invention, that is, a dispensing device and method will be described with reference to the drawings. The dispensing device suctions a liquid sample with a dispensing tip and discharges a predetermined amount of the suctioned liquid sample to perform dispensing. The dispensing device includes a pressure sensor configured to measure an internal pressure of the dispensing device, and a type of the dispensing tip is determined based on a pressure waveform measured by the pressure sensor. The dispensing method for a dispensing device for suctioning a liquid sample with a dispensing tip and discharging a predetermined amount of the suctioned liquid sample to perform dispensing, includes: measuring an internal pressure of the dispensing device; and determining a type of the dispensing tip based on a measured pressure waveform.

[0025] The drawings shown below show specific embodiments according to the invention, but these drawings are for the purpose of understanding the invention, and are not to be used for limiting interpretation of the invention. In the present specification, the pressure means an internal pressure of a pipe of an dispensing device, and is detected by the pressure sensor mounted on the device.

[0026] FIG. **1** is a diagram showing a dispensing device **100** that performs pressure-type liquid level detection according to the present disclosure. The dispensing device **100** includes a base **101** having an L-shape as a whole, and a motor **102**, which is a drive unit, provided on an upper portion of the base **101**. The base **101** is rotatably provided with a screw shaft **104** implemented by a trapezoidal screw, a ball screw or the like that is connected to a rotating shaft of the motor **102** via a coupling **103**.

[0027] The screw shaft **104** is provided with a slider **106** through which the screw shaft **104** passes, and a nut **105** screwed to the screw shaft **104**. The slider **106** is connected to a linear guide **107** provided on the base **101**, and the nut **105** and the slider **106** are vertically movable or slidable along a direction of an arrow S shown in the figure. The slider **106** is joined to a piston **108** protruding downward, and is configured to move vertically instead of rotating. As described above, the piston **108** and the piston receiving portion **109** form a pipette mechanism. When the piston **108** is operated, a pressure in a system pipe changes, and the pipette mechanism is equipped with a pressure sensor **113** that measures the change in pressure. A measurement value of the pressure sensor **113** is input to a control computer **116**, which is a control unit, and is sequentially stored in a memory of the control computer **116**.

[0028] A vertical movement of the piston **108** of the pipette mechanism serves as a pump. A tip **110** is mounted to a tip end of the piston receiving portion **109** of the pipette mechanism. A tip removal portion **111** is provided above the tip **110**. The tip removal portion **111** is provided with a U-shaped notch or a through hole having a diameter smaller than a diameter of an opening portion of the tip **110**. The tip removal portion **111** is normally biased upward by a spring member **112** such as a spring connected to an upper end of the tip removal portion **111** and the base **101**, and is configured to move vertically along the arrow S. In order to ensure dispensing into small containers installed in various places in the device, the dispensing device **100** is installed on an automatic stage (not shown) which is freely driven in a horizontal direction and a vertical direction. The control computer **116** controls the dispensing motor **102**, which is the drive unit, the automatic stage, and the like.

[0029] A liquid **114** to be dispensed and a liquid reservoir **115** storing the fluid are provided, and it is necessary to acquire information on liquid level height of the liquid **114** to be dispensed. In the case of pressure-type liquid level detection, the piston **108** is driven in a suction or discharge direction, and a pressure value at that time is measured by the pressure sensor **113** while air suction or air discharge is performed. When the entire dispensing device **100** is driven downward in a vertical direction by the automatic stage or the like ((a) of FIG. **1**) and comes into contact with a liquid level of the liquid **114** to be dispensed ((b) of FIG. **1**) while the air suction or the air discharge is performed, a change in pressure value occurs at the time of the air suction or the air discharge by suctioning or discharging a minute amount of the liquid **114** to be dispensed, this change in pressure value is captured, the automatic stage and the piston **108** in the vertical direction are stopped and the liquid level is detected.

[0030] FIG. **2** is an example of a pressure waveform **200** obtained when the liquid level is detected by a discharge method. In the discharge method, a pressure generated when the dispensing device **100** connected to the automatic stage is driven in a vertically downward direction while the piston **108** is driven in the discharge direction is measured by the pressure sensor **113**. When a tip end of the tip comes into contact with the liquid level, the tip end portion is blocked by the liquid, and the pressure is increased to a positive pressure side due to the discharged air. A pressure waveform **201** is a waveform obtained when a small volume dispensing tip is used. A pressure waveform **202** is a waveform obtained when a large volume dispensing tip is used.

