# **United States Patent**

## **Bernard**

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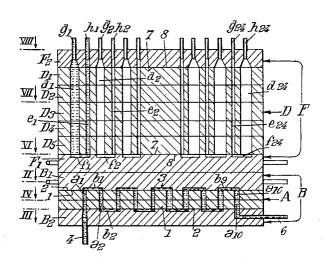
[54]		FOR PORTIONING AND ING LIQUID SAMPLES		
[72]	Inventor:	Claude Bernard, 4, rue Saint Georges, 35, Rennes, France		
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[58]	Field of Sea	rch23/253, 259, 230; 73/423 A,		
	73/425.	4; 222/133; 141/130, 238, 237; 137/625.48, 552.5		
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Primary Examiner—Joseph Scovronek Attorney—Gerard J. Weiser				

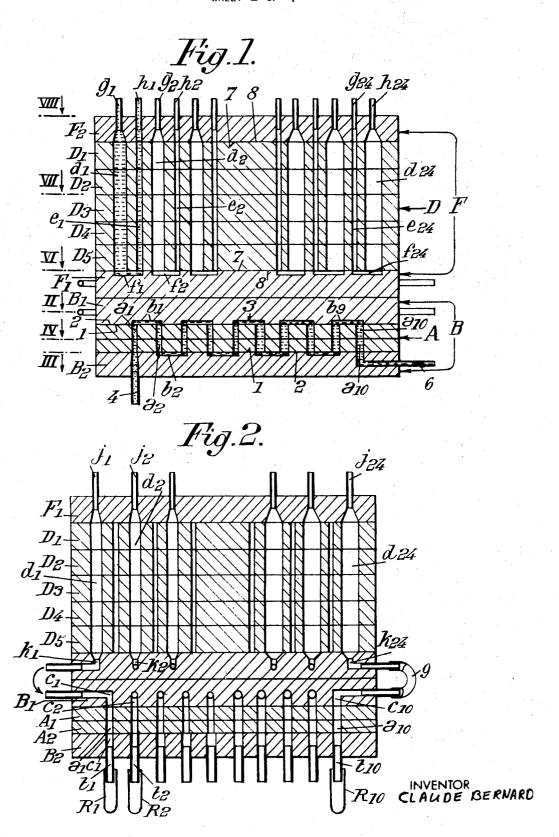
## 7] ABSTRACT

The device is intended to portion a liquid sample into several portions of determined volume. It comprises members that are relatively displaceable from a first relative position to a second relative position. One of these members comprises a series of portion-receiving channels defining the above-mentioned volumes. The other member comprises a first series of channels which put the portion-receiving channels in communication with one another and with the exterior so that they can be filled with the liquid, in the first relative position, and a second series of channels communicating with the portion-receiving channels for collecting the portions retained in these latter channels, in the second relative position.

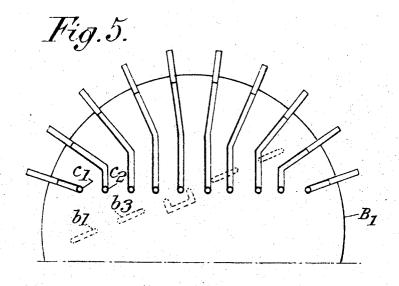
### 14 Claims, 10 Drawing Figures

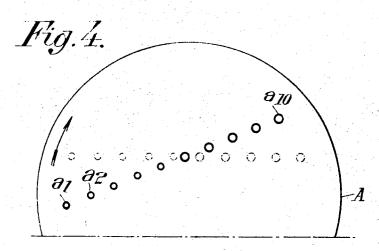


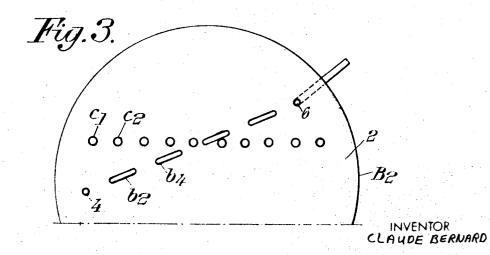
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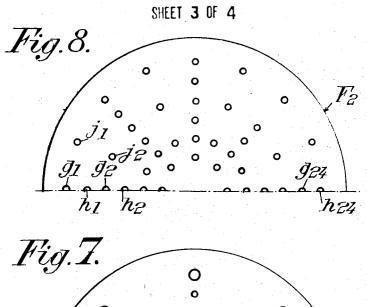


