

Nov. 30, 1965

M. J. E. GOLAY

3,220,164

RECIRCULATION CHROMATOGRAPHY

Filed July 18, 1962

4 Sheets-Sheet 1

Fig. 1.

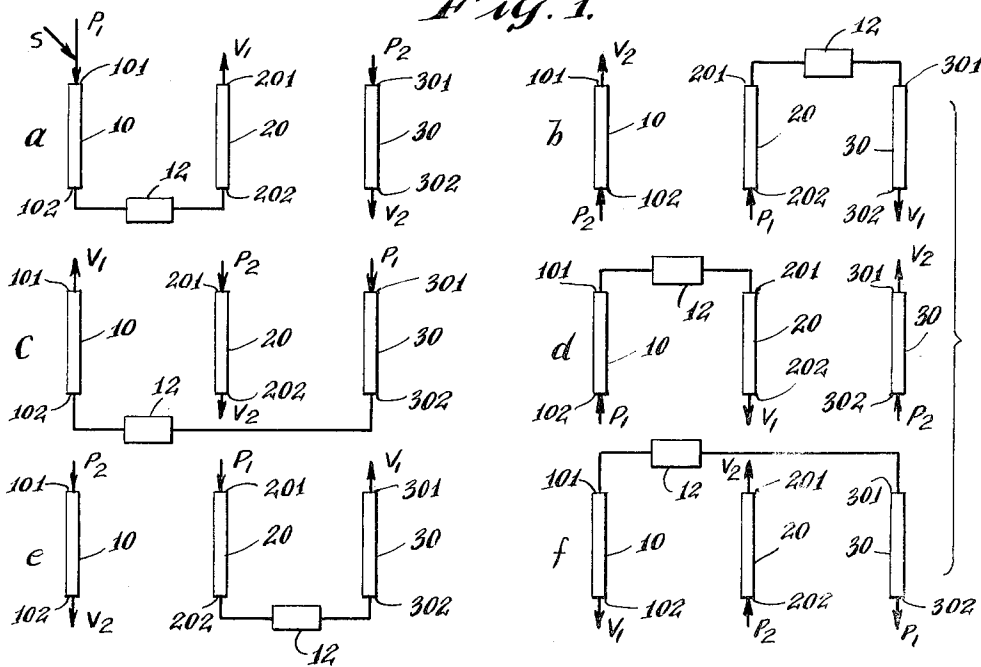
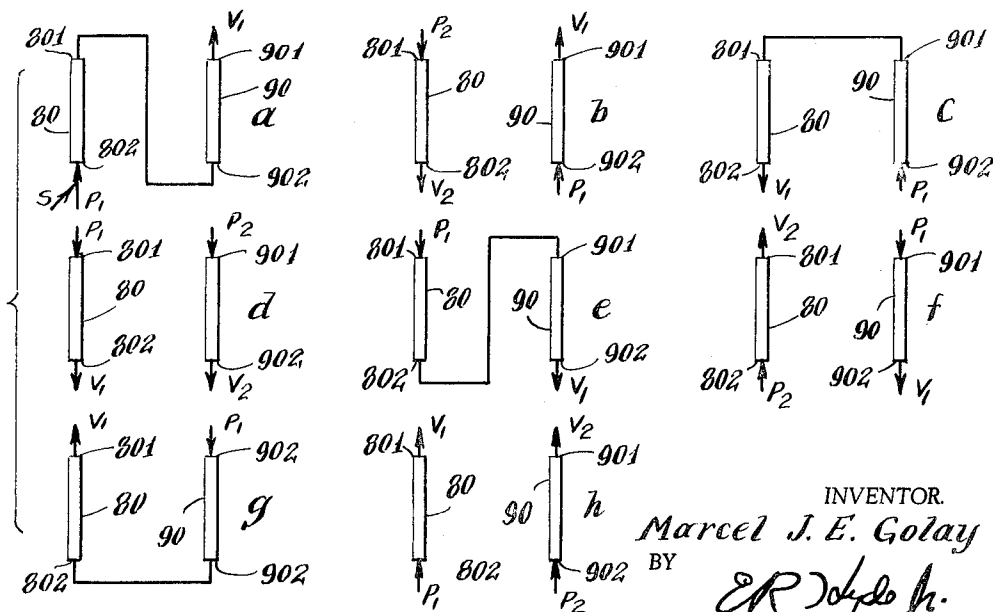


Fig. 5.



INVENTOR.
Marcel J. E. Golay
 BY *ER Joly Jr.*
 ATTORNEY.