[0031] Although a piston drive speed and an automatic stage drive speed can be freely set, the pressure waveforms **201** and **202** shown here are waveforms measured using the same operation parameters. A pressure before the start of air discharge **203** is an atmospheric pressure **204**.

[0032] At air discharge **205**, the piston **108** begins to move in the discharge direction and the pressure increases to a pressure value **206**. The piston **108** begins to come into contact with the liquid **114** to be dispensed from a time point **207**, and approximate straight lines **209** and **210** are obtained based on the pressure values that change during a time **208**. In addition to capturing these changes in pressure, the control computer **116** performs control to stop the piston **108**

and the automatic stage at a time point **213** at which the pressure value exceeds pressure threshold values **211** and **212** that are obtained from a previous experiment and stored in the memory. The information on the liquid level height is acquired by the above operations. At the time point **213**, maximum pressure values **214** and **215** were measured, respectively.

[0033] FIG. **3** is an example of a pressure waveform **300** when the liquid level is detected by a suction method. A pressure generated when the dispensing device **100** connected to the automatic stage is driven in the vertically downward direction while the piston **108** is driven in the suction direction is measured by the pressure sensor **113**. A pressure before the start of air suction **301** is an atmospheric pressure **302**. The pressure is reduced to a pressure value **304** due to air suction **303**, and the tip end of the tip starts to come into contact with the dispensing liquid **114** from a time point **305**, and the liquid is suctioned into the tip.

[0034] A pressure waveform **306** is a waveform obtained when a small volume dispensing tip is used. A pressure waveform **307** is a waveform obtained when a large volume dispensing tip is used. Although the piston drive speed and the automatic stage drive speed can be freely set, the pressure waveforms **306** and **307** shown here are waveforms measured using the same operation parameters.

[0035] Approximate straight lines **309** and **310** are obtained from the pressure values that change during a time **308**. The control computer **116** stops the piston **108** and the automatic stage at a time point **313** at which the pressure value exceeds the pressure threshold values **311** and **312** that are obtained from verification in advance and stored in the memory, in addition to capturing changes in these pressures based on measurement values of the pressure sensor **113**. The information on the liquid level height is acquired by the above operations. Minimum pressure values measured at the time points **313** are **314** and **315**, respectively.

[0036] FIG. **4** is a diagram showing a processing flow S**400** of a normal dispensing method. Next, with reference to FIG. **4**, operations S**401** to S**410** during dispensing performed by the dispensing device will be described.

(S**401**)

[0037] Pressure waveform data is started to be acquired, and the atmospheric pressure **204** and the atmospheric pressure **302**, which serve as references at the time of the liquid level detection determination, are measured and stored in the memory or the like of the control computer **116**.

(S**402**)

[0038] In order to acquire information on the liquid level height, the automatic stage is driven to move vertically downward toward the liquid level. At this time, the piston **108** can be freely set to operate in the suction direction or the discharge direction. The pressure value **206** is measured by the pressure sensor **113** when the piston **108** is operated in the discharge direction, and the pressure value **304** is measured when the piston **108** is operated in the suction direction.

(S**403**)

[0039] At the liquid level contact time points **207** and **305**, the tip end of the tip reaches and comes into contact with the liquid level.

(S**404**)

[0040] When the piston **108** is operated in the discharge direction, the approximate straight line **209** or **210** is obtained from the pressure that changes from the liquid level contact time point **207**. When the piston **108** is operated in the suction direction, the approximate straight line **309** or **310** is obtained from the pressure that changes from the liquid level contact time point **305**. Conditions under which the liquid level is detected and the piston **108** and the automatic stage are stopped are that the pressure exceeds the pressure threshold value obtained from the previous experiment and that a slope of the approximate straight line is equal to or greater than a certain value.

(S**405**)

[0041] A stopped position in the vertical direction is stored in the memory.