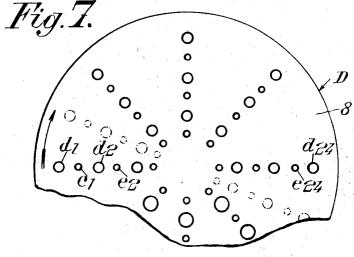
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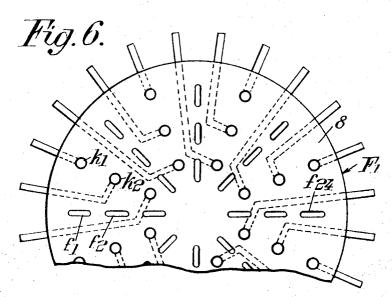






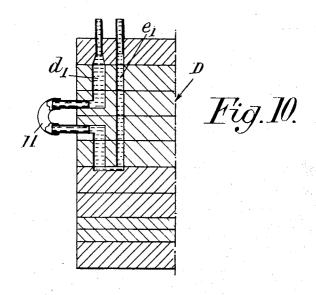


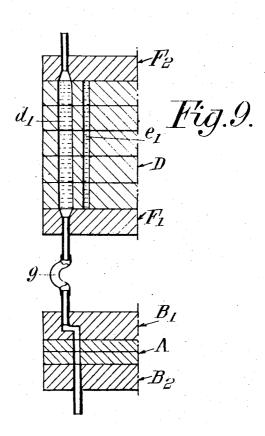




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INVENTOR CLAUDE BERNARD

#### DEVICE FOR PORTIONING AND TITRATING LIQUID SAMPLES

This invention relates to devices for portioning and titrating liquid samples; and it is more particularly, but not exclusively, concerned with such devices which are intended for biological titrations, for example of the content of different constituents in a sample of blood.

An object of this invention is to provide a practical device which is precise and rapid to use, and in which a plurality of titrations on different portions of the same liquid sample can 10 be performed simultaneously, particularly in the case of blood.

In accordance with this invention, the device comprises a first member and at least one second member comprising surfaces of contact adapted to slide on one another so as to per- 15 mit relative movement of one of these members with respect to the other, in particular from a first relative position to a second relative position, the first member (portioning member) comprising a series of channels (portion channels) opening at its surface of contact and each having a determined 20 volume, the second member (transfer member) comprising a first series of channels (transfer channels) in positions such that they put the portion channels in communication with each other and with the exterior, in said first relative position, and a second series of channels (delivery channels) in positions such that they communicate individually with the portion channels, in said second relative position.

According to a particularly advantageous embodiment of block" and a "filling block," in contact with one another and adapted for relative movement, in particular between a first relative position and a second relative position, the reagent block comprising a series of channels of respective determined volumes (reagent channels) and a series of supply channels for these reagent channels, these supply channels being normally isolated from the reagent channels, and the filling block comprising a first series of channels (communication channels) in positions such that they put the supply channels in communication with the reagent channels and the exterior, in said first relative position of the two blocks, and a second series of channels (emptying channels) arranged in this filling block such that they permit the emptying of the reagent channels, in particular through the portion channels of 45 the portioning member mentioned above when those portion channels communicate with the exterior, in the second relative position of the two blocks.

The invention includes certain other features which are preferably used at the same time, but which can, in certain cases, be used separately; these features will be described more explicitely hereafter.

The invention is particularly applicable to devices for performing biological titrations.

In any case, the invention will be well understood from the 55 following complementary description, as well as the accompanying drawings, which complementary description and drawings are, of course, given merely by way of example.

### IN THE DRAWINGS:

FIGS. 1 and 2 show axial sections of a device in accordance with one embodiment of this invention, with the members occupying distinct relative positions;

FIGS. 3 to 8 are partial sections along the respective planes III to VIII of FIG. 1; and

FIGS. 9 and 10 are partial vertical sections of variants of the device according to FIGS. 1 and 2.

Before beginning the description of a preferred embodiment of the invention, it will be recalled that it is usual to perform several analyses, in particular titrations of several con- 70 stituents such as the urea, the glucose, the cholesterol, etc., on the same sample of blood. These analyses thus require the portioning of this sample into successive portions of determined volumes, and the realization of each of these titrations on a different portion.

