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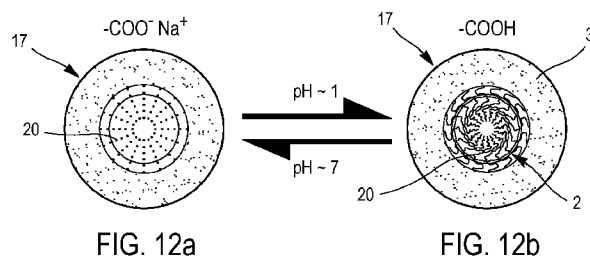
(54) Title: NANO-VALVE COMPRISING A NANOPOROUS MEMBRANE WHEREIN THE PORES ARE FUNCTIONAL-
IZED WITH A POLYELECTROLYTE AND AT LEAST TWO ELECTRODES

FIG. 12a

FIG. 12b

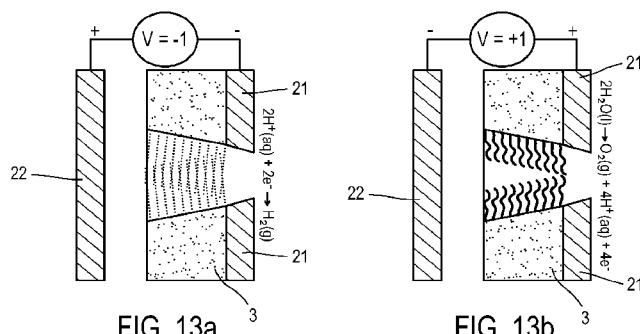


FIG. 13a

FIG. 13b

(57) Abstract: A variable diameter nanoporous device comprising: - a functionalised radio-grafted track-etched membrane (FRTEM) containing at least one nanopore which is radio-grafted with a polyelectrolyte such as the polyacrylic acid, - at least two electrodes adapted to provide a variable potential difference in a region near the electrodes of an aqueous solution, the pH of said region is intended to vary as a function of the potential difference due to electrolysis; the membrane and the two electrodes are arranged in the aqueous solution in such a way that the nanopore is included in said region; the effective diameter or hydrophilicity of the polyelectrolyte changing as a function of the potential difference.



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"Nano-valve device comprising nanoporous membrane."

5 The present invention relates generally to nanoporous membranes, and more particularly to a novel arrangement for controlling the diameter of nanopores realised inside nanoporous polymeric membranes.

 Because of its excellent mechanical and physicochemical properties, poly(vinylidene fluoride) (PVDF) has found wide-spread industrial applications
10 and research interest since the 1960s. Especially, PVDF membranes are produced for separation and filtration. Often, these membranes are chemically and/or physically modified in order to match specific applications, e.g. ion-exchange membranes. As such, hydrophilic PVDF membranes have been studied and applied for non-conventional fields such as drug delivery.

15 The document "Tailoring bulk and surface grafting of poly(acrylic acid) in electron-irradiated PVDF", M.-Cl. Clochard et al, Polymer 45 (Nov2004) 8683-8694, discloses a process to endow hydrophobic membranes with hydrophilic properties using electron beam irradiation. Several parameters governing the structure and morphology of PVDF-g-PAA films have been determined and
20 technique for specially grafting-through and/or surface-grafting is disclosed.

 Numerous processes for the synthesis of nanoporous polymeric membranes exist. One of them, called track etched technique, uses swift heavy ion irradiation.

 The document "Grafting of acrylic acid on etched latent tracks induced by
25 swift heavy ions on polypropylene films", Mazzei et al., Nuclear Instruments and Methods in Physics Research B 266 (march 2008) 3170-3173, describes a systematic study of the grafting process on nuclear tracks that involves different polymers and monomers. This document concerns a stack of foils irradiated by swift heavy ions. The irradiation step leads to the formation of the so-called
30 latent tracks. The etching procedure removes active sites of the latent tracks thus producing pores of different length and diameter. Active sites remaining after the etching procedure were used to graft acrylic acid (AA) on the tracks. This document discloses the fact that the effective diameter of the pores evolves as a function of pH solution during grafting procedure.

35 The document US 2006/0163071, Siwy et al., describes a nanodevice, such as a polymeric foil, for controlling the flow of charged particles in

electrolytes. This document describes an electrolytic bath container divided by a polymeric foil into a first and second compartments. Each compartment comprises an electrode connected to a voltage supply. The nanodevice comprises an asymmetric pore forming a hole through said foil. An electrically
5 conductive layer surrounds the narrow opening of the pore. An electric potential is thus created inside the pore and allows controlling ionic current through the pore. This system is limited to a container which is hermetically divided in two compartments. The electrodes are used to directly control the charged particles in electrolytes.

10 An object of the present invention is to control the effective diameter of pores inside a membrane. Further, it is an object of the present invention to create a nano valve that can be opened and closed at will.

15 The present invention is a variable diameter nanoporous device comprising:

- a functionalised radio-grafted track-etched membrane FRTEM containing at least one nanopore which is radio-grafted with a polyelectrolyte,
- at least two electrodes adapted to provide a variable potential difference
20 in a region, near the electrodes, of an aqueous or solvent polar solution, the pH of said region is intended to vary as a function of the potential difference due to electrolysis; the functionalised radio-grafted track-etched membrane FRTEM and the two electrodes are arranged in the aqueous solution in such a way that the nanopore is included in said region; the effective diameter or hydrophilicity of
25 the polyelectrolyte changing as a function of the potential difference.

A polyelectrolyte is a macromolecular substance, which has the power to dissociate when dissolved in water or in any other ionizing medium, to give at least one ion. In other words, a polyelectrolyte is a polymer containing at least one ionisable monomer.

30 In particular, the polyelectrolyte can give polyions, such as polyanions, when dissociated in water. A polyelectrolyte can be a polyacid, a polybasic, a polysalt or polyampholytes (contain both acidic (cationic) and basic (anionic) functional groups). In the present invention, it is preferably a polyacid and preferably a strong polyacid. In general, a polyelectrolyte according to the
35 invention is a pH dependent polymer.

Preferably, the functionalised radio-grafted track-etched membrane FRTEM is based on a poly(vinylidene fluoride) PVDF film, and the polyelectrolyte is polyacrylic acid PAA. In other words, in the presence of vinyl monomer, such as acrylic acid (AA), a radical polymerization takes place by radio grafting process to specifically functionalise the nanopore wall with hydrogel.

In other words, the structure of the polyelectrolyte, as the polyacrylic acid (PAA), depends on pH. It is hydrophobic when it is in the protonated form, low pH, and hydrophilic in the deprotonated form, high pH. The pH can be changed near an electrode surface due to the electrolysis of water. Negative voltages reduce protons (H^+) at the electrode surface which results in an increase in pH. Positive voltages can oxidize or break H_2O into O_2 and H^+ at the electrode surface, decrease in pH. If PAA is near an electrode (within a few microns, ~ 10 microns) the form of its structure can be changed by pH changes near the electrode due to electrolysis. This can be used to switch the PAA in the pores of functionalised radio grafted track-etched membranes (FRTEM) between the hydrophilic phase and the hydrophobic phase by applying a voltage to electrodes. This is useful as a device for the separation and analysis of protein residues. This effect could also be exploited to make nanovalves for micro and nanofluidics or as variable diameter nanofilters.

The device according to the invention can be used as a bistable nanovalve that behaves as a switch, or it can be used as a progressive nanovalve by progressively changing the diameter of the nanopore.

The device according to the invention acts on acrylic acid grafted on the nanopore wall in order to change the diameter of said nanopore. On the contrary, document US 2006/0163071 acts directly on the charged particles without changing the diameter of the pore.

