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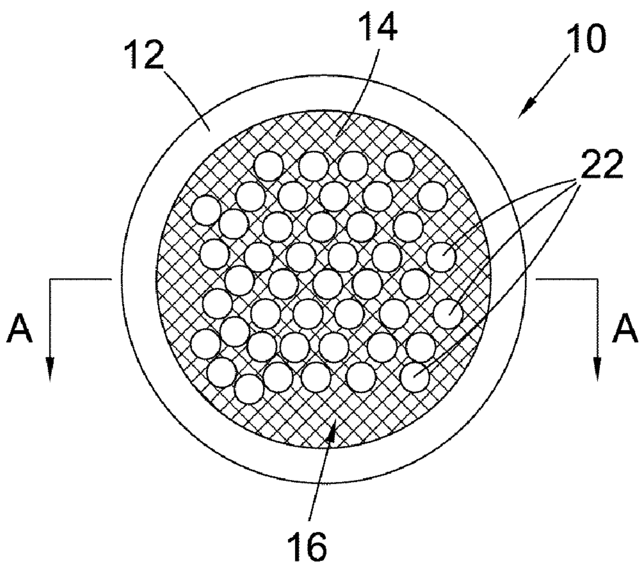

Fig. 1

(57) Abstract: Embodiments of the invention extend to a membrane assembly (10) having a membrane (14) and one or more structures (22) formed on the surface of the membrane. Further embodiments extend to a method of manufacturing a membrane assembly.

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MEMBRANE ASSEMBLY

TECHNICAL FIELD

Embodiments of the invention relate to a membrane assembly and, in particular, a membrane assembly having structures adhering to a surface of a membrane of the membrane assembly.

BACKGROUND

Embodiments of the invention are concerned with the use of membranes which are used to partition environments or chambers. In many such applications it is useful to be able to control or monitor the environments or chambers partitioned by the membrane. In certain applications therefore, it is useful to have various structures which may be used to control or mitigate flow, for example, and sensors in the vicinity of the membrane.

It is known to provide membranes with seals such as an O-ring which acts as a reusable seal. For example, GB 1 271 860 discloses a seal for a membrane which adheres to the surface of the membrane.

EP 1 547 5676 discloses a membrane and a membrane microstructure with channels attached to the surface of a membrane. Plates are provided on either surface of the membrane and the plates have channels formed therein. In manufacture, a thermoformed structure which includes a plate for a first surface of the membrane is covered by a precursor material and this is then bonded to the other thermoformed structure, for the opposing surface of the membrane, in a heat treatment stage which also turns the precursor material into a membrane. This disclosure relies on two distinct steps for forming a structure for the surface of the membrane and adhering that structure to the surface. This is significantly more expensive and complex than a process where the structure can be formed and bonded at the same time.

Furthermore, it is known to use a clamp or sample holder removed and distinct from the membrane to retain a sample or sensor in place in chambers partitioned by a membrane. However, such arrangements are complex and expensive. Furthermore, in the relatively small chambers encountered in micro-fluidic applications, there is often insufficient space to accommodate a separate holder or sensor.

SUMMARY

Aspects of the invention are set out in the accompanying claims.

It is an object of embodiments of the invention to provide a membrane assembly having structures formed on a surface of the membrane whilst reducing the overall size of such an assembly.

It is a further object of embodiments of the invention to provide such membrane assemblies which are capable of withstanding the operational environment where microfluidic behaviour occurs.

According to a first aspect the invention extends to a membrane assembly comprising a membrane, the membrane having a first surface and a second surface so that material may move from the first surface to the second surface through the membrane, the membrane further having at least one edge, the membrane assembly further comprising a structure bonded to said first or said second surface and located in a region of said membrane spaced from said edge,

wherein the structure is formed by a process of injection moulding and wherein the structure is bonded to said first or said second surface by the process of injection moulding.

The membrane assembly may include a seal which, when in use, seals the membrane, in which case the region spaced from the edge of the membrane may comprise a region of said membrane sealed by said seal. The seal may encompass the edge of the membrane and may be formed by injection moulding. In an embodiment, the seal is formed by the same injection moulding process used to form the structure.

In one embodiment, the structure comprises one or more pillars, which are useful for increasing or maximizing surface area or for interaction with the fluid.

In a further embodiment, the structure comprises one or more wells which may be used for isolating cell cultures on a surface of the membrane. Alternatively, or in addition, the structure may comprise supports for retaining a tissue sample in position relative to the membrane surface.

The structure may extend from an edge of the membrane into the region. In certain embodiments, the structure extends over the edge of the membrane. This has the advantage of allowing the structure to interface elsewhere (for example with an electrical circuit) without interfering with the membrane (for example the sealing properties of the seal).

The structure may be an electrode. Preferably, the membrane assembly includes two or more electrodes for measuring an electrical current, resistance and/or potential. Where the membrane assembly includes an injection-moulded seal, the electrode may be retained in place by the seal.