(S**406**)

[0042] When the liquid level is detected by an operation of the piston **108** in the discharge direction, the piston is moved to a predetermined amount suction start position from a position separated vertically upward from the liquid level of the liquid **114** to be dispensed. When the liquid level is detected by an operation of the piston **108** in the suction direction, a minute amount of liquid suctioned during a liquid level entry time **308** is discharged at a position vertically above the liquid level of the liquid **114** to be dispensed. Thereafter, the piston **108** is moved to a predetermined suction start position.

(S**407**)

[0043] The set predetermined amount of liquid is suctioned.

[0044] (S**408**)

[0045] The dispensing device **100** is driven vertically and horizontally by the automatic stage to which the dispensing device **100** is mounted, and is moved to a predetermined discharge position.

(S**409**)

[0046] A predetermined amount of liquid is discharged.

[0047] In the discharge method described above, since the sample is not suctioned at the time of detection, there is no surplus liquid remaining in the tip. In the suction method, there is a possibility that the presence or absence of clot or the like, which causes clogging of the tip at the time of suction, can be detected before the start of the dispensing main suction.

First Embodiment

[0048] The present embodiment is an example of a dispensing device and method for determining a type of a tip based on an approximate straight line of a change in pressure which is obtained by discharging a minute amount of air or suctioning a minute amount of air in a state where a tip end of the tip is in contact with the liquid in advance. A tip determination method according to the present embodiment will be described with reference to FIGS. **5** and **6**.

[0049] FIG. **5** shows an example of a pressure waveform **500** obtained when a minute amount of air is discharged into the liquid. A pressure waveform **501** is a waveform obtained when a small volume dispensing tip is used. A pressure waveform **502** is a waveform obtained when a large volume dispensing tip is used. A pressure value **504** is measured by the pressure sensor in a state where the tip end of the tip is in contact with the liquid. When a minute amount of air is discharged during a time **505** starting from a time point **503**, pressure values **508** and **507** are measured at a piston stop time point **506**, respectively.

[0050] Approximate straight lines **509** and **510** are obtained from a change in pressure obtained during the time **505**. As is clear from the figure, since these approximate straight lines have characteristics for each type of tip, it is possible to determine the type of the tip by comparing the pressure value at the time of stop or a slope of the approximate straight line with a value measured in advance.

[0051] FIG. **6** is an example of a pressure change waveform **600** obtained when a minute amount of liquid is suctioned. A pressure waveform **601** is a waveform obtained when a small volume dispensing tip is used. A pressure waveform **602** is a waveform obtained when a large volume dispensing tip is used. A pressure value **603** is measured by the pressure sensor in a state where the tip end of the tip is in contact with the liquid. When a minute amount of liquid is suctioned during a time **605** starting from a time point **604**, the pressure values **608** and **607** are measured at a piston stop time point **606**, respectively.

[0052] Approximate straight lines **609** and **610** are obtained from a change in pressure obtained during the time **605**. Since these approximate straight lines have characteristics for each type of tip, it is possible to determine the type of the tip by comparing the pressure value at the time of stop or the slope of the approximate straight line with a value measured in advance.

[0053] According to the dispensing device, a liquid level detection method using the pressure waveform, and a tip type determination method of the present embodiment, a type of a tip being used can be determined based on a difference in characteristics of the pressure waveform, the relation between the pressure waveform during suction and the suction time, and the like.

Second Embodiment

[0054] A second embodiment is a tip type determination method using a pressure waveform obtained at the time of liquid level detection. Steps S**701** to S**712** of a tip type determination flow S**700** using the liquid level detection in FIGS. **3** and **7** will be described with reference to FIGS. **8** and **9**. An operation processing subject of the tip type determination flow S**700** is the control computer **116**, which is a control unit, or the like.

(S**701**)

[0055] Pressure waveform data is started to be acquired, and the atmospheric pressure **204** and the atmospheric pressure **302**, which serve as a reference at the time of the liquid level detection determination, are measured by the pressure sensor **113** and stored.

(S**702**)

[0056] In order to acquire the information on the liquid level height, the automatic stage is driven to move vertically downward toward the liquid level. At this time, the piston **108** can be freely set to operate in the suction direction or the discharge direction. A pressure value **206** is measured by the pressure sensor **113** when the piston **108** is operated in the discharge direction, and a pressure value **304** is measured when the piston **108** is operated in the suction direction.

