

DESCRIPTION

Title of Invention: CAPILLARY ELECTROPHORESIS DEVICE AND CAPILLARY ELECTROPHORESIS ANALYSIS METHOD

Technical Field

[0001]

The present invention relates to a device and a method for analyzing components contained in a sample solution by capillary electrophoresis.

Background Art

[0002]

In the present description, a pressure is defined as a pressure to be added to an atmospheric pressure (approximately 1 atm) which is a reference. That is, the atmospheric pressure is set to 0 atm. For convenience, a pressure of 0 atm to 7 atm is referred to as a low pressure, and a pressure exceeding 7 atm is referred to as a high pressure. 1 atm is about 0.1 MPa.

[0003]

A capillary electrophoresis device is an automatic device that performs electrophoresis separation and analysis of various types of components contained in a sample solution by charge and size. For example, Applied BiosystemsTMSeqStudioTMFlex Series Genetic Analyzers (hereinafter referred to as a device A) sold by Thermo Fisher Scientific can perform DNA sequencing and DNA fragment analysis as described in NPL 1. Although the device A can perform parallel analysis using eight or 24 capillaries, one capillary will be mainly described in present description (the same description applies to other capillaries). The DNA fragments are negatively charged, and therefore, electrophoresis of the DNA fragments occurs from a cathode to an anode with a sample-injection end of the capillary as a cathode side and a sample-elution end as an anode side. In the device A, a high pressure can be applied to the sample-elution end of the capillary by a plunger type pressurizing mechanism. The sample-elution end is

connected to a flow path containing a polymer solution, and a syringe containing the polymer solution is connected to the flow path. An anode buffer solution tank containing the anode buffer solution is also connected to the flow path, the anode buffer solution in the anode buffer solution tank is connected to the polymer solution in the flow path, and a valve is placed at a boundary therebetween. In a state in which the valve is closed, the plunger type pressurizing mechanism mechanically pushes a plunger of the syringe in, so that a pressure of the polymer solution inside is increased to a high pressure of about 70 atm at maximum, practically 35 atm. At this time, the sample-injection end is vented to atmospheric pressure, and therefore, the capillary can be filled with a high-viscosity polymer solution.

[0004]

On the other hand, when the valve is opened, an inside of the anode buffer solution tank and the sample-elution end are vented to the atmospheric pressure. The cathode has a pipe shape, and the sample-injection end of the capillary is inserted through the cathode to integrate the cathode and the sample-injection end. The anode is not integrated with the sample-elution end of the capillary, but is inserted into the anode buffer solution tank and immersed in the anode buffer solution. In a state in which both ends of the capillary are vented to the atmospheric pressure, the sample-injection end is immersed in the sample solution, and a voltage is applied between both electrodes, that is, both ends of the capillary, so that the sample can be injected into the capillary by an electric field. Electrophoresis (referred to as atmospheric pressure electrophoresis) can be performed by immersing the sample-injection end in a cathode buffer solution and applying a voltage to both ends of the capillary in a state in which both ends of the capillary are vented to the atmospheric pressure.

[0005]

A PA 800 Plus Pharmaceutical Analysis System (hereinafter referred to as device B) sold by Sciex is a capillary electrophoresis device of a type different from that of the device A, and can analyze proteins such as antibodies as described in NPL 2. The device B can analyze both a negatively charged component and a positively charged component. When a negatively charged component is analyzed, the negatively charged component is subjected to electrophoresis from the cathode to the anode with the sample-injection end of the capillary as

a cathode side and the sample-elution end as an anode side.

[0006]

On the other hand, when a positively charged component is analyzed, the positively charged component is subjected to electrophoresis from the anode to the cathode with the sample-injection end of the capillary as the anode side and the sample-elution end as the cathode side. Hereinafter, for simplicity, a case of analyzing a sample including a negatively charged component will be described. In the device B, a low pressure can be independently applied to both ends of the sample-injection end and the sample-elution end of the capillary by an air type pressurizing mechanism. In addition, both ends can be independently vented to the atmospheric pressure. The cathode has a pipe shape, and the sample-injection end of the capillary is inserted through the cathode to integrate the cathode and the sample-injection end. In addition, the anode also has a pipe shape, and the sample-elution end of the capillary is also inserted through the anode to integrate the sample-elution end and the anode. The air type pressurizing mechanism can increase the pressure in the container to about 7 atm at the maximum by inserting any capillary end into the container in which the solution is stored, immersing the capillary end in the solution, and introducing compressed air into the container in a state in which the container has a sealed structure. When the sample-elution end of the capillary is immersed in the polymer solution, a low pressure of 5 atm is applied by the air type pressurizing mechanism, and the sample-injection end is vented to the atmospheric pressure, the capillary can be filled with the polymer solution from the sample-elution end toward the sample-injection end (alternatively, when the sample-injection end of the capillary is immersed in the polymer solution, a low pressure of 5 atm is applied by the air type pressurizing mechanism, and the sample-elution end is vented to the atmospheric pressure, the capillary can be filled with the polymer solution from the sample-injection end toward the sample-elution end). In addition, when the sample-injection end of the capillary is immersed in the sample solution, a low pressure of 1 atm is applied by the air type pressurizing mechanism, and the sample-elution end is vented to the atmospheric pressure, the sample can be injected into the capillary by pressure. Alternatively, when the sample-elution end of the capillary is immersed in the anode buffer solution, the sample-injection end is immersed in the sample solution, and a voltage is

applied to both ends of the capillary, the sample can be injected into the capillary by an electric field. Atmospheric pressure electrophoresis can be performed by immersing the sample-elution end of the capillary in an anode buffer solution, immersing the sample-injection end in a cathode buffer solution, and applying a voltage across both ends of the capillary. Further, by applying an equal low pressure of 1 atm to both ends of the capillary by the air type pressurizing mechanism during electrophoresis (both-ends pressurizing mechanism), the generation of bubbles in the polymer solution inside the capillary can be prevented, and electrophoresis analysis can be stabilized.

[0007]

The device shown in FIG. 10 of PTL 1 (hereinafter referred to as a device C) can perform DNA sequencing and DNA fragment analysis using a capillary having a short effective length. In the device C, the sample-injection end is directed vertically downward, the sample-elution end is directed vertically upward, and the entire capillary is erected in a vertical direction. The sample-elution end is connected to an anode buffer tank containing the anode buffer solution via a flow path containing the polymer solution. Here, in order to prevent the polymer solution in the capillary from falling due to gravity, the cathode buffer tank has a sealed structure. In addition, similarly to the device A, the capillary can be filled with a high-viscosity polymer solution by applying a high pressure of 35 atm to the sample-elution end of the capillary by the plunger type pressurizing mechanism. In addition, a low pressure of 1 atm can be applied to the sample-injection end by an air type pressurizing mechanism. Further, since the cathode buffer tank has a sealed structure, the polymer solution can be more effectively prevented from falling due to gravity. In this state, when the sample-injection end is immersed in the sample solution, and a voltage is applied to both ends of the capillary, the sample can be injected into the capillary by an electric field.

[0008]

The plunger type pressurizing mechanism moves a solid in a direct contact with the liquid stored in the sealed container to compress the liquid and increase the pressure. A volume change of the solid and the liquid with respect to the pressure is smaller than that of the gas, and therefore, a high pressure can be obtained by a small movement of the solid. That is, the

plunger type pressurizing mechanism is a method suitable for applying a high pressure to the liquid stored in the sealed container. Even when a small amount of gas is contained in the sealed container, the increase in pressure due to the subsequent movement of the individual is increased when the volume of the gas is sufficiently reduced by pressurization. In addition, even when a small amount of gas is sandwiched between the liquid and the solid, and the solid that is in an indirect contact with the liquid stored in the sealed container is moved, a high pressure can be similarly obtained by the plunger type pressurizing mechanism.

[0009]

In contrast, the air type pressurizing mechanism compresses the liquid and increases the pressure by compressing the gas (increasing the density of the gas) that is in a direct contact with the liquid stored in the sealed container to increase the pressure. The volume change with respect to the pressure of the gas is large, and therefore, a large device is required to generate the compressed air. Therefore, it is necessary to place the sealed container and the large device at separate positions and connect them using an air tube, a connector, a valve, or the like. As a result, the volume and surface area of the compressed air to be handled also increase, so that a small pressure generates a large force, and leakage or rupture is likely to occur. For the above reasons, it is generally difficult to increase the pressure of compressed air to a high pressure, and compressed air having a low pressure of 5 atm or less is practically used. That is, the air type pressurizing mechanism is a method suitable for applying a low pressure to the liquid stored in the sealed container. In addition, even when a small amount of solid is sandwiched between the liquid and the gas, and the gas that is in indirect contact with the liquid stored in the sealed container is compressed, a low pressure can be similarly obtained by the air type pressurizing mechanism.

Citation List

Patent Literature

[0010]

PTL 1: JP2001-124736A

Non Patent Literature

[0011]

NPL 1: SeqStudio™ Flex Series Genetic Analyzer with Instrument Software v1.1,
USER GUIDE

https://assets.thermofisher.com/TFS-Assets/LSG/manuals/100104689_SeqStudioFlex_v1_RUO_UG.pdf

NPL 2: PA 800 Plus Pharmaceutical Analysis System, Methods Development Guide
<https://sciex.com/content/dam/SCIEX/pdf/customer-docs/user-guide/pa-800-plus-methods-development-guide.pdf>

Summary of Invention

Technical Problem

[0012]

In capillary electrophoresis, an injection amount of a sample using the electric field injection is proportional to the sample concentration when the sample concentration is low, but is saturated with respect to the sample concentration when the sample concentration is high. On the other hand, an injection amount of the sample using the pressure injection is proportional to a sample concentration regardless of the sample concentration. Therefore, in order to prepare a sample having a high concentration and obtain a larger injection amount, pressure injection may be superior to electric field injection. Further, as compared with the electric field injection, in the pressure injection, a linear relationship is obtained between the sample concentration and a peak intensity in a wide concentration range of the sample. From the above description, the pressure injection is expected to be superior to the electric field injection in terms of an improvement in sensitivity and an improvement in quantitative properties. In addition, both-end pressurizing function during electrophoresis contributes to preventing the generation of bubbles and stably obtaining high separation performance by increasing the pressure of the polymer solution inside the capillary. In particular, it is important to improve the decrease in the separation ability due to the generation of bubbles when injecting a large amount of high-concentration samples.

[0013]

The pressure injection of the sample and the pressurization at both ends during electrophoresis are expected to exhibit the same effects even when the DNA sequencing and the DNA fragment analysis are performed. The DNA sequencing and the DNA fragment analysis were performed in the device A using a high-viscosity polymer solution POP-7TM Polymer, for 3500/SeqStudioTM Flex (Thermo Fisher Scientific, hereinafter, POP-7) for the DNA sequencing and the DNA fragment analysis. The filling with the polymer solution was performed by applying a high pressure of 35 atm by the plunger type pressurizing mechanism, and therefore, the filling with the polymer solution could be performed within a practical time of about 5 minutes even though the polymer solution had a high viscosity. However, in the device A, the air type pressurizing mechanism cannot be used, and therefore, the pressure injection of the sample and the pressurization at both ends during electrophoresis (both-end pressurization electrophoresis) cannot be performed.

[0014]

Therefore, the DNA sequencing and the DNA fragment analysis were attempted using the device B including an air type pressurizing mechanism at both ends of a capillary. The sample-elution end of the capillary was immersed in a high-viscosity polymer solution POP-7, and a low pressure of 5 atm was applied by an air type pressurizing mechanism to vent the sample-elution end to the atmospheric pressure. However, the viscosity of POP-7 was greater than the viscosity of a polymer solution for protein analysis (for example, SDS-MW Gel Buffer manufactured by Sciex) normally used in the device B, and the filling speed of the polymer solution was significantly reduced. Therefore, filling with the polymer solution cannot be performed within a practical time. Therefore, it is difficult to perform the DNA sequencing and the DNA fragment analysis using the device B.

[0015]

Next, the DNA sequencing and the DNA fragment analysis were performed using the device C. Similarly to the device A, the high-viscosity polymer solution POP-7 could be subjected to the filling with the polymer solution within a practical time by applying a high pressure of 35 atm by the plunger type pressurizing mechanism provided at the sample-elution

end. On the other hand, it was found that the pressure injection of the sample cannot be performed even though a low pressure of 1 atm can be applied to the sample-injection end by the air type pressurizing mechanism provided at the sample-injection end. This is because the anode buffer tank to which the sample-elution end is connected has a sealed structure and cannot be vented to the atmospheric pressure, so that the pressure applied to the sample-injection end is transmitted to the entire polymer solution inside the capillary, and no pressure difference occurs between both ends of the capillary.

[0016]

In view of the above, the invention proposes a capillary electrophoresis technique for achieving any one of providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (2) "capable of performing pressure injection of a sample" (a first object); providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (3) "capable of performing pressurization at both ends during electrophoresis" (a second object); and providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", (2) "capable of performing pressure injection of a sample", and (3) "capable of performing pressurization at both ends during electrophoresis" (a third object).

Solution to Problem

[0017]

In order to solve the above problems, the invention proposes a capillary electrophoresis device including a first liquid system with which a first capillary end of a capillary is in contact; a second liquid system with which a second capillary end of the capillary is in contact; a power supply configured to apply a voltage between the first liquid system and the second liquid system; a first pressurizing mechanism configured to compress a first gas in direct or indirect contact with a first interface of the first liquid system to increase a first pressure of the first liquid

system; a first depressurizing mechanism configured to reduce the first pressure of the first liquid system; a second pressurizing mechanism configured to move a solid in direct or indirect contact with a second interface of the second liquid system to increase a second pressure of the second liquid system; and a second depressurizing mechanism configured to reduce the second pressure of the second liquid system. The second liquid system has a second gas in direct or indirect contact with a third interface different from the second interface, which is an interface inside a container holding a liquid when the capillary is filled with the liquid.

[0018]

Additional features related to the present disclosure will be clarified based on the description of the present description and the accompanying drawings. Aspects of the present disclosure may be achieved and implemented using elements, combinations of various elements, the following detailed description, and accompanying claims.

The description of the present description is merely a typical illustration and does not limit the scope of the claims or application examples of the present disclosure in any sense.

Advantageous Effects of Invention

[0019]

According to an aspect of the invention (the configuration of the device F: the device F will be described below), the filling with the polymer solution within a practical time can be performed using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis, and pressure injection of the sample can also be performed. Therefore, in DNA sequencing and DNA fragment analysis, sensitivity can be improved by a larger sample injection amount than the related art, and highly quantitative analysis can be performed. In addition, according to another aspect of the invention (the configuration of the device I: the device I will be described below), in addition to the effect of the device F, both-end pressurization electrophoresis can be performed. Therefore, the generation of bubbles can be prevented, and high separation performance can be stably obtained.

Brief Description of Drawings

[0020]

FIG. 1 is a diagram showing a configuration example of a related device 1 in which atmospheric pressure electrophoresis is performed.

FIG. 2 is a diagram showing a configuration example of the related device 1 in which filling with a polymer solution at a high pressure is performed.

FIG. 3 is a diagram showing a configuration example of the related device 1 in which electric field injection of a sample is performed.

FIG. 4 is a diagram showing a configuration example of a related device 2 in which both-end pressurization electrophoresis is performed.

FIG. 5 is a diagram showing a configuration example of the related device 2 in which a low pressure polymer solution filling is performed.

FIG. 6 is a diagram showing a configuration example of the related device 2 in which electric field injection of a sample is performed.

FIG. 7 is a diagram showing a configuration example of a capillary electrophoresis device according to Modified Example 1, in which atmospheric pressure electrophoresis is performed.

FIG. 8 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 1) according to Modified Example 2, in which atmospheric pressure electrophoresis is performed.

FIG. 9 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 1) according to Modified Example 2, in which filling with a polymer solution at a high pressure is performed.

FIG. 10 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 1) according to Modified Example 2, in which pressure injection of a sample is performed.

FIG. 11 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 2) according to Modified Example 3, in which atmospheric pressure electrophoresis is performed.

FIG. 12 is a diagram showing a configuration example of the capillary electrophoresis

device (Embodiment 2) according to Modified Example 3, in which filling with a polymer solution at a high pressure is performed.

FIG. 13 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 2) according to Modified Example 3, in which pressure injection of a sample is performed.

FIG. 14 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 2) according to Modified Example 3, in which both-end pressurization electrophoresis is performed.

FIG. 15 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 3) according to Modified Example 4, in which filling with a polymer solution at a high pressure is performed.

FIG. 16 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 3) according to Modified Example 4, in which pressure injection of a sample is performed.

FIG. 17 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 4) according to Modified Example 5, in which both-end pressurization electrophoresis is performed.

FIG. 18 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 4) according to Modified Example 5, in which filling with a polymer solution at a high pressure is performed.

FIG. 19 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 4) according to Modified Example 5, in which pressure injection of a sample is performed.

FIG. 20 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 5) according to Modified Example 6, in which both-end pressurization electrophoresis is performed.

FIG. 21 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 6) according to Modified Example 7, in which both-end pressurization electrophoresis is performed.

FIG. 22 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 7) according to Modified Example 8, in which both-end pressurization electrophoresis is performed.

FIG. 23 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 7) according to Modified Example 8, in which filling with a polymer solution at a high pressure is performed.

