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DEVICE FOR SUPPLYING SEGMENTIZED SAMPLES OF A FLUIDAL MEDIUM TO AN ANALYSIS APPARATUS

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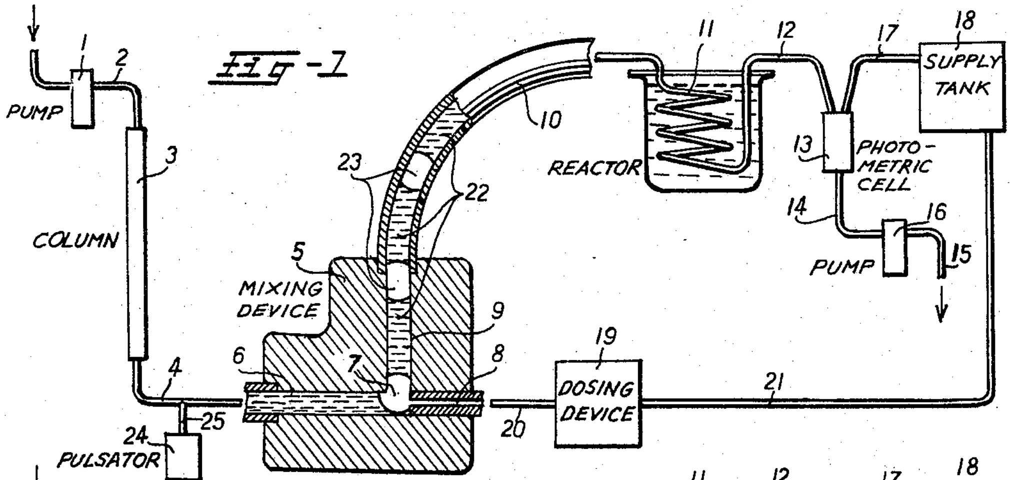