In a further embodiment, the structure is an optode.

Further embodiments of the invention extend to a method of forming a membrane assembly comprising:

providing a membrane, the membrane having a first surface and a second surface so that material may move from the first surface to the second surface through the membrane, the membrane further having at least one edge,

bonding a structure to said first or second surface in a region of said membrane spaced from said edge,

wherein the structure is formed by a process of injection moulding and wherein the structure is bonded to said first or said second surface by the process of injection moulding.

The method may further comprise encasing an edge of the membrane with a seal, said seal delimiting said region spaced from said edge. The seal may be formed by injection-moulding. In an embodiment, the seal is formed by the same injection moulding process used to form the structure.

The edge may define a border between the first and second surfaces.

The structure may be adhered to said surface of said membrane, for example by an adhesive, or other known manners of adhering such structures together which may, in certain embodiments, depend on the materials of which the structure and the membrane are composed.

In certain embodiments, a further structure is bonded to a surface of the membrane opposed to the surface on which the initial structure was bonded.

The method may comprise forming the structure with the use of a mould, in which case the method may further comprise the step of preparing the mould by coating one or more surfaces of said mould with enzymes or other biochemical compounds. This helps to create an active layer on top of the injection moulded structures or to provide a surface functionality on the structures.

The method may further comprising the step of coating one or more surfaces of said membrane with enzymes or other biochemical compounds, which may be applied before or after an injection-moulding process.

Embodiments of the invention extend to a membrane assembly, and a method of manufacturing a membrane assembly with a structure bonded to one or more surfaces of the membrane at a region spaced from an edge of the membrane. The membrane functions to allow material to pass through the membrane. During use, the majority of this passage occurs in a region of the membrane located away from an edge of the membrane. Therefore, in certain embodiments, the region of the membrane spaced from the edge is that region of the membrane through which the majority of material passes.

In embodiments where the membrane includes more than one edge, the region may be spaced from an outer edge of the membrane.

DESCRIPTION OF ACCOMPANYING FIGURES

Embodiments of the invention are described with reference to the accompanying schematic diagrams where:

Figure 1 is a plan view of a membrane assembly according to an embodiment of the invention;

Figure 2 is a cross-section of the membrane assembly of Figure 1 along the line A-A;

Figure 3 is a plan view of a membrane assembly according to a further embodiment of the invention;

Figure 4 is a cross-section of the membrane assembly of Figure 3 along the line B-B;

Figure 5 is a cross-section of a membrane assembly according to a further embodiment of the invention;

Figure 6 is a plan view of a membrane assembly according to a further embodiment of the invention;

Figure 7 is a cross-section of the membrane assembly of Figure 6 taken along the line D-D, showing the membrane assembly in use;

Figure 8 is a plan view of a membrane assembly according to a further embodiment of the invention;

Figure 9 is a plan view of a membrane assembly according to a further embodiment of the invention;

Figure 10 is a plan view of a membrane assembly according to a further embodiment of the invention;

Figure 11 is a cross-section of a membrane assembly of Figure 10 taken along the line E-E;

Figure 12 is a plan view of a membrane assembly according to a further embodiment of the invention;

Figure 13 is a cross-section of a membrane assembly of Figure 10 taken along the line D-D;

Figure 14 is a schematic plan view of a die for moulding a membrane assembly according to an embodiment of the invention; and

Figure 15 is a flow diagram of a method for constructing a membrane assembly according to an embodiment of the invention.

DESCRIPTION OF EMBODIMENTS

Embodiments of the invention are described hereafter with reference to the accompanying diagrams.

Figure 1 illustrates a membrane assembly 10 according to an embodiment of the invention. The membrane assembly 10 comprises a disc-shaped membrane 14 and a seal 12. The seal 12, here in the form of an O-ring, completely surrounds an edge of the membrane. It is to be realised however that embodiments of the invention are not limited to disc-shaped membranes; membranes of the invention may take many other forms. Only an upper surface 16 of the membrane 14 is visible in Figure 1.

Figure 2 is a cross-section of the membrane assembly of Figure 1 taken along the line A-A. As illustrated in this Figure, the membrane has two surfaces 16 and 18. For the sake of convenience, the surface 16 is here designated the upper surface and surface 18 is designated the lower surface. The seal 12 covers the edge 20 of the membrane 14 as well as a portion of both the upper 16 and lower 18 surfaces. In this embodiment therefore, the seal 12 delimits an area of the membrane 14 which is spaced from the edge 20. Referring back to Figure 1, the area of the membrane spaced from the edge is, in this embodiment, the area of the membrane visible in this Figure.

The manner in which a membrane having a seal may be manufactured is disclosed in the applicant's co-pending Luxembourg application number 91961 also entitled "Membrane Assembly". The entire contents of this application is incorporated herein by reference. In particular it is noted that the formation of structures in a region spaced from the edge of a membrane, as occurs in embodiments of the current invention, may also be carried out on the arrangements illustrated in Luxembourg application number 91961.