FIG. 24 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 7) according to Modified Example 8, in which pressure injection of a sample is performed.

FIG. 25 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 8) according to Modified Example 9, in which both-end pressurization electrophoresis is performed.

FIG. 26 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 8) according to Modified Example 9, in which filling with a polymer solution at a high pressure is performed.

FIG. 27 is a diagram showing a configuration example of the capillary electrophoresis device (Embodiment 8) according to Modified Example 9, in which pressure injection of a sample is performed.

FIG. 28 is a diagram showing a configuration example of a capillary electrophoresis device (Embodiment 9) according to Modified Example 10, in which both-end pressurization electrophoresis is performed.

FIG. 29 is an electropherogram obtained by electric field injection using the capillary electrophoresis device (Embodiment 2) according to Modified Example 3.

FIG. 30 shows a relationship between an electric field injection time and a peak area in FIG. 29.

FIG. 31 is an electropherogram obtained by pressure injection using Modified Example 3 (Embodiment 2).

FIG. 32 shows a relationship between a pressure injection time and a peak area in FIG. 31.

FIG. 33 shows steps of capillary electrophoresis analysis using electric field injection.

FIG. 34 shows steps of capillary electrophoresis analysis using pressure injection.

FIG. 35 shows steps of capillary electrophoresis analysis using pressure injection and both-end pressurization electrophoresis.

Description of Embodiments

[0021]

A configuration of a capillary electrophoresis device of the invention (Modified Example) and characteristics of an analysis method will be described in comparison with a related method. Hereinafter, in order to simplify the description, a capillary electrophoresis device using one capillary is mainly handled, but this method may be used for a multi-capillary electrophoresis device using a plurality of capillaries.

In the following embodiments, a plurality of devices having different configurations will be referred to as a device A, a device B, and the like respectively (note that the devices A, B, and C are also described in the background art). In the following description, in order to handle a plurality of different devices, the plurality of devices having different configurations will be described in detail as Related Example 1, Related Example 2, and the like regarding a related method (Related Example) and will be described in detail as Modified Example 1, Modified Example 2, and the like as a novel method (Modified Example) with reference to the drawings. However, a mutual correspondence relationship is described each time.

[0022]

Each device is provided with a temperature control device for maintaining a temperature of a capillary constant, but the description of the temperature control device is omitted in the description of each drawing. For example, when DNA sequencing and DNA fragment analysis are performed, the temperature of the capillary is preferably adjusted to 60°C.

[0023]

As shown in the upper left of each drawing of the present description, a right-handed XYZ orthogonal coordinate system is defined in each drawing. That is, in each drawing, an X axis is taken in a horizontal direction, a rightward direction is taken as a positive direction of the

X axis, a Z axis is taken in a direction perpendicular to the X axis, an upward direction is taken as a positive direction of the Z axis, a Y axis is taken in a direction perpendicular to a paper surface, and a backward direction with respect to the paper surface is taken as a positive direction of the Y axis. In each drawing, the same reference numerals are given to components having the same structure and the same function.

[0024]

In the present description, the entire liquid (a buffer solution, a polymer solution, a sample solution, etc.) in which a capillary end (a sample-injection end or a sample-elution end) is immersed is defined as a liquid system. The liquid system is a continuous series of liquids (does not need to be contained in one container), and can change every time (for example, when the liquid system is divided by a valve, the liquid system is reduced). A composition of one liquid system does not need to be uniform (for example, when the buffer solution and the polymer solution are in contact with each other without mixing, they may be collectively referred to as one liquid system).

[0025]

<Related Example 1>

FIGS. 1 to 3 are diagrams showing a configuration example of a capillary electrophoresis device (corresponding to a device A) according to Related Example 1 and an analysis method using the capillary electrophoresis device. A sample-injection end 2 of one capillary 1 is disposed on a right side, a sample-elution end 3 is disposed on a left side, and each of the sample-injection end 2 and the sample-elution end 3 is disposed vertically downward (toward a -Z-axis direction). A plunger type pressurizing mechanism is provided on an anode side (sample-elution end side). FIG. 1 shows a state in which electrophoresis (atmospheric pressure electrophoresis) is performed in Related Example 1. A sample is injected from the sample-injection end 2 into the capillary 1 (outer diameter: 360 μm , inner diameter: 50 μm) filled with a polymer solution 18 (POP-7), the sample is electrophoresed in the capillary toward the sample-elution end 3, and a plurality of different components contained in the sample are separated by the electrophoresis based on the charge and size. The sample-injection end 2 is inserted into a pipe-shaped cathode 4, and the two are integrated. A cathode buffer solution

tank 8 storing a cathode buffer solution 6 and a sample solution tank 11 storing a sample solution 10 are fixed onto a cathode stage 12, and the cathode stage 12 is coupled to an XYZ axis drive mechanism (not shown). Of course, other containers such as a plurality of sample solution tanks storing different samples are also fixed onto the cathode stage 12, but the other containers are not shown for simplicity. The sample-injection end 2 equipped with the cathode 4 is inserted into the cathode buffer solution tank 8 and immersed in the cathode buffer solution 6. The sample-elution end 3 is connected to an acrylic T block 15 filled with the polymer solution 18 using a connector 14, and immersed in the polymer solution 18. An inverted T-shaped flow path is formed inside the T block 15, and the flow path is filled with the polymer solution 18. A pressure-resistant syringe 16 and a polymer solution tube 19 are also connected to the T block 15, and the two are filled with the polymer solution 18 (which are not shown although they are connected using connectors). Each connection portion is sealed so that the contents do not leak out even when a pressure of the polymer solution inside increases (having a pressure resistance performance). An anode buffer solution tank 9 storing an anode buffer solution 7 is fixed onto an anode stage 13. An end of the polymer solution tube 19 opposite to the T block 15 is inserted into the anode buffer solution tank 9 and immersed in the anode buffer solution 7. A polymer solution valve 20 is placed at a boundary between the polymer solution 18 and the anode buffer solution 7 at an end portion of the polymer solution tube 19. The polymer solution valve 20 has a plunger portion that moves up and down (Z-axis direction), and when the plunger portion moves upward (+Z-axis direction), the polymer solution valve 20 is opened, and when the plunger portion moves downward (-Z-axis direction), the polymer solution valve 20 is closed.

[0026]

Although only the plunger portion of the polymer solution valve 20 is shown in FIG. 1, the polymer solution valve 20 actually includes a solenoid mechanism (not shown) for moving the plunger portion up and down and a connection mechanism (not shown) for interlocking the solenoid mechanism and the plunger portion. The cylindrical anode 5 is inserted into the anode buffer solution tank 9 and immersed in the anode buffer solution 7. The anode 5 and the cathode 4 are connected to a DC power supply 21 by an electric wire 22. A voltage is applied between the anode 5 and the cathode 4, that is, a voltage is applied between the sample-elution

end 3 and the sample-injection end 2 of the capillary 1 to perform atmospheric pressure electrophoresis. A vertical height (Z coordinate) of an interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and a vertical height (Z coordinate) of an interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. For example, a difference in height between the two liquid surfaces may be 1 mm or less. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis. A position on the capillary 1 where electrophoresis is performed by a certain distance from the sample-injection end 2 is used as a detection position, and a polyimide coating of the capillary in a vicinity of the detection position is removed in advance. The detection position is irradiated with a laser beam 24 emitted from a laser light source 23, and fluorescence emitted from the detection position is detected by a fluorescence detection device (not shown).

[0027]

FIG. 2 shows a state in which the capillary 1 is filled with the polymer solution 18 at a high pressure in the capillary electrophoresis device according to Related Example 1. With this filling, the polymer solution 18 already filled in the capillary 1 can be replaced with the newly filled polymer solution 18. The polymer solution valve 20 is closed to mechanically push the plunger 17 of the pressure-resistant syringe 16 using a motor, and pressure is applied to the polymer solution 18 inside. The polymer solution 18 in the polymer solution tube 19, the polymer solution 18 in the T block 15, and the polymer solution 18 in the pressure-resistant syringe 16 form a continuous liquid system. The liquid system fills a sealed space, and the sealed space contains almost no air. In addition, the sample-elution end 3 is immersed in the liquid system. In this state, since the plunger 17 as a solid directly pressurizes the polymer solution 18 as a liquid at the interface 104 between the plunger 17 and the polymer solution 18, a high pressure of about 70 atm at the maximum can be obtained. Even if a gas such as air is introduced between the plunger 17 and the polymer solution 18, the plunger 17 can indirectly pressurize the polymer solution 18, and the same high pressure can be obtained when a volume of the gas is sufficiently small. The high pressure is transmitted to the entire liquid system including the sample-elution end 3.

[0028]

In each drawing of the present description, the polymer solution under atmospheric pressure is indicated by a vertical dotted line pattern, and the polymer solution under high pressure is indicated by a checkered pattern. Therefore, in FIG. 1, the liquid system under atmospheric pressure is indicated by a vertical dotted line pattern, and in FIG. 2, the liquid system under high pressure is indicated by a checkered pattern. Since the sample-injection end 2 is under atmospheric pressure, a high pressure difference is generated between the sample-elution end 3 and the sample-injection end 2, and the capillary 1 is filled with the polymer solution 18 from the sample-elution end 3 toward the sample-injection end 2. The pressure applied to the liquid system can be controlled by controlling a force of the motor that pushes the plunger 17 in. Actually, a high pressure of 35 atm is applied to the liquid system to fill the capillary 1 with the polymer solution 18 at a high pressure. After the filling with the polymer solution, the mechanical pushing-in of the plunger 17 is stopped, the plunger 17 and the mechanical pushing mechanism are separated, and the pressure applied to the liquid system is reduced to substantially zero. However, in practice, some pressure may remain. Therefore, the polymer solution valve 20 is opened to vent the sample-elution end 3 and the liquid system to the atmospheric pressure.

[0029]

FIG. 3 shows a state in which a sample is being injected into the capillary 1 by an electric field in Related Example 1. The sample-injection end 2 is inserted into the sample solution tank 11 and immersed in the sample solution 10 by a movement of the cathode stage 12 using the XYZ axis drive mechanism. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 of the capillary 1 for a certain period of time to inject the sample into the capillary 1 by the electric field from the sample-injection end 2. At this time, the vertical height (Z coordinate) of an interface 105 between the sample solution 10 and air (that is, a liquid surface of the sample solution 10) and the vertical height (Z coordinate) of the interface 102 (that is, the liquid surface of the anode buffer solution 7) do not need to be equalized necessarily. When these heights deviate, the polymer solution 18 inside the capillary 1 may move due to gravity. However, if the time of electric field injection is short, the

influence is small.

[0030]

Thereafter, the sample-injection end 2 is inserted into the cathode buffer solution tank 8 and immersed in the cathode buffer solution 6 by the movement of the cathode stage 12 using the XYZ axis drive mechanism. Returning to the state shown in FIG. 1, a voltage is applied between the sample-elution end 3 and the sample-injection end 2, and both ends of the capillary 1 are placed under atmospheric pressure to perform electrophoresis (atmospheric pressure electrophoresis). The vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis.

[0031]

As described above, the capillary electrophoresis device according to Related Example 1 does not include an air type pressurizing device, and therefore, pressure injection of a sample cannot be performed, and pressurization at both ends during electrophoresis cannot be performed.

[0032]

<Related Example 2>

FIGS. 4 to 6 show a configuration of a capillary electrophoresis device (corresponding to the device B) according to Related Example 2 and an analysis method using the capillary electrophoresis device. Hereinafter, a description of a portion overlapping with Related Example 1 will be partially omitted, and a portion different from Related Example 1 will be mainly described. An air type pressurizing mechanism is provided on a cathode side (sample-injection end side), and an air type pressurizing mechanism is also provided on an anode side (sample-elution end side).

[0033]

FIG. 4 shows a state in which electrophoresis (both-end pressurization electrophoresis) is performed in the capillary electrophoresis device according to Related Example 2. The

sample-injection end 2 is inserted into the pipe-shaped cathode 4, and the two are integrated. The cathode buffer solution tank 8 storing the cathode buffer solution 6 and the sample solution tank 11 storing the sample solution 10 are fixed onto the cathode stage 12, and the cathode stage 12 is coupled to the XYZ axis drive mechanism (not shown). Of course, other containers such as a plurality of sample solution tanks storing different samples, a polymer solution tank storing a polymer solution, and a waste liquid tank storing a waste liquid can also be fixed onto the cathode stage 12, but these containers are not illustrated for simplicity.

[0034]

An O-ring 33 is placed at an edge of an upper end of each of the cathode buffer solution tank 8 and the sample solution tank 11. A fixed block 31 has a plane parallel to the XY plane and facing the -Z direction. With the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the cathode buffer solution tank 8 together with the cathode 4 and immersed in the cathode buffer solution 6. At the same time, with a movement of the cathode stage 12 in the +Z direction, the O-ring 33 is pressed against a flat surface portion of the fixed block 31 and compressed to seal the cathode buffer solution tank 8.

[0035]

A gap among the capillary 1, the cathode 4, and the fixed block 31 is sealed. At this time, the cathode buffer solution tank 8 contains the cathode buffer solution 6 and air 34 in contact with the cathode buffer solution 6. The air 34 is connected to a compressed air source 25 or the atmosphere by a cathode pressurizing valve 28 and a cathode release valve 29 via an air tube 30. The pressure of the compressed air discharged from the compressed air source 25 can be adjusted and controlled to a constant low pressure of 0 atm to 7 atm.

[0036]

As shown in FIG. 4, when the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, the air 34 is connected to the compressed air source 25, the compressed air flows into the cathode buffer solution tank 8 via the air tube 30, and the pressure of the air 34 increases until it becomes equal to the pressure of the compressed air discharged from the compressed air source 25. At the same time, the pressure of the cathode buffer

solution 6 contained in the cathode buffer solution tank 8 also increases until it becomes equal to the pressure of the compressed air discharged from the compressed air source 25. In each drawing of the present description, air under atmospheric pressure is indicated by a blank pattern, and air under a low pressure is indicated by a dot pattern. The buffer solution under atmospheric pressure is indicated by a horizontal dotted line pattern, and the buffer solution under low pressure is indicated by a horizontal solid line pattern. Therefore, in FIG. 4, the air 34 under the low pressure is indicated by a dot pattern, and in FIG. 5, the air 34 under atmospheric pressure is indicated by a blank pattern. In FIG. 4, the cathode buffer solution 6 under the low pressure is indicated by a horizontal solid line pattern, and in FIG. 5, the cathode buffer solution 6 under atmospheric pressure is indicated by a horizontal dotted line pattern. These patterns are commonly used in other drawings.

[0037]

The anode side has a device configuration similar to that of the cathode side. The sample-elution end 3 is inserted into the pipe-shaped anode 5, and the two are integrated. The anode buffer solution tank 9 storing the anode buffer solution 7 and the polymer solution tank 32 storing the polymer solution 18 are fixed onto the anode stage 13, and further, the anode stage 13 is coupled to an XYZ axis drive mechanism (not shown). Of course, other containers such as a plurality of sample solution tanks storing different samples and a waste liquid tank storing a waste liquid can also be fixed onto the anode stage 13, but these containers are not illustrated for simplicity.

[0038]

The O-ring 33 is placed at an edge of an upper end of each of the anode buffer solution tank 9 and the polymer solution tank 32. The fixed block 31 has a plane parallel to the XY plane and facing the -Z direction. With a movement of the cathode stage 13 using the XYZ axis drive mechanism, the sample-elution end 3 is inserted into the anode buffer solution tank 9 together with the anode 5 and immersed in the anode buffer solution 7. At the same time, with a movement of the anode stage 13 in the +Z direction, the O-ring 33 is pressed against the flat surface portion of the fixed block 31 and compressed to seal the anode buffer solution tank 9. A gap among the capillary 1, the anode 5, and the fixed block 31 is sealed. At this time, the

anode buffer solution tank 9 contains the anode buffer solution 7 and air 35 in contact with the anode buffer solution 7. The air 35 is connected to the compressed air source 25 or the atmosphere by an anode pressurizing valve 26 and an anode release valve 27 via the air tube 30. [0039]

As shown in FIG. 4, when the anode pressurizing valve 26 is opened, and the anode release valve 27 is closed, the air 35 is connected to the compressed air source 25, the compressed air flows into the anode buffer solution tank 9 via the air tube 30, and the pressure of the air 35 increases until it becomes equal to the pressure of the compressed air discharged from the compressed air source 25. At the same time, the pressure of the anode buffer solution 7 contained in the anode buffer solution tank 9 also increases until it becomes equal to the pressure of the compressed air discharged from the compressed air source 25. Similarly to the cathode side, in FIG. 4, the air 35 under the low pressure is indicated by a dot pattern, and in FIG. 5, the air 35 under atmospheric pressure is indicated by a blank pattern. In FIG. 4, the anode buffer solution 7 under the low pressure is indicated by a horizontal solid line pattern, and in FIG. 5, the anode buffer solution 7 under atmospheric pressure is indicated by a horizontal dotted line pattern.