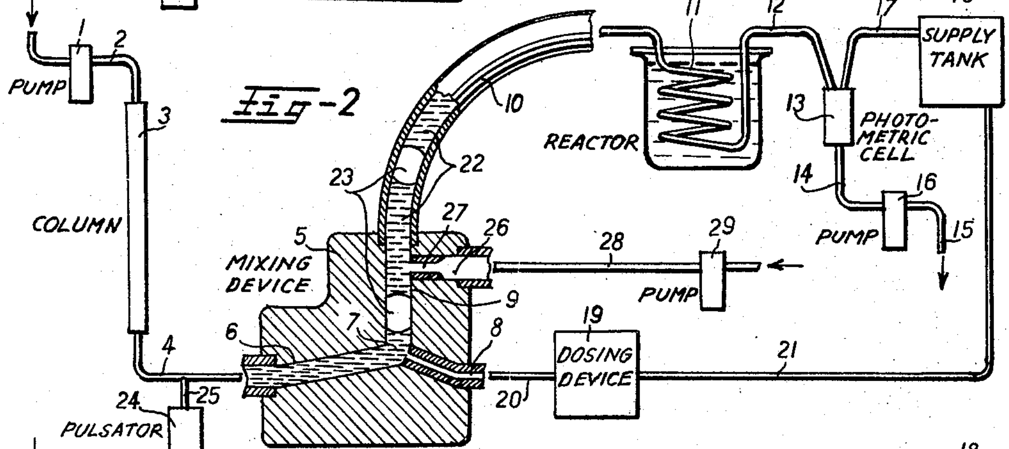

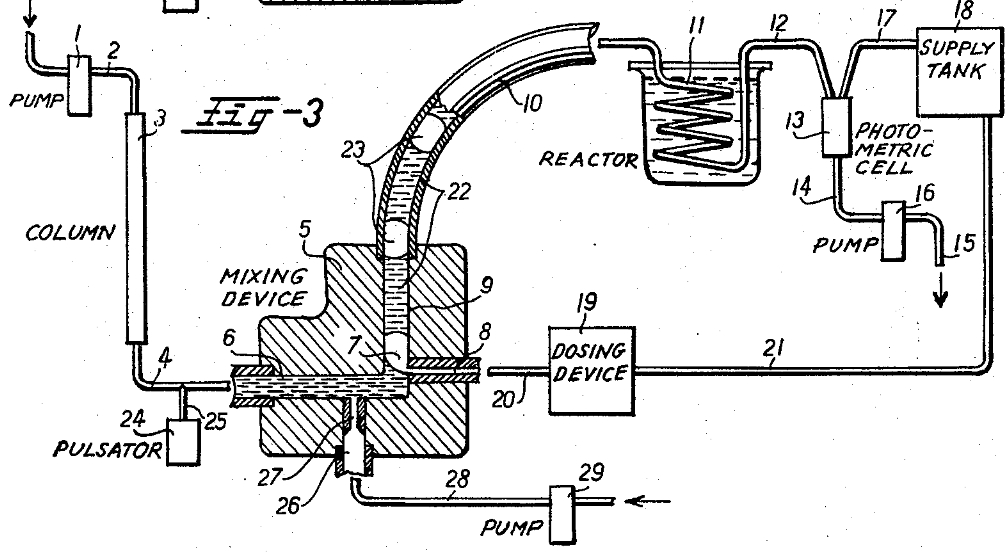

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DEVICE FOR SUPPLYING SEGMENTIZED SAMPLES OF A FLUIDAL MEDIUM TO AN ANALYSIS APPARATUS

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Claims priority, application Czechoslovakia, Mar. 26, 1965, 2,024/65
Int. Cl. E03b *1/00*; F17d *1/00*
U.S. Cl. 137—1 5 Claims

ABSTRACT OF THE DISCLOSURE

Predetermined equal or programmed quantities of at least one segmentizing fluidal medium are forceably fed in equal or programmed periods into the stream of a basic fluidal medium which uninterruptedly flows for example from a chromatographic column with uniform velocity or with programmatically changing velocity possibly effected by a periodically pulsating pump, the periods of said forceable feeding alternating with the periods when the stream of the segmentizing medium is at rest.

This application is a continuation of Ser. No. 534,210 filed Mar. 14, 1966, now abandoned.

The invention relates to a method of, and a device for, dividing flowing media into individual sections separated from each other by sections of another medium not intermixing with the medium of an adjacent section.

For many problems in laboratory techniques and also in industrial microtechniques it is of importance to transport a medium through a tubing having more or less capillary dimensions, in such a manner that its individual parts differing from other parts by its composition or by its concentration should not intermix while flowing through the tubing. It is known that to this end a continuous flow of a medium is divided into individual sections by introducing into the stream of the medium another medium not mixing with the first one, in order to create separate cushions or segments which separate the various sections of the said first medium from each other, and also cause as little as possible of the first medium to stick to the walls of the tubing.

Existing methods achieve division of a medium into individual sections by leading both media through separate tubinbs to the place where the two media combine, in such a manner that while drawing the two media in a more or less continuous manner, their sections or segments alternate. Another gaseous medium creates by virtue of the action of capillary forces the conditions under which individual bubbles of this other gaseous medium enter the tubing for joint guiding of both media, in such a manner that there are created gaseous cushions moving between individual sections of the first medium separated from each other by these bubbles, through another tubing where the two media are guided together in the shape of sections separated from each other.