(S**703**)

[0057] At the liquid level contact time points **207** and **305**, the tip end of the tip reaches and comes into contact with the liquid level.

(S**704**)

[0058] Conditions under which the piston and the automatic stage are stopped at the time of liquid level detection are that the pressure exceeds the pressure threshold value stored in advance and that the slope of the approximate straight line is equal to or greater than a certain value.

[0059] When the piston is operated in the discharge direction and a large volume dispensing tip is used, at the time point **213**, the piston stops, and an approximate straight line **210** is obtained from the pressure waveform **202**. The case where a pressure threshold value and a slope condition of the approximate straight line related to a liquid level detection operation are set as parameters for the large volume dispensing tip will be considered. Since when a small volume dispensing tip is used in this state, a set pressure threshold value and the slope condition are set to be smaller than conditions for the small volume dispensing tip, the time until the liquid level is detected and the piston is stopped is shortened. Therefore, a pressure waveform corresponding to the small volume dispensing tip has a shape indicated by **801**. At a time point **802**, the piston stops, and an approximate straight line **803** is obtained.

[0060] When the piston is operated in the suction direction, for a large volume dispensing tip, the piston stops at the time point **313**, and an approximate straight line **310** is obtained from the pressure waveform **307**. Similarly, the case where a pressure threshold value and a slope condition of the approximate straight line related to a liquid level detection operation are set as parameters for the large volume dispensing tip will be considered. Since when a small volume dispensing tip is used in this state, a set pressure threshold value is larger and the slope condition is smaller than conditions for the small volume dispensing tip, the time until the liquid level is detected and the piston is stopped is shortened.

[0061] Therefore, a pressure waveform corresponding to the small volume dispensing tip has a shape indicated by **901**. At a time point **902**, the piston stops, and an approximate straight line **903** is obtained.

(S**705**)

[0062] A pressure waveform acquired in a liquid level detection process of S**701** to S**704** is used. When the piston is operated in the discharge direction and the liquid level detection is performed, a type of the tip is determined based on the approximate straight lines **210** and **803**. When the piston is operated in the suction direction and the liquid level detection is performed, the type of the tip is determined based on the approximate straight lines **310** and **903**.

[0063] Here, a pressure P measured by the pressure sensor **113** will be considered by taking the liquid level detection in which the piston is operated in the suction direction as an example. A pressure ΔP is considered to be $\Delta P=2\times\sigma/(D/2)$.

σ represents a surface tension of the liquid, and D represents a tip end inner diameter of the tip. From this equation, it can be seen that a suction pressure value has the surface tension σ of the suction liquid and the tip end inner diameter D of the tip as parameters.

[0064] In the small volume dispensing tip and the large volume dispensing tip described as examples, since a tip end inner diameter of the small volume dispensing tip is smaller than that of the large volume dispensing tip, it can be seen that the change in pressure per unit time from the time point **313** shown in FIG. **3** is large. It can be seen that when the same liquid is suctioned, the change in pressure, that is, the slope of the approximate straight line is larger in the tip having a small tip end. Therefore, it can be said that tips having different tip end diameters have different feature data in the slope of the obtained approximate straight line.

[0065] An air volume in the tip varies depending on a dispensing volume. A tip with a large dispensing volume generally has a large internal air volume in order to suction more liquid. When an amount of air, which is a compressive fluid, is large, a delay occurs in a value detected by the pressure sensor, so that the slope of the approximate straight line per unit time is larger for a tip having a smaller tip volume. That is, it can be seen that the slopes of the approximate straight lines have different characteristics even when the tip end diameters of the tips are the same.

[0066] By using these characteristics and comparing these characteristics with the pressure waveforms obtained from verification results in advance, it is determined whether an appropriate tip is being used.

(S**706**)

[0067] An error notification that a tip inappropriate for the dispensing is mounted is output. When a tip having a sufficient volume for the dispensing amount is mounted, the dispensing itself is possible. However, since the air volume inside the tip is large, there is a possibility that the required dispensing accuracy cannot be satisfied. Here, by detecting an error in the mounted tip, it is possible to ensure the dispensing accuracy of the specification.

(S**707**)

[0068] A stopped position in the vertical direction is stored.

