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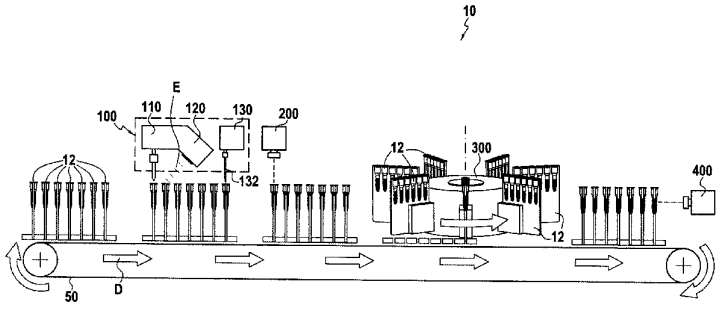


FIG.1

(57) Abstract : The invention relates to a device for filling at least one receptacle (12) of gel card type initially sealed by a cap. The invention is characterized by the fact that the filling device comprises a piercing member (110) for perforating the cap, means (120) for eliminating the electrostatic charges capable of being borne by the receptacle, and filling means (130) for filling the receptacle after perforation of the cap and elimination of the electrostatic charges.

(57) Abrégé : L'invention concerne un dispositif de remplissage d'au moins un réceptacle (12) de type carte gel initialement fermé par un opercule. L'invention se caractérise par le fait que Ie dispositif de remplissage comporte un organe de perçage (110) pour perforer l'opercule, des moyens (120) pour supprimer les charges électrostatiques susceptibles d'être portées par le réceptacle, et des moyens de remplissage (130) pour remplir le réceptacle après perforation de l'opercule et suppression des charges électrostatiques.

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# Gel card filling device comprising an ionizer

The present invention relates to the field of devices for performing medical analyses.

Traditionally, such devices, also called analysis machines, make it possible to automate certain protocols, such as for example pipetting liquids into gel cards. This protocol consists of pouring a predetermined quantity of liquid into a reactive well of a gel card containing one or more reagents. This liquid can for example be a blood sample, or any other type of human sample.

In a known manner, a gel card is a receptacle containing one or more reactive wells that are initially sealed by a cap. After having pierced the cap and poured the liquid, chemical reactions occur between the poured liquid and the reagent(s) of the card.

Generally, the quantity of liquid poured is very small, in the vicinity of several microliters, so that one generally refers to a "dose." What is more, the filling of the wells must respect certain quality criteria. Among these criteria, we will more particularly mention those relative to the creation of an air gap between the dose of liquid dispensed into the well and the reagent previously present at the bottom of the well, as well as the criterion relative to the absence of liquid splashes on the inner wall of the well. Splashes most often come from more or less significant, but still random, fracturation of the dispensed dose of liquid.

The presence of an air gap has the effect of provisionally prohibiting physical contact between the dispensed dose of liquid and the reagent. One interest is of controlling the moment from which the chemical reaction must begin. In practice, the gel cards are incubated and centrifuged after dispensing the liquid dose thereby leading to the chemical reaction.

The absence of splashes in turn is necessary in order to prevent a fraction of the dose of liquid from remaining stuck to the walls of the well and thus being removed from the incubated and centrifuged reactive mixture.

To resolve the first problem, document US 5 780 248 proposes the use of consumable accessories made from plastic, said accessory being formed by an insert provided with six cavities with a pointed lower end. Moreover, the lower ends of the cavities are provided with a very small hole. This accessory is intended to be manually planted in a gel card, the ends of the cavities perforating the cap sealing the wells of the gel card. Each of the cavities of the accessory is housed in a well of the gel card. Then, a dose of liquid is dispensed into each of the cavities of the accessory. Using that accessory, the operator does not need to worry about whether an air gap is formed, inasmuch as the cavity isolates the dispensed liquid dose from

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the reagent contained at the bottom of the well. It also appears that the use of such accessories makes it possible to decrease the presence of splashes.

However, this solution has several drawbacks: the accessories must be purchased, stored and handled. What is more, the installation of the accessories on the gel cards must necessarily be done manually, which is inconvenient and not very fast.

Thus, a need exists to propose a device for filling at least one receptacle of the gel card type initially sealed by a cap, allowing automatic filling while resolving the aforementioned drawbacks.

**Object of the Invention**

It is an object of the invention to overcome or substantially ameliorate one or more of the above disadvantages, or at least to provide a useful alternative.