The taking of these successive portions from the sample of blood to be titrated, as well as the preparation of determined volumes of appropriate reagents which are to be added to each of these portions, are long and fastidious operations. Furthermore, the results can be erroneous, if all these analyses are not made at the same instant after the blood has been taken from the patient.

The device according to the present invention eliminates to a large extent these disadvantages, and permits taking practically simultaneously the different portions or well determined volumes of the sample of blood to be analyzed. This device comprises a first member A and at least one second member B comprising surfaces of contact 1 and 2 adapted to slide on one another so as to permit relative movement of one of these members with respect to the other, in particular from a first relative position to a second relative position, the first member A (portioning member) comprising, for example, a series of channels  $a_1, a_2, \dots a_{10}$  (portion channels) opening at its surface of contact 1 and each having a determined volume, the second member B (transfer member) comprising a first series of channels  $b_1, b_2 \dots b_9$  (transfer channels) in positions such that they put the portion channels in communication with each other and with the exterior, in said first relative position (FIG. 1), and a second series of channels  $c_1, c_2, \dots c_{10}$  (delivery channels) in positions such that they communicate individually with the portion channels, in said second relative position

Thus one can introduce the sample of blood to be analyzed prising supplementary members, in particular a "reagent" supplementary members, in particular a "reagent" and a "filing black" and a "filing black". and the transfer channels, when the portioning member and the transfer member are in their first relative position, for example by means of a pipette and a syringe (not shown) respectively connected to the tubes 4 and 6 opening out of this channel 3 towards the exterior. The modification of the relative positions of the portioning member A and the transfer member B results in the elimination of the communication of the portion channels  $a_1, a_2, \dots$  with one another, and consequently, results in a portioning of the initial liquid sample, each of the portion channels  $a_1, a_2, \dots$  then retaining its own volume of blood.

> The bringing of the portioning member and the transfer member into said second relative position, represented in FIG. 2, then permits the emptying of the portion channels  $a_1, a_2, ...$  $a_{10}$  via the delivery channels  $c_1, c_2, \dots c_{10}$ , for example as represented in FIG. 2, which are then in alignment with with portion channels. The delivery channels can be prolonged by outlet tubes  $t_1, t_2, \dots t_{10}$  opening into recipients  $R_1, R_2, \dots R_{10}$ . The volume of blood received by each of these recipients is 50 exactly determined by the volume of each of the portion chan-

Needless to say this volume can vary from one portion channel to another according to the cross section of each of these portion channels. In variants of the device, which will be described later on, various embodiments of the portioning member or the like will be described in which the volume of each of the portion channels is made variable, and consequently regulable, as a function of the imperatives of each of the titrations performed on the same sample of blood.

In an advantageous embodiment of the invention, the portioning member A is constituted by a circular plate traversed from one side to the other by the portion channels  $a_1, a_2, ...,$ and the transfer member is constituted by two coaxial circular plates B1, B2 in contact with the first plate on its two faces, the transfer channels  $b_1$ ,  $b_2$ , .... being constituted by grooves formed in the surfaces of contact 2 of the two circular plates B<sub>1</sub>, B<sub>2</sub> of the transfer member such that, in a first relative angular position of the portioning plate with respect to the transfer plates, these grooves make the communication between the portion channels two by two, alternately on one side and then on the other side of the portioning plate, so as to form a continuous crenelated channel 3.

Similarly, the delivery channels  $c_1, c_2, ...$  and the tubes  $t_1, t_2$ , ... are advantageously disposed in the plates B1, B2 of the 75 transfer member such that, in the said second relative position, they align themselves with the portion channels  $a_1, a_2, \ldots$ , the delivery channels of the lower plate  $B_2$  opening into the recipients  $R_1, R_2, \ldots$ , as has been described above, and the delivery channels of the upper plate  $B_1$  communicating with sources of air permitting the emptying of the portion channels into the corresponding recipients, or preferably, with the members which also supply the predetermined volumes of reagents appropriate for the titrations to be performed on each of the portions which were previously isolated in the portion channels.