Preferably, the polymer nanopores consist of tubules through the entire thickness of the functionalised radio-grafted track-etched membrane. The membrane could be in a shape of a cylinder or parallelepiped in which tubules are all parallel and perpendicular to two opposite sides of the membrane. The thickness of the membrane could substantially be of $9\text{ }\mu\text{m}$ and the nanopores could present a diameter between 20 and 100 nm. Moreover, each side of the membrane could present a diameter of substantially 400mm^2 .

Advantageously, nanoporous membranes according to the present invention have better diffusion profiles than porous sponge like films due to 2D

diffusion as opposed to 3D diffusion, such as glassy carbon, and an uniform distribution of pore diameter and length.

In preferred embodiment, the membrane is specifically grafted inside the nanopores. The synthesis of functionalized radio grafted membranes comprises notably steps of irradiation to activate radicals, chemical etching and radiografting. The remanence of radicals within the nanopore walls after etching allows to radio graft specifically inside the nanopores and not the membrane surface.

According to a preferred embodiment of the invention:

- 10 - one of said two electrodes is a surface electrode arranged on one side of the functionalised radio-grafted track-etched membrane FRTEM, said surface electrode comprising an aperture so that the nanopore remains open,
- the other electrode is disposed in the same solution as the functionalised radio-grafted track-etched membrane FRTEM, for example at
15 opposite side of the surface electrode.

The two electrodes can be connected to a single voltage generator.

In general, each surface electrode may be a sputtered metallic layer that enters the nanopores some hundreds of nm.

According to another embodiment of the invention:

- 20 - one of said two electrodes is composed of two surface electrodes respectively arranged on each side of the functionalised radio-grafted track-etched membrane FRTEM perpendicularly with respect to the nanopore, each surface electrode comprising an aperture so that the nanopore remains open, said two surface electrodes being connected together;
- 25 - the other electrode is disposed next to, contactless, the functionalised radio-grafted track-etched membrane FRTEM.

According to another embodiment of the invention, the two electrodes are two surface electrodes respectively arranged on each side of the functionalised radio-grafted track-etched membrane FRTEM perpendicularly with respect to
30 the longitudinal axis of the nanopore, each surface electrode comprising an aperture so that the nanopore remains open.

According to an advantageously variant embodiment of the invention, the nanoporous device comprises:

- a plurality of nanopores, and
- 35 - said at least two electrodes comprises a plurality of independent surface electrodes arranged on one side of the functionalised radio-grafted track-etched

membrane FRTEM, each surface electrode being associated with a nanopore and comprising an aperture so that the associated nanopore remains open;

- said at least two electrodes further comprises at least another electrode disposed next to the functionalised radio-grafted track-etched membrane FRTEM at opposite sides of the surface electrodes, each surface electrode providing an independent potential difference with respect to said at least another electrode.

Advantageously, the potential difference between said at least two electrodes is obtained by means of a potentiostat or power supply. The voltage can be variable inside a range of +/- ~1.5 volts.

The present invention also concerns an application of the variable diameter nanoporous device in which the hydrophobicity of the poly-electrolyte changes as a function of the potential difference, said change being reversible with the control of the electrodes such that nanopore effective diameter is driven in a controllable manner.

For the purpose of illustrating the invention, there is shown in the drawings a form that is presently preferred; it being understood, however, that this invention is not limited to the precise arrangements and instrumentalities.

Figure 1 is a schematic view illustrating Track-etch process: I) swift heavy Ions irradiation forms damaged zones in the polymer bulk along the ion pathway called latent tracks, II) the latent tracks are chemically etched forming nanopore of biconical shape at the early stage and III) if the track etch rate is sufficiently higher than the bulk etch rate, biconical nanopores become cylindrical;

Figure 2 is a graph illustrating the electron paramagnetic resonance (EPR) spectra per mass unit (mg-1) for a heavy ion irradiated film;

Figure 3 is a graph illustrating the radical decay from EPR results versus time;

Figure 4 is a graph illustrating a FTIR spectra of swift heavy ion $^{58}\text{Ni}^{25+}$ irradiated PVDF-g-PAA for different etching times (AA concentration 100% v/v, fluence 109cm^{-2} , Mohr's salt 0.25% w/w, radiografting at 60°C for 1 hour); the maximum corresponds to O-C=O stretching (1701 cm^{-1}) and gives evidence of COOH groups radiografted PAA chains;

Figure 5 is a schematic view of a membrane cut in order to view nanopore walls;

Figure 6 shows a schematic cut-away side view of a membrane with gold electrodes on top and bottom sides;

5 Figure 7 shows a perspective view of the membrane of figure 6;

Figures 8-10 are schematic views illustrating the fixing of the membrane into a membrane-holder;

10 Figures 11a and 11b show a variable diameter nanoporous device according to the invention immersed in an aqueous solution and controlled by a voltage generator,

Figures 12a and 12b are schematic top views of the pH response of a polyacrylic acid (PAA) FRTEM pore,

15 Figures 13a and 13b are schematic cut views of the pH response of a PAA FRTEM pore,

Figures 14a and 14b are schematic cut views of the pH response of the structure of a PAA inside a pore,

Figures 15a, 15b and 15c show a hydrophilic chromatography in which the polyacrylic acid (PAA) varies from hydrophilic phase to hydrophobic phase,

20 Figures 16a and 16b show a variable diameter nanoporous device according to the invention with a both sides metalized FRTEM by a same electrode, during hydrophilic phase (Fig 16a) and hydrophobic phase (Fig 16b),

Figure 17 shows a variable diameter nanoporous device according to the invention with a both sides metalized FRTEM by respectively two electrodes each
25 at a different voltage,

Figure 18 shows a membrane with nine independent electrodes.

While the invention is susceptible to various modifications and alternative forms, specific embodiments thereof are shown by way of example in the
30 drawings and will herein be described in detail. It should be understood, however, that the drawings and detailed description thereto are not intended to limit the invention to the particular form disclosed, but on the contrary, the intention is to cover all modifications, equivalents and alternatives falling within the spirit and scope of the present invention as defined by the appended claims.

35 In accordance with the preferred embodiment, the method and device according to the invention relates to the following materials and processes:

Materials: Poly(vinylidene fluoride) (PVDF) films of 9 μm thickness provided by PiezoTech SA®, Saint Louis (France). Toluene, potassium hydroxide, potassium permanganate, potassium disulfite, acrylic acid (AA),
5 Mohr's salt $((\text{NH}_4)_2\text{Fe}(\text{SO}_4)_2 \cdot 6\text{H}_2\text{O})$, sulphuric acid, EDC ($\text{C}_8\text{H}_{17}\text{N}_3\text{HCl}$), phosphate buffer saline (PBS), tBuOK ($\text{C}_4\text{H}_9\text{OK}$ 95%) purchased from Sigma-Aldrich®, and Alexa Fluor R 488 hydrazide ($\text{C}_{21}\text{H}_{15}\text{N}_4\text{NaO}_{10}\text{S}_2$) purchased from Invitrogen®.

Irradiation: Prior to irradiation, PVDF films are toluene-extracted for 24 h. Swift heavy ion irradiation was performed at the GANIL, Caen (France). Films
10 are irradiated with Kr ions (10.37 MeV/amu, fluence 107 to 10^{10} cm^{-2}) under He atmosphere. In two cases, samples are stored at -20°C under N_2 atmosphere until chemical etching and radio grafting.

Chemical etching: PVDF irradiated films are chemically etched using permanganate solution (0.25 M) in a highly alkaline medium (KOH 10 M) at
15 65°C with different etching times from 0.5 to 3 h. Membranes obtained are washed in potassium disulfide solution (15%) then dried at 50°C under vacuum.

Radio grafting: PVDF films of initial size $20 \times 20 \text{ mm}^2$, are weighed. The film was immersed at room temperature in a radio grafting solution containing acrylic acid and Mohr's salt (0.25%w/w). After 15 minutes of bubbling nitrogen
20 at room temperature, the sample was introduced into a thermostated water bath at 60°C for 1 hour. Membranes are washed with water and then Soxhlet-extracted in boiling water in order to extract free homopolymer. Functionalised membranes are dried at 50°C under vacuum.