(S**708**)

[0069] When the liquid level is detected by an operation of the piston **108** in the discharge direction, the piston is moved to a predetermined amount suction start position from a position separated vertically upward from the liquid level of the liquid **114** to be dispensed. When the liquid level is detected by an operation of the piston **108** in the suction direction, a minute amount of liquid suctioned during a liquid level entry time **308** is discharged at a position vertically above the liquid level of the liquid **114** to be dispensed. Thereafter, the piston **108** is moved to a predetermined suction start position.

(S**709**)

[0070] A set predetermined amount of liquid is suctioned.

(S**710**)

[0071] The dispensing device **100** is driven vertically and horizontally by the automatic stage to which the dispensing device **100** is mounted, and is moved to a predetermined discharge position.

(S**711**)

[0072] A predetermined amount of liquid is discharged.

[0073] According to the present embodiment, it is possible to perform the tip type determination using the pressure waveform obtained at the time of the liquid level detection.

Third Embodiment

[0074] The first embodiment and the second embodiment describe an effective determination method when there is a large difference in the tip volume or the tip end diameter. For example, in a case of tips having dispensing volumes of 10 microliters and 20 microliters, the differences in both the volume and the tip end diameter are small, so that determination cannot be made in the first embodiment and the second embodiment. In such a case, a type of a tip is determined using a method shown in the present embodiment.

[0075] Tip type determination according to the present embodiment will be described with reference to FIGS. **10** and **11**. Here, it is assumed that a commercially available disposable tip with a filter is used.

[0076] FIG. **10** is an example of a pressure waveform **1000** obtained when a liquid is suctioned. A pressure waveform **1001** is a pressure waveform obtained when excessive liquid is suctioned beyond a tip volume. In a pre-suction time **1002**, the automatic stage is moved in the vertically downward direction to a liquid level height stored in advance. The liquid is suctioned in a suction time **1003**, and the suctioned liquid enters the filter at an excess suction time **1004**, and a pressure is reduced. A dotted line **1005** in FIG. **10** indicates a normal pressure waveform.

[0077] FIG. **11** is an operation flow S**1100** according to the present embodiment. A tip type determination method will be described below with reference to flows S**1101** to S**1108**.

(S**1101**)

[0078] Pressure waveform data is started to be acquired, and an atmospheric pressure that serves as a reference is measured and stored.

(S**1102**)

[0079] The automatic stage to which the dispensing device **100** is connected is moved in the vertically downward direction to a pre-stored liquid level height at which the liquid can be suctioned, and the liquid is started to be suctioned.

(S**1103**) Tip Type Determination based on Suction Pressure Waveform

[0080] A type is determined based on a change in suction pressure waveform continuously acquired from S**1101**. Operation parameters for suction are set to values verified by a dispensing test or the like, based on liquid physical constants (viscosity, surface tension, specific gravity, contact angle) and dispensing amounts of various liquids. Therefore, it is possible to calculate a suction amount at any time.

[0081] That is, it is possible to predict when the volume will be exceeded for each tip based on the operation parameters for suction. When the suction is performed normally, a suction pressure remains stable at a certain pressure, and returns to a positive pressure side when the suction stops. The suction pressure decreases when the liquid reaches the filter beyond the tip volume.

[0082] For example, a case of using two types of tips having dispensing volumes of 10 microliters and 20 microliters is considered. When a 20-microliter dispensing operation is performed with a tip having a volume of 10 microliters, the tip volume is exceeded at a certain time. When the suction pressure decreases at a certain time, it can be determined that excessive suction is being performed beyond the tip volume, so that the type of the tip can be determined.

(S**1104**)

[0083] A suction operation is stopped, and the type of the tip is determined.

(S**1105**)

[0084] Based on a determination result, an error notification that a tip inappropriate for the dispensing is mounted is output.

(S**1106**)

[0085] The suction operation is completed.

(S**1107**)

[0086] The dispensing device **100** is driven vertically and horizontally by the automatic stage to which the dispensing device **100** is mounted, and is moved to a predetermined discharge position.

(S**1108**)

[0087] A predetermined amount of liquid is discharged.

[0088] According to the present embodiment, it is possible to determine the type of a tip with a smaller dispensing volume.