**Summary**

According to a first aspect of the present disclosure, there is provided a device for filling at least one receptacle of the gel card type initially sealed by a cap, the filling device including a piercing member to perforate the cap, means for eliminating the electrostatic charges that may be borne by the receptacle, and filling means to fill the receptacle after perforation of the cap and elimination of the electrostatic charges.

The inventors have in fact noted that the elimination of the electrostatic charges on the receptacle makes it possible to clearly avoid the formation of splashes on the inner walls of the receptacle. In fact, it happens that the electrostatic charges borne by the receptacle tend to dislocate the liquid dose when it leaves the filling means. It follows that certain fractions of the dose adhere against the inner wall of the receptacle, due to the attraction forces created by the electrostatic charges.

It is therefore understood that the filling device according to the present disclosure advantageously makes it possible to prevent splashes from forming. Furthermore, embodiments of the present disclosure do not require the use of consumables, unlike the prior devices. Another interest of embodiments of the present disclosure is that they allow automatic filling.

What is more, the formation of the air gap is favored by the absence of electrostatic force tending to deflect the dose released by the filling means.

Preferably, the receptacle is a card, of the gel card type, which includes a plurality of wells sealed by the cap, each of the wells containing one or more reagents.

Advantageously, the piercing member includes a piercing rake provided with a plurality of piercing tips that are intended to penetrate the wells while passing through the cap.

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One interest of the rake is that it makes it possible to pierce several holes in the cap all at once, these holes being those through which the filling means pour the liquid into the wells.

Preferably, the rake includes as many tips as the number of wells of the gel card, as a result of which the operation for piercing the cap of a gel card is performed a single time.

Particularly advantageously, the means for eliminating the electrostatic charges comprise an ionizer. The latter generates a flow of alternatingly positively and negatively charged ions, this ion flow being sent toward the receptacle, preferably after the cap has been perforated. This alternation makes it possible to eliminate the electrostatic charges borne by the wells of the gel card.

Preferably, the ionizer can and is intended to generate an electrical field producing a corona effect. Said corona effect, known in itself, is also called crown effect.

According to one preferred embodiment, the filling device has an intake direction for the receptacles toward the piercing member and the ionizer is made up of at least one ionization ramp extending transversely relative to said intake direction. Said ramp is preferably arranged as close as possible to the piercing zone in order to ionize the gel card right after the cap is pierced.

Furthermore, the ionizer preferably includes a plurality of electrodes targeting a zone in which the receptacle is intended to be located during piercing of the cap of said receptacle.

Without going beyond the scope of the present disclosure, it would also be possible to use an ionizer provided with means for blowing ionized air toward the gel card.

Preferably, the ionization ramp extends between the two mobile arms that bear the piercing rake, owing to which it is possible to ionize the gel card immediately after the piercing operation.

According to a second aspect of the present disclosure, there is provided a medical analysis machine to analyze the chemical reactions taking place in at least one receptacle that comprises a plurality of wells containing one or more reagents while being sealed by at least one cap, said machine including a filling device as described above, means for bringing said receptacle toward said filling device, and means for analyzing the chemical reactions that can occur in the wells of the receptacle after the filling means have poured a quantity of liquid into each of the wells.

The machine preferably includes a plurality of receptacles made up of similar or different gel cards.

Advantageously, the machine according to the present disclosure also includes a checking station to verify the positioning of the liquid poured into the wells by the filling means.

Preferably, said checking station includes a camera as well as image processing means making it possible to identify the presence or absence of an air gap and any splashes.

According to a third aspect of the present disclosure, there is provided a method for filling a receptacle of the gel card type provided with a plurality of wells sealed by a cap, comprising:

- a step of piercing the cap of the receptacle in order to open the wells;
- a step of eliminating electrostatic charges that may be borne by the receptacle; and
- a filling step during which a quantity of liquid is poured into each of the wells of the receptacle.

Preferably, this method is implemented by the filling device according to the present disclosure, as described above.

Advantageously, the step of eliminating the electrostatic charges consists of ionizing the wells of the receptacle by generating an electrical field producing a corona effect.

Preferably, but not necessarily, the step for eliminating electrostatic charges is carried out after the piercing step. One interest is to be able to ionize the air contained inside the wells.

Advantageously, the step for filling the wells is carried out with at least one pipette, and during said filling step, said pipette extends coaxially to one of the wells.