Infra-red spectroscopy: FTIR spectra of PVDF films are obtained with a
25 Nicolet Magna-IR 750 spectrometer equipped with a DGTS detector. Spectra are recorded in an attenuated total reflection mode (ATR) using a diamond-crystal with single reflection. Spectra are collected by accumulating 32 scans at a resolution of 2 cm^{-2} .

Confocal Scanning Laser Microscopy (CSLM): Measurements are
30 performed at LLB (CEA-Saclay, France) with a Leica TCS-SP2 using an Ar laser (488 nm). Samples are observed in water with a 40x dry objective of numerical aperture 0.85.

Electrode fabrication: the gold layers, $\sim 45\text{nm}$ are sputtered (EMITECH K550, UK) through a mask with 3 mm diameter holes.

The synthesis of functionalized radio grafted membranes is described according to figures 1-4. With respect to figure 1, a track-etch process is described. This process comprises three steps:

- I) latent track formation along the ion pathway through a polymer film 1,
- 5 II) symmetrical attack of latent tracks by hydrolysis at early stage of the process, and
- III) formation of cylindrical pores 2.

In other words, for the preparation of a functionalised radio grafted track-etched membrane 3 (FRTEM), polymer film 1 is first bombarded by swift heavy
10 ions and the formed tracks along the ion passage are revealed under alkaline chemical treatment.

The obtained nanoporous polymer membrane 3 does not need to undergo a subsequent e-beam irradiation to increase radical proportion in polymer bulk submicronic pore diameter. Indeed, after etching times inferior to one hour, the
15 radical residues within nanopore walls were found sufficiently numerous to pursue a radiografting from the pore walls 2.

Figure 2 shows an electron paramagnetic resonance (EPR) spectra per mass unit (mg-1) for a heavy ion irradiated film before etching (latent tracks)
20 and after 1 hour of track etching. In the latter case, the non-horizontal baseline is due to paramagnetic impurities (KMnO₄ from the etching bath). Figure 3 shows the radical decay from EPR results versus time. Radicals are always presents even after 1 hour of track etching.

Concerning the functionalisation, in the presence of vinyl monomer, such
25 as acrylic acid (AA), a radical polymerization takes place by radio grafting process to specifically functionalise the nanopore walls with carboxylate hydrogel as shown from FTIR spectra in figure 4. This polymerization is specific to the nanopore walls and does not occur on the membrane surface. The selectivity of the grafting is checked by labelling of the amine functionalised
30 surface of the PVDF nanoporous membrane by a fluorescent probe specific to the amines and the poly(acrylic acid) inside the pores by a second fluorescent probe specific to the acid groups.

Figures 5-10 describe a non limitative embodiment of a both sides metalized membrane. A nanoporous device 13 according to the invention is
35 shown. The nanosensor is based on the membrane 3, the shape of which is a cylinder of 9µm thick and of 400 mm² diameter, with 10⁶ to 10¹⁰ nanopores per

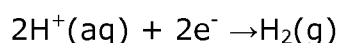
cm² of 50 nm diameter. Once the membrane has been functionalised, gold is sputtered on each side of the membrane 3 in figure 6 : a bottom electrode 4 of 45nm thick and a top electrode 5 of 45nm thick. The sputtering is made as known by one ordinarily skilled in the art, in such a way that the nanopores remain open. The gold layers can cover or not the entire surface. On figure 7 the perspective view of the membrane shows the top electrode 5 and the bottom electrode 4. On figures 8-10, the bottom layer 4 is contacted with silver paste 6 to copper contacts 7 lithographically patterned on 1.5 cm² plexiglass plackets 8. The top layer 5 is contacted with a gold wire 9 and silver paste to other copper contacts 10 on the same placket 8. The membrane 3 is then covered with waterproof tape, Kapton, 3M, except for a 2 mm diameter circular area 11 in the centre of the membrane, which will serve as a window for exposure of the membrane to the aqueous solution. The copper leads are not completely covered by the tape and remain outside of the solution so they can be connected to a potentiostat via a bridge 12.

Figures 11a is a cut view illustrating a variable diameter nanoporous device 14 according to the invention immersed in an aqueous solution (water) 15 and controlled by a potentiostat or a voltage generator 16. The variable diameter nanoporous device 14 comprises a PVDF membrane 17 radiografted with polyacrylic acid PAA 20 (PAA FRTEM) inside the nanopore 18. More precisely, said nanopore 18 consists in a conical tubule through the entire thickness of the PVDF membrane 17 with pH sensitive polyacrylic acid hydrogel attached to the nanopore wall 19. For drawing simplicity, only a single nanopore is represented, but the PVDF membrane 17 may include several nanopores arranged as a matrix or not. A gold layer is directly sputtered on a side (see figure 11b) of the PVDF membrane 17 in order to form a surface electrode 21. Figure 11b is a top view of a part of device 14. It is shown that the surface electrode 21 covers the disk-shaped PVDF membrane 17. As known by a person skilled in the art, gold is sputtered in such a way that the nanopore apertures on both sides remain open. A counter electrode 22 is also immersed in the aqueous solution 15 next to, but not in contact with, the PVDF membrane 17 at opposite side of the surface electrode 21. The counter electrode 22 is a metallic or gold disk arranged parallel to the surface of the PVDF membrane. For example, the conical nanopore 18 is disposed with the large aperture facing the reference membrane.

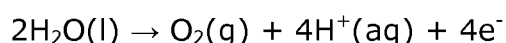
The surface electrode 21 is connected to an output of the voltage generator 16 via wire 23. The counter electrode 22 is connected to a cathode output of the voltage generator 16 via wire 34. The voltage generator 16 provides a potential difference between the counter electrode 22 and surface electrode 21. According to the present invention, this potential difference is variable for example between -1 (minus one) and +1. The voltage generator 16 provides automatically or not a variable potential difference which results in a variation of the pH of the aqueous solution within a few microns of the electrode 21 and 22. The nanopore 18 is contained in the region 25 which is within a few microns of the electrode. Advantageously, the variation of the pH causes a reversible phase change in the polyacrylic acid between a hydrophobic phase and a hydrophilic phase as shown on figures 12-14.

Figures 12a, 12b, and 13a, 13b, respectively, show how the structure of polyacrylic acid (PAA) 20 depends on pH. It is hydrophobic in the protonated form (Fig 12b), low pH, and hydrophilic in the deprotonated form (Fig 12a), high pH. The pH is changed near the electrode surface 21 due to the electrolysis of water. This can be used to expand or contract PAA 20 radiografted in the nanopore 18 (figure 11) of the PAA FRTEM 17 to open and to close the nanopore or change their effective pore diameter or hydrophilicity by applying a voltage to the surface electrode 21. Figures 13a and 13b illustrate a side view of the PAA FRTEM 17 of figure 12.

The hydrophilic phase (Fig 13a) is obtained with a pH around 7.4 for a potential difference $V=-1$ volt, the anode being connected to the surface electrode 21 which is connected to a PAA FRTEM surface. Electrolysis of water occurs near the surface electrode 21 as follows:



The hydrophobic phase (Fig 13b) is obtained with a pH around 1.4 for a potential difference $V=+1$ volt, the cathode of the voltage generator 16 being connected to the reference electrode 22. Electrolysis of water occurs near the surface electrode 21 as follows:



Figures 14a and 14b show how the structure of polyacrylic acid (PAA) depends on pH inside a biconical nanopore. During the hydrophilic phase (Fig 14a), at pH 13, carboxylic acids of PAA are totally dissociated. The resulting electrostatic repulsions swell the PAA chains. The nanopore becomes permeable and favours ion diffusion. Reversely, during hydrophobic phase (Fig 14b), at acidic pH 1, the collapse of radiografted PAA chains inside the nanopore causes a dense PAA layer on the nanopore wall reducing any ion flow stream through the nanopore.

