Aug. 7, 1973 S. D. RAINS 3,751,357

ELECTROPHORESIS SYSTEM AND GEL FRAME

Filed May 24, 1971 2 Sheets-Sheet 1

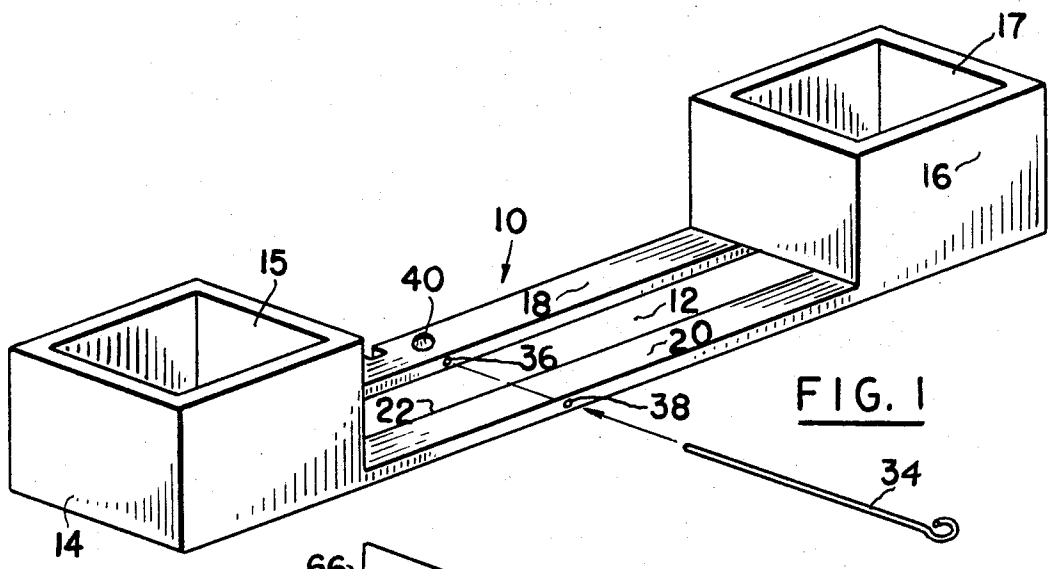

FIG. 1

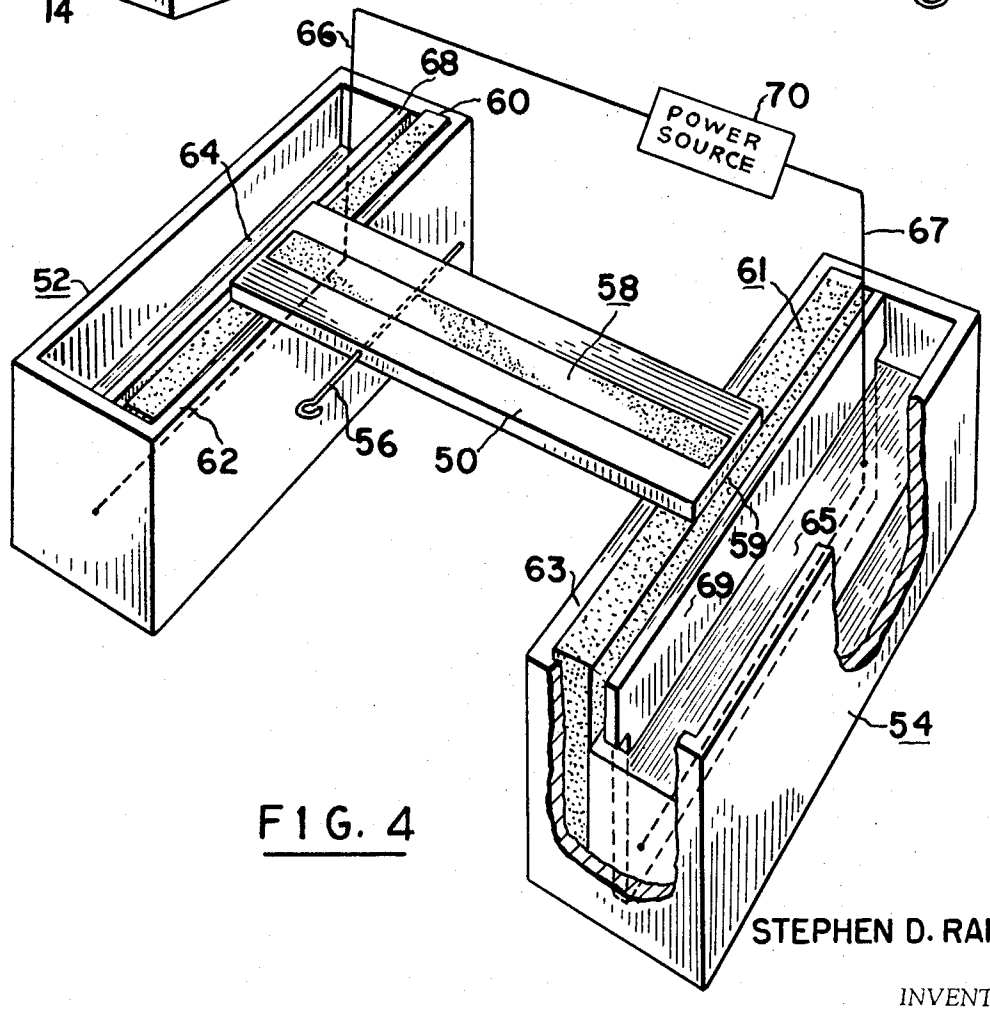

FIG. 4

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ELECTROPHORESIS SYSTEM AND GEL FRAME

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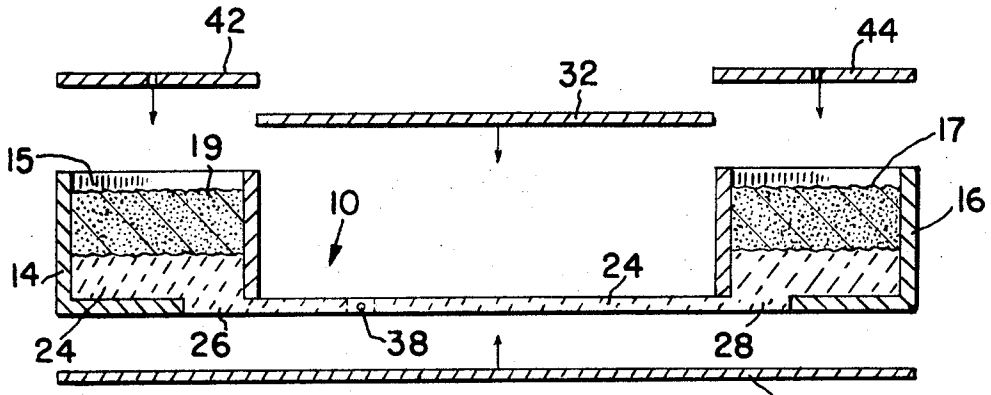

FIG. 3

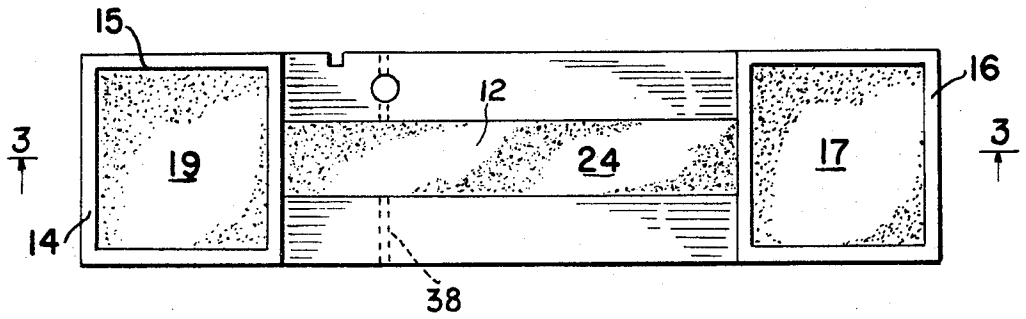

FIG. 2

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3,751,357

ELECTROPHORESIS SYSTEM AND GEL FRAME

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Int. Cl. B01k 5/00
U.S. Cl. 204—299 20 Claims

ABSTRACT OF THE DISCLOSURE

A gel frame for use in chemical analysis and, particularly, for electrophoresis testing, utilizing buffer chambers having a migration portion positioned therebetween, a wire-like element traversing the migration portion and a gel situated in the migration portion extending to or into the buffer chambers to engage a gel or a buffer solution for use in the chemical analysis.