Nov. 30, 1965

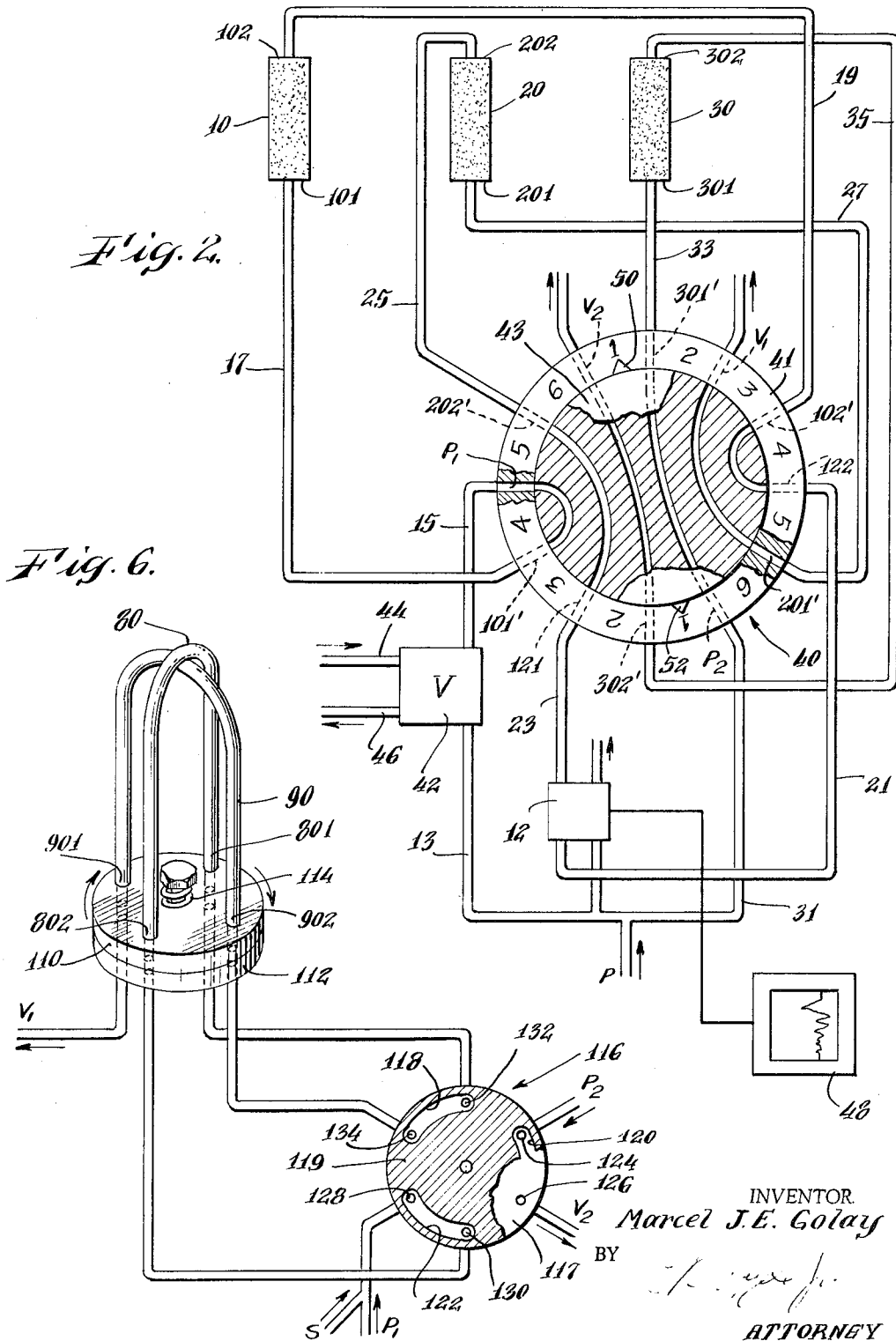
M. J. E. GOLAY

3,220,164

RECIRCULATION CHROMATOGRAPHY

Filed July 18, 1962

4 Sheets-Sheet 2



INVENTOR.
Marcel J.E. Golay

ATTORNEY

Nov. 30, 1965