One interest is to prevent the end of the pipette from coming into contact with droplets of reagent that can be located on the inner wall of the well, and therefore to avoid any contamination of the pipette.

According to the present disclsoure, a complementary manner of avoiding the contamination of the pipette is to place the lower end of the pipette slightly below the cap during the filling step. Preferably, the lower end of the pipette is placed several millimeters under the cap.

Preferably, during the filling step, an air gap is created between the poured liquid and another liquid previously present in the wells. In other words, an air gap is created between the reagent contained in each of the wells and the poured doses.

Lastly and advantageously, the method according to an aspect of the present disclosure also includes a step of verifying the positioning of the liquid poured at the end of the filling step. One primarily verifies the proper production of the air gaps.

The invention will be better understood and its advantages will better appear upon reading the following detailed description, of an embodiment illustrated as a non-limiting example. The description refers to the drawings, in which:

- figure **1** diagrammatically illustrates a medical analysis machine according to the invention, which includes a filling device according to the invention;
- figure **2** is a frontal view of a receptacle intended to be used with the machine of figure **1**;

- figure **3** is a perspective view of one preferred embodiment of the filling device according to the invention;
- figure **4** is a detailed view of the ionization ramp of the filling device of figure **3**; and
- figure **5** shows the formation of an air gap between the reagent contained in a well of the receptacle of figure **2** and a dose of liquid dispensed by a pipette of the machine of figure **1**.

Figure **1** shows a very diagrammatic and non-limiting illustration of a medical analysis machine **10** according to the invention.

This machine **10** uses consumable receptacles, in this case gel cards **12** provided with wells **14**, also well known. Figure **2** shows that each of the gel cards **12** of this example includes six wells **14** emerging in an upper wall **12a** of the gel card. These wells **14** therefore have openings **16** formed in the upper wall **12a** of the gel card, these openings **16** initially being sealed by a cap **18** that extends in a longitudinal direction **L** of the gel card **12**. In that example, the cap **18** consists of a thin strip sealed to the upper wall of the gel card **12**.

As understood using figure **2**, each well **14** of the gel card **12** contains, in a known manner, a reagent **R**, said reagent being able to be different from one well to the next.

More specifically, each well **14** is formed by a substantially cylindrical upper cavity **14a** connected to a lower cavity **14b** that is also substantially cylindrical via a tapered intermediate cavity. The upper cavity **14a** has a diameter substantially larger than that of the lower cavity **14b**, and the upper **14a** and lower **14b** cavities are coaxial with a shared axis **A**. As shown in figure **2**, the reagent is contained in the lower cavity **14b**, the reagent level being situated slightly below the upper end of the lower cavity **14b**, while the upper cavity **14a**, initially empty, emerges in the upper wall **12a** of the gel card **12**.

It happens that the gel cards **12**, made from plastic, have a propensity to bear electrostatic charges $\mathbf{C}^+$, $\mathbf{C}^-$; it is thought that they are generated during impacts that the gel cards **12** may undergo during handling thereof.

Referring again to figure 1, one sees that the machine includes a conveyor **50** that makes it possible to move the gel cards **12** of the machine **10** in an intake direction **D**. Of course, any other type of conveyor can be used without going beyond the scope of the present invention.

Considered in the intake direction **D**, the machine **10** successively includes a filling device **100** according to the invention, an audit station **200** to verify the position of the liquid poured into the wells by the filling device, a compressor impeller

**300**, then means **400** for analyzing the chemical reactions likely to occur in the wells of the gel card.

The gel cards **12** are first conveyed toward the filling device **100**, the latter being intended to fill the wells of the gel cards **12** with a liquid in a predetermined quantity.

To that end, the filling device **100** according to the invention first includes a piercing member **110** to perforate the caps **18** of the gel cards.

According to one essential aspect of the invention, the filling device **100** also includes means **120** for eliminating the electrostatic charges that may be borne by the gel cards. And of course, the filling device also includes filling means **130** to fill the wells of the gel cards after perforation of the cap and elimination of the electrostatic charges. It is specified that, according to the preferred embodiment of the invention, the filling means **140** are automatic. However, and without going beyond the scope of the present invention, they may also be made up of a manual pipette handled by an operator.

The piercing member **110** and the means **120** for eliminating the electrostatic charges will first be described in more detail using figures **3** and **4**.