Referring back to Figure 1 of the current matter, the embodiment illustrated in Figure 1 further comprises a plurality of pillars 22 which are bonded to both the upper 16 and the lower 18 surface of the membrane 14 in the area of the membrane spaced from the edge. The pillars 22 serve to increase the surface area of the membrane 14. This is useful in tissue engineering, cell trapping, rare cells isolation etc.

The manner of manufacture of the membrane assembly 10 is described below with reference to Figure 15.

Figure 3 is a plan view of a membrane assembly 40 according to a further embodiment of the invention. Similar to the embodiment of Figures 1 and 2, the membrane assembly includes a membrane 44 and a seal 42 which covers an edge 54 of the membrane (Figure 4). The seal therefore delineates an area of the membrane spaced from the edge.

The membrane 44 includes an upper surface 56 and a lower surface 58 as illustrated in Figure 4. In Figure 3 only the upper surface 56 is visible. As further illustrated in Figure 3, the membrane assembly 40 further comprises a plurality of cell wells 52 formed by transverse walls 48 and 50. The transverse walls 48 and 50 are bonded to the upper surface 56 of the membrane 44 in the area of the membrane spaced from the edge.

Figure 4 is a cross-section of the membrane assembly 40 of Figure 3 taken along the line B-B. As illustrated in this Figure, transverse walls 48 and 50 are also bonded to the lower surface 58 of the membrane 44.

The cell wells 52 provide a structure which allows multiple isolated enclosures in which cells may be cultured or alternative experiments carried out. Although transverse walls 48 and 50 are described as being distinct, it is to be realised that in the embodiment illustrated, these walls are formed by injection moulding and are therefore formed simultaneously from a single mould. Therefore, the walls surrounding cells 52 are integrally formed. An alternative arrangement includes wall-delimited enclosures or wells on one side of the membrane.

The embodiment illustrated in Figures 3 and 4 has square-shaped cell wells 52. It is to be realised however that other shapes and sizes for such cell wells are also possible. As described in greater detail below, the shape and size of these wells is only limited by the precision machining of the corresponding mould used to form these.

Figure 5 illustrates a cross-section of a membrane assembly 60 according to a further embodiment of the invention. The membrane assembly 60 is similar to the membrane assembly 40 illustrated in Figures 4 and 5. The same reference numerals have been used to refer to the same elements of this membrane assembly. The membrane assembly 60 includes a membrane 44 and a seal 42 encasing an edge 54 of the membrane. Transverse walls (only one type of which, transverse walls 50, are shown in this Figure), which are bonded to upper 56 and lower 58 surfaces of the membrane 44, define cell wells 52.

The membrane assembly 60 of Figure 5 differs from that of Figures 3 and 4 in that it includes an upper cover 62 covering the cell wells 52 formed on the upper surface 56 of membrane 44 and a lower cover 64 covering the cell wells 52 formed on the lower surface 58 of the membrane 44. The upper 62 and lower 64 covers form part of a larger containment structure which is not illustrated here. The upper 62 and lower 64 covers thereby create a channel through which fluid may flow to the cell wells 52. Where the membrane assembly 60 is dimensioned accordingly, the channel formed by upper 62 and lower 64 covers may be used for microfluidic applications.

Figure 6 illustrates a membrane assembly 80 according to a further embodiment of the invention. The membrane assembly 80 includes a membrane 82 having an edge 84 (see Figure 7) and a seal 86 covering the edge. The membrane 82 has an upper surface 90 and a lower surface 88. The seal 86 covers the edge 84 and a portion of the upper 90 and lower 88 surfaces of the membrane. Therefore, the seal 86 delineates an area of the membrane spaced from the edge 84.

A second seal 92 is formed in the area of the membrane spaced from the edge 84 on the upper surface 88 of the membrane 82.

Figure 7 illustrates a cross-section of the membrane assembly 80. This Figure illustrates the membrane assembly 80 in use. As illustrated, in use, the upper surface 88 on which the second seal 92 is formed is situated so that it faces a sample sensor 94 mounted on a holder 96. The second seal 92 contacts the holder to thereby form a sealed cavity 100. A sample 98 is situated in the cavity 100 in contact with the sensor 94. In an alternative embodiment, the sample sensor is fabricated monolithically on a holder.

In this embodiment, the sample 98 is a tissue sample and the sensor 94 monitors properties such as electrical pathways in the sample 98. Therefore, the second seal 92 forms a holder for the sample 98 ensuring that the sample is retained in position relative to the sensor 94 and protects the sample 98 from the ambient environment. The second seal 92 advantageously prevents the sample from moving or lifting with the movement of fluid which would cause it to loose contact with the sensor 94.

The embodiment of Figures 6 and 7 include a second seal 92 to isolate the sample 98 and to help retain the sample 98 in position. In further embodiments, it is desirable to retain the sample in position, but is not necessary to also isolate the sample.