M. J. E. GOLAY

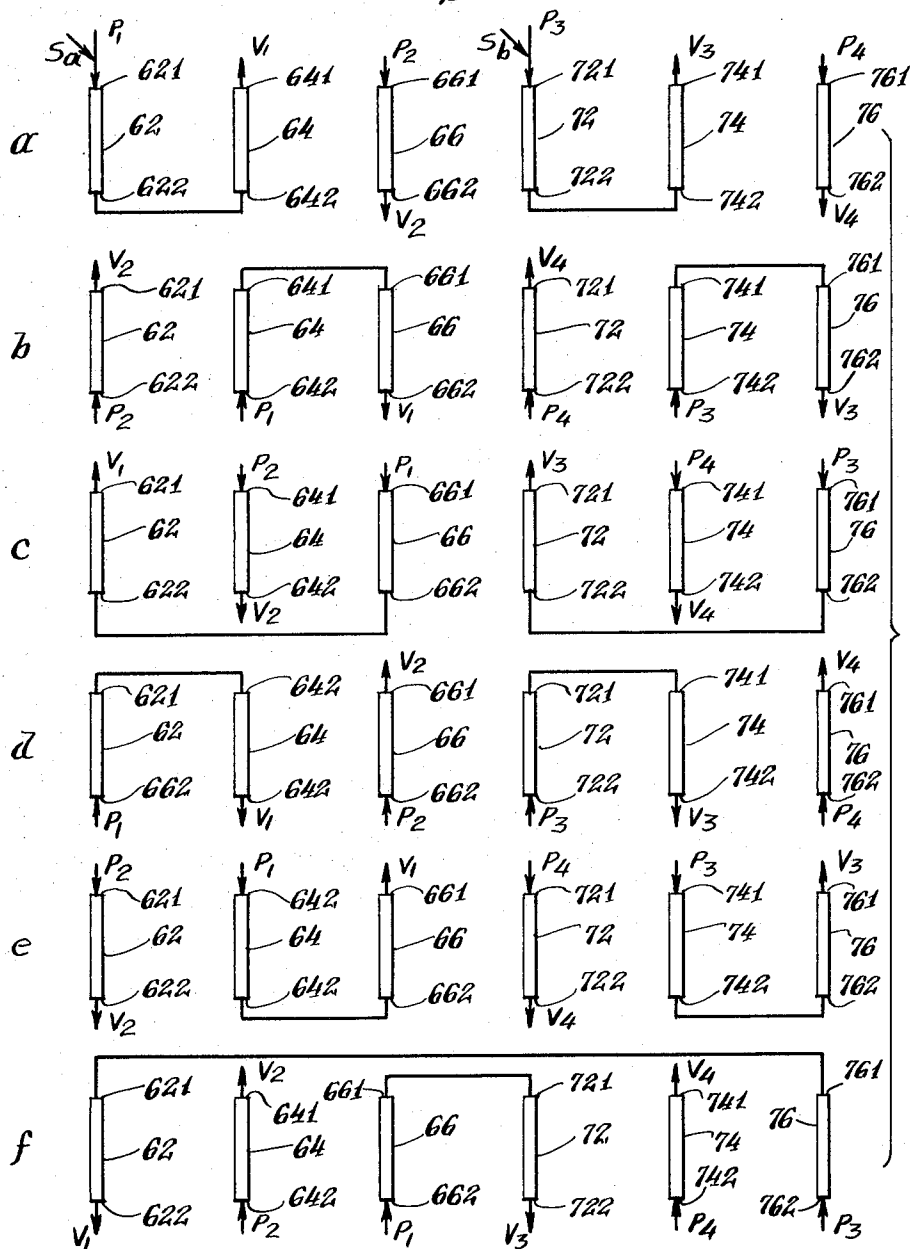
3,220,164

RECIRCULATION CHROMATOGRAPHY

Filed July 18, 1962

4 Sheets-Sheet 3

Fig. 3.



INVENTOR
Marcel J. E. Golay
 BY *ER Hyde Jr.*
 ATTORNEY.