The piercing member **110** includes a piercing rake **112** that is provided with six tips **114**, these tips being intended to penetrate the wells of the gel card while passing through the cap **18** so as to create a series of holes **17** in the cap. The gel cards **12** also including six wells **14**, it is understood that the rake **112** makes it possible to produce six holes **17** at once in the cap of each of the gel cards **12**.

As seen in figure **3**, this rake **112** extends transversely relative to the intake direction **D**.

What is more, the tips **114** of the rake **112** preferably have flats **114a** in order to favor the piercing of the cap **18**.

Furthermore, a pair of spring blades **116** extending between the tips **114** is provided to facilitate the disengagement of the piercing rake **112** after perforating the cap **18**.

Lastly, it is specified that the rake **112** is locked to a rake holder **113** by a locking member **118** making it possible to disassemble the rake **112**. Furthermore, this rake holder **112** includes two mobile arms **113a, 113b** between which the rake **112** extends, these arms being connected to pivoting connecting rods **115** that make it possible to bring the rake **112**, following a circular translational movement, from an idle position (shown in figure **3**) toward a working position in which the tips **114** perforate the cap **18** of the gel card.

According to one advantageous aspect of the invention, the means **120** for eliminating the electrostatic charges comprise an ionizer **122** here made up by an ionization ramp that is powered by traditional power means not shown here.

This ionization ramp **122** is immobile relative to the machine and extends transversely relative to the intake direction **D** between the arms cavities **113a** and **113b** of the rake holder **113**. As seen in figure **3**, the ionization ramp **122** is situated below the tips **114** of the rake **112** when the latter is in its idle position. Said ramp **122** is also arranged so that the tips **114** of the rake **112** do not touch the rake during movement of the rake **112** toward its working position.

Furthermore, figure **3** shows that the ionization ramp **122** includes several electrodes **124**, in this case five, protruding from the bottom of a longitudinal groove **126**.

In reference now to figure **4**, one can see that the ionization ramp **122** is mounted on a holder **128** having a fastening foot **129**. The ramp is tilted by about 60° relative to the vertical so that the electrodes **124** of the ramp target a zone in which the gel card is located during the piercing operation of the cap **18**. Preferably, the distance between the ionization ramp and the openings **16** of the wells **14** is between 15 and 30 mm. In this particular case, the electrodes **124** of the ionization ramp **122** serve to generate an electrical field **E**, of the corona type, around wells **14** of the gel card **12**. To that end, one can for example choose a power supply of the auto-transformer type delivering a sinusoidal wave, with a frequency of 50 Hz, with a potential difference of 4 KV and fan-out of 2.5 mA on each electrode.

We will now explain the filling method used by the filling device **100** according to the invention.

As shown in figure **3**, the gel cards **12** are successively brought near the piercing member **110**, in a housing **102** extending transversely relative to the intake direction **D**, so that, during the piercing operation, the gel card **12** is maintained in a vertical plane transverse to the intake direction **D**.

When the piercing member **110** is actuated, the rake **112** tilts in its working position following the circular translational movement described above, so that the tips **114** of the rake **112** perforate the cap **18**. Then, the rake **112** is brought back into its idle position as shown in figure **3**. At the end of the piercing step, the cap **18** is pierced with six holes **20** at the wells **14**.

After this piercing step, the ionization ramp is activated so as to generate an electrical field with a corona effect around the wells **14**. As explained above, this corona effect electrical field generates ionized air that results in eliminating the electrostatic charges $C^+$, $C^-$ that may be borne by the wells of the gel cards **12**. Preferably, the ionization duration of the wells **14** is between 1 and 1.5 second.

After the ionization step, the gel card **12** is brought toward the filling means **170**. The latter include at least one pipette **132** visible in figure **5**. As shown in that figure, the pipette **132** is successively inserted into each of the upper cavities **14a** of the wells **14** through the holes **20** formed in the cap **18** following the piercing operation. During the insertion of the pipette into one of the wells **14** through the hole **20**, the lower end **132a** of the pipette is brought to several millimeters below the cap, while the pipette is arranged coaxially relative to said well.

Then, the pipette **132** pours a dose **134** of liquid, that is to say about 10 µl, into the upper cavity **14a**, as shown in figure **5** for the wells situated close to the left edge of the gel card **12**.

Very preferably, an air gap **136** is created between the dose **134** and the reagent contained in the lower cavity **14b** of the wells **14**. This air gap is situated essentially below the tapered intermediate cavity.

At the end of the filling step, the gel card **12** is brought into the checking station **200** in order to verify the presence of air gaps **136.**

After this, the gel card **12** is incubated, then centrifuged owing to the compressor impeller **300**.