BACKGROUND OF THE INVENTION

(1) Cross-reference to related applications

This invention is related to the invention described in the concurrently-filed and copending applications entitled, "Method of and Apparatus for Depositing a Fluid in a Gel," Ser. No. 146,262, filed May 24, 1971, for inventors Stephen D. Rains and Leon L. Wheeless, Jr., and "Immunoelectrophoresis Gel Tray," Ser. No. 146,388, filed May 24, 1971, for inventor Stephen D. Rains.

(2) Field of the invention

This invention relates to apparatus and a system for carrying a gel for electrophoresis analysis of a fluid sample and, more particularly, to either self-contained or separate electrophoresis units for supporting a gel and solutions provided for connection to electrodes for energizing an electrical field across the gel having apparatus for introducing a fluid sample.

(3) Description of the prior art

In the past, apparatus available for use in the field of electrophoresis has involved the use of awkward and cumbersome devices which frequently resulted in inaccurate and inconsistent results. For example, in the apparatus as disclosed in U.S. Pat. No. 3,432,414 entitled "Electrophoretic Process With Continuous Scanning," issued to R. N. Rand on Mar. 11, 1969, there is disclosed, as best seen in FIG. 4, an apparatus for carrying a sample fluid comprising a string **49** stretched across an applicator **26** for positioning on the surface of the migration layer **6**. It will readily be appreciated that there is a great deal of difficulty experienced in consistently depositing a fluid sample onto the string in the proper quantity without causing over-saturation to the string with the resulting blotting of the sample when the string is placed in position on the surface of the migration layer.

Another known method which is equally difficult for the hereinbefore mentioned processes involves the use of an applicator having the facility for introducing a fluid in a relatively thin line upon the gel. The disposition of the fluid upon the gel is controllable in thickness only. It is fairly obvious that the accuracy of the operator may vary as he draws the applicator across the gel which may, accordingly, result in a fluid deposition line of varying dimensions. Generally, this device has no means for controlling the speed of the movement of the operator's hand when traversing the gel, the amount or rate of fluid being dispensed and further the direction of the motion. In addition, in the prior art devices it has generally been necessary to make the gel solution immediately prior to the test to be conducted and to cast the gel within the respective frames allowing it to set for a short period

thereafter. The resulting multiplicity of steps complicated the job and created a number of unnecessary steps and further necessitated a great deal of the operator's time to conduct each singular test.

Prior to applicant's present invention the results obtained from the previously mentioned devices have been somewhat unsatisfactory and undependable. It was, at times, necessary in the past to repeat the tests to corroborate and verify the previously obtained results.

SUMMARY OF THE INVENTION

This invention provides for an electrophoresis gel frame having a migration portion interposed between, and in communication with, buffer chambers disposed at opposite ends of the frame for receiving electrodes to create an electrical field for causing migration of a fluid sample. The invention further provides for an accurate dependable device, easy and inexpensive to manufacture, convenient to store and handle and for all practical purposes disposable.

Embodiments according to the principles of the present invention can be constructed from a great variety of materials. It, however, has been found during the process of the experiments run that synthetic materials, particularly those belonging to the plastic family, work exceedingly well. The need for holding especially close tolerances which, correspondingly, increase manufacturing costs are essentially eliminated. This has decided advantages over the electrophoresis gel frames heretofore known in the field, particularly, for example, the gel frame disclosed in the previously mentioned R. N. Rand patent.