Nov. 30, 1965

M. J. E. GOLAY

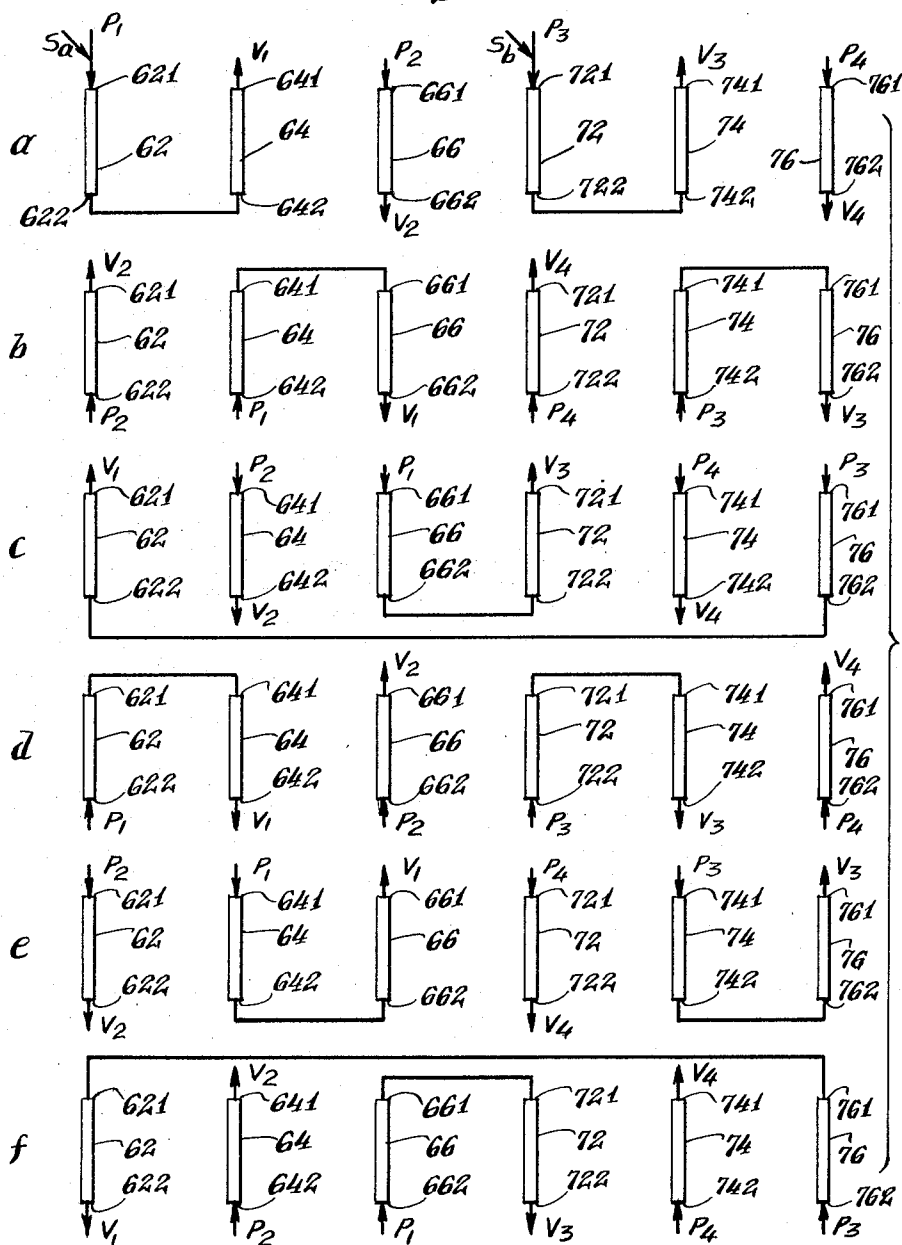
3,220,164

RECIRCULATION CHROMATOGRAPHY

Filed July 18, 1962

4 Sheets-Sheet 4

Fig. 4.



INVENTOR

Marcel J. E. Golay

BY

ER Hyde Jr.

ATTORNEY.

1

3,220,164

RECIRCULATION CHROMATOGRAPHY

Marcel J. E. Golay, Rumson, N.J., assignor to The Perkin-Elmer Corporation, Norwalk, Conn., a corporation of New York

Filed July 18, 1962, Ser. No. 210,642
13 Claims. (Cl. 55—67)

This invention relates to chromatography and, more particularly, to method and apparatus for recirculating a mixture of components through a plurality of separating columns.

Chromatography is a well known method for separating a mixture of components into its various constituents. Various chromatographic techniques are available to those skilled in the art, such as gas-liquid, gas-solid, liquid-liquid, and liquid-solid chromatography. As an example of the gas-liquid technique, a column of suitable length is packed with an inert material such as crushed fire brick or kieselguhr. This material is coated with a suitable non-volatile liquid. A carrier gas such as helium or hydrogen is passed through the column. This particular apparatus, therefore, comprises a stationary liquid phase and a mobile gas phase. The liquid phase is chosen with a view to the desired separation of a gas or vapor sample to be analyzed. The multicomponent sample is injected into the moving carrier stream which thereupon forces it through the column. As the sample passes through the column, its components are selectively retarded because of their various affinities for the liquid phase. The eluant from the column is carrier gas containing "bands" of the various components physically displaced from one another.

The above description is a somewhat idealized conception. In practice, it may be quite difficult to completely separate the various materials from one another. For example, in the analysis of a complex hydrocarbon mixture, the "lighter" components will elute far in advance of the "heaviest" components. Between light and heavy ends there may be a number of similar components which can be separated from one another only with great difficulty or by passage through an exceptionally long column. The terms "light" and "heavy," as used in this context, do not necessarily refer to weight, but are indicative of retention times within the column. The "light" ends are those which elute first, while the "heavy" ends are those components most strongly retained.

It is, therefore, the primary object of this invention to provide method and apparatus for separating, in columns of relatively short length, those components which would normally require excessively long passage through a partitioning agent.

It is another object of this invention to provide such a method and apparatus wherein the components of interest may be continuously recirculated.

It is another object of this invention to provide method and apparatus wherein the light ends of a sample may be continuously vented.

It is another object of this invention to provide such a method and apparatus wherein the heavy ends of such a sample may be continuously backflushed and eventually vented.

It is another object of this invention to provide such a method and apparatus wherein a relatively short length of partitioning material may have the separation capabilities of a much greater length of material.

Other objects, features, and advantages of this invention will be apparent from the following description, the appended claims, and the figures of the attached drawings wherein:

FIG. 1 is a schematic diagram illustrating one arrangement of columns in accordance with this invention;

2

FIG. 2 is a schematic diagram of a valving arrangement capable of performing the functions illustrated in FIG. 1;

FIG. 3 illustrates another embodiment of the invention;

FIG. 4 illustrates a still further embodiment of the invention;

FIG. 5 illustrates still another embodiment of this invention; and

FIG. 6 illustrates a valving arrangement for achieving the arrangements illustrated in FIG. 5.

In accordance with this invention, a chromatographic separation is carried out by a method which comprises passing a mixture of fluid components sequentially and repeatedly through a plurality of chromatographic separating columns. Simultaneously with such passage, components ahead of a preselected portion of the mixture are removed and components behind the preselected portion are backflushed. The preselected portion is periodically passed into a previously backflushed column.