The result of the chemical reactions taking place in the wells **14** is then analyzed using means **400** for analyzing chemical reactions. Such means, otherwise known, generally include a reader making it possible to visualize the result of the reaction(s) in the wells **14** of the gel card **12**.

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**The claims defining the invention are as follows:**

1. A device for filling at least one receptacle of the gel card type initially sealed by a cap, said device including a piercing member to perforate the cap, means for eliminating the electrostatic charges that may be borne by the receptacle, and filling means to fill the receptacle after perforation of the cap and elimination of the electrostatic charges.

2. The filling device according to claim **1**, wherein the receptacle is a card, which includes a plurality of wells sealed by the cap, each of the wells containing one or more reagents.

3. The filling device according to claim **2**, wherein the piercing member includes a piercing rake provided with a plurality of piercing tips that are intended to penetrate the wells while passing through the cap.

4. The filling device according to either one of claims **2** or **3**, wherein the filling means comprise at least one pipette.

5. The filling device according to any one of claims **1** to **4**, wherein the means for eliminating the electrostatic charges comprise an ionizer.

6. The filling device according to claim **5**, having an intake direction for the receptacle toward the piercing member, wherein the ionizer is made up of an ionization ramp extending transversely relative to said intake direction.

7. The filling device according to either one of claims **5** or **6**, wherein the ionizer includes a plurality of electrodes targeting a zone in which the receptacle is intended to be located during piercing of the cap of said receptacle.

8. The filling device according to any one of claims **5** to **7**, wherein the ionizer is intended to generate an electrical field producing a corona effect.

9. A medical analysis machine for analyzing chemical reactions taking place in at least one receptacle that comprises a plurality of wells containing one or more reagents while being sealed by at least one cap, said machine including a filling device according to any one of claims **1** to **8**, means for bringing said receptacle toward said filling device, and means for analyzing the chemical

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reactions that can occur in the wells of the receptacle after the filling means have poured a quantity of liquid into each of the wells.

10. The machine according to claim 9, wherein it also includes a checking station to verify the positioning of the liquid poured into the wells by the filling means.

11. A method of filling a receptacle of the gel card type provided with a plurality of wells sealed by a cap, comprising:

a step of piercing the cap of the receptacle in order to open the well;

a step of eliminating electrostatic charges that may be borne by the receptacle; and

a filling step during which a quantity of liquid is poured into each of the wells of the receptacle.

12. The filling method according to claim 11, wherein the step for eliminating the electrostatic charges consists of ionizing the well of the receptacle by generating an electrical field producing a corona effect.

13. The filling method according to claim 11 or 12, wherein the step of eliminating the electrostatic charges is carried out after the piercing step.

14. The filling method according to any one of claims 11 to 13, wherein the step of filling the wells is carried out with at least one pipette, and, during said filling step, said pipette extends coaxially to one of the wells.

15. The filling method according to any one of claims 11 to 14, wherein the filling step is carried out with at least one pipette having a lower end, and, during said filling step, the lower end is placed slightly below the cap.

16. The filling method according to any one of claims 11 to 15, wherein, during the filling step, an air gap is created between the poured liquid and another liquid previously present in the wells.

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17. The filling method according to any one of claims 11 to 16, further including a step of verifying the positioning of the liquid poured at the end of the filling step.