Figure 15 shows a hydrophylic chromatography which is possible by scanning the surface electrode potential, resulting in a separation of species based on their hydrophilicity. For a potential $V=0$, the PAA FRTEM presents a mixed phase. This could be used in protein analysis.

The nanoporous device according to the invention is a new way to make switchable hydrophilic nanoporous separation devices for protein analysis and nanoscale valves.

Figure 16 shows the use of a second surface electrode 26 at opposite side of the first surface electrode 21, but both being connected together. The both sides of the PAA FRTEM are at the same potential. At high pH, it is easier for ions to pass through the nanopore but difficult for hydrophobic species to pass. At low pH, it is difficult for ions to pass but easy for hydrophobic species to pass.

Referring now to figure 17, a variable diameter nanoporous device according to the invention is shown with a both sides metalized PAA FRTEM 27. The nanopore 30 has a biconical shape and is radiografted with polyacrylic acid (PAA) hydrogel. A surface electrode 28, 29 is realized on each lateral side of the PAA FRTEM 27. The two surface electrodes are at different potential. For each surface electrode 28, 29, the sputtered gold layer enters the nanopore 30 from 100nm to 500nm depending on nanopore shape and diameter. This embodiment with both sides metalized PAA FRTEM enhances the control of the PAA structure.

For a positive potential difference, for example +2V, between the surface electrode 29 with respect to the surface electrode 28, the production of H^+ at surface electrode 29 side causes a local decrease in pH. The PAA 31, at surface electrode 29 side, is in hydrophobic condensed phase. Reversely, the loss of H^+ at surface electrode 28 side causes a local increase in pH. The PAA 32, at surface electrode 28 side, is in hydrophilic swollen phase.

According to another aspect of the invention, there is provided on figure 18 a PAA FRTEM 33 for hydrophilic separations. This PAA FRTEM comprises nine independent nanopores 34a-42a with nine independent corresponding surface electrodes 34b-42b deposited through a mask. Each surface electrode can be contacted to a voltage. With this configuration the hydrophobicity of the PAA FRTEM at each surface electrode can be independently controlled. This allows the parallel analysis or separation of species based on their hydrophobicity.

The nanoporous device according to the present invention enables one to change the hydrophobicity of nanopores in nanoporous membranes by applying a voltage to the membrane while the membrane is in solution. In other words, the effective diameter of the nanopores varies as the hydrophobicity of the polyelectrolyte changes as a function of the potential difference. This may have applications for hydrophilic analysis of proteins and as filters.

Numerous variations and modifications will become apparent to those skilled in the art once the above disclosure is fully appreciated. It is intended that the following claims be interpreted to embrace all such variations and modifications. For example, an electrode can be sputtered, evaporated or integrated on a side of the membrane. The polyelectrolyte may be poly(acrylic acid) PAA, poly(methylacrylic acid) or other hydro gel type polymers.

The aqueous solution may be an aqueous electrolyte or polar solvent electrolyte solution.

Claims

1. A variable diameter nanoporous device comprising:
 - a functionalised radio-grafted track-etched membrane (FRTEM) containing
 - 5 at least one nanopore which is radio-grafted with a polyelectrolyte,
 - at least two electrodes powered by a potentiostat or a power supply in order to provide a variable potential difference in a region in an aqueous or solvent polar solution, the pH of said region is intended to vary as a function of the potential difference due to electrolysis; the functionalised radio-grafted track-
 - 10 etched membrane (FRTEM) and the two electrodes are arranged in the aqueous solution in such a way that the nanopore is included in said region; the effective diameter of said at least one nanopore or hydrophilicity of the polyelectrolyte changing as a function of the potential difference.
- 15 2. Device according to claim 1, characterised in that the polyelectrolyte is polyacrylic acid PAA.
3. Device according to claim 1 or 2, characterised in that the nanopore consists of tubule through the entire thickness of the functionalised radio-
- 20 grafted track-etched membrane (FRTEM).
4. Device according to any of preceding claims, characterised in that:
 - one of said two electrodes is a surface electrode arranged on one side of the functionalised radio-grafted track-etched membrane (FRTEM), said surface
 - 25 electrode comprising an aperture so that the nanopore remains open,
 - the other electrode is disposed in the same solution as the functionalised radio-grafted track-etched membrane (FRTEM).
5. Device according to any of claims 1-3, characterised in that:
 - 30 - one of said two electrodes is composed of two surface electrodes respectively arranged on each side of the functionalised radio-grafted track-etched membrane (FRTEM) perpendicularly with respect to the nanopore, each surface electrode comprising an aperture so that the nanopore remains open, said two surface electrodes being connected together;
 - 35 - the other electrode is disposed next to the functionalised radio-grafted track-etched membrane (FRTEM).

6. Device according to any of claims 1-3, characterised in that the two electrodes are two surface electrodes respectively arranged on each side of the functionalised radio-grafted track-etched membrane (FRTEM) perpendicularly with respect to the nanopore, each surface electrode comprising an aperture so that the nanopore remains open.

7. Device according to any of preceding claims, characterised in that it comprises:

- a plurality of nanopores, and
- said at least two electrodes comprises a plurality of independent surface electrodes arranged on one side of the functionalised radio-grafted track-etched membrane (FRTEM), each surface electrode being associated with a nanopore and comprising an aperture so that the associated nanopore remains open;
- said at least two electrodes further comprises at least another electrode disposed next to the functionalised radio-grafted track-etched membrane (FRTEM) at opposite side of the surface electrodes, each surface electrode providing an independent potential difference with respect to said at least another electrode.

8. Device according to any of preceding claims, characterised in that the potential difference between said at least two electrodes is obtained by means of a potentiostat (16), the voltage of which being variable inside a range less than five volts.

9. Device according to any of preceding claims, characterised in that the functionalised radio-grafted track-etched membrane (FRTEM) is based on a poly(vinylidene fluoride) PVDF film.

10. Device according to any of claims 4-9, characterised in that each surface electrode is a sputtered metallic layer that enters the nanopores on some hundreds of nm.

11. Device according to any of preceding claims, characterised in that the thickness of the functionalised radio-grafted track-etched membrane (FRTEM)

is substantially of 9 μm and the nanopore presents a diameter between 20 and 100 nm.