Although the two media enter the common tubing through cross-sections which are narrowed closely in front of the mixing place, there arise substantial irregularities in the size of the individual sections of the first and of second medium. This is due to the fact that while the two media are separated into sections, conditions are affected by many factors which are difficult to control, such as: instantaneous hydrodynamic conditions at the inlet into the mixing place; the very variable detailed distribution of the capillary forces on the boundary between two liquids and on the boundary of the individual liquids and the surrounding walls. Even such an imperfect separation into individual sections might certainly mean many advantages in comparison with the case where the stream of the first medium would not be divided at all. But this division in accordance with known methods is not satisfactorily regular due to the above mentioned reasons. Such methods can therefore not be used in highly exacting modern analytical processes such as the modern highly effective methods for analysing mixtures of the amino acids and similar materials. In such cases it is essential to divide the flow of the first medium in a highly accurate manner to ensure sections of the two media which are either accurately identical, or in accordance with a general program with respect to the size of the first and of the second medium. The first medium becomes usually additionally mixed with another material entering into reaction therewith. A very important condition is to achieve in each section perfect mixing of a very accurate amount of the first medium with a very accurate dose of another material. The time of passage through the entire further equipment must also be maintained very accurately. For example in the case where the second medium is a gaseous one, the individual doses forming its sections must also be very accurate to ensure that in the case of subsequent expansion, for example under higher temperature, the entire process takes place under accurately constant, or accurately programmed operational conditions. Even small disturbances with respect to any of the above mentioned conditions leads to irregularities in the analytic result.

It is a general object of the invention to eliminate the drawback of the known state of art.

The invention is based on the fact that the unsatisfactory results of existing methods are due in the first place to the fact that sufficient attention has not been payed to achieve regular dosing, regular movement and regular alternation of the individual sections of the two media, and that an accurately controlled supply of the media permits dosing into a tubing with a wide range of inner diameter, for example from 0.2 mm. to 2 mm., and that the use of tubings with diameters as large as possible within admissible limits has various advantages.

The invention also teaches that sometimes it may be convenient to alternate sections of more than two media and even also to admit regularly into some sections of the medium another material in accordance with a certain law.

Finally, the invention makes also, use of the fact that a regular and uniform division may also be enhanced by pulsations of at least one of the flowing media.

The main feature of the invention resides in the fact that one of the media is divided into sections of programmed size and that into the stream of this medium moving at a programmed speed is pressed or forced at regular intervals a dose determining a section of the programmed size of at least one further medium, and that a dose of another medium may be forced into an already created section of another medium.

In most cases the method in accordance with the invention is carried out in that at regular intervals there are forced into the stream of the medium moving at a regular rate equal doses of another medium or of other media. In dependence on the specific weight of the media, other media are forced into the first medium flowing either in the upward or downward direction. In accordance with the invention, another medium is pumped with advantage from a space in which there is an overpressure which is approximately equal to the overpressure in the tubing into which the medium is being forced. The regular course of the process may sometimes be enhanced in that the movement of at least one medium is affected by pulsations, particularly at the place where another medium is let in.

For the correct course of the process it is of course necessary that the media whose sections are in contact are inert with respect to each other.

The device for carrying out the method in accordance with the invention consist, like other known devices used for carrying out the known methods mentioned in the introduction, of a body in which there is provided a duct for the fundamental medium, and into the first duct opens a second duct for an additional medium.

In accordance with the invention more than one duct for additional media may open into this first duct, or a duct for another additional medium may open into the duct for the first additional medium.

The main features of the device in accordance with the invention resides in the fact that the duct for the additional medium is connected to an accurately dosing pump. A duct extending preferably vertically in which the alternating sections of the medium are created possesses preferably a larger inner diameter than the duct opening into it through which passes a continuous uninterrupted stream of the medium.

The invention will be best understood from the following specification to be read in conjunction with the accompanying drawing illustrating three preferred examples of carrying out the invention. The diagram includes circuits and partial units which are of importance for some applications of the invention.

Referring now more particularly to FIG. 1, pump **1** is connected by tube **2** with column **3**, and further by tube **4** with the body of a mixer **5**. In this body **5**, the supply tube **4** for the first medium is continued by a duct **6** which meets, at the place marked **7**, with a duct **8** for supplying another medium. At the mixing place **7** there begins a duct **9** for leading separate sections of the first and of the second medium. The duct **9** opens into a tube **10** which leads away the media in the shape of a stream divided into individual sections of alternating media. Tube **10** opens into further equipment, for example capillary reactor **11** to which is joined by means of tube **12** for example a photometric measuring cell **13**. This cell **13** is connected by means of tube **14** with the drain or outlet **15** either directly or through a suction pump **16**, or in a similar manner with an outlet dosing device.