The manner in which the novel advantages of the invention are achieved will be apparent from FIG. 1. FIG. 1 discloses a novel sequence of chromatographic column connections proceeding from (a) through (f). The operative sequence for purposes of illustration begins with FIG. 1(a); three columns, 10, 20, 30 are connected by suitable valving arrangements as shown. End 101 of column 10 is connected to a first source of carrier gas P_1 . A sample may be injected through S. End 102 of column 10 is directly connected to end 202 of column 20 to allow flow of components directly from column 10 into column 20. Between ends 102 and 202 a detector 12 is positioned to detect the eluant from column 10. End 201 of column 20 is vented to vent V_1 . It will thus be seen that in the embodiment of FIG. 1(a) columns 10 and 20 are connected in series so that the carrier gas and the entrapped sample will pass through them in series. For purposes of illustration, it will be assumed that the three columns are identical. However, this need not necessarily be the case and is not to be construed as a limiting condition.

During the time that columns 10 and 20 are so connected for the passage of sample, column 30 is being flushed by a stream of carrier gas entering end 301 from source P_2 and passing to a vent V_2 .

For purposes of this illustration, it is assumed that a mixture is being separated wherein the components of particular interest fall somewhere in the mid-range between the light and heavy components present in the sample.

At a time when the components of interest have passed into column 20, the lighter ends of the sample will have been partially removed by venting through V_1 . At this point in time, the columns are switched to the configuration shown in FIG. 1(b). End 202 of column 20 is now connected to carrier source P_1 . End 201 of column 20 is now connected to end 301 of column 30 through detector 12. End 302 of column 30 is vented through vent V_1 . During the period columns 20 and 30 are in this series relationship, end 102 of column 10 is connected to carrier source P_2 and end 101 is discharged through vent V_2 .

As explained relative to FIG. 1(a), the light ends of the sample were previously partially vented through V_1 . The heavier ends which lagged the components of interest were partially retained in column 10. It will now (FIG. 1(b)) be noted that column 10 is being backflushed by pure carrier gas whereby the heavy-end components retained therein are partially or wholly removed and the column prepared for later use. It will be understood that the carrier gas pressure at P_2 may be higher (or lower) than the pressure at P_1 . Also, although referred to as

3

"carrier" gas, the gas used for this purpose may be completely different if required for the backflushing operation.

By further reference to FIG. 1(b), it will be noted that the series arrangement of columns 20 and 30 once more permits the venting of the lighter ends to V₁. As the components of interest pass into column 30 the columns may be rearranged to the configuration shown in FIG. 1(c). In FIG. 1(c) it will be noted that pure carrier gas from P₁ enters the system at column end 301, forcing the sample out end 302 and into end 102 of column 10. From end 101, the sample passes to vent V₁. It is important to note at this point that column 10 is a column that has been backflushed in previous step b and is thereby prepared to take new sample. Column 20 has now been removed from the sample flow system and is being backflushed by carrier gas passing from P₂ to V₂.

By following the sequence from FIG. 1(a) through FIG. 1(f) it will be noted that this general sequence of valving continues. As the components of interest progress from column to column, the lighter ends are continuously being vented and the heavy ends are continually being backflushed.

From the arrangement shown in FIG. 1(f) the valving proceeds to the arrangement shown in FIG. 1(a). This recirculation may proceed for as long a period as necessary to resolve the components of interest.

It is to be noted that the backflushing referred to herein need not be total. It is only necessary that backflushing be continued until the heavier ends remaining in the column will stay ahead of the desired components and, therefore, vent before the next switching operation.

It will be noted that the net result of this arrangement is the provision of a column of greatly increased length, insofar as the components of interest are concerned. This is accomplished by use of a limited amount of partition material and a switching scheme which prevents the overlapping of the light and heavy ends as might normally be expected in a recirculation technique.

In FIG. 2 there is illustrated a suitable mechanical arrangement for performing the sequence of operations illustrated in FIG. 1. In FIG. 2, columns 10, 20, and 30 of FIG. 1 are connected through a twelve port rotary valve 40 having a body portion 41 and a rotor 43. Six of the twelve ports of valve 40 are numbered to correspond with the column end to which each is connected. A "prime" symbol distinguishes the reference number of the port from that of the column end. The additional ports of valve 40 are lettered or numbered in accordance with the diagram of FIG. 1 insofar as practicable. Four of the remaining ports in the valve are thus labeled V₁, V₂, P₁ and P₂. The remaining two ports are connected across detector 12 and are thus labeled 121 and 122. A source of carrier gas P supplies both P₁ and P₂ as illustrated. In addition, carrier gas may be employed in the reference side of detector 12 if a thermal conductivity bridge detector is employed. It will also be noted that carrier gas from P flows through a valve 42 in its passage to P₁. Valve 42 is representative of a sample injection valve such as that disclosed in U.S. Patent 2,757,541 which issued August 7, 1956, to E. S. Watson, et al. A continuous sample supply passes through valve 42 via lines 44, 46. A recorder 48 is illustrated as connected to detector 12.