Figures 8 and 9 illustrate two embodiments where structures are provided to retain the sample in place without also isolating the sample from the immediate environment (although sealing of the membrane as a whole is still provided for).

Figure 8 illustrates a membrane assembly 110 comprising a membrane 112 with a seal 114 encasing an edge of the membrane 112. The seal 114 delineates a region of a surface of the membrane spaced from the edge in the same manner as discussed above with reference to the embodiments of Figures 1 to 7. A sample retainer is formed on an upper surface of the membrane 112 comprising two crescent-shaped structures 116 and 118.

Figure 9 illustrates a membrane assembly 120 comprising a membrane 122 with a seal 124 encasing an edge of the membrane 122. The seal 124 delineates a region of a surface of the membrane spaced from the edge. Membrane assembly 120 further comprises a sample retainer comprised of five structures 126, 128, 130, 132 and 134 bonded to an upper surface of the membrane in the region spaced from the edge.

The sample retainers of the embodiments of Figures 8 and 9 help to ensure that the position of the sample relative to the membrane remains constant, but still allow communication between the sample and its surrounding environment.

In the embodiments illustrated in Figures 1 to 9, the structure bonded to the first or second surface is completely located in the region of the membrane spaced from the edge of the membrane (when viewed in plan). In further embodiments, a portion of the structure is located in the region spaced from the edge and a further portion extends outside of this region. In certain embodiments, a portion of the structure extends over an edge of the membrane (when viewed in plan).

Figure 10 illustrates a plan view of a membrane assembly 140 comprising a membrane 142 having an edge 144 and a seal 146 encasing the edge 144. The membrane 142 has an upper surface 148 and a lower surface 150. The seal 146 delineates a region of the membrane 142 spaced from the edge 144. The membrane assembly further comprises two electrodes 150 and 152 bonded to the upper surface of the membrane 142. As illustrated, each of the electrodes 150 and 152 is partly located in the region spaced from the edge delineated by the seal 146, but also includes a portion which extends over the edge (when viewed in the plan view of Figure 10 or the cross-section of Figure 11).

As illustrated in both Figures 10 and 11, the seal is formed over the electrodes 150 and 152 and therefore helps to retain the electrodes in place.

In embodiments of the invention described in greater detail below, the electrodes may be formed by injection moulding conducting polymers such as PEDOT-PSS. In further embodiments, the electrodes are formed on the surface of the membrane 142 by stencil or mask lithography, or are formed by the use of conducting adhesives (e.g. silver-filled thermoplastic adhesives). In yet further embodiments, photopolymerisation, photolithography, chemical vapour deposition or direct writing techniques may be used to form the electrodes.

The embodiment of Figures 10 and 11 includes two electrodes, electrodes 150 and 152. In further embodiments of the invention, more than two electrodes may be bonded to the surface of the membrane. In yet another embodiment, two electrodes, are placed on opposite sides of the membrane. Alternatively, or in addition, a coating which is sensitive to currents or changes in electric fields may be used. All such embodiments are useful for measuring various electrical properties of a sample or of the environment surrounding the sample. For example, such embodiments have use in drug partitioning studies, creation of bio- and chemical sensors and for measuring ion transport across epithelial layers (often involving the use of an Ussing chamber).

In further embodiments of the invention, structures which have sensing properties other than those relating to electricity are bonded to the surface of the membrane.

Figures 12 and 13 illustrate a membrane assembly 180 comprising a membrane 182 having an edge 184 and upper 186 and lower 188 surfaces. A seal 190 completely encases the edge and delineates an area of the upper surface 186 spaced from the edge 184. Two structures 192 and 194 are bonded to the upper surface 186 in this region spaced from the edge 184.

The structures 192 and 194 are optodes formed from luminescent or fluorescent compounds which react to the concentration of a specific analyte. In this manner further sensors may be incorporated into embodiments of the invention.

As described, the structures, including the seals, of the above described embodiments are bonded to the membrane. In certain embodiments, these structures are bonded to the membranes through a process of injection moulding.

Furthermore, because the seal is bonded to the membrane, embodiments of the invention are able to withstand greater pressures than known arrangements having a mechanical join between the membrane and the seal. In one comparative test carried out by the inventors, a membrane assembly according to an embodiment of the invention was able to withstand pressures over 20 times greater than known assemblies (tested at up to 50 μl/min flow rates through 0.45 μm membranes).

Embodiments of the invention are particularly well suited to establishing cultures in chambers having relatively small dimensions. A particular application of embodiments of the invention relates to microfluidics. Microfluidics concerns the study of fluid behaviour in small channels where a channel is an enclosed space in which a fluid is constrained. In these applications, the membrane of embodiments of the invention forms a portion of such a channel and, for this reason, in certain embodiments of the invention, the dimensions of the components of membrane assemblies are constrained.

The seals of membrane assemblies according to embodiments of the invention, and of plural membrane structures, are composed of a deformable, pliable material. This ensures that the sealing properties of these assemblies and structures are improved.