All mentioned spaces including the mixing place **7** may be maintained constantly under overpressure, for example by connecting the photometric cell **13** by means of the tube **17** with the container **18** in which there is maintained a constant overpressure.

Besides the body **5** for mixing, the most important element of the device for carrying out the method in accordance with the invention is a dosing device **19** which is connected by tube **21** with the container **18** intended for maintaining overpressure in the entire system.

The device illustrated in FIG. 1 intended for chromatography works in the following manner: The pump **1** of eluents drives these eluents through the chromatographic column **3** into duct **6** practically at a uniform rate since any possible pulsations of the pump **1** are absorbed by the resilience of the preceding elements connected in the circuit, such as particularly the column **3**.

As long as the dosing device **19**, for example an accurate pump for dosing individual doses of the second medium, do not force this second medium into the mixing place **7**, the first medium which in the case considered is an eluate discharged from the column **3**, flows at a uniform rate into duct **9** and tube **10**. However, as soon as the dosing device **19** discharges quickly a predetermined dose, for example of argon, into the mixing place **7** through the duct **8**, a bubble is quickly growing in the mixing place **7** in such a manner that it interrupts the communication between the ducts **6** and **9** and that it separates the medium in duct **6** from the same medium in duct **9**. The thus produced bubble is torn away by the stream of the first medium from the mouth of duct **8** and it is carried by duct **9** together with the stream of the first medium.

This process is repeated each time a new dose of the second medium is forced by the dosing device **19** into the mixing place **7**. Therefore, in duct **9** and in the tube **10** following thereafter, as well as in other parts of the device. there move sections **22** of the first medium separated from each other. These sections are accurately of the same size, or accurately programmed. Accurately of the same size, or of the same accurately programmed size are also sections **23** of the second medium which has been forced in the individual cycles into the mixing place **7** by the dosing device **19**.

In many applications, the device acording to FIG. 1 may be operated without overpressure, that is under circumstances where the pressure in the individual ducts **4, 8, 9** and tubes **10** until outlet **15** do not differ much from the ambient atmospheric pressure. In some cases advantages may be obtained if the entire system of spaces connected with each other is maintained under overpressure with respect to the ambient atmosphere; the value of the atmosphere may be, in accordance with circumstances, only 0.1 atm. or even several atm. In each case, the dosing device **19** must be able to force the respective doses into into the mixing place **7**. If the device is under overpressure, the dosing device **19** can perform its function if it acts as a compressor compressing the necessary doses of gases to the necessary pressure, and then force these dose into duct **20** and **8** into the place **7**. This imposes increased requirements on the dosing device **19**, particularly in the case of larger overpressure and a required high dosing accuracy. Conditions are made easier if the dosing device **19** will not draw in gas without overpressure, but conveniently with the same or a simlar overpressure like in the mixing place **7**. This can be easily achieved in that the dosing device **19** will draw in the second medium from the pressure container **18** through the connecting tube **21**. The dosing device **19** may be for example an accurate piston or a finger-operated peristaltic micropump.

Accurate dosing can also be obtained from a dosing device designed as a small space which is opened by an inlet and outlet valve into communication with the container of the second medium which in this case must have a substantially higher pressure than the pressure in the mixing place **7**; the outlet valve is closed; then the inlet valve is closed and the outlet valve is opened, and from the dosing space is discharged into duct **8** and the mixing place **7** a dose of the second medium which corresponds to the conditions under which it accummlates in the closed dosing space due to pressure changes caused by the connection to the container of the medium and to the duct **8**.