Valve 40 may be operated either manually or automatically. When operated automatically, it may be actuated by detector 12 or by a suitable timer. As illustrated, the rotor 43 of valve 40 includes six passages symmetrically arranged about a diameter of the valve. Pointers 50, 52 indicate the position of the valve rotor and are indexed in accordance with valve position indicating numerals running from "1" through "6." In the position illustrated by FIG. 2, columns 10, 20 and 30 are connected as shown in FIG. 1(a). At the beginning of the cycle, valve 42 is actuated to inject a sample into the flowing carrier gas stream passing through conduit 13 from P. The carrier

4

and the measured sample volume pass through conduit 15 and into valve 40 through port P₁. From valve 40 they pass sequentially through conduit 17, column 10, conduit 19, valve 40, conduit 21, detector 12, conduit 23, valve 40, conduit 25, column 20, conduit 27, valve 40, to vent V₁. End 101 receives the sample, ends 102 and 202 are interconnected through detector 12 and end 201 is vented as shown in FIG. 1(a). While this arrangement is in effect, carrier gas is simultaneously passing from P through conduit 31, port P₂, Port 301', conduit 33, and is backflushing column 30 by flowing from 301 to 302 and thence via conduit 35 and valve 40 to vent V₂.

It will now be noted that a rotation of valve 40 to bring pointers 50, 52 into alignment with indexing numerals "2" will result in the valving arrangement shown in FIG. 1(b). Similarly, each of positions 3, 4, 5, and 6 corresponds to the arrangements illustrated, respectively, in FIGS. 1(c), 1(d), 1(e) and 1(f).

FIGS. 3 and 4 each illustrate an assemblage of six columns 62, 64, 66, 72, 74, 76, the ends of each column being numbered by adding the digit "1" or "2" to the reference numeral of the column. Each of these embodiments has the advantage of allowing the injection of two samples simultaneously. In each instance, the sample is injected into column ends 621 and 721. For purposes of convenience, the two samples of each figure are designated S_a and S_b. There are now four sources of carrier gas in each embodiment which are labeled respectively P₁, P₂, P₃, and P₄. P₁ and P₃ represent carrier gas sources used to recirculate the sample components. P₂ and P₄ represent sources of flushing gas which may or may not be similar to the carrier. There are also four vents, V₁, V₂, V₃ and V₄. V₁ and V₃ of each figure vent the light ends from the second of the series-connected columns. V₂ and V₄ in each instance are the backflushing vents from the column being prepared for reuse. A comparison of FIGS. 3(a)-3(e) with FIGS. 1(a)-1(e) will indicate that each group of three columns, meaning 62, 64, 66 and 72, 74, 76 is similar to the correspondingly numbered portions of FIG. 1. In FIG. 3(f) however, when sample S_a has entered column 66, end 661 is connected to discharge into end 721 of column 72 of the second group. Similarly, when sample S_b has entered column 76, end 761 is connected to discharge into end 621 of column 62. This will be seen to cause each of samples S_a and S_b to be injected into the second circuit of three columns. Consequently, each sample is caused to make a complete recirculating tour of a column group, passing through each column twice and in reversed direction and thereupon passing into the second group of three columns wherein the same circulation takes place.

In FIG. 4 a somewhat similar arrangement is shown. However, in this sequence of operation, each sample S_a and S_b passes sequentially through all six columns in series.

It will be noted that in each of FIGS. 3 and 4 the recirculation provides the same advantages as discussed relative to FIGS. 1 and 2. Thus, while components of interest are being continuously recirculated, light ends are being vented, heavy ends are being backflushed, and a new section of column is being continually presented to the advancing components.

It should be noted here that in the foregoing description I have referred to the venting of light ends and the backflushing of heavy ends. This description presupposes in each instance that the analyst or other user is primarily interested in the separation of mid-range components. However, this notation is for convenience and ease of illustration only. The necessary valving of the column sections may be performed whenever desired in accordance with the location of the particular components of interest. It may be, for example, that the components which it is desired to separate are at the lightest end of the mixture. In such an instance, the light ends, of course, would not be allowed to vent. However, the il-

5

illustrations would be the same and backflushing would still continue. Pure carrier gas, however, would be vented or would be recycled as desired.

Similarly, if the analyst desired to separate the heaviest ends, the backflushing step would be omitted but the light ends would continue to vent as before.

In FIG. 5 there is illustrated a two column variation of this invention. In this embodiment, two pressure sources for carrier gas may be required. One source serves to supply carrier gas for the normal chromatographic separation. The other source serves to flush the previously loaded column by a short high pressure injection of carrier or flushing gas to prevent the fastest desired components from overtaking the slow components during the remainder of the cycles. The manner in which this technique is employed will be more apparent from FIGS. 5(a) through 5(h). These diagrams illustrate a sequence of separation utilizing chromatographic columns 80 and 90. Following the previously described notation, the respective ends of the column are designated by the column reference numeral followed by the digit "1" or "2." In order to illustrate this embodiment of the invention, it will be assumed that a sample is injected into the carrier gas flowing from source P_1 into column end 802. The components of interest pass through column 80, out end 801, and into end 902 of column 90. Simultaneously, lighter ends may vent from V_1 while heavier components are retained in column 80. When the components of interest have entered column 90, the columns may be switched to the embodiment of FIG. 5(b). In FIG. 5(b) it will be noted that column 80 is connected to the previously described high pressure source P_2 of carrier or flushing gas and vents through a vent V_2 . The heavy flow resulting from the increased backflushing pressure allows the time during which the arrangement of FIG. 5(b) exists to be short. During this backflushing period, the components of interest remain in column 90. When backflushing of column 80 has proceeded sufficiently far, the columns are switched to the arrangement shown in FIG. 5(c). The components of interest are now circulated to newly backflushed column 80, light ends vent from V_1 , and heavy ends remain in column 90. From this position, the column valving is rearranged to permit the high pressure backflushing of column 90 as shown in FIG. 5(d). After this short backflush period the columns are switched to the position shown in FIG. 5(e). By following the diagrams through FIG. 5(h) it will be seen that this sequence continues. The components of interest are circulated from one column to the other, light ends are always allowed to vent and heavy ends are being backflushed during short, high pressure backflushing periods. The components of interest are thus continuously passed to newly backflushed sections of column. From the configuration shown in FIG. 5(h) the columns are rearranged once again to the arrangement shown in FIG. 5(a). The components of interest are thereby continuously recirculated for as long a period as may be required to effect their separation.