In the embodiments illustrated in Figures 1 to 13 and described above, the region spaced from the edge of the membrane is the region delineated by the seal encasing the edge of the respective membranes of those membrane assemblies. Therefore, the region spaced from the edge is that region of the upper surface of the membrane visible when the membrane assembly is viewed in plan.

What is important in certain embodiments of the invention is that the structures be formed on the membrane in that region where the membrane is functionally active. Therefore, in certain embodiments of the invention, the edge of a membrane delimits the boundary between two surfaces of the membrane which functions to partition a chamber in fluid communication with one of the surfaces from a chamber in fluid communication with the other of the surfaces. In such embodiments, the region spaced from the edge may be that region where the majority of material passes through the membrane moving from one chamber to the other.

A further embodiment of the invention relates to a method of forming a membrane assembly. Figure 14 is a schematic plan view of a die 200 for moulding a membrane assembly according to an embodiment of the invention. The die 200 is shaped from a suitable material such as polycarbonate. The die 200 includes two portions, a top portion 202 and a bottom portion 204. Both the top 202 and bottom

204 portions have four holes formed therein. The holes 206 of the top portion extend through the portion whereas the holes 208 of the bottom portion extend part of the way through that portion. The top portion 202 and the bottom portion 204 each have respective ports 216 and 218 through which liquid material may be introduced into the mould during an injection moulding technique. It is to be realised that the depiction of Figure 14 is not to scale. For example, the size of the ports 216 and 218 has been exaggerated in Figure 14 for the sake of illustration.

In use of the mould 200, screws 214 are threaded through the holes 206 and 208 to bind the top portion 202 to the bottom portion 204 to form a mould. In an alternate embodiment, the screws extend through and are engaged by nuts. The mould 200 of Figure 14 is used to construct the membrane assembly 80 of Figure 6. In the configuration illustrated in Figure 14, the top portion 202 has been bound to the bottom portion 204 in the manner described and this creates an elongate void 210 in which the membrane 82 of the membrane assembly 80 of Figure 6 resides during an injection moulding process. The mould further includes a rounded void 212 located at either end of the membrane (when viewed in the cross-section of Figure 14). The seal 86 encasing the edges of the membrane 82 is formed in the void 212. The mould 200 further forms a void 214 in which the structure (seal) 92 is formed.

As described below, the seal 86 and structure 92 are formed, and bonded or adhered to the surface of the membrane 82, by means of a process of injection moulding. Since the structures are bonded to the membrane during the same process in which they are formed, membrane assemblies of embodiments of the invention are substantially cheaper and quicker to manufacture than devices where the structures (or seals) are manufactured in a different step to that where they are adhered or bonded to the surface of the membrane.

The complete process 220 of manufacturing a membrane assembly using a mould such as the mould 160 is illustrated in Figure 15. In a first step, step 222, the mould is prepared by machine-milling of polycarbonate. This will depend on the type of assembly to be constructed. Preparation of the mould also involves cleaning the mould from impurities. In the following step, step 224, a provided membrane is positioned in the mould. Where the mould comprises a die such as die 200 illustrated in Figure 14, the membrane is placed in the elongate void 210 so that the edges of the membrane are located over the void 212.

In the following step, step 226, the mould is fastened. Where the mould comprises die 200 this step includes fastening the mould by locating and tightening screws 212 in the holes 206 and 208.

In step 228 liquid prepolymer is injected into the mould. In embodiments of the invention, the seal (which is formed by the molten prepolymer once it has set) encases the edge of the membrane. Therefore, the mould is formed so that the molten prepolymer injected into the die is able to flow around the relevant edge of the membrane. In the die 200 of Figure 14, the molten prepolymer is injected into the ports 216 and 218 so that it encases the edge of the membrane located in the void 210. The molten prepolymer also flows into the void 214 of the die.

Once the liquid prepolymer has been injected into the mould in step 228, it is cured in step 230. This step will depend on the type of polymer used. In this embodiment polydimethylsiloxane is used and the curing involves exposing the mould to a temperature of 80° C for a period of two hours.

The curing process will not only cause the prepolymer to set, but will also ensure that the prepolymer is bonded to the membrane Therefore, the injection moulding provides for a single process for forming the structure on the surface of the membrane and bonding this structure to the surface of the membrane.

In certain embodiments, the membrane is porous and, in this case, the molten prepolymer flows into the pores of the membrane during the injection moulding process. When the prepolymer is cured to form the structure, the structure is then engaged with the surface of the membrane and with the pores, thereby forming a secure and steadfast interface between the membrane and the structure.