The present invention provides for including a gel in a migration portion of a gel frame in communication with buffer solutions contained in buffer chambers. The resulting gel frame may then be stored until a later date when the sample fluid will be introduced into the gel and the electrophoresis process carried out. This greatly facilitates set-up procedures, handling, and also reduces the time required for performing the electrophoresis operation. After completion of the operation for electrophoresis study, the operator may, if he so chooses, dispose of the frame without incurring great expense. The device of the present invention thereby further eliminates the need for a cleaning station and the accompanying materials necessary to prepare the frames for subsequent reuse. In addition, the device of the present invention will decrease the number of trained personnel necessary to perform the required operations.

A further embodiment of the present invention provides for an electrophoresis gel frame having separate buffer chambers, which for convenience purposes may or may not be fixed. A removable electrophoresis migration tray is provided to be bridged between the separate buffer chambers. The embodiment of this description may be constructed from a variety of materials, although, as previously discussed, synthetic materials, such as plastic, work very well.

In operation the buffer chambers have introduced into them the necessary substances to enable the electrophoresis process to take place. The prepared migration tray, or trays as the case may be, is then disposed so as to bridge the gap between the buffer chambers and also to make intimate contact with the gel in the tray and a compatible substance in the buffer chamber. A continuous path is thereby provided between the migration tray and the buffer chambers. Electrodes are disposed within the buffer chambers and then energized to facilitate the process of electrophoresis across the migration tray.

It is, of course, readily seen that the buffer chambers, as well as the migration tray, may be prepared in separate and remote preparation areas, stored for a period

of time and then brought together for use in the desired electrophoresis processes. It will also be easily seen that the buffer chambers may be used frequently and, particularly, may be used to conduct more than one test simultaneously. The resulting number of steps required to perform the operations, as well as the number of personnel required, will be favorably reduced.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is a perspective view of an apparatus according to the principles of the present invention;

FIG. 2 is a top plan view of the apparatus;

FIG. 3 is a cross-sectional view of the apparatus of FIG. 2 taken along line 3—3 of FIG. 2; and

FIG. 4 is a perspective view of a further embodiment, according to the principles of the present invention, showing a plurality of buffer tanks having an electroplhoresis tray placed therebetween.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

In FIGS. 1, 2 and 3 a gel frame **10** is shown which comprises a migration portion **12** extending between the buffer chambers **14** and **16** which are disposed at respective ends of the frame **10**. The gel frame **10** generally shown in FIG. 1 consists of a migration portion **12** which comprises two spaced apart and parallelly disposed runners **18** and **20** extending between the buffer chambers **14** and **16** to define therebetween a generally rectangular aperture **22** for supporting a gel material **24** which is best seen in FIG. 2. The gel may comprise, for example, a medium such as is defined in U.S. Pat. No. 3,399,127 entitled "Electrophoresis Medium Using Agarose and Carrageenan," issued to R. N. Rand et al.

A gelatinous fluid is made and then poured into the respective buffer chambers **14** and **16** through openings **15** and **17**, respectively. The gelatinous fluid then proceeds to flow through openings **26** and **28**, as best seen in FIG. 3, which communicate the buffer chambers **14** and **16** respectively with the rectangular aperture **22** of the migration portion **12** of the frame **10**. The gelatinous fluid fills the rectangular aperture **22** completely while the buffer chambers **14** and **16** are filled to a level approximately three times the thickness of the fluid contained within the rectangular aperture **22**. To provide for an even distribution of the gelatinous fluid within the rectangular aperture **22** of the migration portion **12** there may be provided a thin, relatively smooth and flat film or plate **30** positioned at the underside of the frame **10** for supporting the gel **24** in the fluid state. A further thin, relatively smooth and flat film or plate **32** may be provided for containing the gelatinous fluid in the upper area of the migration portion **12**, as best seen in FIG. 3. The use of thin films or plates **30** and **32** provide for uniformly regular and flat upper and lower surfaces on the gel **24**. This feature will greatly insure accurate and true readings of the migration path across the migration portion **12**. These readings may, of course, be made by any suitable known apparatus available in the field. It will be appreciated that any variations in the thickness of the gel would cause false and inaccurate readings when the migration path is analyzed and the use of the upper and lower thin films or plates **32**, **30**, respectively, greatly insures generally parallel upper and lower surfaces of the gel **24**. An accurate reading is therefore assured. It will be further appreciated that the thin films or plates **30** and **32**, respectively, would protect the gel during shipping, prevent dehydration during the process of electrophoresis and, further act as heat sinks and heat conduits.