**BIO-RAD INNOVATIONS**

By Patent Attorneys for the Applicant

COTTERS

**Patent & Trade Mark Attorneys**

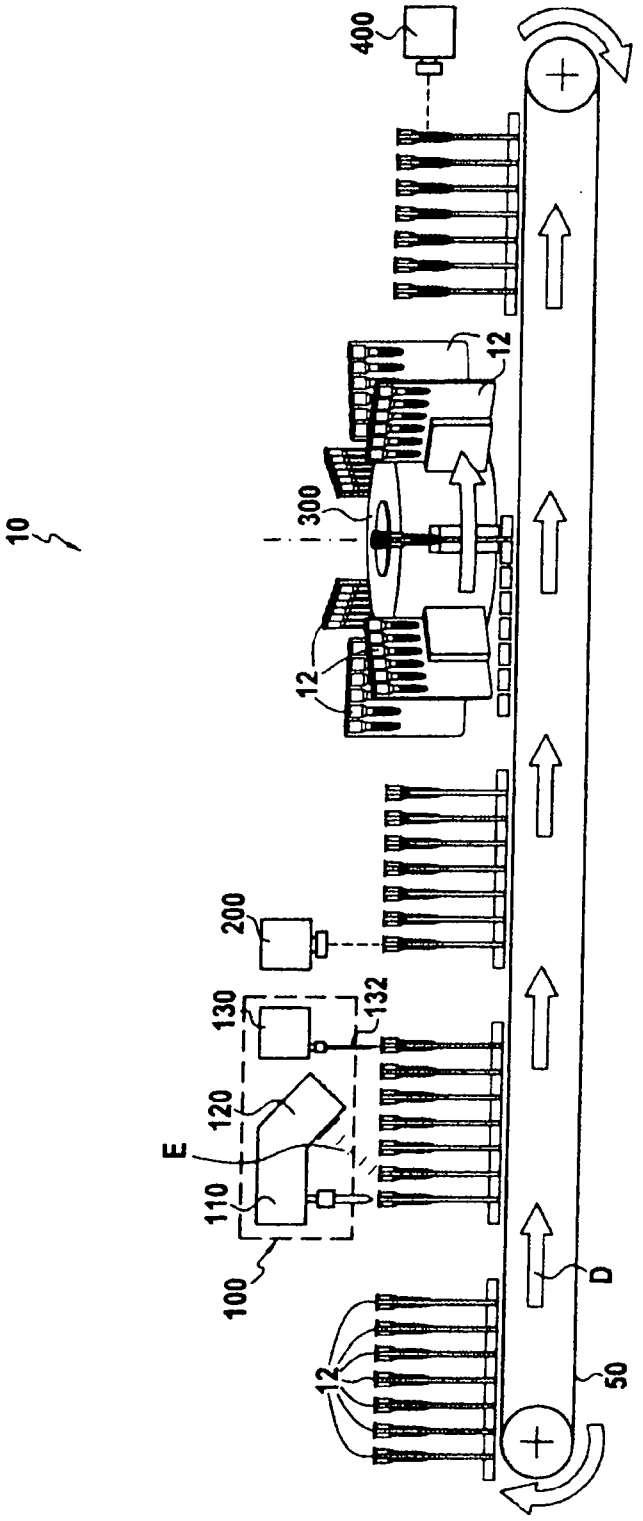


FIG.1