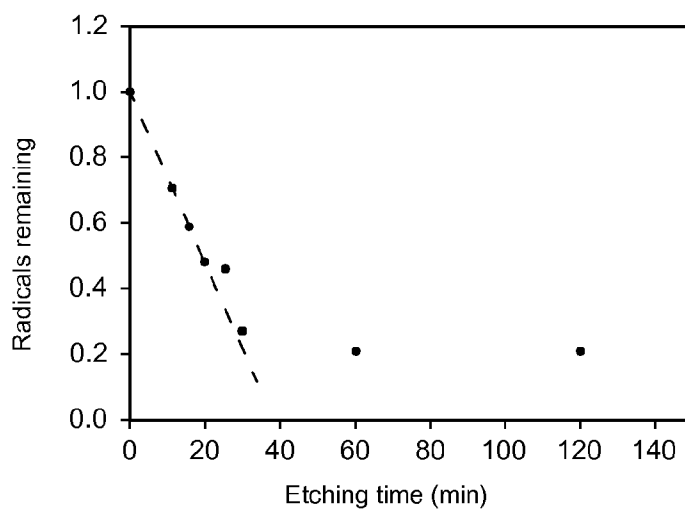
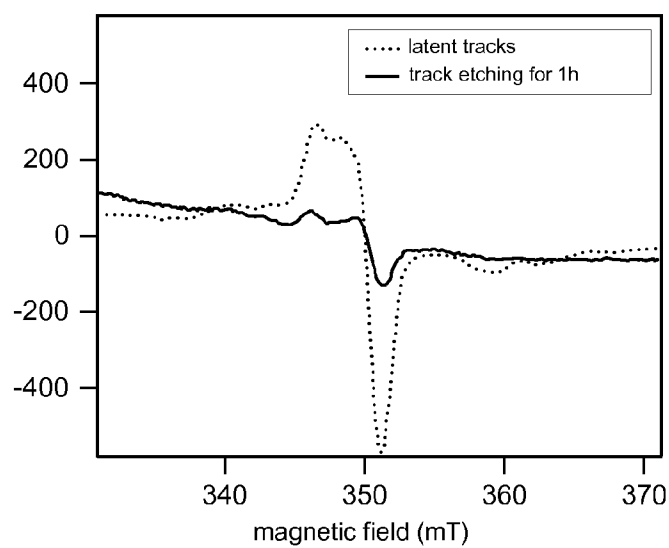
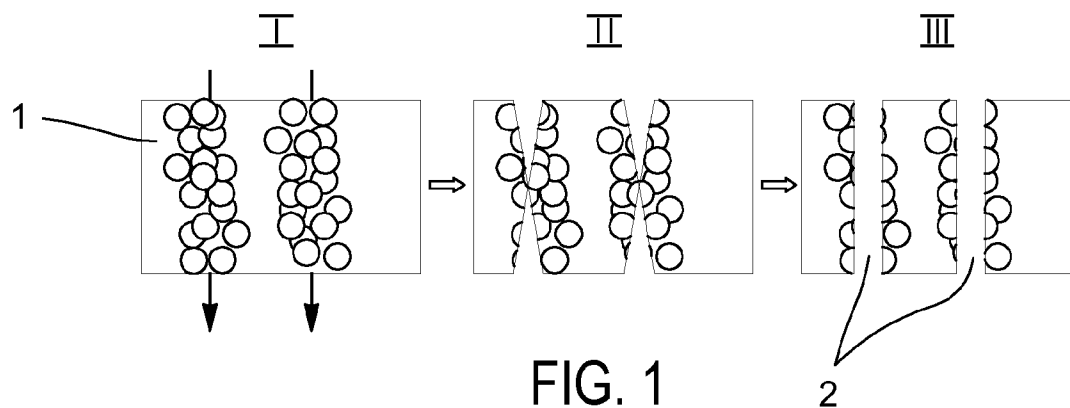
12. Application of a variable diameter nanoporous device according to any of
5 preceding claims for the separation and analysis of protein residues.

13. Application of a variable diameter nanoporous device according to any of claims 1-11, as nanovalves for micro and nanofluidics.

10 14. Application of a variable diameter nanoporous device according to any of claims 1-11, as variable diameter nanofilters.

15 15. Application of a variable diameter nanoporous device according to any of claims 1-11, in which the hydrophobicity of the poly-electrolyte changes as a function of the potential difference, said change being reversible with the control of the electrodes such that nanopore effective diameter is driven in a controllable manner.

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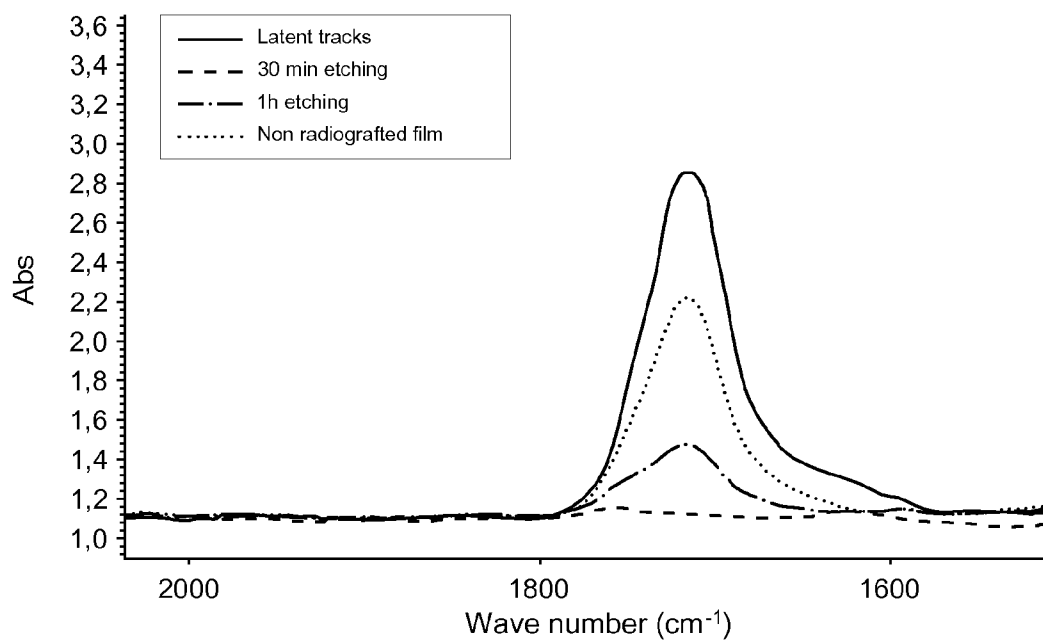