A wire-like element **34**, as best seen in FIG. 1, is provided for utilization in introducing a fluid sample into the formed gel **24**. The wire-like element **34** extends through openings **36** and **38** in the runners **18** and **20** respectively of the migration portion **12**. A fluid sample well **40** is positioned, for example, in migration runner **18** above and connected to the opening **36**. As can easily be seen, the fluid sample may be disposed in the fluid well **40** by any convenient methods, such as, for example, those described in the hereinbefore concurrently-filled applications Ser. Nos. 146,262 and 146,388. Similarly, the fluid sample is disposed through the gel **24** by the wire-like element **34**, as defined in the hereinbefore mentioned patent application.

After the gelatinous material is introduced into the frame **10**, as previously described, and after it has set, a buffer solution **19** is introduced through openings **15** and **17** of buffer chambers **14** and **16** respectively. The buffer solution **19** may be composed of any well-known buffer material such as those defined in the Rand Pat. No. 3,434,-414. This arrangement, which is best seen in FIG. 2, provides for easy introduction of the electrophoresis electrodes without difficulty in setting the apparatus up and without transferring the migration portion **12** from one work area to another. In addition, embodiments according to the present invention are such that they do not necessitate the need for baffles such as those described in the immediately previously mentioned R. N. Rand patent. Baffles may, however, be incorporated to better control the electrophoresis process, if it is so desired.

After the buffer solution is introduced into the buffer chambers **14** and **16** end caps **42** and **44** may be placed over the openings **15** and **17** of the buffer chambers **14** and **16** respectively to thereby contain in cooperation with thin films **30** and **32** the gel and buffer constituents within the frame **10**. The provision of the end caps **42** and **44** on the buffer chambers **14** and **16**, respectively further provides for a convenient package for both handling and storage.

In an alternate embodiment illustrated in FIG. 4 there is shown an electrophoresis migration tray **50** bridged across two similarly constructed electrophoresis buffer tanks **52** and **54**. The process of electrophoresis is similar to the process of electrophoresis hereinbefore discussed. The structures differ, however, in that the tray **50** is, itself, devoid of buffer tanks. The migration tray **50** must therefore be placed upon the buffer tanks **52** and **54** to complete the electrophoresis process. After the electrophoresis process has been completed the migration tray **50** may be readily removed for analysis or replacement by a further migration tray. The embodiment of FIG. 4 is ideally suited for making the buffer tanks **52** and **54** as a relatively fixed structure for including an enclosure for performing the electrophoresis process. Alternately, the embodiments disclosed may be individually movable to enable an operator to selectively place the tanks as he desires. Additionally, it is easily appreciated that a plurality of trays **50** may be placed to bridge the area between the buffer tanks **52** and **54** in order to run any desired number of tests.

In the detail, the trays **50** may be similar to embodiments according to the principles of the invention included in the concurrently-filed Rains et al. patent application hereinbefore mentioned. The tray structure would be similar in that it would have a wire-like element **56** situated therethrough for introducing a fluid sample into a gel area **58** which is contained within and extends the length of the tray **50**. The tray **50** is designed so that the gel area **58** is exposed at the bottom portion for placement upon the gel slabs **60** and **61** in each of the buffer tanks **52** and **54**, respectively. The gel slabs **60**, **61** are formed contiguous with one wall of the respective buffer tanks **52** and **54** and extend slightly above the uppermost ledges **62** and **63** of the buffer tanks **52**, **54**, respectively, in order to make intimate contact with the bottom side **59** of the gel portion **58** in the tray **50**.