For this purpose, an apparatus is advantageously used which cooperates with the above-mentioned device such that each of the reagents can be introduced practically simultaneously in the recipients  $R_1,\,R_2,\,\ldots$ , after these recipients have received the different portions of blood, the introduction of each of the reagents into the corresponding portion of blood being advantageously effected through the corresponding portion channels and the corresponding delivery channels, when the portioning member and the transfer member are brought into their second relative position.

According to a preferred embodiment of the invention, this apparatus is constituted by a device comprising a member D (reagent block) provided with channels of respective determined volumes adapted to receive the corresponding volumes 25 of diluents or of reagents and also cooperating with another member F (filling block), by the intermediary of surfaces of contact 7 and 8 permitting relative displacement of these blocks one with respect to the other, in particular from a first relative position to a second relative position; the reagent 30 block comprises a series of, for example 24, channels  $d_1, d_2, \dots$  $d_{24}$  of respective determined volumes (reagent channels) and a series of supply channels  $e_1, e_2, \dots e_{24}$  for these reagent channels, these supply channels being normally isolated from the reagent channels; the filling block comprises a first series of 35 channels  $f_1, f_2, \dots f_{24}$  (communication channels) in positions such that they put the supply channels  $e_1, e_2, \ldots$  in communication with the reagent channels  $d_1, d_2, \dots$  and the exterior, in said first relative position of the two blocks, and a second series of channels (emptying channels)  $k_1, k_2, \dots k_{24}$  arranged in 40 this filling block such that they permit the emptying of the reagent channels - in particular through the portion channels and the delivery channels of the portioning member A when these channels communicate with each other — in the second relative position of the two blocks D, F.

In a particularly advantageous embodiment of the invention, represented in FIGS. 1 and 2, the reagent block D and the filling block F are also constituted by circular plates coaxial with the portioning plate A and with the transfer plate B of the portioning device described above. More particularly, the reagent block D is constituted by a circular plate traversed from one face to the other by the supply channels and the reagent channels, which are normally isolated from one another, and the filling block is constituted by two coaxial circular 55 plates, namely a lower plate F<sub>1</sub> and an upper plate F<sub>2</sub>, in contact with the first plate on its two faces 7; the communication channels then comprising, on the one hand, grooves  $f_1, f_2, ...$ formed in the surface of contact of the lower plate F<sub>1</sub> (FIG. 1) with the reagent plate D, such that they put the reagent channels in communication one by one with the supply channels, in a first relative angular position of the blocks D and F and, on the other hand, openings  $g_1, h_1, g_2, h_2, ...$  in the upper plate  $F_2$ positioned to ensure the communication of the filling channels and of the reagent channels with the exterior, in this first angular relative position of the blocks.

In this first relative angular position, it is thus possible to fill each of the reagent channels by the intermediary of the corresponding supply channel, as represented for one of them in FIG. 1. The change of relative position of the reagent block with respect to the filling block results in the isolation of each of the reagent channels with its contents whose volume is thus determined. These volumes can be different from one reagent channel to another according to the values given to their cross sections which can be different.

The filling plates F are, moreover, provided with orifices or emptying channels  $k_1, k_2, \ldots$  which come, in a second relative angular position of the blocks, into alignment with each of the reagent channels  $d_1, d_2, \ldots$ , in particular for permitting the emptying of each of them into one of the recipients  $R_1, R_2, \ldots$ , in order to dilute or transform chemically the constituent to be titrated of the corresponding portion of blood received in the same recipient, from one of the portion channels mentioned above.

In an advantageous embodiment of the invention, the emptying channels  $k_1, k_2, ...$  and the delivery channels  $c_1, c_2, ...$  are interconnected by conduits 9 (FIG. 2) so that the emptying of the reagent channels can be effected by the intermediary of the corresponding portion channels. In this latter case, one of the plates  $B_1$  (the central plate) of the transfer member, which cooperates, on one of its faces, with the portioning plate, also constitutes one of the plates  $F_1$  of the filling block, which cooperates, on its other face, with the reagent plate (FIGS. 1 and 2); the portioning and reagent plates are adapted to be brought simultaneously from their first respective relative angular positions with respect to the central plate (or vice verse) by rotations of equal angular values.