FIG. 4

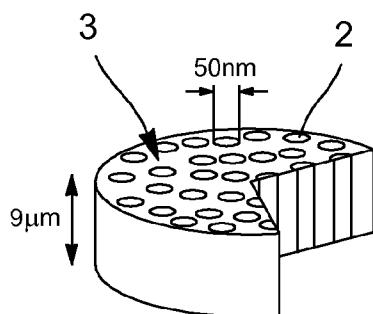


FIG. 5

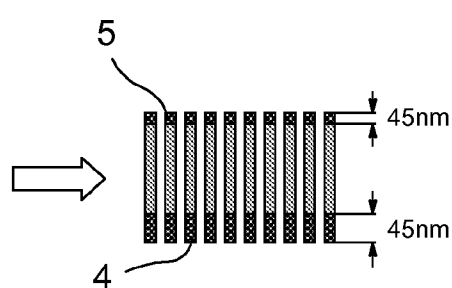


FIG. 6

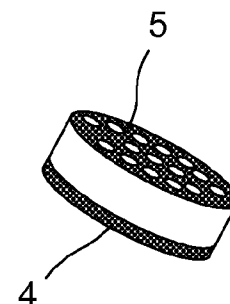


FIG. 7

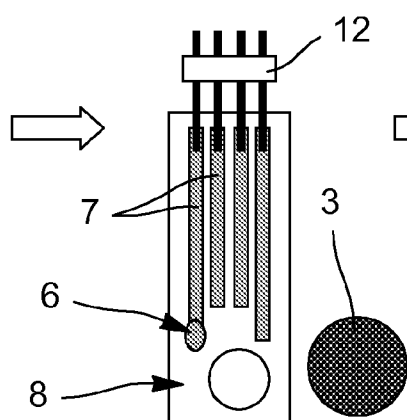


FIG. 8

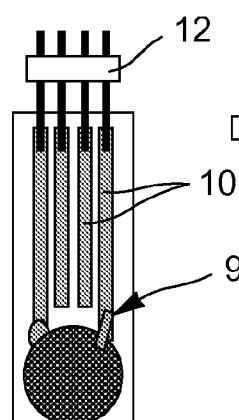


FIG. 9

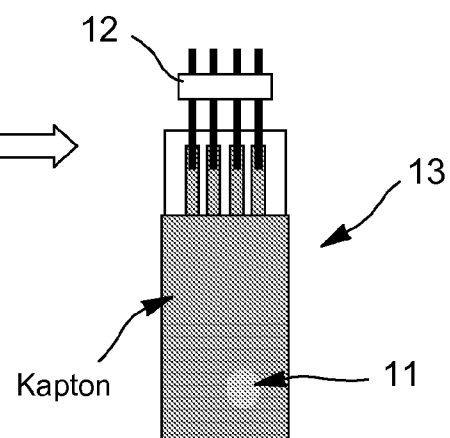


FIG. 10

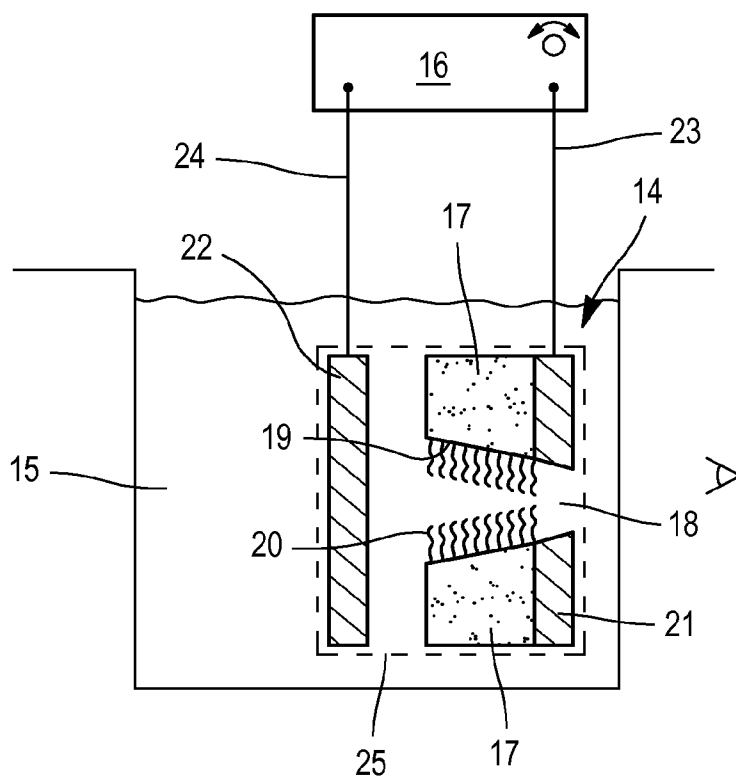


FIG. 11a

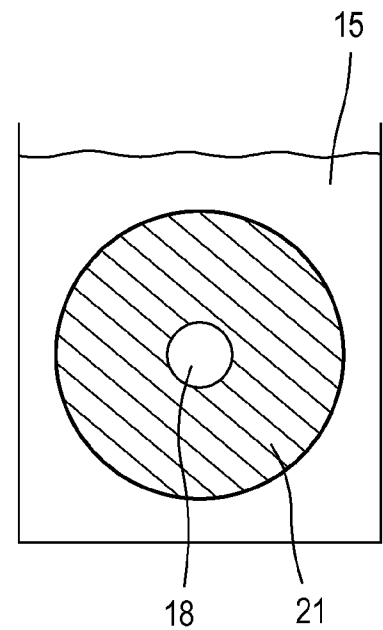


FIG. 11b

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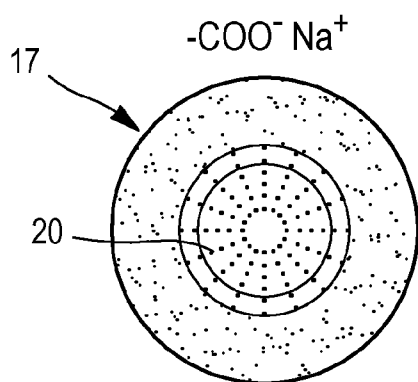