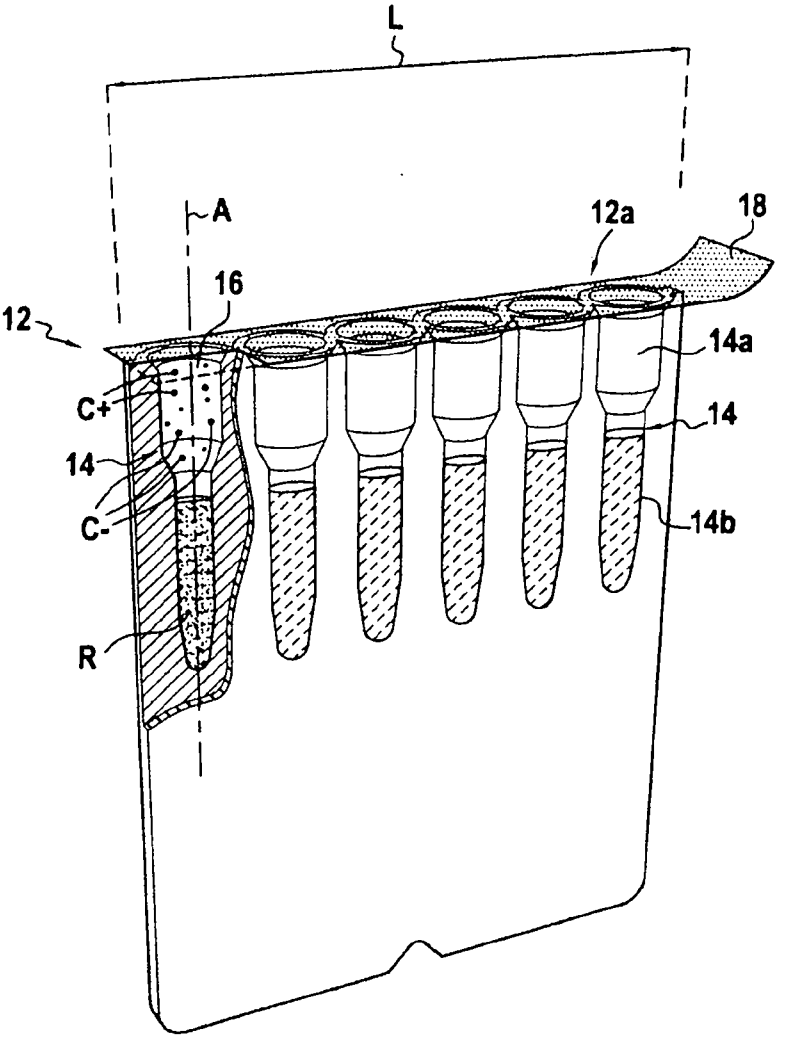


FIG.2

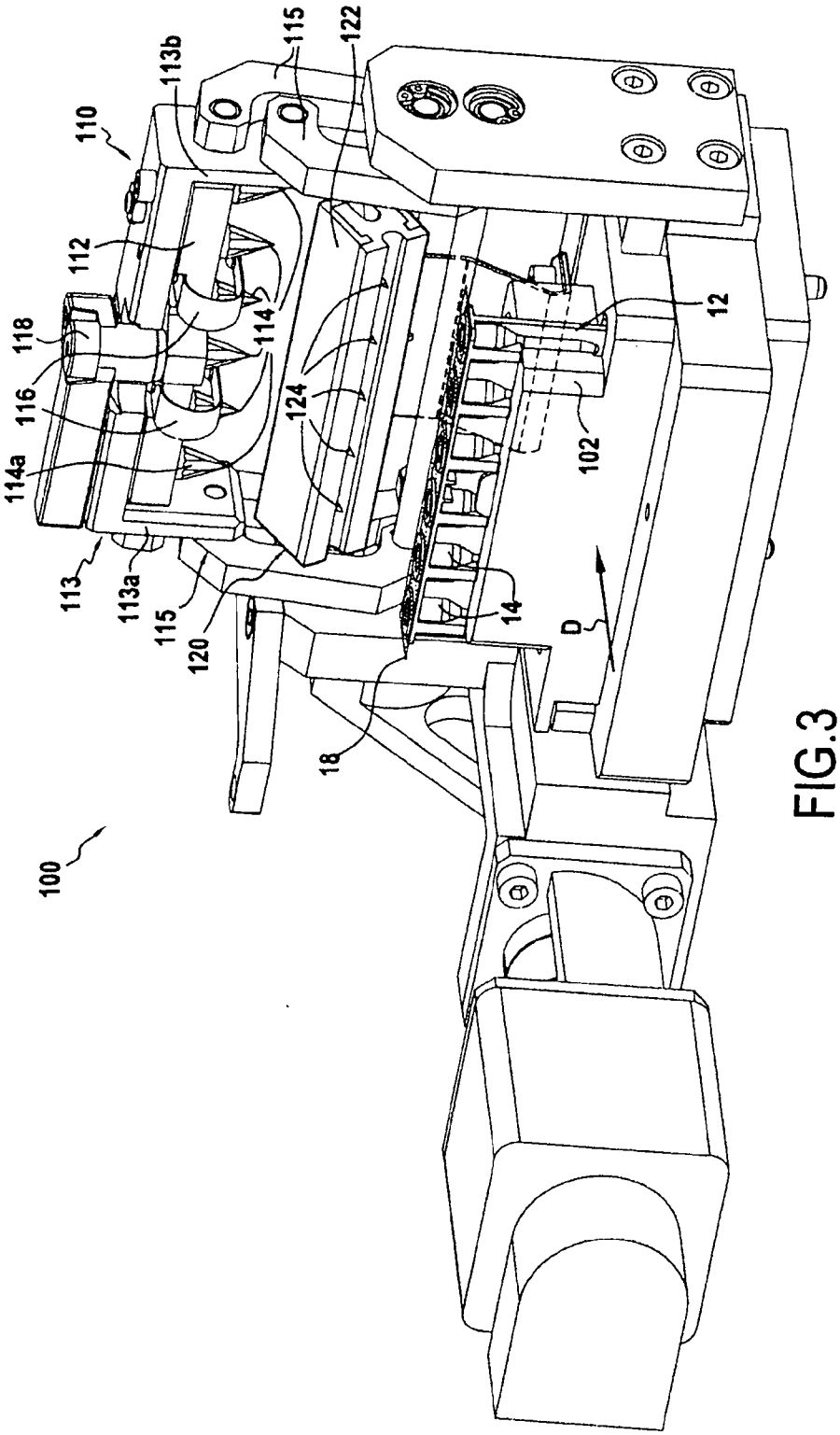
100
110
112
113
113a
113b
114
114a
115
116
118
120
122
124
12
14
18
102
D