The emptying channels  $k_1, k_2, \ldots$  and the delivery channels  $c_1, c_2, \ldots$  in the central plate can be, for example as shown in FIGS. 5 and 6, deviated towards the lateral surfaces of the central plate  $B_1$  (or  $F_1$ ), the connections being established by exterior flexible conduits 9 at the lateral surface of the central plate.

The connections can also be established as shown in FIG. 9, the central plate then being previously separated into two parts.

In particular in the case in which the titration of one of the portions requires the use of several separate reagents, the delivery channel corresponding to one of the portion channels can be connected in this manner to several emptying channels for collecting the contents of several reagent channels.

The different superimposed plates of the device shown in FIGS. 1 and 2 can be made of plastic material, for example Teflon, these plates being pressed against one another, for example by springs.

Whatever be the variants envisaged above, the simultaneous 45 emptying of each of the portion channels and of the associated reagent channel (or channels) into the corresponding recipient R can be ensured by simultaneously bringing, in particular, the portioning plate A and the reagent plate D into their second relative positions with respect to the other mem-50 bers of the device.

The disposition of the different types of channels in the different members or blocks of the device shown in FIGS. 1 and 2 is also clearly visible in FIGS. 3 to 8 which are transverse cross sections at different levels of the device, whose parts occupy the relative positions shown in FIG. 1.

In this embodiment, there are 10 portion channels  $a_1, a_2, \ldots$   $a_{10}$  disposed in a line (FIG. 4) in the portioning plate A, and 24 reagent channels  $d_1, d_2, \ldots, d_{24}$  respectively associated with their supply channels  $e_1, e_2, \ldots, e_{24}$  disposed in eight radii of a section transverse to the axis of the reagent plate D (FIG. 7).

When the above-mentioned members and blocks occupy their first relative positions, the portion channels  $a_1$ ,  $a_2$ , .... are put in communication two by two, alternately on one face and then on the other face of the portioning plate A, by grooves  $b_1$ ,  $b_2$ , .... (FIGS. 3 to 5). Similarly, the reagent channels  $d_1$ ,  $d_2$ , .... are respectively put in communication with their supply channels  $e_1$ ,  $e_2$ , .... by the intermediary of the grooves  $f_1$ ,  $f_2$ , .... (FIG. 6), these reagent and supply channels being also put in communication with the exterior by the channels  $g_1$ ,  $h_1$ ,  $g_2$ ,  $h_2$  .... formed in the upper plate  $F_2$ . In this position, each of the reagent channels (such as  $d_1$ ) can be filled by the intermediary of its supply channel  $h_1$  by a simple circulation of the corresponding reagent in the continuous conduit that they form with the corresponding communication groove, such as  $f_1$ .

The bringing of the different members and blocks of the apparatus into their second respective positions (FIG. 2) is then effected by the simultaneous rotation of the portioning member A and the reagent block D, by 22.5°, about their common axis. As the other parts of the apparatus remain fixed, it will be observed that only the sections represented in FIGS. 4 and 7 will have moved. The portion channels  $a_1, a_2, \ldots$  will come to occupy the positions represented in broken lines in FIG. 4, in alignment with the delivery channels  $c_1, c_2, \ldots$  (and the associated tubes  $t_1, t_2, \ldots$ ) of the plates of the transfer member, on opposite sides of the portioning member (FIGS. 3 to 5).

Similarly, the reagent channels  $d_1$ ,  $d_2$ , .... will come to occupy the positions shown in broken lines, for a part of them, in FIG. 7, in alignment with the emptying channels  $k_1$ ,  $k_2$ , .... in the lower plate  $F_1$  of the filling member (FIG. 6) and with the openings  $j_1$ ,  $j_2$ , .... communicating with the atmosphere or with sources of air under pressure (FIG. 8).

Thus each of the recipients  $R_1$ ,  $R_2$ , .... receives finally the portion of blood retained previously in the corresponding portion channel and one or several portions of reagent, according as this portioning channel has been previously put in communication with one or several reagent channels by the intermediary of conduits such as 9.

As indicated above, the volume of each of the portion channels and of the reagent channels can be determined by its cross section. According to advantageous variants of the device according to the invention, the volumes of these channels can be regulated to different values by constituting the 30 portioning member and the reagent block by stacks of discs of unit thickness, variable in number, due to which the height of each of these channels can be regulated.