FIG. 12a

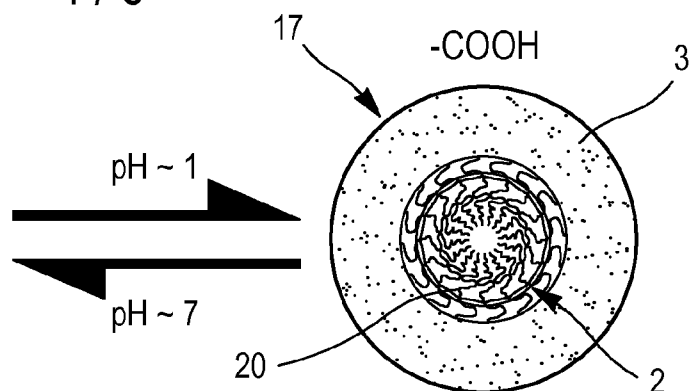


FIG. 12b

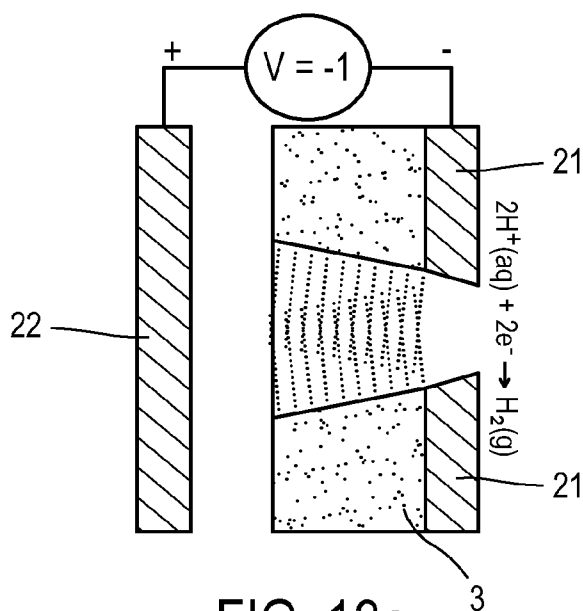


FIG. 13a

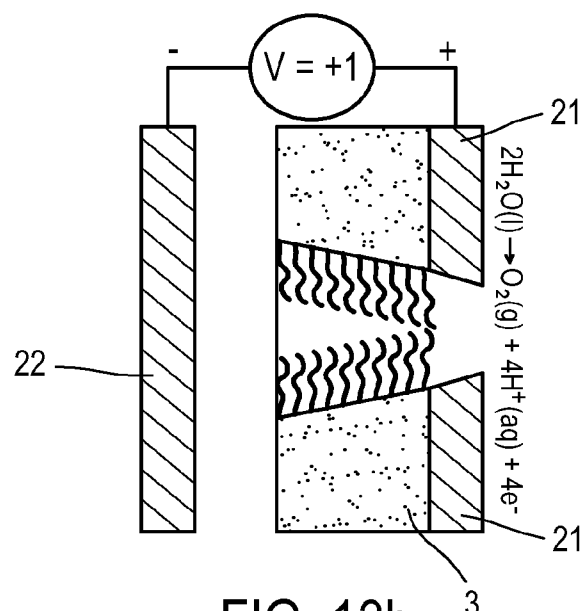


FIG. 13b

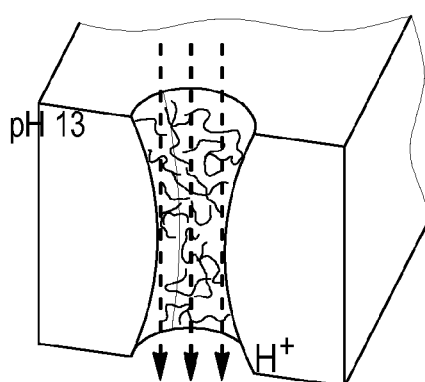


FIG. 14a

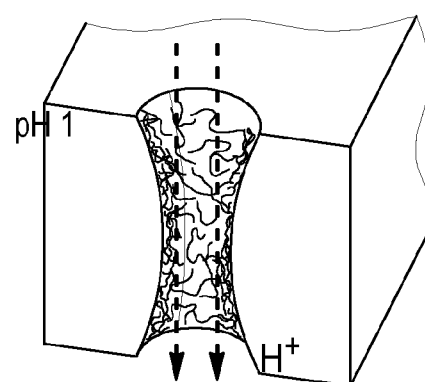
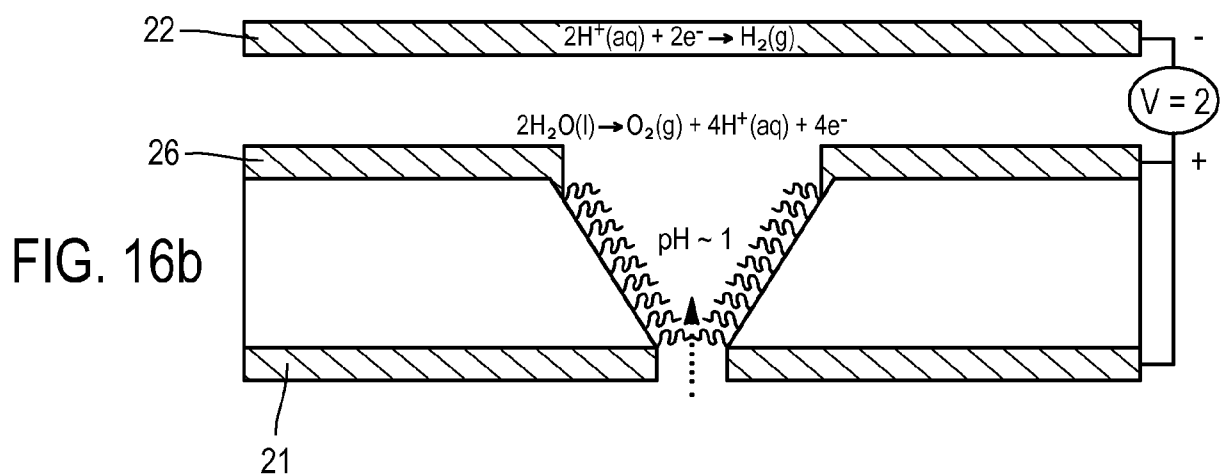
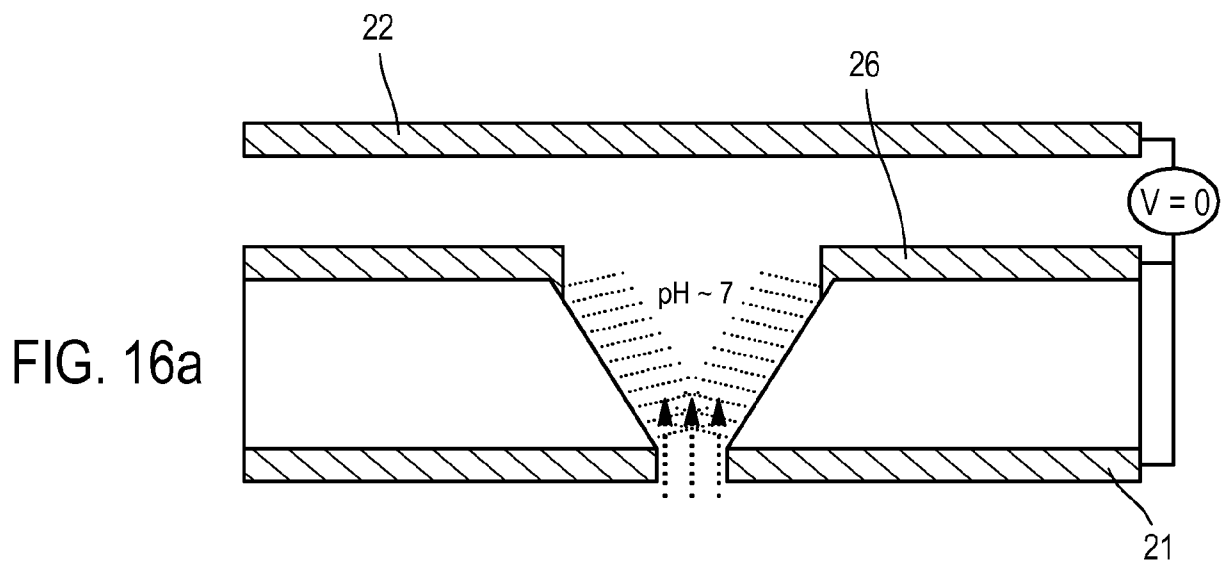
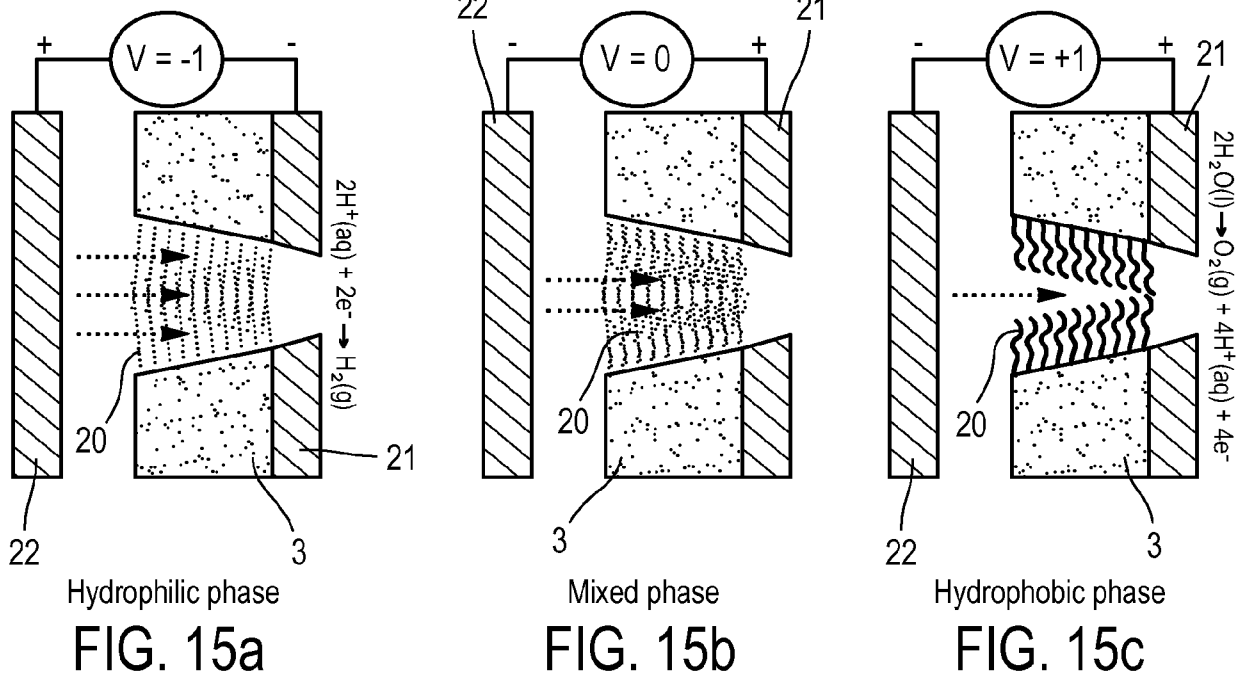