[0089] The invention is not limited to the embodiments described above and includes various modifications. For example, the embodiments described above are described in detail for better understanding of the invention, and the invention is not necessarily limited to embodiments including all configurations described above.

[0090] Further, although an example of creating a program that implements a part or all of the configurations, functions, and control computers described above and the like is mainly described, it is needless to say that a part or all of them may be implemented by hardware, for example, by designing an integrated circuit. That is, all or a part of functions of a processing unit may be implemented by, for example, an integrated circuit such as an application specific integrated circuit (ASIC) or a field programmable gate array (FPGA) instead of the program.

REFERENCE SIGNS LIST

[0091] **100** dispensing device
[0092] **101** base
[0093] **102** motor
[0094] **103** coupling
[0095] **104** screw shaft
[0096] **105** nut
[0097] **106** slider
[0098] **107** linear guide
[0099] **108** piston
[0100] **109** piston receiving portion
[0101] **110** disposable tip
[0102] **111** tip removal portion
[0103] **112** spring member
[0104] **113** pressure sensor
[0105] **114** liquid to be dispensed
[0106] **115** liquid reservoir
[0107] **116** control computer

1. A dispensing device for suctioning a liquid sample with a dispensing tip and discharging a predetermined amount of the suctioned liquid sample to perform dispensing, the dispensing device comprising:
- a pressure sensor configured to measure an internal pressure of the dispensing device, wherein
- a type of the dispensing tip is determined based on a pressure waveform measured by the pressure sensor.

2. The dispensing device according to claim **1**, wherein
- the type of the dispensing tip is determined by using a pressure waveform obtained at the time of liquid level detection as the pressure waveform.

3. The dispensing device according to claim **2**, further comprising:
- a pipette mechanism configured to perform suction and discharge; and
- a drive unit configured to drive the pipette mechanism, wherein
- the dispensing tip is mounted on the pipette mechanism, and the drive unit drives the pipette mechanism in a suction or discharge direction.

4. The dispensing device according to claim **3**, further comprising:
- a control unit configured to control the drive unit based on an output of the pressure sensor.

5. The dispensing device according to claim **4**, wherein
- the control unit stops the drive unit and determines the type of the dispensing tip when it is detected that the dispensing tip reaches a liquid level.

6. The dispensing device according to claim **5**, wherein
- the control unit outputs an error notification when it is determined that an inappropriate dispensing tip is mounted as a result of determining the type of the dispensing tip.

7. The dispensing device according to claim **5**, wherein
- the control unit stores a liquid level position when it is determined that an appropriate dispensing tip is mounted as a result of determining the type of the dispensing tip.

8. The dispensing device according to claim **1**, wherein
- a dispensing tip with a filter is used as the dispensing tip, and
- the type of the dispensing tip is determined based on the pressure waveform obtained when a liquid is suctioned beyond a specification volume of the dispensing tip with a filter.

9. A dispensing method for a dispensing device for suctioning a liquid sample with a dispensing tip and discharging a predetermined amount of the suctioned liquid sample to perform dispensing, the dispensing method comprising:

measuring an internal pressure of the dispensing device; and

determining a type of the dispensing tip based on a measured pressure waveform.

10. The dispensing method according to claim **9**, wherein

the type of the dispensing tip is determined by using a pressure waveform obtained at the time of liquid level detection as the pressure waveform.

11. The dispensing method according to claim **10**, further comprising:

driving the dispensing tip in a suction or discharge direction.

12. The dispensing method according to claim **11**, wherein

the driving is stopped and the type of the dispensing tip is determined when it is detected that the dispensing tip reaches a liquid level.

13. The dispensing method according to claim **12**, further comprising:

outputting an error notification when it is determined that an inappropriate dispensing tip is mounted as a result of determining the type of the dispensing tip.

14. The dispensing method according to claim **12**, further comprising:

storing a liquid level position when it is determined that an appropriate dispensing tip is mounted as a result of determining the type of the dispensing tip.

15. The dispensing method according to claim **9**, wherein

a dispensing tip with a filter is used as the dispensing tip; and

the type of the dispensing tip is determined based on the pressure waveform obtained when a liquid is suctioned beyond a specification volume of the dispensing tip with a filter.

* * * * *