FIG.3

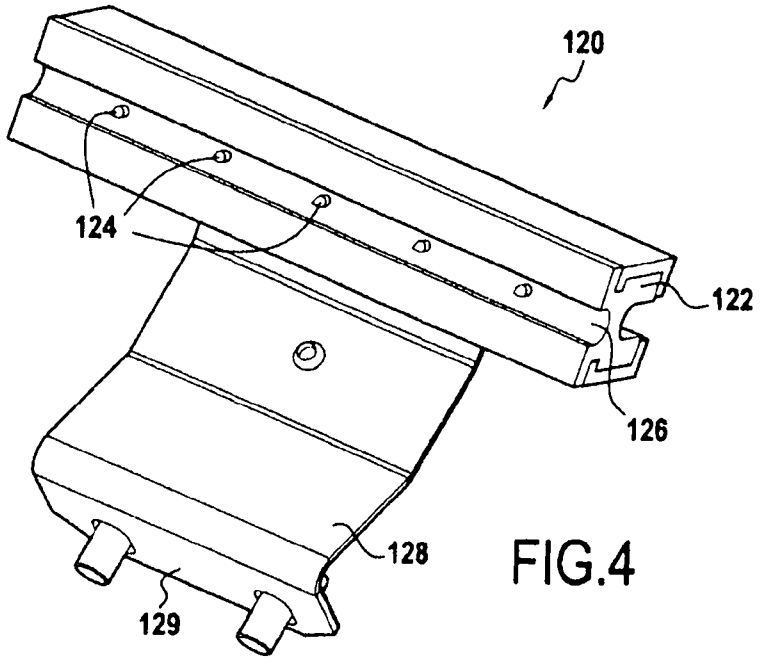
120
124
122
126
128
129

FIG.4

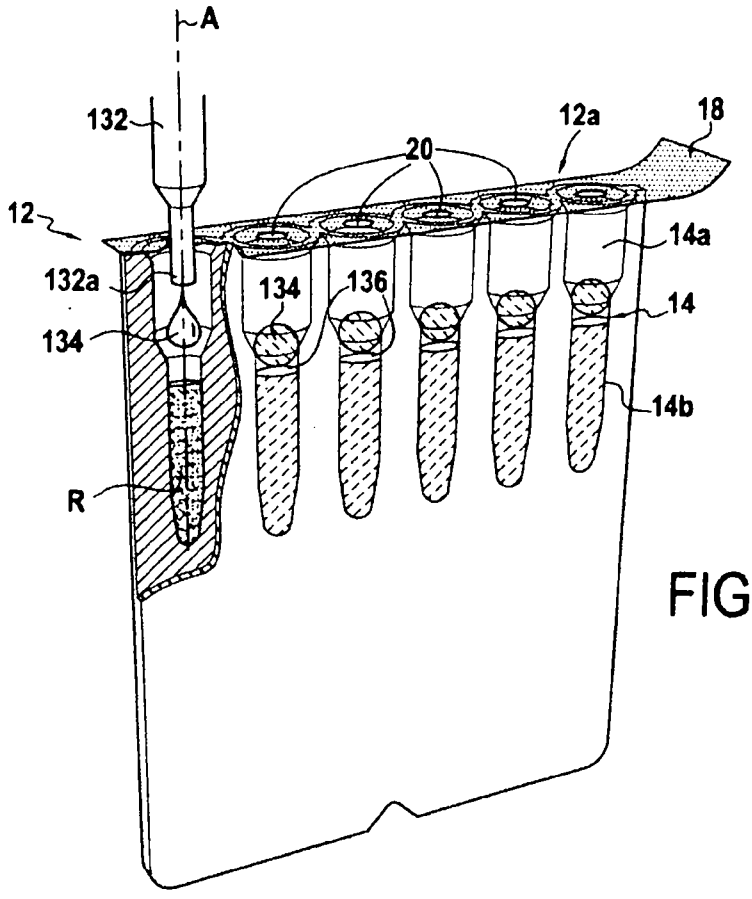
A
132
12a
18
20
12
14a
132a
134
136
14
134
14b
R

FIG.5