The structures may be formed by injection moulding by any one of the following materials:

Acrylonitrile butadiene styrene (ABS)
Acrylic (PMMA)
Celluloid
Cellulose acetate
Cycloolefin Copolymer (COC)
Ethylene-Vinyl Acetate (EVA)
Ethylene vinyl alcohol (EVOH)
Fluoroplastics (PTFE, alongside with FEP, PFA, CTFE, ECTFE, ETFE)
Ionomers
Kydex, a trademarked acrylic/PVC alloy
Liquid Crystal Polymer (LCP)
Polyacetal (POM or Acetal)
Polyacrylates (Acrylic)
Polyacrylonitrile (PAN or Acrylonitrile)
Polyamide (PA or Nylon)
Polyamide-imide (PAI)
Polyaryletherketone (PAEK or Ketone)
Polybutadiene (PBD)
Polybutylene (PB)
Polybutylene terephthalate (PBT)
Polycaprolactone (PCL)
Polychlorotrifluoroethylene (PCTFE)
Polyethylene terephthalate (PET)
Polycyclohexylene dimethylene terephthalate (PCT)
Polycarbonate (PC)
Polyhydroxyalkanoates (PHAs)
Polyketone (PK)
Polyester
Polyethylene (PE)
Polyetheretherketone (PEEK)
Polyetherketoneketone (PEKK)
Polyetherimide (PEI)

Polyethersulfone (PES)- see Polysulfone
Polyethylenechlorinates (PEC)
Polyimide (PI)
Polylactic acid (PLA)
Polymethylpentene (PMP)
Polyphenylene oxide (PPO)
Polyphenylene sulfide (PPS)
Polyphthalamide (PPA)
Polypropylene (PP)
Polystyrene (PS)
Polysulfone (PSU)
Polytrimethylene terephthalate (PTT)
Polyurethane (PU)
Polyvinyl acetate (PVA)
Polyvinyl chloride (PVC)
Polyvinylidene chloride (PVDC)
Styrene-acrylonitrile (SAN)

Similarly, the membrane may be formed from any one of the following:
Mixed cellulose Esters (MCE)
Cellulose Acetate
PTFE
PolyPropylene
Nylon
Polycarbonate
Polyester
Ceramic
Glass fiber
Silver
Polyethersulfone
polyvinylidene difluoride (PVDF)
Polytetrafluoroethylene (PTFE)
Nitrocellulose
PVC

Once the polymer of the seals has set, the assembly is removed in step 232. For example, where the die 200 is used, this involves removing the screws located in holes 206 and 208.

At a final step, step 234, the stays are removed with an appropriate cutting edge and the membrane assembly undergoes final preparation appropriate to the use to which it will be put. Such final preparation may include sterilization and packaging.

This process may also be adapted to manufacture the membrane assemblies described and illustrated here. For many such membrane assemblies, the structure may be formed and bonded to the surface of the membrane in a region spaced from the edge at the same time as the formation of the seal which encases the edge. However, for other embodiments, such as the membrane assembly 140 illustrated in Figures 10 and 11, the structures (in this case electrodes 150 and 152) are formed on the surface of the membrane before the seal is formed by injection moulding. In such a case, the process 220 of Figure 15 will include a further step, step 240, located between step 222 and step 224 where the structures are formed on the surface of the membrane.

The process described above and illustrated in Figure 15 has been selected to manufacture membrane assemblies in a laboratory environment. It has the advantage that curing does not require complex or expensive equipment and the process can be adapted to design changes relatively easily. However, the process is relatively material and time intensive. Therefore, for mass production of membrane assemblies, the production process and materials used for the production would be altered. Many different types and forms of injection moulding are known and many may be applied to embodiments of the invention. For example, the dies may be constructed from mild steel and held together during the manufacturing process by applied pressure instead of screws. Known bio-compatible thermoset and thermoplastic resins and polymers may be used for the seal and the membrane. Prior to injection moulding, the moulds may be coated with enzymes or other biochemical compounds to create an active layer on top of the injection moulded structures or to provide a surface functionality on the structures. Alternatively, such compounds may be applied after the injection moulding process, e.g. on the surface of the membrane.

In the embodiments of the membrane assembly, and the method of manufacturing this as described above, the membrane has a single edge. In further embodiments, the membrane may include more than the single edge. For example, the membrane may be formed with a void describing an inner edge (such arrangements are described in co-pending Luxembourg application number 91961). In this case, the region spaced from the edge in which the structure is formed is the region spaced from the outer edge. Therefore, embodiments of the invention extend to membrane assembly having a membrane with a void formed therein and a structure formed close to or incorporating an edge defined by the void.

It will be appreciated by the person skilled in the art that various modifications may be made to the above described embodiments without departing from the scope of the present invention.

CLAIMS

1. A membrane assembly comprising a membrane, the membrane having a first surface and a second surface so that material may move from the first surface to the second surface through the membrane, the membrane further having at least one edge, the membrane assembly further comprising a structure bonded to said first or said second surface and located in a region of said membrane spaced from said edge,

wherein the structure is formed by a process of injection moulding and wherein the structure is bonded to said first or said second surface by the process of injection moulding.

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2. The membrane assembly according to claim 1 further comprising a seal.

3. The membrane assembly according to claim 2 wherein the region spaced from the edge of the membrane comprises a region of said membrane sealed by said seal.