Buffer solutions **64**, **65** are provided within the buffer chambers **52** and **54** respectively so that intimate contact is made with the gel slabs **60** and **61**. The buffer solutions **64** and **65** are further provided to receive therein electrodes **66** and **67**, respectively, which may be formed, for example, of platinum wire. To preclude migration of the

acid and base formed in an electrolytic process such as the one herein described, and more fully described in the Rand Pat. No. 3,432,414, baffle plates **68** and **69** are provided in buffer tanks **52** and **54**, respectively, and positioned to be disposed between the electrodes **66, 67** and the gel slabs **60** and **61**. The gel slabs **60** and **61** are formed in the baffle tanks **52** and **54** and about the baffle plates **68** and **69** so that a continuous path of buffer solution is provided around and under the baffle plates **68** and **69**. The tray **50**, the buffer tanks **52** and **54** and the baffle plates **68** and **69** may be formed of any suitable material, such as, for example, plastic. A power source **70** is provided which energizes the electrodes **66** and **67** and completes the process of electrophoresis.

I claim:

1. A device for supporting a gel useable as a medium in analyzing chemical constituents by chemical separation, comprising:

a pair of receiving chambers containing buffer solution and a gel said chambers to be disposed apart from each other;

a generally flat and relatively thin frame having a perimeter defining an opening in the frame said frame positioned to communicate one chamber with the other chamber;

a gel disposed within and supported by the opening of the frame and formed to be in intimate contact with the gel in the chambers; and

means for providing a pressure reduction between a first point and a second point within the gel disposed within and supported by the opening in the frame to move chemical constituents from the first point to the second point within the gel.

2. The device as defined in claim **1**, wherein the means is disposed within the gel and is a wire-like element.

3. The device as defined in claim **1**, further comprising removable plates disposed upon the frame for positioning in intimate contact with the gel to be carried by the frame to assure smooth, parallel surfaces on the gel.

4. The device as defined in claim **1**, further comprising covers for placement over the receiving chambers.

5. The device as described in claim **6**, wherein the covers are removable.

6. The device as described in claim **7**, wherein the covers are perforated to permit the insertion of electrodes therethrough and into the receiving chambers.

7. The device as defined in claim **1**, further comprising means for introducting an electrical current to the chemical constituents to facilitate the electrophoresis process.

8. The device as defined in claim **7**, wherein the means for introducing an electrical current to the chemical constituents are electrodes disposed within the buffer solution and extending the length thereof.

9. The device as defined in claim **8**, wherein the electrodes are formed of a non-corrodible material.

10. The device as defined in claim **9**, wherein the electrodes are formed of platinum.

11. The device as defined in claim **1**, wherein the means for providing a pressure reduction between a first point and a second point within the gel is a filament to be disposed and movable within the supported gel from the first point to the second point to create a pressure reduction between said first and second points to move chemical constituents under the influence of the created pressure differential from the first point to the second point.

12. The device as defined in claim **2**, wherein the wire-like element is formed of a thread-like material.

13. A device for supporting a gel useable as a medium in analyping chemical constituents by chemical separation, comprising:

a pair of receiving chambers containing a buffer solution and gel said chambers to be spaced apart from each other;

a generally flat and relatively thin frame having a perimeter defining an opening said frame positioned to communicate one receiving chamber with the other receiving chamber;

a gel disposed within and supported by the opening of the frame and formed to be in intimate contact with the gel in the receiving chambers; and

means for flowing chemical constituents by capillary action from a first point and a second point within the gel disposed within and supported by the generally flat and relatively thin frame.

14. The device as defined in claim **13** wherein the means for flowing chemical constituents from a first point to a second point within the gel is an element having absorbent qualities to permit the chemical constituents to be absorbed therein when the element is at least in part immersed in the chemical constituents.

15. The device as defined in claim **1**, further comprising baffle plates disposed within the receiving chambers.

16. The device as described in claim **13**, further comprising removable plates disposed upon the frame for positioning in intimate contact with the gel to be carried by the frame to assure smooth, parallel surfaces on the gel.

17. The device as defined in claim **13**, further comprising removable covers for placement over the receiving chambers.

18. The device as defined in claim **13**, further comprising means for introducing an electrical current to the chemical constituents to facilitate the electrophoresis process.

19. The device as defined in claim **18**, wherein the means for introducing an electrical current to the chemical constituents are electrodes disposed within the buffer solution and extending the length thereof.

20. The device as defined in claim **13**, further comprising baffle plates disposed within the receiving chambers.

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U.S. Cl. X.R.

204—180 G; 23—253 R