FIG. 14b

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FIG. 17

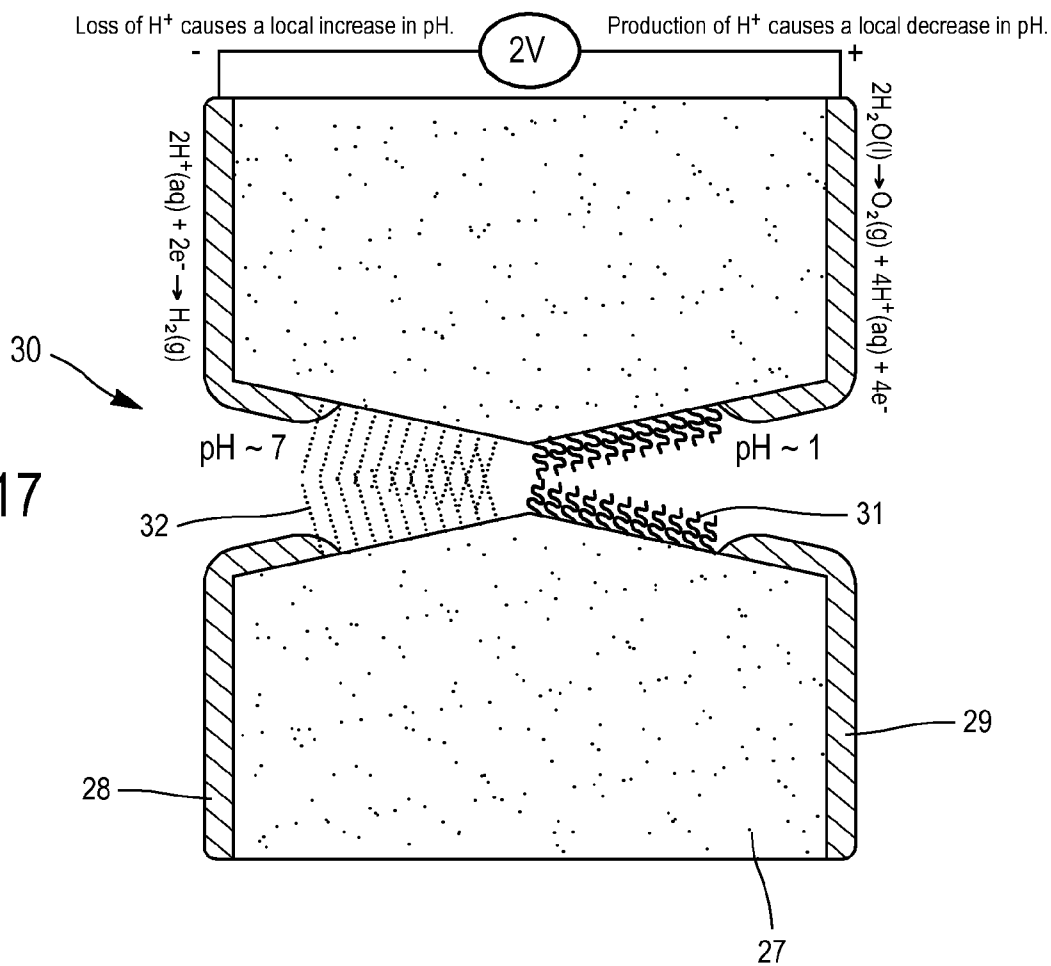
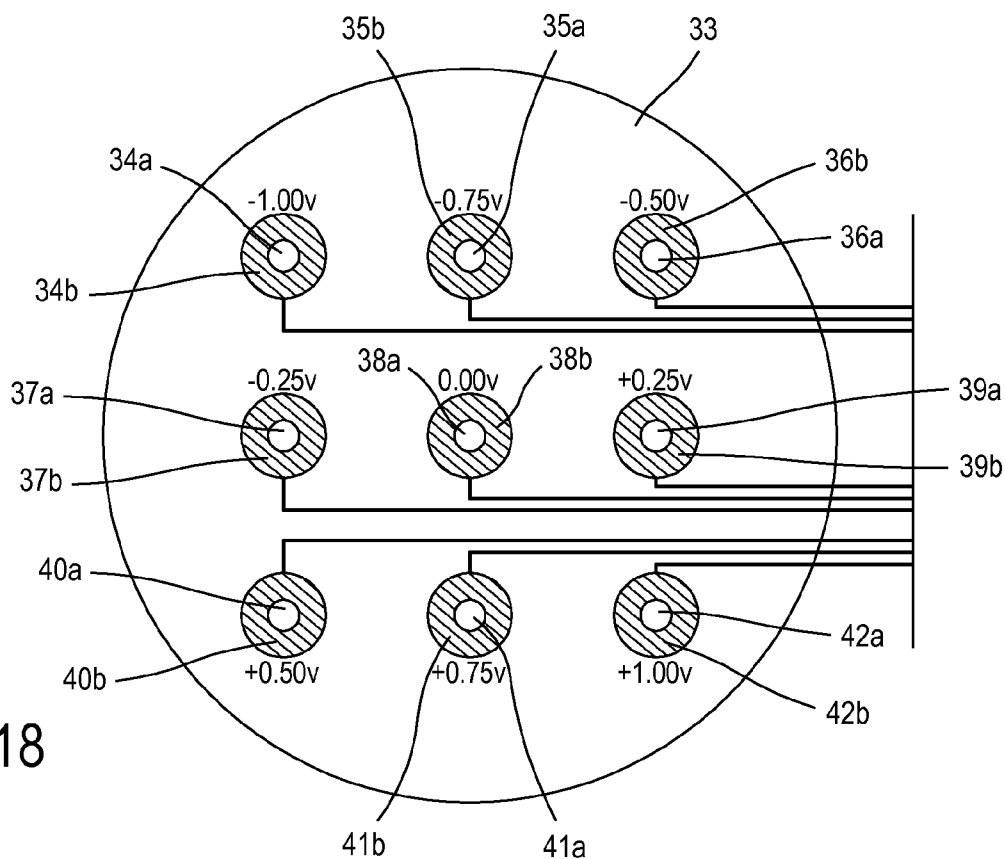


FIG. 18



INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2010/053653

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N33/487 B01D69/10 B01D61/02
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G01N B01D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2007/140252 A (UNIV DREXEL [US]; ELABD YOSSEF A [US]; PALMESE GIUSEPPE R [US]) 6 December 2007 (2007-12-06)	1,4-6,15
Y	* abstract; figures 1,7 page 16, columns 5-12	2,3,7, 9-15
X	US 2008/025875 A1 (MARTIN CHARLES R [US] ET AL) 31 January 2008 (2008-01-31) paragraphs [0070], [0076], [0077], [0090], [0107], [0122], [0164]; figures 2-4	1,8

☒ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

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"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

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Date of the actual completion of the international search

21 June 2010

Date of mailing of the international search report

28/06/2010

Name and mailing address of the ISA/

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Fax: (+31-70) 340-3016

Authorized officer

Klein, Marc-Oliver

INTERNATIONAL SEARCH REPORT

International application No

PCT/EP2010/053653

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	CUSCITO ET AL: "Nanoporous beta-PVDF membranes with selectively functionalized pores" NUCLEAR INSTRUMENTS & METHODS IN PHYSICS RESEARCH, SECTION - B: BEAM INTERACTIONS WITH MATERIALS AND ATOMS, ELSEVIER, AMSTERDAM, NL, vol. 265, no. 1, 17 November 2007 (2007-11-17), pages 309-313, XP022349433 ISSN: 0168-583X the whole document	2,3,9, 11-15
Y	WO 2005/033685 A (EPIGEM LTD [GB]; HARVEY THOMAS GRIERSON [GB]) 14 April 2005 (2005-04-14) * abstract; claims 1-32; figures 1,10,13,16	7
Y	EP 1 441 213 A (AGILENT TECHNOLOGIES INC [US]) 28 July 2004 (2004-07-28) * abstract; figure 1 paragraph [0057]	10
A	YOSHIHIRO ITO ET AL: "Signal-responsive gating by a polyelectrolyte pelage on a nanoporous membrane" NANOTECHNOLOGY, IOP, BRISTOL, GB, vol. 9, no. 3, 1 September 1998 (1998-09-01), pages 205-207, XP020067153 ISSN: 0957-4484 the whole document	1

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2010/053653

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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WO 2005033685 A	14-04-2005	NONE	
EP 1441213 A	28-07-2004	JP 2004233356 A	19-08-2004
		US 2004144658 A1	29-07-2004