4. The membrane assembly according to claim 2 or claim 3 wherein the seal encases the edge of the membrane.

5. The membrane assembly according to any of claims 2 to 4 wherein the seal is formed by injection moulding.

6. The membrane assembly according to claim 5 wherein the seal is formed by the same injection moulding process used to form the structure.

7. The membrane assembly according to any preceding claim comprising one or more structures bonded to said first surface and to said second surface.

8. The membrane assembly according to any preceding claim wherein the structure extends from an edge of the membrane into the region.

9. The membrane assembly according to claim 8 wherein the structure extends over the edge of the membrane.

10. The membrane assembly according to any preceding claim wherein the structure comprises any one or a combination of:

one or more pillars; one or more wells; a sample retaining structure; a second seal; and supports for retaining a tissue sample in position relative to the membrane surface.

11. The membrane assembly according to any of claims 1 to 9 wherein the structure comprises one or more electrodes.

12. The membrane assembly according to claim 11 comprising two or more electrodes for measuring an electrical current, resistance and/or potential.

13. The membrane assembly according to claim 12 further comprising an injection moulded seal formed to retain said one or more electrodes in position on a surface of the membrane.

14. The membrane assembly according to any of claims 1 to 9 wherein the structure comprises one or more optodes.

15. A method of forming a membrane assembly comprising:

providing a membrane, the membrane having a first surface and a second surface so that material may move from the first surface to the second surface through the membrane, the membrane further having at least one edge, bonding a structure to said first or said second surface in a region of said membrane spaced from said edge,

wherein the structure is formed by a process of injection moulding and wherein the structure is bonded to said first or said second surface by the process of injection moulding.

16. The method according to claim 15 further comprising encasing an edge of the membrane with a seal, said seal delimiting said region spaced from said edge.

17. The method according to claim 15 or claim 16 wherein said seal and/or said structure is formed by injection moulding.

18. The method according to claim 17 wherein the seal is formed by the same injection moulding process used to form the structure.

19. The method according to any of claims 15 to 18 wherein said structure is adhered to said surface of said membrane.

20. The method according to any of claims 15 to 19 further comprising bonding a further structure to a surface opposed to the surface on which the initial structure was bonded.

21. The method according to any of claims 15 to 20 wherein said structure is formed by a mould, said method further comprising the step of preparing the mould by coating one or more surfaces of said mould with enzymes or other biochemical compounds.

22. The method according to any of claim 15 to 21 wherein said structure is formed by a mould, said method further comprising the step of coating one or more surfaces of said membrane with enzymes or other biochemical compounds.

23. The method according to claim 22 wherein said step of coating is applied before or after an injection-moulding process.