The reagent plate is, for example in the construction represented in FIGS. 1 and 2, constituted by five discs  $D_1$ ,  $D_2$ , 35  $D_3$ ,  $D_4$  and  $D_5$ . Similarly, the portioning plate A is constituted by two superimposed discs  $A_1$  and  $A_2$ . By modifying the number of discs of these plates, one can thus modify the volumes of the portions of blood and of the portions of the reagents to be added to each of these portions of blood in a considerable number of ratios.

This variation of the volume of each of these channels can, according to still another variant of the invention shown in FIG. 10, be obtained by the intermediary of exterior derivation conduits 11 of variable lengths, the volume retained in each of the reagent channels, for example  $d_1$ , being then directly a function of this length.

This results in an infinite choice of dilutions possible for each of the portions of blood isolated in the portion channels.

The cleaning of the apparatus before using it again can be accomplished easily by bringing the different blocks and members into the first relative positions mentioned above (FIG. 1) and by passing cleaning liquids, for example in the opposite direction, in the different channels then put in communication.

This device permits the realization of several practically simultaneous titrations in infinitely variable conditions on the same sample of blood or on any other liquid sample.

This invention is not limited to the particular application nor to the particular embodiments which have been described in detail. Many variants are possible: in particular, it is possible to combine several of these devices together; alternatively, in the case of simplified titrations requiring only a single addition of reagent to each of the isolated portions of blood, the device can comprise the same number of portion channels and reagent channels, formed respectively in the portioning member and in the reagent block, such that they come into alignment when this member and this block are brought into their second relative position.

What I claim is:

1. A device for portioning a liquid sample into several portions of respectively determined volumes, and for permitting their possible dilution or titration, said device comprising a first member and at least one second member comprising sur-

faces of contact adapted to slide on one another so as to permit relative movement of one of these members with respect to the other, between a first relative position and a second relative position, the first member (portioning member) comprising a series of channels (portion channels) opening at its surfaces of contact and each having a determined volume, the second member (transfer member) comprising a first series of channels (transfer channels) in positions such that they put the portion channels in communication with one another and with the exterior in said first relative position, and a second series of channels (delivery channels) in positions such that they communicate individually with the portion channels in said second relative position.

2. A device according to claim 1, further comprising a member (reagent block) having channels adapted to receive determined volumes of different reagents or dilution liquids (reagent channels) and adapted to communicate individually with the portion channels, when the portioning member and the transfer member are in their second relative position.

3. A device according to claim 1, further comprising an apparatus comprising a third member (reagent block) and a fourth member (filling block) having surfaces of contact permitting relative displacement of these blocks one with respect to the other, between a first relative position and a second relative position, said reagent block comprising a series of channels of respective determined volumes (reagent channels) and a series of supply channels, normally isolated from the reagent channels, said filling block comprising a first series of channels (communication channels) in positions such that they put the supply channels in communication with the reagent channels and the exterior for said first relative position of the two blocks, and a second series of channels (emptying channels) in positions such that they permit the emptying of the reagent channels for said second relative position of the two blocks, each of said emptying channels being connected to one of said delivery channels.

4. A device according to claim 1, in which said portioning member is constituted by at least one circular plate traversed from one face to the other face by the portion channels, and the transfer member is constituted by two coaxial circular plates in contact with the first plate on its two faces, the transfer channels being constituted by grooves formed in the surfaces of contact of the two circular plates of the transfer member such that, in the first relative angular position of the portioning plate with respect to the transfer plates, these grooves make the communication between the portion channels two by two, alternately on one face and then on the other face of the portioning plate, so as to form a continuous crenelated channel.

5. A device according to claim 4, in which the two circular plates of the transfer member further comprise delivery channels formed in these plates such that, in the second relative position of these plates with respect to the portioning plate, these delivery channels come into alignment with the portion channels.

6. A device according to claim 3, in which the reagent block is constituted by a circular plate traversed from one face to the other face by the supply channels and the reagent channels which are normally isolated from one another, and the filling block is constituted by two coaxial circular plates, namely a lower plate and an upper plate, in contact with the first plate on its two faces, the communication channels comprising grooves formed in the surface of contact of the lower plate with the reagent plate such that they put the reagent channels in communication one by one with the supply channels and openings disposed in the upper plate such that they permit the communication of the filling channels and of the reagent channels with the exterior, in a first relative angular position of said blocks.