The entire system in accordance with FIG. 1 has its specific features from the dynamic point of view, these features being related with the resilience of the individual partiol elements, and with the masses which are being moved, that is particularly with the masses of the liquid medium, and so on. Not even the tube **4** which is filled, for example, with a liquid, does not possess zero resilience. A high resilience has tube **10**, and particularly the stream of the two media in the shape of alternating sections **22** and **23** of both media, particularly if one of the media is a gas. On quickly forcing the dose of the second medium into the mixing place **7**, there occurs usually an accelerated movement in the direction into tube **10** particularly because of the resilience of the sections **23** of the gaseous medium in this tube.

If the speed at which the dose of the second medium is forced into the mixing place **7** were too high, vibration of the resilient column in tube **11** might occur with results sometimes desirable, but mostly undesirable. The optimal value of the speed and of the course of forcing in the second medium are chosen from this point of view, and from the point of view of the resilience of the part of the system which lies in front of the mixing place **7**. At any rate, however, it will be advantageous to us a forcing-in speed which is rather high compared with the speed of the normal flow of the first medium.

If the rate of flow of the first medium is so high that it may impede the correct formation of accurately programmed sections of the second medium, conditions can be improved by causing pulsation in the duct **6** for supplying the first medium in such a manner that the rate of flow into the mixing place **7** is reduced even as much as to zero, or into negative values, at the moment when the second medium is forced in from the dosing device **19**. Such superposition of pulsation can be produced in the stream of the first medium in duct **6** for example by a parallel connection of an actively acting pulsator **24** with tube **25** on tube **4** or duct **6**. Such a pulsator may be formed by a piston without any distribution, the space above the piston being constantly connected with the tube **4** or the duct **6**. To achieve such an effect, it is sufficient if, at the time when the second medium enters, the piston of the pulsator **24** sucks away a proper amount of the first medium forcing it back into the tube only after the second medium has been forced from the dosing device **19**.

The emobidment according to FIG. 2 differs from that in FIG. 1 by the fact that into the duct **9** in the body **5** opens a duct **29** by a narrowing **27** for supplying a further liquid medium arriving through the tube **28** from the pump **29**. FIG. 2 shows the moment when just one section **23** of the liquid medium lies in the region of the mouth of the duct **26**, and can at this moment accept a dose of an additional liquid medium injected through duct **26** by the pump **29** working in synchronism with the pump **19**.

The embodiment according to FIG. 2 differs from that of FIG. 2, where a further additional medium is not injected into sections **22** of the first liquid medium which are divided by sections **23** of a gaseous medium, but it is injected into a continuous stream of the first liquid medium before it becomes divided into sections.

It should be understood by those expert in the art that the embodiments according to FIGS. 2 and 3 representing only preferred examples may be combined in any desired manner.

What is claimed is:

1. A method for dividing a liquid stream into segments for analysis comprising conducting a continuous liquid stream into a segmentizing zone through capillary tubing, introducing an immiscible fluid into said stream at said zone in predetermined doses at uniform intervals, whereby sample segments are spaced apart by separating fluid, periodically reducing the fluid pressure in said segmentizing zone while maintaining the source of said segmenting fluid at a substantially uniform pressure greater than said reduced pressure, whereby said segmenting fluid flows into said segmentizing zone when said fluid pressure is reduced.

2. The method according to claim **1** including introducing an additional fluid into said stream in synchronized relation to said immiscible fluid introducing step.

3. Apparatus for dividing a continuous stream of liquid into a plurality of liquid segments for analysis comprising body means containing a segmentizing zone, capillary means for conducting liquid into said zone and out of said zone, means for introducing a fluid into said zone independently of said capillary means, means for supplying a predetermined quantity of fluid into said introducing means, and means for periodically reducing fluid pressure in said zone whereby fluid flows periodically from said introducing means in a predetermined dose, thereby dividing said continuous liquid stream into substantially equal liquid segments.

4. The apparatus according to claim **3** said periodic pressure reducing means includes a displacement pump upstream from said zone for temporarily withdrawing a portion of said continuous stream.

5. The apparatus according to claim **3** wherein said dosing means includes means for conducting a predetermined dose into said fluid injecting means between said periodic pressure reductions of said fluid stream.

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