The illustrations of FIGS. 5(b), 5(d), 5(f), and 5(h) indicate that, during the flushing period, carrier gas source P_1 is connected to the column containing the components of interest. It should be understood, however, that, during this period, this column may be held in a "standby" condition without connection either to source P_1 or to vent V_1 .

A combination of apparatus suitable for performing the above switching arrangements is shown in FIG. 6. In this embodiment, the columns 80, 90 are mounted for rotation. The ends 801, 802, 901, and 902 are directly mounted on valve rotor 110. Rotor 110 is held in rotatable relationship against stator member 112 by means of a suitable compression spring 114. Four ports are contained on the underside of stator 112, in alignment with the equally spaced ends of columns 80 and 90. In addition, a second valve 116 is connected into the cir-

6

cuit for performing the short flushing cycle. Valve 116 contains six ports located in a stator disc 117 and is so arranged that adjacent ports may be interconnected by means of rotatable arcuate passages 118, 120, 122 in rotor disc 119. This valve may be similar to the valve disclosed in United States Patent 2,757,541, previously referred to. Valve 116, however, does not contain a sampling loop. P_2 represents a relatively high pressure source of flushing gas leading to port 124. In the illustrated position the flushing gas is vented from port 126 to vent V_2 . Meanwhile, carrier gas under normal pressure from P_1 passes into port 128 and from port 130 continues to end 802 of column 80. Sample S may also be inserted into the carrier stream from P_1 . From column end 801 the carrier and contained sample pass into port 132 and from port 134 into column end 902. From column end 901, the carrier and separated components may pass to vent V_1 .

It will be noted that the valve positions illustrated in FIG. 6 define the circuitry of FIG. 5(a). At the proper time, as previously described, valve 116 is actuated to interconnect port 132 with 124, 126 with 130, and 128 with 134. It will be seen that, with this combination, the configuration of FIG. 5(b) is achieved. After the lapse of a proper period of time, valve 116 is repositioned to its original state and, at the same time, rotor 110 is rotated in the direction shown by the arrows so that each column end is aligned with the adjacent port of stator 112. This creates the flow condition illustrated in FIG. 5(c). By continuing the relative movements of valves 116 and 110, each of the schematics illustrated by FIGS. 5(a) through 5(h) may be achieved.

A number of modifications of this invention are possible. For example, although arrangements of two, three, and six columns have been described, similar techniques employing other multiples are possible. Also, although dual sample injection has been described relative to FIGS. 3 and 4, a single injection could be employed or a greater number of injections could be made.

The use of plural injections wherein the various samples follow each other about the circuit has the advantage of using a single time control for switching. It will be understood that such a system would require a relatively close matching of the columns from the standpoint of pneumatic resistance. Variations in resistance should be compensated insofar as possible by alternating high and low resistance columns. If "box car" injections (i.e., rather long, square-ended injections of sample) are employed, slight variations in the k' value of the columns would cause an occasional "nipping off" of the box car ends. However, this effect would not be cumulative since the overall passage time of each sample would be the same. The term k' refers to the ratio

$$k' = \frac{F_{11q}}{F_{gas}}$$

and is defined at page xii of Keulemans Gas Chromatography, Reinhold Publishing Corporation, second edition, 1959.

The term "plate" or "theoretical plate" is commonly used in the art of chromatography to define the separating power of a column. A complete description of the term will be found in the Keulemans book cited above but, for present purposes, we may say that the greater the number of plates the greater the separation capability. If each column of a group contains n_1 plates, and if the sample is circulated n_2 times, the effective number of plates becomes $n_1 n_2$. As a spike-injected component is spread over the order of $\sqrt{n_1 n_2}$ plates, the number of distinguishable components contained within a column of n_1 plates is of the order of

$$\sqrt{\frac{n_1}{n_2}}$$

If the user is interested in isolating a single component, n_2 may be made of the order of n_1 .

It is to be understood that this invention is capable of many variations and modifications without departing from the spirit and scope thereof. Accordingly, this invention is to be construed as limited only by the scope of the following claims.