[0040]

As described above, when the pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm, a low pressure of 1 atm is applied to both the cathode buffer solution 6 and the anode buffer solution 7, and a low pressure of 1 atm is applied to both ends, i.e., the sample-injection end 2 and the sample-elution end 3 of the capillary 1. In this state, a voltage is applied between the anode 5 and the cathode 4 to apply a voltage to both ends, i.e., the sample-injection end 2 and the sample-elution end 3 of the capillary 1, thereby performing both-end pressurization electrophoresis. Accordingly, the pressure of the polymer solution 18 in the capillary 1 is increased to 1 atm, the generation of bubbles in the capillary 1 during electrophoresis is prevented, and high separation performance can be stably obtained. Further, the vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid

surface of the anode buffer solution 7) are equalized. For example, the difference in height between the two liquid surfaces may be 1 mm or less. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis.

[0041]

FIG. 5 shows a state in which the capillary 1 is filled with the polymer solution 18 at a low pressure in the capillary electrophoresis device according to Related Example 2. With the movement of the anode stage 13 using the XYZ axis drive mechanism, the sample-elution end 3 is inserted into the polymer solution tank 32 together with the anode 5 and immersed in the polymer solution 18, and at the same time, the O-ring 33 is pressed against the fixed block 31 and compressed to seal the polymer solution tank 32. The pressure of the compressed air discharged from the compressed air source 25 is set to 5 atm. The anode pressurizing valve 26 is opened, and the anode release valve 27 is closed to cause the compressed air to flow into the polymer solution tank 32 via the air tube 30, and the pressure of the polymer solution 18 inside the polymer solution tank 32 and the pressure of the air 36 in contact with the polymer solution 18 are increased to 5 atm.

[0042]

In FIG. 5, the air 36 under a low pressure of 5 atm is indicated by a dot pattern. In addition, in each drawing of the present description, the polymer solution under the atmospheric pressure is indicated by a vertical dotted line pattern, and the polymer solution under the low pressure is indicated by a vertical solid line pattern. Therefore, in FIG. 5, the polymer solution 18 under the low pressure is indicated by a vertical solid line pattern. These patterns are commonly used in other drawings.

[0043]

On the other hand, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to connect the air 34 inside the cathode buffer solution tank 8 to the atmosphere, and the pressure of the air 34 is set to the atmospheric pressure (0 atm). The air 34 is indicated by a blank pattern, and the cathode buffer solution 6 is indicated by a horizontal dotted line pattern indicating the atmospheric pressure. Accordingly, a low pressure difference of 5 atm is generated between the sample-elution end 3 and the sample-injection end 2, and the

capillary 1 is filled with the polymer solution 18 at a low pressure from the sample-elution end 3 toward the sample-injection end 2. After filling with the polymer solution, the anode pressurizing valve 26 is closed, and the anode release valve 27 is opened to discharge a part of the air 36 inside the anode buffer solution tank 9 to the atmosphere via the air tube 30, and the pressure of the polymer solution 18 and the pressure of the air 36 are brought to atmospheric pressure.

[0044]

FIG. 6 shows a state in which a sample is injected into the capillary 1 by pressure in the capillary electrophoresis device according to Related Example 2. With the movement of the anode stage 13 using the XYZ axis drive mechanism, the sample-elution end 3 is inserted into the anode buffer solution tank 9 and immersed in the anode buffer solution 7. The pressure of the anode buffer solution 7 and the pressure of the air 32 inside the anode buffer solution tank 9 are atmospheric pressure. On the other hand, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the sample solution tank 11 and immersed in the sample solution 10, and at the same time, the O-ring 33 is pressed against the fixed block 31 and compressed to seal the sample solution tank 11. The pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm. When the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, the pressure of the sample solution 10 inside the sample solution tank 11 and the pressure of the air 37 in contact with the sample solution 10 increase to 1 atm.

[0045]

In each drawing of the present description, the sample solution under atmospheric pressure is indicated by a horizontal dotted line pattern, and the sample solution under the low pressure is indicated by a horizontal solid line pattern. Therefore, in FIG. 6, the sample solution 10 under the low pressure is indicated by a horizontal solid line pattern. These patterns are commonly used in other drawings. Similarly, the air 37 under the low pressure is indicated by a dot pattern. As described above, a low pressure difference of 1 atm is generated between the sample-injection end 2 and the sample-elution end 3, and the sample solution 10 is injected into the capillary 1 from the sample-injection end 2. After a predetermined time has elapsed,

the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the pressure of the sample solution 10 and the pressure of the air 37 inside the cathode sample solution tank 11 to the atmospheric pressure. The sample can also be injected by an electric field by applying a voltage between the sample-elution end 3 and the sample-injection end 2 in this state.

[0046]

Thereafter, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the cathode buffer solution tank 8 and immersed in the anode buffer solution 6, and at the same time, the cathode buffer solution tank 8 is sealed. When the anode pressurizing valve 26 is opened, the anode release valve 27 is closed, the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, all of the cathode buffer solution 7 and the air 35 inside the anode buffer solution tank 9 and the cathode buffer solution 6 and the air 34 inside the cathode buffer solution tank 8 are pressurized to 1 atm, and the state returns to the state shown in FIG. 4. The compressed air introduced into the anode buffer solution tank 9 and the cathode buffer solution tank 8 originates from the same compressed air source 25, and therefore, the pressure inside the anode buffer solution tank 9 and the pressure inside the cathode buffer solution tank 8 are strictly equal. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform both-end pressurization electrophoresis. Accordingly, the pressure of the polymer solution 18 in the capillary 1 is increased to 1 atm, the generation of bubbles in the capillary 1 during electrophoresis is prevented, and high separation performance can be stably obtained. Further, the vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis.

[0047]

<Modified Example 1>

FIG. 7 shows a configuration example of a capillary electrophoresis device

(corresponding to the device D) according to Modified Example 1. Modified Example 1 is implemented by modifying Related Example 2. However, as a result of the study, it has been found that Modified Example 1 cannot achieve the object of the invention as in the device C of PTL 1.

[0048]

In Modified Example 1, an air type pressurizing mechanism is provided on the cathode side (sample-injection end side), and a plunger type pressurizing mechanism is provided on the anode side (sample-elution end side). FIG. 7 shows a state in which atmospheric pressure electrophoresis is performed in the capillary electrophoresis device according to Modified Example 1. The configuration on the cathode side is the same as that of the related device 2. However, unlike FIG. 4, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the inside of the cathode buffer solution tank 8 to the atmospheric pressure. Similarly to Related Example 2, the sample-elution end 3 is inserted into the pipe-shaped anode 5, and the two are integrated. The pressure-resistant syringe 16 containing the polymer solution 18 and the polymer solution tank 32 containing the polymer solution 18 are coupled and fixed onto the anode stage 13. The sample-elution end 3 is inserted into the polymer solution tank 32 together with the anode 5 and immersed in the polymer solution 18, and at the same time, the polymer solution tank 32 is sealed. However, unlike the related device 2, a sealed structure of the polymer solution tank 32 cannot be easily eliminated.

[0049]

The polymer solution tank 32 and the pressure-resistant syringe 16 have one internal space, and the internal space is filled with the polymer solution 18 to form one liquid system. The internal space contains almost no air. When a voltage is applied between the sample-elution end 3 and the sample-injection end 2 in this state, electrophoresis can be performed. Further, while the cathode buffer solution 6 and the air 34 inside the cathode buffer solution tank 8 are vented to the atmospheric pressure, the plunger 17 of the pressure-resistant syringe 16 is mechanically pushed in, so that the pressure of the polymer solution inside the polymer solution tank 32 and the syringe 16 is increased to 35 atm, and the capillary 1 can be filled with the polymer solution 18 at a high pressure (not shown).

[0050]

However, it has been found that the pressure injection of the sample was not performed even when the sample-injection end 2 was inserted into the sample solution tank 11, the sample solution tank 11 was sealed, and the internal pressure was increased to 1 atm as in Related Example 2 after the mechanical pushing-in of the plunger 17 was stopped. This is because the pressure of the sample-injection end and the pressure of the sample-elution end become equal (1 atm), and a pressure difference cannot be obtained between both ends because the sealed structure of the polymer solution tank 32 is maintained. This structural problem is the same as the problem of the device C in PTL 1. Therefore, Modified Example 1 cannot implement any of the first to third objects of the invention.

[0051]

<Modified Example 2: Embodiment 1>

FIGS. 8 to 10 show a configuration example of a capillary electrophoresis device according to Modified Example 2 (Embodiment 1) and an analysis method using the capillary electrophoresis device. Modified Example 2 (Embodiment 1) is implemented by modifying Related Example 2, and is configured to solve the problem of Modified Example 1.

[0052]

The capillary electrophoresis device according to Modified Example 2 (Embodiment 1) includes an air type pressurizing mechanism on the cathode side (sample-injection end side) and a plunger type pressurizing mechanism on the anode side (sample-elution end side). FIG. 8 shows a state in which atmospheric pressure electrophoresis is performed in Modified Example 2 (Embodiment 1). The configuration on the cathode side is the same as that of Related Example 2. However, unlike FIG. 4, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the inside of the cathode buffer solution tank 8 to the atmospheric pressure. Similarly to Related Example 2, the sample-elution end 3 is inserted into the pipe-shaped anode 5, and the two are integrated. The anode buffer solution tank 9 containing the anode buffer solution 7 and the polymer solution tank 32 to which the pressure-resistant syringe 16 containing the polymer solution 18 is coupled are fixed onto the anode stage 13, and further, the anode stage 13 is coupled to an XYZ axis drive mechanism (not shown).

[0053]

The O-ring 33 is not placed at the edge of the upper end of the anode buffer solution tank 9, and the O-ring 33 is placed at an upper end of the polymer solution tank 32. With the movement of the cathode stage 13 using the XYZ axis drive mechanism, the sample-elution end 3 is inserted into the anode buffer solution tank 9 and immersed in the anode buffer solution 7. Unlike Related Example 2 and Modified Example 1, the anode buffer solution tank 9 is not sealed, and the anode buffer solution 7 inside is vented to the atmospheric pressure. A voltage is applied between the sample-elution end 3 and the sample-injection end 2 of the capillary 1 to perform atmospheric pressure electrophoresis. The vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. For example, the difference in height between the two liquid surfaces may be 1 mm or less. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis.

[0054]

FIG. 9 shows a state in which the capillary 1 is filled with the polymer solution 18 at a high pressure in a capillary electrophoresis device according to Modified Example 2 (Embodiment 1). With the movement of the anode stage 13 using the XYZ axis drive mechanism, the sample-elution end 3 is inserted into the polymer solution tank 32 and immersed in the polymer solution 18, and at the same time, the O-ring 33 is pressed against the fixed block 31 and compressed to seal the polymer solution tank 32. The polymer solution tank 32 and the pressure-resistant syringe 16 are integrated to have one internal space, and the internal space is filled with the polymer solution 18 and contains almost no air. While the cathode buffer solution 6 and the air 34 inside the cathode buffer solution tank 8 are vented to the atmospheric pressure, the plunger 17 of the pressure-resistant syringe 16 is mechanically pushed in to increase the pressure of the polymer solution 18 inside the polymer solution tank 32 and the syringe 16 to 35 atm, and the capillary 1 is filled with the polymer solution 18 at a high pressure. After the filling with the polymer solution, the mechanical pushing-in of the plunger 17 is

stopped, the plunger 17 and the mechanical pushing mechanism are separated, and the pressure applied to the polymer solution 18 is reduced to substantially zero. However, in practice, some pressure may remain. Therefore, with the movement of the anode stage 13 in the -Z-axis direction using the XYZ axis drive mechanism, the compression of the O-ring is released to vent the polymer solution 18 to the atmospheric pressure.

[0055]

FIG. 10 shows a state in which a sample is injected into the capillary 1 by pressure in the capillary electrophoresis device according to Modified Example 2 (Embodiment 1). With the movement of the anode stage 13 using the XYZ axis drive mechanism, the sample-elution end 3 is inserted into the anode buffer solution tank 9 and immersed in the anode buffer solution 7. The pressure of the anode buffer solution 7 inside the anode buffer solution tank 9 is atmospheric pressure.

[0056]

On the other hand, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the sample solution tank 11 and immersed in the sample solution 10, and at the same time, the O-ring 33 is pressed against the fixed block 31 and compressed to seal the sample solution tank 11. The pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm. When the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, the pressure of the sample solution 10 inside the sample solution tank 11 and the pressure of the air 37 in contact with the sample solution 10 increase to 1 atm. As described above, a low pressure difference of 1 atm is generated between the sample-injection end 2 and the sample-elution end 3, and the sample solution 10 is injected into the capillary 1 from the sample-injection end 2. After a predetermined time has elapsed, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the pressure of the sample solution 10 and the pressure of the air 37 inside the cathode sample solution tank 11 to the atmospheric pressure.

[0057]

Thereafter, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the cathode buffer solution tank 8 and

immersed in the anode buffer solution 6, and at the same time, the cathode buffer solution tank 8 is sealed. However, when the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the inside of the cathode buffer solution tank 8 to the atmospheric pressure, the state returns to the state shown in FIG. 8. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform atmospheric pressure pressurization electrophoresis.

[0058]

Therefore, Modified Example 2 (Embodiment 1) can achieve the first object of the invention, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", and (2) "capable of performing pressure injection of a sample". However, Modified Example 2 (Embodiment 1) does not achieve the second and third objects of the invention.

[0059]

In Modified Example 2 (Embodiment 1), not only pressure injection of the sample but also electric field injection can be performed. In FIG. 10, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the sample solution 10 in the sample solution tank 11 and the air 37 in contact therewith to the atmospheric pressure. In this state, the sample can be injected into the capillary 1 by an electric field from the sample-injection end 2 by applying a voltage between the sample-elution end 3 and the sample-injection end 2 for a certain period of time.

[0060]

<Modified Example 3: Embodiment 2>

FIGS. 11 to 13 show a configuration example of a capillary electrophoresis device (corresponding to the device F) according to Modified Example 3 (Embodiment 2). Modified Example 3 (Embodiment 2) is implemented by modifying Related Example 2 (FIGS. 4 to 6). Further, Modified Example 3 has a configuration different from that of Modified Example 2 (FIGS. 8 to 10), but produces an effect equivalent to that of Modified Example 2.

[0061]

The capillary electrophoresis device according to Modified Example 3 (Embodiment 2) includes an air type pressurizing mechanism on the cathode side (sample-injection end side) and a plunger type pressurizing mechanism on the anode side (sample-elution end side). FIG. 11 shows a state in which atmospheric pressure electrophoresis is performed in the capillary electrophoresis device according to Modified Example 3 (Embodiment 2). The configuration on the cathode side is the same as that of Related Example 2. However, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the inside of the cathode buffer solution tank 8 to the atmospheric pressure. On the anode side, first, the sample-elution end 3 and the anode 5 that are integrated are separated, and the anode 5 is changed from a pipe shape to a cylindrical shape. The sample-elution end 3 is connected to the acrylic T block 15 filled with the polymer solution 18 using the connector 14, and immersed in the polymer solution 18. An inverted T-shaped flow path is formed inside the T block 15, and the flow path is filled with the polymer solution 18. The pressure-resistant syringe 16 and the polymer solution tube 19 are also connected to the T block 15, and both are filled with the polymer solution 18 (which are not shown, although they are connected using connectors). A material of the polymer solution tube 19 used in the invention does not necessarily have flexibility.

[0062]

When a high pressure is applied to the polymer solution 18 inside, it is necessary to use a high-pressure-resistant material. Teflon (registered trademark) resin or PEEK can be used. Alternatively, similarly to the T block 15, the flow path may be formed in a block made of acrylic or the like. Each connection portion is sealed so that the contents do not leak out even when the pressure of the polymer solution inside increases. The anode buffer solution tank 9 containing the anode buffer solution 7 is fixed onto the anode stage 13. An end of the polymer solution tube 19 opposite to the T block 15 is inserted into the anode buffer solution tank 9 and immersed in the anode buffer solution 7. The polymer solution valve 20 is placed at a boundary between the polymer solution 18 and the anode buffer solution 7 at an end portion of the polymer solution tube 19. The polymer solution valve 20 has a plunger portion that moves up and down (Z-axis direction), and when the plunger portion moves upward (+Z-axis direction), the polymer

solution valve 20 is opened, and when the plunger portion moves downward (-Z-axis direction), the polymer solution valve 20 is closed.

[0063]

In FIG. 11, the polymer solution valve 20 is opened. Although only the plunger portion of the polymer solution valve 20 is shown in FIG. 11, the polymer solution valve 20 actually includes a solenoid mechanism (not shown) for moving the plunger portion up and down and a connection mechanism (not shown) for interlocking the solenoid mechanism and the plunger portion. The anode 5 is inserted into the anode buffer solution tank 9 and immersed in the anode buffer solution 7. The anode 5 and the cathode 4 are connected to the DC power supply 21 by the electric wire 22. A voltage is applied between the anode 5 and the cathode 4, that is, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 of the capillary 1 to perform atmospheric pressure electrophoresis. The vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. For example, the difference in height between the two liquid surfaces may be 1 mm or less. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis.

[0064]

FIG. 12 shows a state in which the capillary 1 is filled with the polymer solution 18 at a high pressure in the capillary electrophoresis device according to Modified Example 3 (Embodiment 2). With this filling, the polymer solution 18 already filled in the capillary 1 can be replaced with the newly filled polymer solution 18. The polymer solution valve 20 is closed to mechanically push the plunger 17 of the pressure-resistant syringe 16 using a motor, and a high pressure is applied to the polymer solution 18 inside. The polymer solution 18 in the polymer solution tube 19, the polymer solution 18 in the T block 15, and the polymer solution 18 in the pressure-resistant syringe 16 form a continuous liquid system, the liquid system fills the sealed space, and the sealed space contains almost no air. In addition, the sample-elution end 3 is immersed in the liquid system. In this state, since the plunger 17 as a solid directly

compresses the polymer solution 18 as a liquid at the interface 104 with the polymer solution 18, a high pressure of about 70 atm at the maximum can be obtained.