7. A device according to claim 6, in which the two circular plates of the filling block further comprise emptying channels formed in these plates such that, in a second relative angular position of these plates with respect to the reagent plate, the

emptying channels come into alignment with the reagent channels.

- 8. A device for portioning a liquid sample into several portions of respectively determined volumes and for permitting their possible dilution and titration, said device comprising:
  - a portioning member in the form of one circular plate traversed from one face to the other face by portion channels having determined volumes,
  - a transfer member in the form of two coaxial circular plates, namely a lower plate and an upper plate, in slidable contact with the portioning member on the two opposite faces thereof, said transfer member comprising an inlet and an outlet formed in at least one of said plates, in a surface thereof other than said surface of contact, a series of transfer grooves in its surfaces of contact with the por- 15 tioning member in position such that they put said portion channels in communication with each other and said inlet and outlet respectively to form a continuous path for said liquid sample for a first angular relative position of said portioning member and of said transfer member, and a series of delivery channels, including individual outlets, in positions such that they communicate individually with said portion channels in a second angular relative position of said portioning member and of said transfer member,

a reagent block in the form of a circular plate traversed from one face to the other face by a series of reagent channels of determined volumes and a series of supply channels, normally isolated from said reagent channels,

and a filling block in the form of two coaxial circular plates, namely a lower plate and an upper plate, in slidable contact with the reagent block on the two opposite faces thereof, said filling block comprising series of inlets and outlets formed on one of said plates in a surface thereof other than its surface of contact, a series of communication channels in positions such that they put the supply channels in communication individually with the reagent channels and said inlets and outlets for a first angular relative position of said reagent block and of said filling block, and a series of emptying channels in positions such that they permit the emptying of the reagent channels for a second angular relative position of said reagent block and of said filling block,

and conduit means connecting said emptying channels to said delivery channels.

9. A device according to claim 8, in which the upper plate of said transfer member and the lower plate of said filling block form a central plate, the portioning member and the reagent block being adapted to be moved simultaneously to change their relative angular positions with respect to said central 50 plate by rotations of equal angular values, this central plate being provided with conduits interconnecting the emptying channels and the delivery channels.

10. A device according to claim 9, in which the emptying channels and the delivery channels respectively formed in the 55 central plate are deviated towards the lateral surfaces of this

central plate and communicate with one another by removable exterior flexible conduits at these lateral surfaces.

11. A device according to claim 9, in which the upper part and the lower part of said central plate are adapted to be separated from each other for permitting the connections of the emptying channels to the delivery channels.

12. A device according to claim 8, wherein the portioning member and the reagent block are, respectively, constituted by stacks of discs of variable number, as a function of the desired volumes for the portion channels and the reagent channels.

13. A device according to claim 12, in which the reagent channels comprise exterior conduits of variable lengths as a function of the volumes desired for each of these channels.

14. A device for portioning a liquid sample into several portions of respectively determined volumes, and for permitting their dilution or titration, said device comprising

a first member and at least one second member comprising surfaces of contact adapted to slide on one another so as to permit relative movement of one of these members with respect to the other, between a first relative position and a second relative position, the first member (portioning member) comprising a series of channels (portion channels) opening at its surfaces of contact and each having a determined volume, the second member (transfer member) comprising an inlet and an outlet in at least one of its surfaces other than its said surface of contact, a first series of channels (transfer channels) in positions such that they put the portion channels in communication with one another and with said inlet and outlet in said first relative position to form a continuous path for said liquid sample, and a second series of channels (delivery channels), including individual outlets, in position such that they communicate individually with the portion channels in said second relative position;

a third member (reagent block) and a fourth member (filling block) having surfaces of contact permitting relative displacement of these blocks one with respect to the other, between said first relative position and second relative position, said reagent block comprising a series of channels of respective determined volumes (reagent channels) and a series of supply channels, normally isolated from the reagent channels, said filling block comprising series of inlets and outlets in at least one of its surfaces other than its corresponding surface of contact, a first series of channels (communication channels) in positions such that the supply channels are put in communication individually with the reagent channels and the said inlets and outlets for said first relative position of the two blocks, and a second series of channels (emptying channels) in positions such that they permit the emptying of the reagent channels, for said second relative position of the two blocks,

and conduit means connecting said emptying channels to said delivery channels.

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