I claim:

1. Apparatus for chromatographic separation which comprises:

- (a) a plurality of chromatographic separating column means;
- (b) means for passing a mixture of fluid components sequentially and repeatedly through said column means;
- (c) means for removing components which may be ahead of a preselected portion of said mixture;
- (d) means for backflushing and removing components from a previously used column behind said preselected portion; and
- (e) means for periodically passing said preselected portion through said previously used column in the same direction as the direction of backflush.

2. Apparatus for chromatographic separation which comprises:

- (a) a plurality of chromatographic separating column means;
- (b) means for injecting a multi-component fluid sample into a fluid carrier;
- (c) means for passing said sample and carrier sequentially and repeatedly through said column means;
- (d) means for removing components which may be ahead of a preselected portion of said mixture;
- (e) means for backflushing and venting a previously used column to remove components behind said preselected portion; and
- (f) means for periodically passing said preselected portion through said previously used column in the same direction as the direction of backflush.

3. Apparatus for chromatographic separation which comprises:

- (a) a source of carrier gas;
- (b) first and second chromatographic separating columns;
- (c) means for injecting a multi-component fluid sample into said carrier gas;
- (d) means for passing said carrier gas and contained sample into a first end of said first column to effect a component separation therein;
- (e) means for passing a preselected portion of said sample from the second end of said first column into a first end of said second column;
- (f) means for venting the second end of said second column during at least a part of the travel time of said preselected portion therethrough;
- (g) means for backflushing and venting said first column to remove unwanted components therefrom; and
- (h) means for repassing said preselected portion through said first column in the same direction as the direction of backflush.

4. Apparatus for chromatographic separation which comprises:

- (a) a source of carrier gas,
- (b) first, second, and third chromatographic separating columns;
- (c) means for injecting a multi-component fluid sample into said carrier gas;
- (d) means for passing said carrier gas and contained sample into a first end of said first column to effect a component separation therein;
- (e) means for passing a preselected portion of said sample from the second end of said first column into a first end of said second column;
- (f) means for venting the second end of said second

column during at least a part of the travel time of said preselected portion therethrough;

- (g) means for passing said preselected portion from the second end of said second column into a first end of said third column;
- (h) means for backflushing and venting said first column during passage of said preselected portion through said third column; and
- (i) means for passing said preselected portion from the second end of said third column through said first column in the same direction as the direction of backflush.

5. A method of chromatographic separation comprising:

- (a) passing a mixture of fluid components sequentially and repeatedly through a plurality of chromatographic separating columns;
- (b) removing components ahead of a preselected portion of said mixture if there are components present in said mixture which are ahead of said preselected portion;
- (c) backflushing in a previously used column components behind said preselected portion and removing said components behind said preselected portion; and
- (d) passing said preselected portion through said previously used column in the same direction as the direction of backflush.

6. A method of chromatographic separation comprising:

- (a) passing a mixture of fluid components sequentially and repeatedly through a plurality of chromatographic separating columns;
- (b) venting a column to be used to remove components ahead of a preselected portion of said mixture if there are components present in said mixture which are ahead of said preselected portion;
- (c) backflushing and venting a previously used column to remove components behind said preselected portion;
- (d) and passing said preselected portion through said previously used column in the same direction as the direction of backflush.

7. A method of chromatographic separation comprising:

- (a) passing a mixture of fluid components sequentially and repeatedly through a plurality of chromatographic separating columns;
- (b) venting a column to be used before and while a preselected portion of said mixture enters said column to remove components ahead of said preselected portion if there are components present in said mixture which are ahead of said preselected portion;
- (c) backflushing and venting a previously used column after said preselected portion leaves said previously used column to remove components behind said preselected portion;
- (d) and passing said preselected portion through said previously used column in the same direction as the direction of backflush.

8. The method of claim 7 wherein the venting of the column to be used and the backflushing and venting of the previously used column occur simultaneously.

9. A method of chromatographic separation comprising:

- (a) injecting a multiple fluid component sample into a fluid carrier;
- (b) passing said carrier and at least a portion of said sample sequentially and repeatedly through a plurality of chromatographic separating columns;
- (c) venting a column to be used to remove components ahead of a preselected portion of said sample if there are components in said mixture which are ahead of said preselected portion;

9

(d) backflushing and venting a previously used column to remove components behind said preselected portion; and

(e) passing said preselected portion through said previously used column in the same direction as the direction of backflush. 5

10. The method of claim 9 wherein the plurality is two.

11. The method of claim 10 wherein each period of backflushing is short compared to the time of passage of the sample portion through a column. 10

12. The method of claim 9 wherein the plurality is at least three.

13. The method of claim 12 wherein the venting and the backflushing occur simultaneously and while the preselected portion is in a third column. 15

10

References Cited by the Examiner

UNITED STATES PATENTS

2,841,005 7/1958 Coggeshall.

3,112,639 12/1963 Maxwell ----- 73—23.1

FOREIGN PATENTS

874,742 8/1961 Great Britain.

OTHER REFERENCES

Gas Chromatography, by D. H. Desty, 1958, pages 297–299, Academic Press Inc.

REUBEN FRIEDMAN, *Primary Examiner*.