[0065]

Even if a gas such as air is introduced between the plunger 17 and the polymer solution 18, the plunger 17 can indirectly pressurize the polymer solution 18, and the same high pressure can be obtained when a volume of the gas is sufficiently small. The high pressure is transmitted to the entire liquid system including the sample-elution end 3 (in FIG. 12, the liquid system in the high-pressure state is indicated by a checkered pattern). Since the sample-injection end 2 is under atmospheric pressure, a high pressure difference is generated between the sample-elution end 3 and the sample-injection end 2, and the capillary 1 is filled with the polymer solution 18 at a high pressure from the sample-elution end 3 toward the sample-injection end 2. The pressure applied to the polymer solution 18 can be controlled by controlling the force of the motor that pushes the plunger 17 in. Actually, a high pressure of 35 atm is applied to the polymer solution 18 to fill the capillary 1 with the polymer solution 18 at a high pressure. After the filling with the polymer solution, the mechanical pushing-in of the plunger 17 is stopped, the plunger 17 and the mechanical pushing mechanism are separated, and the pressure applied to the liquid system is reduced to substantially zero. The polymer solution valve 20 is opened to vent the sample-elution end 3 and the liquid system to the atmospheric pressure.

[0066]

FIG. 13 shows a state in which a sample is injected into the capillary 1 by pressure in the capillary electrophoresis device according to Modified Example 3 (Embodiment 2). With the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the sample solution tank 11 and immersed in the sample solution 10, and at the same time, the O-ring 33 is pressed against the fixed block 31 and compressed to seal the sample solution tank 11. The pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm. When the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, the pressure of the sample solution 10 inside the sample solution tank 11 and the pressure of the air 37 in contact with the sample solution 10 increase to 1 atm. As described above, a low pressure difference of 1 atm is generated between

the sample-injection end 2 and the sample-elution end 3, and the sample solution 10 is injected into the capillary 1 from the sample-injection end 2. After a predetermined time has elapsed, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the pressure of the sample solution 10 and the pressure of the air 37 inside the sample solution tank 11 to the atmospheric pressure.

[0067]

Thereafter, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the cathode buffer solution tank 8 and immersed in the anode buffer solution 6, and at the same time, the cathode buffer solution tank 8 is sealed. However, when the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the inside of the cathode buffer solution tank 8 to the atmospheric pressure, the state returns to the state shown in FIG. 11. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform atmospheric pressure electrophoresis.

[0068]

Therefore, Modified Example 3 (Embodiment 2) can achieve the first object of the invention, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", and (2) "capable of performing pressure injection of a sample". However, Modified Example 3 (Embodiment 2) does not achieve the second and third objects of the invention.

[0069]

In Modified Example 3 (Embodiment 2), not only pressure injection of the sample but also electric field injection can be performed. In FIG. 13, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the sample solution 10 in the sample solution tank 11 and the air 37 in contact therewith to the atmospheric pressure. In this state, the sample can be injected into the capillary 1 by an electric field from the sample-injection end 2 by applying a voltage between the sample-elution end 3 and the sample-injection end 2 for a certain period of time.

[0070]

As described above, in the capillary electrophoresis device according to Modified Example 3 (Embodiment 2), the cathode side has the same configuration as the cathode side in Related Example 2, while the anode side has the same configuration as the anode side in Related Example 1. Such a combination does not exist in the related art. One of the problems of the configuration of the capillary electrophoresis device according to Modified Example 3 (Embodiment 2) is whether the sample can be injected by pressure according to the method shown in FIG. 13, similarly to the method shown in FIG. 6 of Related Example 2. In FIG. 6, the sample-elution end 3 is immersed in a sufficient amount of the anode buffer solution 7, and the air 32 under the atmospheric pressure is present in the vicinity thereof. In contrast, in FIG. 13, the sample-elution end 3 is immersed in a small amount of the polymer solution 18, and air under atmospheric pressure is present at a distant position via a long flow path 19. That is, there is a fluid resistance between the sample-elution end 3 and the air under atmospheric pressure, and the sample pressure injection from the sample-injection end 2 may be adversely affected, for example, the pressure injection of the sample cannot be efficiently performed. Therefore, the capillary electrophoresis analysis was performed by injecting the sample by an electric field or by pressure using the device according to Modified Example 3 (Embodiment 2), and whether an expected result was obtained was checked by experiment.

[0071]

FIG. 29 shows four electropherograms obtained by fixing a voltage of the electric field injection to 1.8 kV and changing time of the electric field injection to 15 seconds, 30 seconds, 45 seconds, and 60 seconds. The sample solution was a solution obtained by diluting GeneScan™ 500 ROX™ dye Size Standard (Thermo Fisher Scientific) with Hi-Di™ Formamide (Thermo Fisher Scientific). FIG. 30 shows a graph in which an average peak area of a plurality of peaks obtained in each electropherogram shown in FIG. 29 is plotted with respect to the electric field injection time. Since the electric field injection time and the peak area have a relationship of a line passing through the origin, it can be confirmed that the electric field injection is performed as expected. In contrast, FIG. 31 shows four electropherograms obtained by fixing the pressure of the pressure injection to 0.5 atm and changing the time of the

pressure injection to 15 seconds, 30 seconds, 45 seconds, and 60 seconds. The sample solution was the same as those described above. FIG. 32 shows a graph in which an average peak area of a plurality of peaks obtained in each electropherogram shown in FIG. 31 is plotted with respect to the pressure injection time. However, the electropherogram corresponding to the plot with the pressure injection time of 90 seconds is not shown in FIG. 31. Since the pressure injection time and the peak area have a relationship of a line passing through the origin, it can be confirmed that the pressure injection is performed as expected.

[0072]

As described above, according to Modified Example 3 (Embodiment 2), it was found that the electrophoresis analysis can be satisfactorily performed without any problem regardless of whether the electric field injection of the sample or the pressure injection of the sample is used.

[0073]

FIG. 33 shows a detailed example of steps of one capillary electrophoresis analysis using the electric field injection. FIG. 34 shows a detailed example of steps of one capillary electrophoresis analysis using the pressure injection. There are step numbers in the leftmost column, and the steps are carried out in numerical order in each analysis. The function of the next column indicates "filling with polymer solution", "preliminary migration", "electric field injection", "pressure injection", "present migration", and the like, and the corresponding row indicates the details of each step. The term "reference" indicates a reference state in a step. The term "present migration" refers to normal electrophoresis. The left half of the portion of the third and subsequent columns in the table shows states or conditions of "contact target", "sealed/opened", "pressure", and "potential" for "sample-elution end", and the right half thereof shows states or conditions of "contact target", "sealed/opened", "pressure", and "potential" for "sample-injection end". The term "contact target" indicates, in each step, a liquid in which the capillary end is immersed. The term "sealed/opened" indicates whether the space for storing the liquid system in which the capillary end is immersed is sealed or opened to the atmosphere in each step. In each step, regarding "pressure", the pressure applied to the capillary end is indicated by any one of "—", "low pressure", and "high pressure". The symbol "—" means the

atmospheric pressure, that is, 0 atm, the term "low pressure" means a pressure greater than 0 atm and equal to or less than 7 atm, and the term "high pressure" means a pressure greater than 7 atm. In each step, regarding "potential", the potential applied to the capillary end is indicated by any one of "-", "positive potential", and "negative potential". Both ends of the capillary being "-" means that no voltage is applied between both ends, and the "sample-injection end" being "positive potential" and the "sample-elution end" being "negative potential" means that a voltage is applied between both ends. In addition, "↓" indicates the same state or condition as that of the row immediately above.

[0074]

An example of steps of capillary electrophoresis analysis using the electric field injection shown in FIG. 33 will be described in order. FIGS. 11 to 13 are basically followed except for a part. The sample-elution end is connected to the T block filled with the polymer solution, and therefore, the contact target is always the polymer solution.

Step 1: The sample-elution end is under atmospheric pressure, and the sample-injection end is immersed in the cathode buffer solution under atmospheric pressure. This state is used as a reference.

[0075]

Step 2: The cathode stage is moved, and the sample-injection end is inserted into the waste liquid tank and immersed in the waste liquid (water) (the waste liquid tank for storing the waste liquid is not depicted on the cathode stage in FIG. 12).

[0076]

Step 3: The polymer solution valve is closed, and the space for storing the liquid system (the polymer solution tube, the T block, and the polymer solution in the pressure-resistant syringe) with which the sample-elution end is in contact is sealed from the atmosphere.

[0077]

Step 4: The plunger (solid) of the pressure-resistant syringe is mechanically pushed in, a high pressure is applied to the liquid system, and the capillary is filled with the polymer solution from the sample-elution end toward the sample-injection end. The polymer solution overflowing from the sample-injection end is discharged to the waste liquid (in FIG. 12, the

polymer solution overflowing from the sample-injection end is discharged to the cathode buffer solution. The discharged polymer solution contains the component of the previously analyzed sample, which may be carried over to the next analysis. Accordingly, the polymer solution is preferably discharged to the waste liquid rather than being discharged to the cathode buffer solution).

[0078]

Step 5: The mechanical pushing-in of the plunger is stopped, the plunger and the mechanical pushing mechanism are separated from each other, the pressure applied to the liquid system is reduced to substantially zero, and the filling with the polymer solution is ended.

[0079]

Step 6: The polymer solution valve is opened to open the space for storing the liquid system (the anode buffer solution, the polymer solution tube, the T block, and the polymer solution in the pressure-resistant syringe) with which the sample-elution end is in contact to the atmosphere.

Step 7: The cathode stage is moved, the sample-injection end is inserted into the cathode buffer solution tank and immersed in the cathode buffer solution, and the state returns to the reference.

Step 8: Preliminary migration is performed by applying a voltage between the sample-elution end and the sample-injection end.

Step 9: The voltage application is stopped, the preliminary migration is ended, and the state returns to the reference.

Step 10: The cathode stage is moved, and the sample-injection end is inserted into the sample solution tank and immersed in the sample solution.

Step 11: A voltage is applied between the sample-elution end and the sample-injection end to inject the sample by an electric field.

Step 12: The voltage application is stopped, and the electric field injection is ended.

Step 13: The cathode stage is moved, the sample-injection end is inserted into the cathode buffer solution tank and immersed in the cathode buffer solution, and the state returns to the reference.

Step 14: The present migration is performed by applying a voltage between the sample-elution end and the sample-injection end.

Step 15: The voltage application is stopped, the present migration is ended, and the state returns to the reference. When the capillary electrophoresis analysis is performed a plurality of times, steps 1 to 15 may be repeated a plurality of times.

[0080]

The above steps of steps 1 to 15 are preferably carried out in this order. However, as a unit of one capillary electrophoresis analysis, for example, steps 1 to 7 may also be performed after steps 7 to 15 are performed. Even in such a case, when the capillary electrophoresis analysis is performed a plurality of times, a step of performing steps 1 to 15 in order is always included. The characteristics of steps 1 to 15 are the filling with the polymer solution in step 4 and the electric field injection in step 11. That is, the invention is characterized in that step A (step 4) of filling the capillary with a part of the polymer solution by pressing a solid against the polymer solution and applying a high pressure (pressure exceeding 7 atm) to the polymer solution in a state in which the sample-injection end is vented to atmospheric pressure and the polymer solution as a separation medium is brought into contact with the sample-elution end and step B (step 11) of injecting a part of the sample solution into the capillary by applying a voltage between the sample-elution end and the sample-injection end in a state in which the sample solution is brought into contact with the sample-injection end are performed in the order of step A and step B. Alternatively, the invention is characterized in that the analysis includes a step of performing step A and step B in order.

[0081]

An example of steps of capillary electrophoresis analysis using the pressure injection shown in FIG. 34 will be described in order. FIGS. 11 to 13 are basically followed except for a part. Steps 1 to 10 are the same as steps 1 to 10 in FIG. 33, and therefore, the description thereof will be omitted.

Step 11: A space for storing a liquid system (sample solution) with which a sample-injection end is in contact (a space inside a sample solution tank) is sealed from the atmosphere.

Step 12: Compressed air is caused to flow into the space for storing the liquid system

with which the sample-injection end is in contact, and a low pressure is applied to perform pressure injection of the sample.

Step 13: The pressure of the compressed air is set to the atmospheric pressure, and the pressure of the space for storing the liquid system with which the sample-injection end is in contact is brought to atmospheric pressure (step 13 can be omitted).

Step 14: The space for storing the liquid system with which the sample-injection end is in contact is opened to the atmosphere.

Steps 15 to 17 are the same as steps 13 to 15 shown in FIG. 33, and therefore, the description thereof will be omitted.

[0082]

When the capillary electrophoresis analysis is performed a plurality of times, steps 1 to 17 may be repeated a plurality of times. Steps 1 to 17 are preferably carried out in this order. However, as a unit of one capillary electrophoresis analysis, for example, steps 1 to 7 may be performed after steps 7 to 17 are performed. Even in such a case, when the capillary electrophoresis analysis is performed a plurality of times, a step of performing steps 1 to 17 is necessarily performed.

[0083]

The characteristics of steps 1 to 17 are the filling with the polymer solution in step 4 and the pressure injection in step 12. That is, the invention is characterized in that step A (step 4) of filling the capillary with a part of the polymer solution by pressing a solid against the polymer solution and applying a high pressure (pressure exceeding 7 atm) to the polymer solution in a state in which the sample-injection end is vented to atmospheric pressure and the polymer solution as a separation medium is brought into contact with the sample-elution end and step B (step 12) of injecting a part of the sample solution into the capillary by bringing compressed air into contact with the sample solution and applying a low pressure (pressure of 0 atm to 7 atm) to the sample solution in a state in which the sample solution is brought into contact with the sample-injection end are sequentially performed in the order of step A and step B. Alternatively, the invention is characterized in that the analysis includes a step of performing step A and step B in order.

[0084]

<Modified Example 4 (Embodiment 3)>

FIGS. 14 to 16 show a configuration of a capillary electrophoresis device according to Modified Example 4 (Embodiment 3) and an analysis method using the capillary electrophoresis device. Modified Example 4 (Embodiment 3) is implemented by modifying Modified Example 2 (Embodiment 1: FIGS. 8 to 10), and is configured to solve the problem of Modified Example 2 (Embodiment 1).

[0085]

The capillary electrophoresis device according to Modified Example 4 (Embodiment 3) includes an air type pressurizing mechanism on the cathode side (sample-injection end side), and a plunger type pressurizing mechanism and an air type pressurizing mechanism on the anode side (sample-elution end side). FIG. 14 shows a state in which both-end pressurization electrophoresis is performed in the capillary electrophoresis device according to Modified Example 4 (Embodiment 3).

[0086]

The configuration on the cathode side is the same as that of Modified Example 2 (Embodiment 1). However, the pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm, the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to bring the inside of the cathode buffer solution tank 8 into a pressurized state of 1 atm. Regarding the configuration on the anode side, the configuration of the polymer solution tank 32 to which the pressure-resistant syringe 16 containing the polymer solution 18 is coupled is the same as that of Modified Example 2 (Embodiment 1). The configurations of the anode buffer solution tank 9 storing the anode buffer solution 7 and the fixed block 31 are the same as those of Related Example 2 (FIGS. 4 to 6). The anode buffer solution tank 9 storing the anode buffer solution 7 and the polymer solution tank 32 to which the pressure-resistant syringe 16 storing the polymer solution 18 is coupled are fixed onto the anode stage 13, and further, the anode stage 13 is coupled to an XYZ axis drive mechanism (not shown). The O-ring 33 is placed at an upper end of each of the anode buffer solution tank 9 and the polymer solution tank 32. With a movement of the anode stage 13 using the XYZ axis

drive mechanism, the sample-elution end 3 is inserted into the anode buffer solution tank 9 together with the anode 5 and immersed in the anode buffer solution 7. At the same time, with a movement of the anode stage 13 in the +Z-axis direction, the O-ring 33 is pressed against the flat surface portion of the fixed block 31 and compressed to seal the anode buffer solution tank 9. The anode pressurizing valve 26 is opened, and the anode release valve 27 is closed to bring the inside of the anode buffer solution tank 9 into a pressurized state of 1 atm. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform both-end pressurization electrophoresis. Accordingly, the pressure of the polymer solution 18 in the capillary 1 is increased to 1 atm, the generation of bubbles in the capillary 1 during electrophoresis is prevented, and high separation performance can be stably obtained.

[0087]

Further, the vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. For example, the difference in height between the two liquid surfaces may be 1 mm or less. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis.

[0088]

In the present description, the step of opening the anode pressurizing valve 26 in order to introduce the compressed air to the sample-elution end 3 side and the step of opening the cathode pressurizing valve 28 in order to introduce the compressed air to the sample-injection end 2 side are separately described, but these steps are preferably performed simultaneously. Further, the step of opening the anode release valve 27 to vent the sample-elution end 3 side to the atmospheric pressure and the step of opening the cathode release valve 29 to vent the sample-injection end 2 side to the atmospheric pressure are separately described, but these steps are preferably performed simultaneously. This is because when the timings of these steps are shifted, a time zone in which a pressure difference occurs between the sample-elution end 3 and the sample-injection end 2 occurs, and the polymer solution 18 in the capillary 1 moves during

the time zone. In order to easily equalize the timings, it is effective to change the anode pressurizing valve 26 and the cathode release valve 29 to one valve and to change the anode release valve 27 and the cathode release valve 29 to one valve. For the same reason, it is preferable that the speed of the pressure increase and the speed of the pressure decrease are equalized between the sample-elution end 3 side and the sample-injection end 2 side. For this purpose, it is preferable to equalize the flow resistance of air on both sides. Alternatively, it is also effective to slowly increase and reduce the pressure of the compressed air discharged from the compressed air source 25, for example, to increase and reduce the pressure at a speed of 0.5 atm/sec or less or 0.1 atm/sec or less.

[0089]

FIG. 15 shows a state in which the capillary 1 is filled with the polymer solution 18 at a high pressure in the capillary electrophoresis device according to Modified Example 4 (Embodiment 3). With the movement of the anode stage 13 using the XYZ axis drive mechanism, the sample-elution end 3 is inserted into the polymer solution tank 32 and immersed in the polymer solution 18, and at the same time, the O-ring 33 is pressed against the fixed block 31 and compressed to seal the polymer solution tank 32. At this time, the structures of the O-ring 33 and the fixed block 31 are determined such that the polymer solution tank 32 and the air tube 30 are not connected to each other, that is, the polymer solution 18 in the polymer solution tank 32 and the air in the air tube 30 do not come into contact with each other. The polymer solution tank 32 and the pressure-resistant syringe 16 are integrated to have one internal space, and the internal space is filled with the polymer solution 18 and contains almost no air. While the cathode buffer solution 6 and the air 34 inside the cathode buffer solution tank 8 are vented to the atmospheric pressure, the plunger 17 of the pressure-resistant syringe 16 is mechanically pushed in to increase the pressure of the polymer solution inside the polymer solution tank 32 and the syringe 16 to 35 atm, and the capillary 1 is filled with the polymer solution 18 at a high pressure. After the filling with the polymer solution, the mechanical pushing-in of the plunger 17 is stopped, the plunger 17 and the mechanical pushing mechanism are separated, and the pressure applied to the liquid system is reduced to substantially zero.

[0090]

FIG. 16 shows a state in which a sample is injected into the capillary 1 by pressure in the capillary electrophoresis device according to Modified Example 4 (Embodiment 3). With the movement of the anode stage 13 using the XYZ axis drive mechanism, the sample-elution end 3 is inserted into the anode buffer solution tank 9 and immersed in the anode buffer solution 7, and at the same time, the anode buffer solution tank 9 is sealed. The anode pressurizing valve 26 is closed, and the anode release valve 27 is opened to bring the pressure inside the anode buffer solution tank 9 to the atmospheric pressure. On the other hand, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the sample solution tank 11 and immersed in the sample solution 10, and at the same time, the sample solution tank 11 is sealed. The pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm. When the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, the pressure of the sample solution 10 inside the sample solution tank 11 and the pressure of the air 37 in contact with the sample solution 10 increase to 1 atm. As described above, a low pressure difference of 1 atm is generated between the sample-injection end 2 and the sample-elution end 3, and the sample solution 10 is injected into the capillary 1 from the sample-injection end 2. After a predetermined time has elapsed, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the pressure of the sample solution 10 and the pressure of the air 37 inside the cathode sample solution tank 11 to the atmospheric pressure.

[0091]

Thereafter, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the cathode buffer solution tank 8 and immersed in the anode buffer solution 6, and at the same time, the cathode buffer solution tank 8 is sealed. When the anode pressurizing valve 26 is opened, the anode release valve 27 is closed, the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to pressurize the inside of the anode buffer solution tank 9 and the cathode buffer solution tank 8 to 1 atm, the state returns to the state shown in FIG. 14. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform the both-end pressurization electrophoresis. Of course, the atmospheric pressure electrophoresis can also

be performed by closing the anode pressurizing valve 26, opening the anode release valve 27, closing the cathode pressurizing valve 28, and opening the cathode release valve 29 to vent the inside of the anode buffer solution tank 9 and the inside of the cathode buffer solution tank 8 to the atmospheric pressure, and applying a voltage between the sample-elution end 3 and the sample-injection end 2.

[0092]

As described above, Modified Example 4 (Embodiment 3) can achieve all of the following objects: a first object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (2) "capable of performing pressure injection of a sample"; a second object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (3) "capable of performing pressurization at both ends during electrophoresis"; and a third object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", (2) "capable of performing pressure injection of a sample", and (3) "capable of performing pressurization at both ends during electrophoresis".

[0093]

According to Modified Example 4 (Embodiment 3), not only the pressure injection of the sample but also the electric field injection can be performed. In FIG. 16, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the sample solution 10 in the sample solution tank 11 and the air 37 in contact therewith to the atmospheric pressure. In this state, the sample can be injected into the capillary 1 by an electric field from the sample-injection end 2 by applying a voltage between the sample-elution end 3 and the sample-injection end 2 for a certain period of time.

[0094]

<Modified Example 5: Embodiment 4>

FIGS. 17 to 19 show a configuration example of a capillary electrophoresis device

(corresponding to the device H) according to Modified Example 5 (Embodiment 4) and an analysis method using the capillary electrophoresis device. Modified Example 5 (Embodiment 4) is implemented by modifying Modified Example 3 (Embodiment 2: FIGS. 11 to 13), and is configured to solve the problem of Modified Example 3 (Embodiment 2). An air type pressurizing mechanism is provided on the cathode side (sample-injection end side), and a plunger type pressurizing mechanism and an air type pressurizing mechanism are provided on the anode side (sample-elution end side). FIG. 17 shows a state in which both-end pressurization electrophoresis is performed in Modified Example 5 (Embodiment 4). The configuration on the cathode side is the same as that of Modified Example 3 (Embodiment 2). However, the pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm, the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to bring the inside of the cathode buffer solution tank 8 into a pressurized state of 1 atm.

[0095]

The configuration of the anode side is the same as that of Modified Example 3 (Embodiment 2) except for a sealed chamber and a mechanism for introducing the compressed air into the sealed chamber described below. Since the air type pressurizing mechanism is provided on the anode side, a mechanism for sealing the anode buffer solution tank 9 and introducing compressed air into the inside is required. However, the polymer solution valve 20 in Modified Example 3 (Embodiment 2) includes a solenoid mechanism for moving the plunger portion up and down and a connection mechanism for interlocking the solenoid mechanism and the plunger portion. That is, the polymer solution valve 20 largely protrudes from the anode buffer solution tank 9 and has a movable portion. Therefore, it is difficult to seal the anode buffer solution tank 9 using the O-ring 33 and the fixed block 31 as in the related device 2 (FIGS. 4 to 6). Therefore, in Modified Example 5 (Embodiment 4), the anode buffer solution tank 9 and the polymer solution valve 20 are entirely accommodated inside a sealed chamber 38. Further, the sealed chamber 38 is connected to the compressed air source 25 or the atmosphere via the air tube 30 using the anode pressurizing valve 26 and the anode release valve 27.

[0096]

As shown in FIG. 17, when the anode pressurizing valve 26 is opened, and the anode release valve 27 is closed, the compressed air flows from the compressed air source 25 into the sealed chamber 38 via the air tube 30, and the pressure of the air 35 inside the sealed chamber 38 and the anode buffer solution tank 9 increases to the pressure of the compressed air discharged from the compressed air source 25, that is, 1 atm. At the same time, the pressure of the anode buffer solution 7 contained in the anode buffer solution tank 9 is similarly pressurized to 1 atm. As described above, both ends of the cathode side and the anode side are brought into the pressurized state. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform the both-end pressurization electrophoresis. Accordingly, the pressure of the polymer solution 18 in the capillary 1 is increased to 1 atm, the generation of bubbles in the capillary 1 during electrophoresis is prevented, and high separation performance can be stably obtained. Further, the vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. For example, the difference in height between the two liquid surfaces may be 1 mm or less. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis.

[0097]

FIG. 18 shows a state in which the capillary 1 is filled with the polymer solution 18 at a high pressure in the capillary electrophoresis device according to Modified Example 5 (Embodiment 4). The anode pressurizing valve 26 is closed, and the anode release valve 27 is opened to vent the air 35 inside the sealed chamber 38 and the anode buffer solution tank 9 to the atmospheric pressure. In addition, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the air 34 in the cathode buffer solution tank 8 to the atmospheric pressure. In this state, the polymer solution valve 20 is closed, and the plunger 17 of the pressure-resistant syringe 16 is mechanically pushed in by using a motor to apply a high pressure of 35 atm to the inside polymer solution 18 where the sample-elution end 2 is immersed.

[0098]

Since the sample-injection end 2 is under atmospheric pressure, a high pressure difference of 35 atm is generated between the sample-elution end 3 and the sample-injection end 2, and the capillary 1 is filled with the polymer solution 18 at a high pressure of 35 atm from the sample-elution end 3 toward the sample-injection end 2. After the filling with the polymer solution, the mechanical pushing-in of the plunger 17 is stopped, the plunger 17 and the mechanical pushing mechanism are separated, and the pressure applied to the polymer solution 18 is reduced to substantially zero. The polymer solution valve 20 is opened to vent the polymer solution 18 and the sample-elution end 3 to the atmospheric pressure.

[0099]

FIG. 19 shows a state in which a sample is injected into the capillary 1 by pressure in the capillary electrophoresis device according to Modified Example 5 (Embodiment 4). With the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the sample solution tank 11 and immersed in the sample solution 10, and at the same time, the O-ring 33 is pressed against the fixed block 31 and compressed to seal the sample solution tank 11. The pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm. When the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, the pressure of the sample solution 10 inside the sample solution tank 11 and the pressure of the air 37 in contact with the sample solution 10 increase to 1 atm. As described above, a low pressure difference of 1 atm is generated between the sample-injection end 2 and the sample-elution end 3, and the sample solution 10 is injected into the capillary 1 from the sample-injection end 2. After a predetermined time has elapsed, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the pressure of the sample solution 10 and the pressure of the air 37 inside the sample solution tank 11 to the atmospheric pressure.

[0100]

Thereafter, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the cathode buffer solution tank 8 and immersed in the anode buffer solution 6, and at the same time, the cathode buffer solution tank 8 is sealed. The pressure of the compressed air discharged from the compressed air source 25

is set to 1 atm. Next, when the anode pressurizing valve 26 is opened, the anode release valve 27 is closed, the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to pressurize the sealed chamber 38, the inside of the anode buffer solution tank 9, and the inside of the cathode buffer solution tank 8 to 1 atm, the state returns to the state shown in FIG. 17. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform the both-end pressurization electrophoresis. Of course, the atmospheric pressure electrophoresis can also be performed by closing the anode pressurizing valve 26, opening the anode release valve 27, closing the cathode pressurizing valve 28, and opening the cathode release valve 29 to vent the inside of the anode buffer solution tank 9 and the inside of the cathode buffer solution tank 8 to the atmospheric pressure, and applying a voltage between the sample-elution end 3 and the sample-injection end 2.

[0101]

As described above, Modified Example 5 (Embodiment 4) can achieve all of the following objects: a first object of the invention, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (2) "capable of performing pressure injection of a sample"; a second object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (3) "capable of performing pressurization at both ends during electrophoresis"; and a third object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", (2) "capable of performing pressure injection of a sample", and (3) "capable of performing pressurization at both ends during electrophoresis".

[0102]

According to Modified Example 5 (Embodiment 4), not only the pressure injection of the sample but also the electric field injection can be performed. In FIG. 19, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the sample solution 10 in the sample solution tank 11 and the air 37 in contact therewith to the atmospheric

pressure. In this state, the sample can be injected into the capillary 1 by an electric field from the sample-injection end 2 by applying a voltage between the sample-elution end 3 and the sample-injection end 2 for a certain period of time.

[0103]

<Modified Example 6: Embodiment 5>

FIG. 20 shows a configuration example of a capillary electrophoresis device according to Modified Example 6 (Embodiment 5). Modified Example 6 (Embodiment 5) is implemented by modifying Modified Example 3 (Embodiment 2: FIGS. 11 to 13), and is configured to solve the problem of Modified Example 3 (Embodiment 2). The capillary electrophoresis device according to Modified Example 6 (Embodiment 5) includes an air type pressurizing mechanism on the cathode side (sample-injection end side), and a plunger type pressurizing mechanism and an air type pressurizing mechanism on the anode side (sample-elution end side).

[0104]

FIG. 20 shows a state in which both-end pressurization electrophoresis is performed in the capillary electrophoresis device according to Modified Example 6 (Embodiment 5). The configuration on the cathode side is the same as that of Modified Example 3. However, the pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm, the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to bring the inside of the cathode buffer solution tank 8 into a pressurized state of 1 atm.

[0105]

In Modified Example 6 (Embodiment 5), since the air type pressurizing mechanism is provided on the anode side, the polymer solution valve 20 in Modified Example 3 (Embodiment 2) is removed, and the anode buffer solution tank 9 is sealed using the O-ring 33 and the fixed block 31 as in Related Example 2 (FIGS. 4 to 6). Instead of the polymer solution valve 20 located at a boundary between the anode buffer solution 7 in the anode buffer solution tank 9 and the polymer solution 18 in the polymer solution tube 19, a compressed air-side polymer solution valve 39 is placed on the polymer solution tube 19 between the anode buffer solution tank 9 and the T block 15. This configuration is characterized in that the compressed air-side

polymer solution valve 39 is disposed between the sample-elution end 3 and the interface 102 between the anode buffer solution 7 and air (i.e., the liquid surface of the anode buffer solution 7).

[0106]

In FIG. 20, the compressed air-side polymer solution valve 39 is opened. In addition, the anode buffer solution tank 9 is connected to the compressed air source 25 or the atmosphere via the air tube 30 using the anode pressurizing valve 26 and the anode release valve 27. However, the structure of the sealed anode buffer tank 9 is different from that of the capillary electrophoresis device according to Related Example 2 in the following points. In Related Example 2, the sample-elution end 3 of the capillary 1 and the anode 5 are inserted into the sealed anode buffer tank 9 and immersed in the cathode buffer solution 7.

[0107]

In contrast, in the capillary electrophoresis device according to Modified Example 6 (Embodiment 5), the sample-elution end 3 of the capillary 1 is not inserted into the sealed anode buffer tank 9, and instead, the anode 5 and the polymer solution tube 19 are inserted into the sealed anode buffer tank 9 and immersed in the cathode buffer solution 7. As shown in FIG. 20, when the anode pressurizing valve 26 is opened, and the anode release valve 27 is closed, the compressed air flows from the compressed air source 25 into the anode buffer solution tank 9 via the air tube 30, and the pressure inside the anode buffer solution tank 9 increases to the pressure of the compressed air discharged from the compressed air source 25, that is, 1 atm. As described above, both ends of the cathode side and the anode side are brought into the pressurized state. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform the both-end pressurization electrophoresis. Accordingly, the pressure of the polymer solution 18 in the capillary 1 is increased to 1 atm, the generation of bubbles in the capillary 1 during electrophoresis is prevented, and high separation performance can be stably obtained. Further, the vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. Accordingly, the

polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis.

[0108]

According to Modified Example 6 (Embodiment 5), it was found that the first to third objects of the invention can be achieved, but the following problems are present. In the state shown in FIG. 20, when a pressure of 1 atm is applied to the inside of the anode buffer solution tank 9, the polymer solution 18 with which the inside of the polymer solution tube 19, the inside of the T block 15, and the inside of the pressure-resistant syringe 16 are filled is also brought into a pressurized state of 1 atm. At this time, the plunger 17 of the pressure-resistant syringe 16 may receive a force in a direction of being pulled out from the pressure-resistant syringe 16, and the plunger 17 may move in a direction of being pulled out from the pressure-resistant syringe 16. When the plunger 17 actually moves, the pressure of the polymer solution 18 with which the inside of the polymer solution tube 19, the inside of the T block 15, and the inside of the pressure-resistant syringe 16 are filled changes, so that the balance of the pressurization at both ends of the capillary 1 is lost, the polymer solution 18 inside the capillary 1 moves, and the separation ability of electrophoresis decreases. Therefore, the first to third objects of the invention are achieved after solving the above problems.

[0109]

<Modified Example 7: Embodiment 6>

FIG. 21 shows a configuration example of a capillary electrophoresis device according to Modified Example 7 (Embodiment 6) (when performing both-end pressurization electrophoresis). Modified Example 7 (Embodiment 6) is implemented by modifying Modified Example 6 (Embodiment 5: FIG. 20), and is configured to solve the problem of Modified Example 6 (Embodiment 5).

[0110]

Modified Example 7 (Embodiment 6) is different from Modified Example 6 (Embodiment 5) in that a plunger stopper 41 capable of fixing the plunger 17 of the pressure-resistant syringe 16 is added. As one of the units for mechanically pushing the plunger 17 of the pressure-resistant syringe 16, an X-axis drive mechanism (not shown) including a stepping

motor can be used. In order to maintain the pressure of the polymer solution 18 inside the pressure-resistant syringe 16 at a desired pressure, a drive force in the -X-axis direction of a drive unit of the x-axis drive mechanism may be set to a corresponding constant value (specifically, "pressure" = "drive force" ÷ "cross-sectional area of pressure-resistant syringe"). For this purpose, the drive force may be measured using a load sensor or the like, and the operation of the drive unit may be controlled so that the drive force becomes a constant value. Alternatively, a value of a current for driving the stepping motor may be controlled so that the stepping motor steps out when the drive force exceeds the constant value.

[0111]

The most basic configuration of the plunger stopper 41 is in a state in which the drive unit of the X-axis drive mechanism and the plunger 17 are coupled. The plunger stopper 41 is operated by continuing excitation of the stepping motor in a state in which the drive unit is stationary. When the excitation of the stepping motor is continued in a state in which the drive unit is stationary, a static torque acts on the stepping motor. Therefore, the movement of the plunger 17 can be stopped. However, when the torque applied to the stepping motor by the force acting on the drive unit exceeds the maximum static torque, the drive unit is driven.

[0112]

However, the coupling of the drive unit of the X-axis drive mechanism and the plunger 17 causes the following problem. In FIG. 21, the compressed air discharged from the compressed air source 25 is set to 1 atm, the anode pressurizing valve 26 is opened, the anode release valve 27 is closed, the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to make the inside of the anode buffer solution tank 9 and the inside of the cathode buffer solution tank 8 have a low pressure of 1 atm. From this state, the anode pressurizing valve 26 is closed, the anode release valve 27 is opened, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the inside of the anode buffer solution tank 9 and the inside of the cathode buffer solution tank 8 to the atmospheric pressure. Further, the compressed air-side polymer solution valve 39 is closed to form a liquid system in which the polymer solution 18 inside a section of the polymer solution tube 19 between the compressed air-side polymer solution valve 39 and the T block 15, the T block 15,

and the pressure-resistant syringe 16 are coupled. With the drive of the X-axis drive mechanism, the plunger 17 of the pressure-resistant syringe 16 is mechanically pushed in, the pressure of the liquid system is increased to a high pressure of 35 atm, and the capillary 1 can be filled with the polymer solution 18. Here, even when the drive of the X-axis drive mechanism is stopped to stop the filling with the polymer solution, and the plunger 17 is stationary, the high-pressure state of the liquid system is maintained (to be exact, the pressure is slowly reduced with the filling with the polymer solution), and the filling with the polymer solution continues. When the compressed air-side polymer solution valve 39 is opened in this state, the liquid system is vented to the atmospheric pressure, and the filling with the polymer solution is stopped.

[0113]

However, at the same time as opening the compressed air-side polymer solution valve 39, a large amount of the polymer solution 18 in the polymer solution tube 19 is rapidly discharged into the cathode buffer solution 7, and the pressure of the liquid system rapidly decreases. These phenomena are not preferable because they cause waste of the polymer solution 18, generation of bubbles, and the like. In order to avoid these phenomena, it is necessary to decrease the pressure of the liquid system by moving the drive unit of the X-axis drive mechanism in the +X-axis direction and moving the plunger 17 in the direction of being pulled out from the pressure-resistant syringe 16. However, it is unclear how much distance the drive unit needs to be moved in the +X-axis direction to bring the pressure of the liquid system to atmospheric pressure, and it is difficult to predict this distance. In addition, when the movement distance becomes slightly greater than the optimum value, the pressure of the liquid system becomes negative.

[0114]

In order to solve the above problem, the drive unit of the X-axis drive mechanism and the plunger 17 are not coupled, and when the drive unit moves in the -X-axis direction, the drive unit comes into contact with the plunger 17 and the plunger 17 can be pushed into the pressure-resistant syringe 16, whereas when the drive unit moves in the +X-axis direction, the drive unit is separated from the plunger 17, and the plunger 17 can be prevented from moving in a direction

of being pulled out from the pressure-resistant syringe 16. When the drive unit is shifted from the state of moving in the -X-axis direction to the state of moving in the +X-axis direction, the state of filling with the polymer solution 18 can be switched to a non-filling state. Even if the drive unit is separated from the plunger 17, a slight residual pressure may remain in the liquid system. However, when the residual pressure of such a degree is present, the influence is small even if the liquid system is vented to the atmospheric pressure by opening the compressed air-side polymer solution valve 39.

[0115]

However, when the drive unit of the X-axis drive mechanism and the plunger 17 are not coupled, the static torque of the stepping motor does not function as the plunger stopper 41. In this case, as shown in FIG. 21, a device different from the X-axis drive mechanism functions as the plunger stopper 41 that directly restricts the operation of the plunger 17.

[0116]

As described above, Modified Example 7 (Embodiment 6) can achieve the first to third objects of the invention after solving the problem of Modified Example 6 (Embodiment 5). According to Modified Example 7 (Embodiment 6), not only the pressure injection of the sample but also the electric field injection can be performed.

[0117]

<Modified Example 8: Embodiment 7>

FIGS. 22 to 24 show a configuration of a capillary electrophoresis device (corresponding to the device I) according to Modified Example 8 (Embodiment 7). Modified Example 8 (Embodiment 7) is implemented by modifying Modified Example 6 (Embodiment 5: FIG. 20), and is configured to solve the problem of Modified Example 6 (Embodiment 5). Modified Example 8 (Embodiment 7) is different from Modified Example 6 (Embodiment 5) in that the T block 15 and the pressure-resistant syringe 16 are connected by a plunger-side polymer solution tube 43, and a plunger-side polymer solution valve 40 is added on the plunger-side polymer solution tube 43 between the T block 15 and the pressure-resistant syringe 16. The configuration of Modified Example 8 (Embodiment 7) is characterized in that the plunger-side polymer solution valve 40 is disposed between the sample-elution end 3 and the interface 104

between the plunger 17 and the polymer solution inside the pressure-resistant syringe 16. The capillary electrophoresis device according to Modified Example 8 (Embodiment 7) includes an air type pressurizing mechanism on the cathode side (sample-injection end side), and a plunger type pressurizing mechanism and an air type pressurizing mechanism on the anode side (sample-elution end side).

[0118]

FIG. 22 shows a state in which both-end pressurization electrophoresis is performed in the capillary electrophoresis device according to Modified Example 8 (Embodiment 7). In the previous stage of FIG. 22, the anode pressurizing valve 26 is closed, the anode release valve 27 is opened, the compressed air-side polymer solution valve 39 is opened, and the plunger-side polymer solution valve 40 is opened to vent the inside of the anode buffer tank 9, the inside of the polymer solution tube 19, the inside of the T block 15, the inside of the plunger-side polymer solution tube 43, and the inside of the pressure-resistant syringe 16 to the atmospheric pressure. In this state, the plunger-side polymer solution valve 40 is closed.

[0119]

Next, the pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm, the anode pressurizing valve 26 is opened, and the anode release valve 27 is closed to pressurize the inside of the anode buffer tank 9, the inside of the polymer solution tube 19, and the inside of the T block 15 to 1 atm.

[0120]

Meanwhile, the sample-injection end 2 is inserted into the cathode buffer solution tank 8, and the cathode buffer solution tank 8 is sealed in a state in which the sample-injection end 2 is immersed in the cathode buffer solution 6. The cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to pressurize the inside of the cathode buffer solution tank 8 to 1 atm. As a result, both ends are brought into a pressurized state as shown in FIG. 22. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform the both-end pressurization electrophoresis. Accordingly, the pressure of the polymer solution 18 inside the capillary 1 is increased to 1 atm, the generation of bubbles in the capillary 1 during electrophoresis is prevented, and high separation performance can be stably

obtained. Further, the vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis.

[0121]

On the other hand, the polymer solution 18 in the T block 15 in which the sample-elution end 3 is immersed, and the polymer solution 18 in the pressure-resistant syringe 16 are divided by the plunger-side polymer solution valve 40, and therefore, the pressure of one does not affect the other. That is, the pressure of 1 atm in the polymer solution 18 in the T block 15 does not move the plunger 17 of the pressure-resistant syringe 16. Conversely, the movement of the plunger 17 does not change the pressure of the polymer solution 18 in the T block 15.

[0122]

FIG. 23 shows a state in which the capillary 1 is filled with the polymer solution 18 at a high pressure in the capillary electrophoresis device according to the Modified Example 8 (Embodiment 7). The anode pressurizing valve 26 is closed, and the anode release valve 27 is opened to vent the inside of the anode buffer solution tank 9 to the atmospheric pressure. The cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the inside of the cathode buffer solution tank 8 to the atmospheric pressure. In this state, the compressed air-side polymer solution valve 39 is closed, and the plunger-side polymer solution valve 40 is opened, and the plunger 17 of the pressure-resistant syringe 16 is mechanically pushed in using a motor to apply a high pressure of 35 atm to the polymer solution 18 in which the sample-elution end 2 is immersed. Since the sample-injection end 2 is under atmospheric pressure, a high pressure difference of 35 atm is generated between the sample-elution end 3 and the sample-injection end 2, and the capillary 1 is filled with the polymer solution 18 at a high pressure of 35 atm from the sample-elution end 3 toward the sample-injection end 2. After the filling with the polymer solution, the mechanical pushing-in of the plunger 17 is stopped, the plunger 17 and the mechanical pushing mechanism are separated, and the pressure applied to the polymer solution 18 is reduced to substantially zero. The compressed air-side

polymer solution valve 39 is opened to vent the sample-elution end 3 to the atmospheric pressure.
[0123]

FIG. 24 shows a state in which a sample is injected into the capillary 1 by pressure in the capillary electrophoresis device according to Modified Example 8 (Embodiment 7). With the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the sample solution tank 11 and immersed in the sample solution 10, and at the same time, the sample solution tank 11 is sealed. When the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, the pressure of the sample solution 10 inside the sample solution tank 11 and the pressure of the air 37 in contact with the sample solution 10 increase to 1 atm. As described above, a low pressure difference of 1 atm is generated between the sample-injection end 2 and the sample-elution end 3, and the sample solution 10 is injected into the capillary 1 from the sample-injection end 2. After a predetermined time has elapsed, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the pressure of the sample solution 10 and the pressure of the air 37 inside the sample solution tank 11 to the atmospheric pressure.

[0124]

Thereafter, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the cathode buffer solution tank 8 and immersed in the anode buffer solution 6, and at the same time, the cathode buffer solution tank 8 is sealed.

[0125]

Next, the plunger-side polymer solution valve 40 is closed. Thereafter, the anode pressurizing valve 26 is opened, and the anode release valve 27 is closed to pressurize the inside of the anode buffer tank 9, the inside of the polymer solution tube 19, and the inside of the T block 15 to 1 atm. On the other hand, when the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to pressurize the inside of the cathode buffer solution tank 8 to 1 atm, the state returns to the state shown in FIG. 22. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform the both-end pressurization electrophoresis.

[0126]

As described above, Modified Example 8 (Embodiment 7) can achieve all of the following objects: a first object of the invention, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (2) "capable of performing pressure injection of a sample"; a second object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (3) "capable of performing pressurization at both ends during electrophoresis"; and a third object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", (2) "capable of performing pressure injection of a sample", and (3) "capable of performing pressurization at both ends during electrophoresis". Of course, the sample can also be injected by an electric field using the capillary electrophoresis device according to Modified Example 8 (Embodiment 7).

[0127]

FIG. 35 shows a detailed example of steps of one capillary electrophoresis analysis using the pressure injection and both-end pressurization electrophoresis. The notation method is the same as that in FIGS. 33 and 34. The steps will be described in order. FIGS. 22 to 24 are basically followed except for a part. Steps 1 to 15 are the same as steps 1 to 15 in FIG. 34, and therefore, the description thereof will be omitted.

[0128]

Step 16: A space for storing a liquid system (cathode buffer solution) with which the sample-injection end is in contact (a space inside the cathode buffer solution tank) is sealed from the atmosphere. At the same time, a space (a space inside the anode buffer solution tank, the polymer solution tube, the T block, and the pressure-resistant syringe) for storing the liquid system (the anode buffer solution, and the polymer solution in the polymer solution tube, the T block, and the pressure-resistant syringe) with which the sample-elution end is in contact is sealed from the atmosphere.

[0129]

Step 17: The same compressed air is caused to flow into the space for storing the liquid system with which the sample-injection end is in contact and the space for storing the liquid system with which the sample-elution end is in contact, and a low pressure is applied to pressurize both ends.

Step 18: A voltage is applied between the sample-elution end and the sample-injection end to perform both-end pressurization electrophoresis.

Step 19: The voltage application is stopped, and only both-end pressurization is performed.

[0130]

Step 20: The pressure of the compressed air is brought to atmospheric pressure, and the pressure of the space for storing the liquid system with which the sample-injection end is in contact and the pressure of the space for storing the liquid system with which the sample-elution end is in contact are brought to atmospheric pressure (step 20 can be omitted).

[0131]

Step 21: The space for storing the liquid system with which the sample-injection end is in contact is opened to the atmosphere. At the same time, the space for storing the liquid system with which the sample-elution end is in contact is opened to the atmosphere. Accordingly, the state returns to the reference.

[0132]

When the capillary electrophoresis analysis is performed a plurality of times, steps 1 to 21 may be repeated a plurality of times. Steps 1 to 21 are preferably carried out in this order. However, as a unit of one capillary electrophoresis analysis, for example, steps 1 to 7 may also be performed after steps 7 to 21 are performed. Even in such a case, when the capillary electrophoresis analysis is performed a plurality of times, a step of performing steps 1 to 21 is necessarily performed.

[0133]

The steps 1 to 21 are characterized by the filling with the polymer solution in step 4, the pressure injection in step 12, and both-end pressurization electrophoresis (present migration)

in step 16. The invention is characterized in that the following steps are performed in the order of step A, step B, and step C: step A (step 4) of filling the capillary with a part of the polymer solution by pressing a solid against the polymer solution and applying a high pressure (pressure exceeding 7 atm) to the polymer solution in a state in which the sample-injection end is vented to the atmospheric pressure and the polymer solution as the separation medium is brought into contact with the sample-elution end; step B (step 12) of injecting a part of the sample solution into the capillary by applying a low pressure (pressure of 0 atm to 7 atm) to the sample solution by bringing compressed air into contact with the sample solution in a state in which the sample solution is brought into contact with the sample-injection end; and step C3 (step 16) of applying a low pressure (pressure of 0 atm to 7 atm) by bringing the compressed air into contact with the cathode buffer solution in a state in which the cathode buffer solution is brought into contact with the sample-injection end, applying a low pressure (pressure of 0 atm to 7 atm) to the liquid system by bringing the compressed air into contact with the liquid system containing the polymer solution with which the sample-elution end is in contact in a state in which the polymer solution is brought into contact with the sample-elution end, and applying a voltage between the sample-elution end and the sample-injection end. Alternatively, the invention is characterized in that the analysis includes a step of performing step A and step B in order.

[0134]

The component of the sample eluted from the sample-elution end by capillary electrophoresis slowly moves toward the anode 5. Such a component may be injected into the capillary again during filling with the polymer solution in the subsequent analysis, and there is a possibility of carryover. In order to reduce such a possibility, the following configuration is effective. When a position where a flow path from the anode buffer solution tank 9 to the sample-elution end 3 intersects with a flow path from the pressure-resistant syringe 16 to the sample-elution end 3 is referred to as an intersection, a distance between the sample-elution end 3 and the intersection is preferably as small as possible. The distance between the sample-elution end 3 and the intersection is preferably 10 mm or less, more preferably 1 mm or less, and most preferably 0 mm.

[0135]

<Modified Example 9: Embodiment 8>

FIGS. 25 to 27 show a configuration example of a capillary electrophoresis device according to Modified Example 9 (Embodiment 8). Modified Example 9 (Embodiment 8) is implemented by modifying Modified Example 8 (Embodiment 7: FIGS. 22 to 24), and achieves the object of the invention more effectively than Modified Example 8 (Embodiment 7). Modified Example 9 (Embodiment 8) is different from Modified Example 8 (Embodiment 7) in that the compressed air-side polymer solution valve 39 and the plunger-side polymer solution valve 40 in Modified Example 8 (Embodiment 7) are replaced with a rotary valve 42. With this modification, the two valves can be made into one valve, and automation of the device becomes easy. The capillary electrophoresis device according to Modified Example 9 (Embodiment 8) includes an air type pressurizing mechanism on the cathode side (sample-injection end side), and a plunger type pressurizing mechanism and an air type pressurizing mechanism on the anode side (sample-elution end side).

[0136]

FIG. 25 shows a state in which both-end pressurization electrophoresis is performed in the capillary electrophoresis device according to Modified Example 9 (Embodiment 8). The rotary valve 42 used in the capillary electrophoresis device according to Modified Example 9 (Embodiment 8) has six ports. In the rotary valve 42 shown in FIG. 25, a port at the 1 o'clock position of a timepiece is referred to as a port 1, a port at the 3 o'clock position of the timepiece is referred to as a port 2, a port at the 5 o'clock position of the timepiece is referred to as a port 3, a port at the 7 o'clock position of the timepiece is referred to as a port 4, a port at the 9 o'clock position of the timepiece is referred to as a port 5, and a port at the 11 o'clock position of the timepiece is referred to as a port 6.

[0137]

The rotary valve 42 includes an automatic rotation mechanism, and takes either one position of a position A and a position B by rotation. At the position A, the port 2 is coupled to the port 3, the port 4 is coupled to the port 5, and the port 6 is coupled to the port 1. At the position B, the port 1 is coupled to the port 2, the port 3 is coupled to the port 4, and the port 5 is coupled to the port 6. As shown in FIG. 25, the polymer solution tubes 19 are respectively

connected to the port 4 and the port 5, the polymer solution tube 19 connected to the port 4 is connected to the anode buffer solution tank 9, and the polymer solution tube 19 connected to the port 5 is connected to the T block 15. In addition, the plunger-side polymer solution tubes 43 are respectively connected to the port 1 and the port 2, the plunger-side polymer solution tube 43 connected to the port 2 is connected to the pressure-resistant syringe 16, and the plunger-side polymer solution tube 43 connected to the port 1 is connected to the T block 15. Further, the port 3 and the port 6 are sealed. In FIG. 25, the rotary valve 42 is at the position A. Accordingly, the two polymer solution tubes 19 are coupled, and the anode buffer solution tank 9 and the T block 15 are connected by the polymer solution tubes 19.

[0138]

Further, the two plunger-side polymer solution tubes 43 are separated, and the pressure-resistant syringe 16 and the T block 15 are not connected. That is, the anode buffer solution 7 in the anode buffer solution tank 9, the polymer solution 18 in the polymer solution tube 19, the polymer solution 18 in the T block 15, and the polymer solution 18 in the plunger-side polymer solution tube 43 between the T block 15 and the rotary valve 42 form a continuous liquid system A, and the sample-elution end 3 is immersed in the liquid system A. The pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm. The sample-injection end 2 is inserted into the cathode buffer solution tank 8, and the cathode buffer solution tank 8 is sealed in a state in which the sample-injection end 2 is immersed in the cathode buffer solution 6. The cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to apply a pressure of 1 atm to the air 34 and the cathode buffer solution 6 inside the cathode buffer solution tank 8.

[0139]

On the other hand, the anode pressurizing valve 26 is opened, and the anode release valve 27 is closed to apply a pressure of 1 atm to the air 35 and the anode buffer solution 7 inside the cathode buffer solution tank 9. Thus, a pressure of 1 atm is applied to the liquid system A.

[0140]

As described above, both ends of the cathode side and the anode side in FIG. 25 are brought into the pressurized state. In this state, a voltage is applied between the sample-elution

end 3 and the sample-injection end 2 to perform both-end pressurization electrophoresis. Accordingly, the pressure of the polymer solution 18 in the capillary 1 is increased to 1 atm, the generation of bubbles in the capillary 1 during electrophoresis is prevented, and high separation performance can be stably obtained.

[0141]

Further, the vertical height (Z coordinate) of the interface 101 between the cathode buffer solution 6 and air (that is, a liquid surface of the cathode buffer solution 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis. Further, since the polymer solution 18 in the T block 15 in which the sample-elution end 3 is immersed, and the polymer solution 18 in the pressure-resistant syringe 16 are not connected, the pressure of one does not affect the other. That is, the pressure of 1 atm in the polymer solution 18 in the T block 15 does not move the plunger 17 of the pressure-resistant syringe 16. Conversely, the movement of the plunger 17 does not change the pressure of the polymer solution 18 in the T block 15.

[0142]

FIG. 26 shows a state in which the capillary 1 is filled with the polymer solution 18 at a high pressure in the capillary electrophoresis device according to Modified Example 9 (Embodiment 8). The anode pressurizing valve 26 is closed, and the anode release valve 27 is opened to vent the inside of the anode buffer solution tank 9 to the atmospheric pressure. The cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the inside of the cathode buffer solution tank 8 to the atmospheric pressure. In this state, the rotary valve 42 is set to the position B. Accordingly, the two polymer solution tubes 19 are separated, and the anode buffer solution tank 9 and the T block 15 are not connected. In addition, two plunger-side polymer solution tubes 43 are coupled, and the pressure-resistant syringe 16 and the T block 15 are connected by the plunger-side polymer solution tube 43. That is, the polymer solution 18 in the pressure-resistant syringe 16, the polymer solution 18 in the plunger-side polymer solution tube 43, the polymer solution 18 in the T block 15, and the polymer

solution 18 in the polymer solution tube 19 between the T block 15 and the rotary valve 42 form a continuous liquid system B, and the sample-elution end 3 is immersed in the liquid system B. [0143]

In this state, the plunger 17 of the pressure-resistant syringe 16 is mechanically pushed in using a motor to apply a high pressure of 35 atm to the liquid system B. Since the sample-injection end 2 is under atmospheric pressure, a high pressure difference of 35 atm is generated between the sample-elution end 3 and the sample-injection end 2, and the capillary 1 is filled with the polymer solution 18 at a high pressure of 35 atm from the sample-elution end 3 toward the sample-injection end 2. After the filling with the polymer solution, the mechanical pushing-in of the plunger 17 is stopped, the plunger 17 and the mechanical pushing mechanism are separated, and the pressure applied to the polymer solution 18 is reduced to substantially zero. In this state, the rotary valve 42 is set to the position A, and the liquid system A and the sample-elution end 3 are vented to the atmospheric pressure. At this time, even if some pressure remains in the polymer solution 18 in the pressure-resistant syringe 16, the sample-elution end 3 is not affected, and thus there is no problem.

[0144]

FIG. 27 shows a state in which a sample is injected into the capillary 1 by pressure in the capillary electrophoresis device according to Modified Example 9 (Embodiment 8). With the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the sample solution tank 11 and immersed in the sample solution 10, and at the same time, the sample solution tank 11 is sealed. When the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, the pressure of the sample solution 10 inside the sample solution tank 11 and the pressure of the air 37 in contact with the sample solution 10 increase to 1 atm. As described above, a low pressure difference of 1 atm is generated between the sample-injection end 2 and the sample-elution end 3, and the sample solution 10 is injected into the capillary 1 from the sample-injection end 2. After a predetermined time has elapsed, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the pressure of the sample solution 10 and the pressure of the air 37 inside the sample solution tank 11 to the atmospheric pressure.

[0145]

Thereafter, with the movement of the cathode stage 12 using the XYZ axis drive mechanism, the sample-injection end 2 is inserted into the cathode buffer solution tank 8 and immersed in the anode buffer solution 6, and at the same time, the cathode buffer solution tank 8 is sealed. Next, the anode pressurizing valve 26 is opened, and the anode release valve 27 is closed to pressurize the air 35 inside the anode buffer solution tank 9 and the liquid system A to 1 atm. On the other hand, when the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed to pressurize the air 34 inside the cathode buffer solution tank 8 and the cathode buffer solution 6 to 1 atm, the state returns to the state shown in FIG. 25. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform both-end pressurization electrophoresis.

[0146]

As described above, Modified Example 9 (Embodiment 8) can achieve all of the following objects: a first object of the invention, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (2) "capable of performing pressure injection of a sample"; a second object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (3) "capable of performing pressurization at both ends during electrophoresis"; and a third object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", (2) "capable of performing pressure injection of a sample", and (3) "capable of performing pressurization at both ends during electrophoresis".

[0147]

In Modified Example 9 (Embodiment 8), not only pressure injection of the sample but also electric field injection can be performed. In FIG. 27, the cathode pressurizing valve 28 is closed, and the cathode release valve 29 is opened to vent the sample solution 10 in the sample solution tank 11 and the air 37 in contact therewith to the atmospheric pressure. In this state,

the sample can be injected into the capillary 1 by an electric field from the sample-injection end 2 by applying a voltage between the sample-elution end 3 and the sample-injection end 2 for a certain period of time.

[0148]

<Modified Example 10: Embodiment 9>

In each of the above-described Modified Examples, in order to simplify the description, each device includes one capillary, and electrophoresis analysis is performed using one capillary in each device. However, the invention is similarly applicable to a case where each device includes a plurality of capillaries and electrophoresis analysis is performed in parallel using the plurality of capillaries. FIG. 28 shows, as an example thereof, a configuration example of a capillary electrophoresis device according to Modified Example 10 (Embodiment 9) in which three capillaries are handled based on Modified Example 8 (Embodiment 7) (when performing both-end pressurization electrophoresis). Of course, the number of three is merely a specific example, and may be any number such as four, eight, 12, and the like.

[0149]

The sample-injection end 2 of each of the three capillaries 1 is inserted into a respective one of the three pipe-shaped cathodes 4, and the sample-injection end 2 and the pipe-shaped cathode 4 are integrated. Three sample-injection ends 2 are oriented in the -Z-axis direction, aligned in the Y-axis direction and the Z-axis direction, and arranged at equal intervals in the X-axis direction. The interval in the X-axis direction is, for example, 9 mm, which is equal to a well interval of a microtiter plate. The three cathode buffer solution tanks 8 in which the cathode buffer solutions 6 are stored are aligned in the Y-axis direction and the Z-axis direction and fixed onto the cathode stage 12 in the X-axis direction at the same intervals as the arrangement intervals of the three sample-injection ends 2 in the X-axis direction, and the cathode stage 12 is further coupled to an XYZ axis drive mechanism (not shown).

[0150]

At least three sample solution tanks 11 in which sample solutions 10 are stored are also fixed onto the cathode stage 12, but are omitted in FIG. 28. The O-ring 33 is placed at an edge of the upper end of each of the three cathode buffer solution tanks 8. With the movement of

the cathode stage 12 by the XYZ axis drive mechanism, the three sample-injection ends 2 are inserted into the three cathode buffer solution tanks 8, respectively, and immersed in the three cathode buffer solutions 6, respectively. At the same time, with the movement of the cathode stage 12 in the +Z direction, the three O-rings 33 are pressed against the flat surface portions of the fixed block 31 and compressed to seal the three cathode buffer solution tanks 8. A gap among the three capillaries 1, the three cathodes 4, and the fixed block 31 is sealed. The three cathode buffer solution tanks 8 contain three cathode buffer solutions 6 and common air 34 in contact with the three cathode buffer solutions 6. The air 34 is integrated inside the fixed block 31 and is connected to the compressed air source 25 or the atmosphere by the cathode pressurizing valve 28 and the cathode release valve 29 via the air tube 30. The pressure of the compressed air discharged from the compressed air source 25 is set to 1 atm.

[0151]

As shown in FIG. 28, when the cathode pressurizing valve 28 is opened, and the cathode release valve 29 is closed, the compressed air flows into the three cathode buffer solution tanks 8 via the air tube 30, and the pressure of the air 34 increases to 1 atm. At the same time, the pressures of the three cathode buffer solutions 6 contained in the three cathode buffer solution tanks 8 also increase to 1 atm.

[0152]

Three detection positions on the three capillaries 1 are arranged on a straight line, the three detection positions are collectively irradiated with the laser beam 24 emitted from the laser light source 23, and fluorescence emitted from the three detection positions is collectively detected by a fluorescence detection device (not shown).

[0153]

The sample-elution ends 3 of the three capillaries 1 are bundled together, connected to the T block 15 using the connector 14, and immersed in the polymer solution 18 in the T block 15. Other components on the anode side (the polymer solution tube 19 containing the polymer solution 18, the compressed air-side polymer solution valve 39, the anode buffer solution tank 9 containing the anode buffer solution 7 and the air 35, the fixed block 31, the plunger-side polymer solution tube 43, the plunger-side polymer solution valve 40, the pressure-resistant

syringe 16 containing the polymer solution 18, and the like) are the same as those in Modified Example 8 (Embodiment 7).

[0154]

As shown in FIG. 28, when the anode pressurizing valve 26 is opened, and the anode release valve 27 is closed, the compressed air flows into the anode buffer solution tank 9 via the air tube 30, and the pressure of the air 35 increases to 1 atm. At the same time, the pressures of the anode buffer solution 7 contained in the anode buffer solution tank 9, the polymer solution 18 contained in the polymer solution tube 19, and the polymer solution 18 contained in the T block 15 also increase to 1 atm. In this state, a voltage is applied between the sample-elution end 3 and the sample-injection end 2 to perform both-end pressurization electrophoresis. Accordingly, the pressure of the polymer solution 18 in the capillary 1 is increased to 1 atm, the generation of bubbles in the capillary 1 during electrophoresis is prevented, and high separation performance can be stably obtained.

[0155]

In addition, the vertical height (Z coordinate) of the interface 101 between each of the three cathode buffer solutions 6 and air (that is, a liquid surface of each of the three cathode buffer solutions 6) and the vertical height (Z coordinate) of the interface 102 between the anode buffer solution 7 and air (that is, a liquid surface of the anode buffer solution 7) are equalized. Accordingly, the polymer solution 18 inside the capillary 1 can be prevented from moving due to gravity during the electrophoresis. Methods such as filling with the polymer solution and the pressure injection of the sample are the same as those in Modified Example 8 (Embodiment 7).

[0156]

As described above, Modified Example 10 (Embodiment 9) can achieve all of the following objects for each of the three capillaries: a first object of the invention, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (2) "capable of performing pressure injection of a sample"; a second object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with

a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis" and (3) "capable of performing pressurization at both ends during electrophoresis"; and a third object, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", (2) "capable of performing pressure injection of a sample", and (3) "capable of performing pressurization at both ends during electrophoresis". In Modified Example 10 (Embodiment 9), not only the pressure injection of the sample but also the electric field injection can be performed.

[0157]

<Summary of Embodiment>

First, the air type pressurizing mechanism provided at the sample-elution end in the device B (Related Example 2) is replaced with a plunger type pressurizing mechanism (Modified Example 1: device D). The configuration of the sample-injection end side is not changed. The sample-elution end is connected to a container filled with a polymer solution, and further, a syringe filled with a polymer solution is connected to the container. Internal spaces of the container and the syringe form one sealed internal space filled with the polymer solution. The sample-elution end and the anode integrated with the sample-elution end are immersed in the polymer solution in the above internal space. When the plunger of the syringe is mechanically pushed in a state in which the sample-injection end is vented to the atmospheric pressure, the pressure of the polymer solution inside can be increased to 35 atm, and the capillary can be filled with the high-viscosity polymer solution. When the sample-injection end is immersed in the sample solution, and a voltage is applied to both ends of the capillary, the sample can be injected into the capillary by an electric field. However, even if the sample-injection end is immersed in the sample solution, and a low pressure of 1 atm is applied by the air type pressurizing mechanism, the sample cannot be injected into the capillary by pressure. This is because, in the device D, the sample-elution end cannot be vented to atmospheric pressure, so that no pressure difference occurs between both ends of the capillary. This problem is the same as the problem of the device C. However, when the sample-injection end of the capillary is immersed in the cathode buffer solution, and a voltage is applied to both ends of the capillary,

electrophoresis can be performed. Therefore, the configuration of the device D cannot achieve any object of the invention.

[0158]

Next, the air type pressurizing mechanism provided at the sample-elution end in the device B is replaced with the plunger type pressurizing mechanism of the device A (Reference Example 1: referred to as device E). The configuration of the sample-injection end side is not changed. The sample-elution end integrated with the anode is connected to a flow path containing the polymer solution, and a syringe containing the polymer solution is connected to the flow path. In addition, the anode buffer tank containing the anode buffer solution is also connected to the flow path, and a valve is placed at the boundary between the anode buffer solution and the polymer solution. When the pressure of the polymer solution inside is increased to 35 atm by mechanically pushing the plunger of the syringe in a state in which the sample-injection end is vented to the atmospheric pressure and the valve is closed, the capillary can be filled with a high-viscosity polymer solution. When the valve is opened, the sample-elution end is vented to the atmospheric pressure. Therefore, when the sample-injection end is immersed in the sample solution, and a low pressure of 1 atm is applied by the air type pressurizing mechanism, the sample can be injected into the capillary by pressure. Alternatively, when the sample-injection end is immersed in the sample solution, and a voltage is applied to both ends of the capillary, the sample can be injected into the capillary by an electric field. When the sample-injection end of the capillary is immersed in a cathode buffer solution, and a voltage is applied to both ends of the capillary, electrophoresis can be performed. However, immersing the anode integrated with the sample-elution end in the polymer solution contained in the flow path adversely affects the electrophoresis analysis as follows. Unlike the anode buffer tank, the flow path has a small inner diameter and a small internal volume per unit length in an electrophoresis direction. Therefore, an ion composition of the polymer solution in the vicinity of the sample-elution end changes along with the electrophoresis, and finally, ion depletion occurs. In addition, the gas generated on a surface of the anode along with the electrophoresis remains as bubbles in the flow path, resulting in a large electric resistance. Further, the components of the sample eluted from the sample-elution end along with the

electrophoresis remain in the flow path, and such components flow back into the capillary due to filling with the polymer solution in the subsequent analysis, which causes a carryover problem. [0159]

Therefore, the integrated anode and sample-elution end in the device E are separated, and the sample-elution end is connected to the flow path containing the polymer solution, and on the other hand, the anode is immersed in the anode buffer solution (Modified Example 3 (Embodiment 2): device F). With the configuration of the device F, the position of the anode does not adversely affect the electrophoresis analysis. Therefore, the filling with the polymer solution can be performed within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis, and pressure injection of the sample can also be performed. Therefore, the device F can achieve the first object of the invention, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", and (2) "capable of performing pressure injection of a sample". However, the sample-elution end is not provided with an air type pressurizing mechanism, and therefore, both-end pressurization during electrophoresis cannot be performed.

[0160]

In order to implement both-end pressurization electrophoresis, a plunger type pressurizing mechanism is placed at the sample-injection end in the same manner as the sample-elution end in the device A (Related Example 1) (Reference Example 2: device G). The configuration of the sample-elution end side is not changed. The sample-injection end integrated with the cathode is connected to a flow path containing the polymer solution, and further, the syringe containing the polymer solution is connected to the flow path. The cathode buffer tank containing the cathode buffer solution is also connected to the flow path, and a valve is placed at a boundary between the cathode buffer solution and the polymer solution. The plunger type pressurizing mechanism increases the pressure of the polymer solution inside by mechanically pushing the plunger of the syringe in a state in which the valve is closed. In addition, when the valve is opened, the sample-injection end is vented to the atmospheric pressure. As described above, independent plunger type pressurizing mechanisms are placed

at both ends of the capillary, and therefore, it is expected that both-end pressurization during electrophoresis can be performed. However, as compared with the air type pressurizing mechanism, the plunger type pressurizing mechanism is suitable for applying a high pressure, but is not suitable for applying a low pressure with a high accuracy and stability. For example, the sliding resistance when the plunger is pushed into the syringe is not constant, and therefore, the internal pressure fluctuates even if a pushing force is constant. In addition, when the air type pressurizing mechanisms are used at both ends of the capillary as in the device B, the pressures at both ends can be equalized by branching and using the same compressed air for each air type pressurizing mechanism. In contrast, when the plunger type pressurizing mechanisms are used at both ends of the capillary as in the device G, it is difficult to equalize the pressures at both ends because the mechanisms are independent of each other. When there is a difference in pressure between both ends, the polymer solution in the capillary moves from a position with a higher pressure to a position with a lower pressure, which adversely affects the separation ability. Further, the sample-injection end is connected to the flow path containing the polymer solution, and therefore, it is difficult to separate the sample-injection end from the flow path and immerse the sample-injection end in the sample solution. Therefore, it is difficult to perform both the pressure injection and the electric field injection of the sample.

[0161]

Based on the above description, a sealed chamber including a set of the anode buffer tank, the valve, and the mechanism for driving the valve is placed, and an air type pressurizing mechanism achieved by introducing compressed air into the sealed chamber is placed in the device F (Modified Example 5 (Embodiment 4): device H). The air in the sealed chamber can also be vented to the atmospheric pressure. The valve and the mechanism for driving the valve largely protrude from the inside of the anode buffer tank and move spatially, and therefore, it is difficult to seal only the anode buffer tank as in the device B. Therefore, a relatively large sealed chamber as described above is placed. By mechanically pushing the plunger of the syringe in a state in which the sample-injection end is vented to the atmospheric pressure, the sealed chamber is opened to atmospheric pressure, and the valve is closed, the pressure of the polymer solution inside can be increased to 35 atm, and the capillary can be filled with a high-

viscosity polymer solution. When the valve is opened, the sample-elution end is vented to the atmospheric pressure. Therefore, when the sample-injection end is immersed in the sample solution, and a low pressure of 1 atm is applied by the air type pressurizing mechanism, the sample can be injected into the capillary by pressure. Alternatively, when the sample-injection end is immersed in the sample solution, and a voltage is applied to both ends of the capillary, the sample can be injected into the capillary by an electric field. When the sample-injection end of the capillary is immersed in a cathode buffer solution, and a voltage is applied to both ends of the capillary, electrophoresis can be performed. In addition, during the electrophoresis, in a state in which the valve is opened, a low pressure of 1 atm is applied to the sample-elution end by the air type pressurizing mechanism achieved by introducing compressed air into the sealed chamber, and at the same time, a low pressure of 1 atm is applied to the sample-injection end by the air type pressurizing mechanism achieved by sealing the cathode buffer tank and introducing compressed air, so that both-end pressurization can be implemented.

[0162]

As described above, the device H can achieve the third object of the invention, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", (2) "capable of performing pressure injection of a sample", and (3) "capable of performing pressurization at both ends during electrophoresis". However, there is a problem in that the structure of the sealed chamber is large and complicated. In addition, the internal volume of the sealed chamber is large, and therefore, it is a problem of taking a long time for the internal pressure to reach a predetermined pressure after the compressed air is introduced.

[0163]

Further, in view of the above description, the valve at the boundary between the anode buffer solution and the polymer solution is removed, the valve 1 is placed on the flow path between the sample-elution end and the anode buffer tank, the valve 2 is also placed on the flow path between the sample-elution end and the syringe in the device F, and at the same time, similarly to the device B, the anode buffer tank has a sealed structure, and an air type

pressurizing mechanism achieved by introducing compressed air into the anode buffer tank is placed (Modified Example 8 (Embodiment 7): device I). However, unlike the device B, the sample-elution end of the capillary is not inserted into the anode buffer tank, and instead, a flow path containing the polymer solution, which is connected to the sample-elution end, is inserted. The anode buffer tank may be vented to the atmospheric pressure. The configuration of the sample-injection end side is not changed. By mechanically pushing the plunger of the syringe in a state in which the sample-injection end is vented to the atmospheric pressure, the valve 1 is closed, and the valve 2 is opened, the pressure of the polymer solution inside can be increased to 35 atm, and the capillary can be filled with a high-viscosity polymer solution. When the anode buffer tank is vented to the atmospheric pressure, and the valve 1 is opened, the sample-elution end is opened to atmospheric pressure. In this state, when the sample-injection end is immersed in the sample solution, and a low pressure of 1 atm is applied by the air type pressurizing mechanism, the sample can be injected into the capillary by pressure. Alternatively, when the sample-injection end is immersed in the sample solution, and a voltage is applied to both ends of the capillary, the sample can be injected into the capillary by an electric field. When the sample-injection end of the capillary is immersed in a cathode buffer solution, and a voltage is applied to both ends of the capillary, electrophoresis can be performed. Further, during the electrophoresis, in a state in which the valve 1 is opened, and the valve 2 is closed, a low pressure of 1 atm is applied to the anode buffer tank and the sample-elution end by the air type pressurizing mechanism, and at the same time, a low pressure of 1 atm is applied to the sample-injection end by the air type pressurizing mechanism, both-end pressurization electrophoresis can be performed.

[0164]

As described above, the device I can achieve the third object of the invention, i.e., providing a capillary electrophoresis device (1) "capable of performing filling with a polymer solution within a practical time using a high-viscosity polymer solution for DNA sequencing and DNA fragment analysis", (2) "capable of performing pressure injection of a sample", and (3) "capable of performing pressurization at both ends during electrophoresis".

Reference Signs List

[0165]

- 1: capillary
- 2: sample-injection end
- 3: sample-elution end
- 4: cathode
- 5: anode
- 6: cathode buffer solution
- 7: anode buffer solution
- 8: cathode buffer solution tank
- 9: anode buffer solution tank
- 10: sample solution
- 11: sample solution tank
- 12: cathode stage
- 13: anode stage
- 14: connector
- 15: T block
- 16: pressure-resistant syringe
- 17: plunger
- 18: polymer solution
- 19: polymer solution tube
- 20: polymer solution valve
- 21: DC power supply
- 22: electric wire
- 23: laser light source or lamp light source
- 24: laser beam or lamp light
- 25: compressed air source
- 26: anode pressurizing valve
- 27: anode release valve

- 28: cathode pressurizing valve
- 29: cathode release valve
- 30: air tube
- 31: fixed block
- 32: polymer solution tank
- 33: O-ring
- 34: air in contact with cathode buffer solution
- 35: air in contact with anode buffer solution
- 36: air in contact with polymer solution
- 37: air in contact with sample solution
- 38: sealed chamber
- 39: compressed air-side polymer solution valve
- 40: plunger-side polymer solution valve
- 41: plunger stopper
- 42: rotary valve
- 43: plunger-side polymer solution tube
- 101: interface between cathode buffer solution and air
- 102: interface between anode buffer solution and air
- 103: interface between anode buffer solution and polymer solution
- 104: interface between polymer solution and plunger
- 105: interface between sample solution and air
- 106: interface between polymer solution and air

CLAIMS

[Claim 1]

A capillary electrophoresis device comprising:

a first liquid system with which a first capillary end of a capillary is in contact;

a second liquid system with which a second capillary end of the capillary is in contact;

a power supply configured to apply a voltage between the first liquid system and the second liquid system;

a first pressurizing mechanism configured to compress a first gas in direct or indirect contact with a first interface of the first liquid system to increase a first pressure of the first liquid system;

a first depressurizing mechanism configured to reduce the first pressure of the first liquid system;

a second pressurizing mechanism configured to move a solid in direct or indirect contact with a second interface of the second liquid system to increase a second pressure of the second liquid system; and

a second depressurizing mechanism configured to reduce the second pressure of the second liquid system, wherein

the second liquid system has a second gas in direct or indirect contact with a third interface of the second liquid system.

[Claim 2]

The capillary electrophoresis device according to claim 1, wherein

the first pressurizing mechanism is a pressurizing mechanism that seals a first space in which the first liquid system is stored from atmosphere and supplies compressed air to the first space, and

the second pressurizing mechanism is a pressurizing mechanism that seals a second space in which the second liquid system is stored from the atmosphere and reduces a volume of the second space.

[Claim 3]

The capillary electrophoresis device according to claim 2, wherein
the first depressurizing mechanism is a first atmospheric pressure opening mechanism that opens the first space to the atmosphere and reduces the first pressure to an atmospheric pressure, and

the second depressurizing mechanism is a second atmospheric pressure opening mechanism that opens the second space to the atmosphere and reduces the second pressure to the atmospheric pressure.

[Claim 4]

The capillary electrophoresis device according to claim 3, wherein
a portion of the second liquid system with which the second capillary end is in contact is a polymer solution as a separation medium, and

in a state in which the first pressure reaches the atmospheric pressure due to the first atmospheric pressure opening mechanism, the second pressurizing mechanism increases the second pressure to fill the capillary with a part of the polymer solution.

[Claim 5]

The capillary electrophoresis device according to claim 3, wherein
a portion of the first liquid system with which the first capillary end is in contact is a sample solution, and

in a state in which the second pressure reaches the atmospheric pressure due to the second atmospheric pressure opening mechanism, the first pressurizing mechanism increases the first pressure to inject a part of the sample solution into the capillary.

[Claim 6]

The capillary electrophoresis device according to claim 3, wherein
when electrophoresis is performed by applying a voltage to the first capillary end and

the second capillary end in a state in which

the first pressure reaches the atmospheric pressure due to the first atmospheric pressure opening mechanism and

the second pressure reaches the atmospheric pressure due to the second atmospheric pressure opening mechanism,

a vertical height of the first interface and a vertical height of the third interface are equalized.

[Claim 7]

A capillary electrophoresis analysis method to be executed by applying a voltage between a first capillary end and a second capillary end of a capillary, the capillary electrophoresis analysis method comprising:

a step 1 of filling, in a state in which the first capillary end is vented to an atmospheric pressure and a polymer solution as a separation medium is brought into contact with the second capillary end, the capillary with a part of the polymer solution by pressing a solid against the polymer solution and pressurizing the polymer solution; and

a step 2 of injecting, in a state in which a sample solution is brought into contact with the first capillary end, a part of the sample solution into the capillary by bringing compressed air into contact with the sample solution and pressurizing the sample solution, wherein

the method is executed in an order of the step 1 and the step 2.

[Claim 8]

A capillary electrophoresis analysis method to be executed by applying a voltage between a first capillary end and a second capillary end of a capillary, the capillary electrophoresis analysis method comprising:

a step 1 of filling, by applying a pressure of 0 atm to the first capillary end and applying a pressure of more than 7 atm to the second capillary end in a state of being in contact with a polymer solution as a separation medium, the capillary with a part of the polymer solution; and

a step 2 of injecting, by applying a pressure of 7 atm or less to the first capillary end in

a state of being in contact with a sample solution and applying a pressure of 0 atm to the second capillary end, a part of the sample solution into the capillary, wherein

the method is executed in an order of the step 1 and the step 2.

[Claim 9]

A capillary electrophoresis device comprising:

a first liquid system with which a first capillary end of a capillary is in contact;

a second liquid system with which a second capillary end of the capillary is in contact;

a power supply configured to apply a voltage between the first liquid system and the second liquid system;

a first pressurizing mechanism configured to compress a first gas in direct or indirect contact with a first interface of the first liquid system to increase a first pressure of the first liquid system;

a second pressurizing mechanism configured to move a solid in direct or indirect contact with a second interface of the second liquid system to increase a second pressure of the second liquid system; and

a third pressurizing mechanism configured to compress a second gas in direct or indirect contact with a third interface of the second liquid system to increase the second pressure of the second liquid system.

[Claim 10]

The capillary electrophoresis device according to claim 9, further comprising:

a first depressurizing mechanism configured to reduce the first pressure of the first liquid system; and

a second depressurizing mechanism configured to reduce the second pressure of the second liquid system.

[Claim 11]

The capillary electrophoresis device according to claim 10, wherein

the first pressurizing mechanism is a pressurizing mechanism that seals a first space in which the first liquid system is stored from atmosphere and supplies compressed air to the first space,

the second pressurizing mechanism is a pressurizing mechanism that seals a second space in which the second liquid system is stored from the atmosphere and reduces a volume of the second space, and

the third pressurizing mechanism is a pressurizing mechanism that seals the second space from the atmosphere and supplies compressed air to the second space.

[Claim 12]

The capillary electrophoresis device according to claim 11, wherein

the first depressurizing mechanism is a first atmospheric pressure opening mechanism that opens the first space to the atmosphere and reduces the first pressure to an atmospheric pressure, and

the second depressurizing mechanism is a second atmospheric pressure opening mechanism that opens the second space to the atmosphere and reduces the second pressure to the atmospheric pressure.

[Claim 13]

The capillary electrophoresis device according to claim 12, wherein

a portion of the second liquid system with which the second capillary end is in contact is a polymer solution as a separation medium, and

in a state in which the first pressure reaches the atmospheric pressure due to the first atmospheric pressure opening mechanism, the second pressurizing mechanism increases the second pressure to fill the capillary with a part of the polymer solution.

[Claim 14]

The capillary electrophoresis device according to claim 12, wherein

a portion of the first liquid system with which the first capillary end is in contact is a

sample solution, and

in a state in which the second pressure reaches the atmospheric pressure due to the second atmospheric pressure opening mechanism, the first pressurizing mechanism increases the first pressure to inject a part of the sample solution into the capillary.

[Claim 15]

The capillary electrophoresis device according to claim 12, wherein
the first pressurizing mechanism and the third pressurizing mechanism use compressed air of equal pressure,

the first pressure and the second pressure are equalized by the first pressurizing mechanism increasing the first pressure, and the third pressurizing mechanism increasing the second pressure, and

a voltage is applied between the first capillary end and the second capillary end to perform capillary electrophoresis.

[Claim 16]

The capillary electrophoresis device according to claim 12, further comprising:
a first valve configured to divide or couple the second liquid system between the third interface and the second capillary end.

[Claim 17]

The capillary electrophoresis device according to claim 12, further comprising:
a second valve configured to divide or couple the second liquid system between the second interface and the second capillary end.

[Claim 18]

The capillary electrophoresis device according to claim 12, wherein
when electrophoresis is performed by applying a voltage to the first capillary end and the second capillary end, a height of the first interface and a vertical height of the third interface

are equalized.

[Claim 19]

A capillary electrophoresis analysis method to be executed by applying a voltage between a first capillary end and a second capillary end of a capillary, the capillary electrophoresis analysis method comprising:

a step 1 of filling, in a state in which the first capillary end is vented to an atmospheric pressure and a polymer solution as a separation medium is brought into contact with the second capillary end, the capillary with a part of the polymer solution by pressing a solid against the polymer solution and pressurizing the polymer solution;

a step 2 of injecting, in a state in which a sample solution is brought into contact with the first capillary end, a part of the sample solution into the capillary by bringing first compressed air into contact with the sample solution and pressurizing the sample solution; and

a step 3 of bringing, in a state in which a buffer solution is brought into contact with the first capillary end, second compressed air into contact with the buffer solution and pressurizing the buffer solution, bringing, in a state in which the polymer solution is brought into contact with the second capillary end, the second compressed air into contact with a liquid system containing the polymer solution and pressurizing the liquid system, and applying a voltage between the first capillary end and the second capillary end, wherein

the method is executed in an order of the step 1, the step 2, and the step 3.

[Claim 20]

A capillary electrophoresis analysis method to be executed by applying a voltage between a first capillary end and a second capillary end of a capillary, the capillary electrophoresis analysis method comprising:

a step 1 of filling, by applying a first pressure of 0 atm to the first capillary end and applying a second pressure of more than 7 atm to the second capillary end in a state of being in contact with a polymer solution as a separation medium, the capillary with a part of the polymer solution;

a step 2 of injecting, by applying a third pressure of 7 atm or less to the first capillary end in a state of being in contact with a sample solution and applying the first pressure to the second capillary end, a part of the sample solution into the capillary; and

a step 3 of performing both-end pressurization electrophoresis by applying a fourth pressure of 7 atm or less to the first capillary end in a state of being in contact with a buffer solution, applying the fourth pressure to the second capillary end in a state of being in contact with the polymer solution, and applying a voltage between the first capillary end and the second capillary end, wherein

the method is executed in an order of the step 1, the step 2, and the step 3.