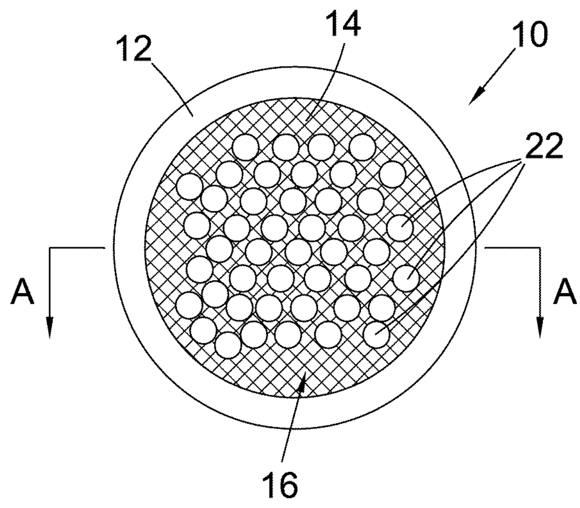


Fig. 1

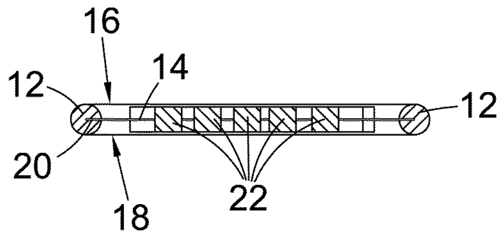


Fig. 2

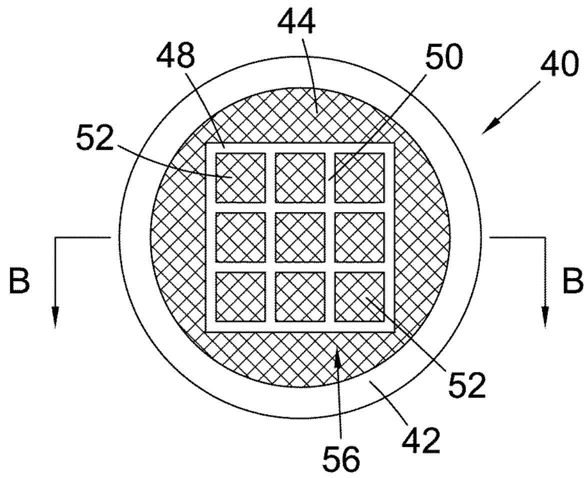


Fig. 3

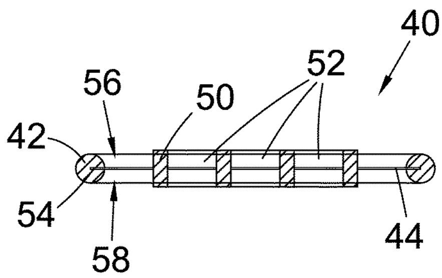


Fig. 4

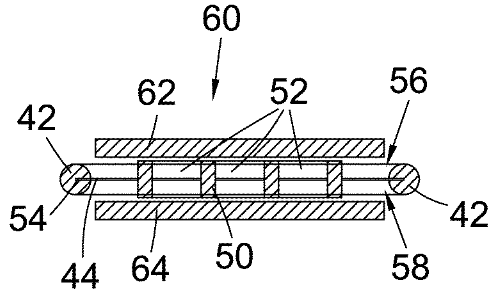


Fig. 5

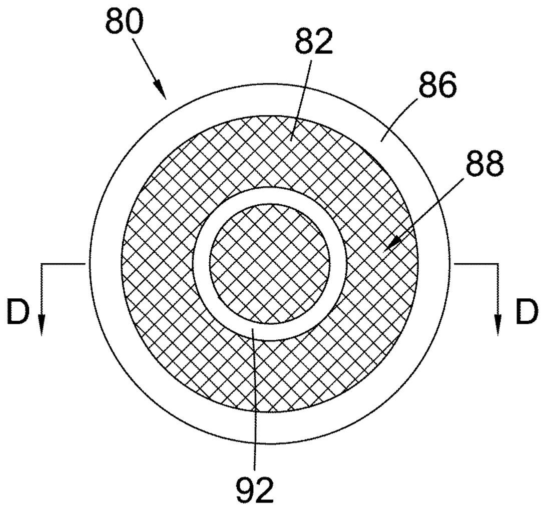


Fig. 6

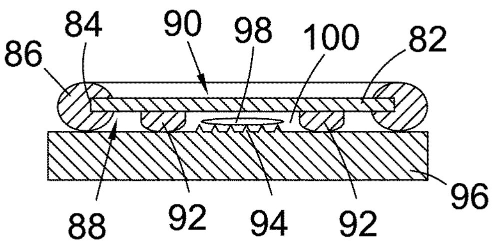


Fig. 7

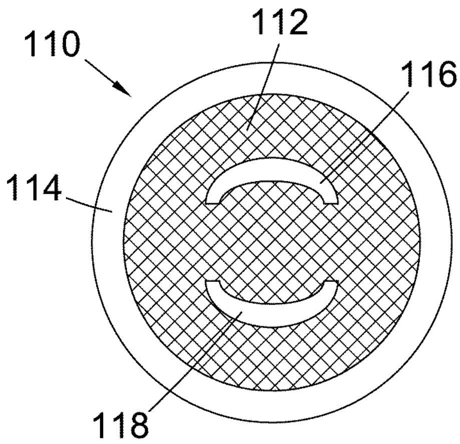


Fig. 8

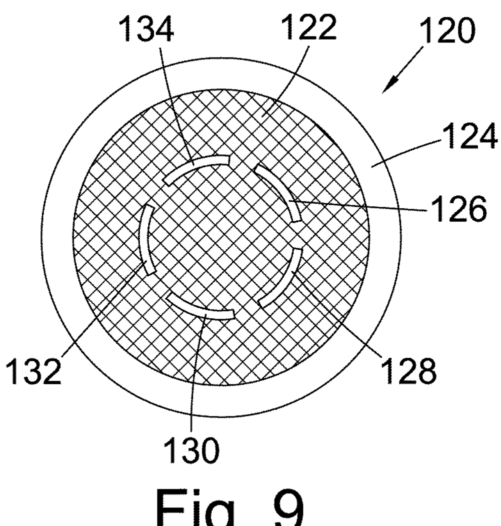


Fig. 9

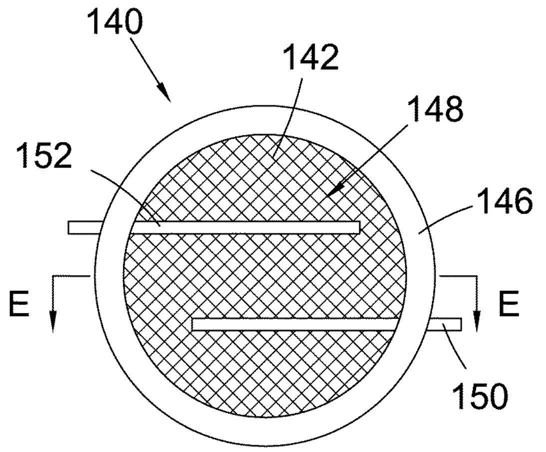
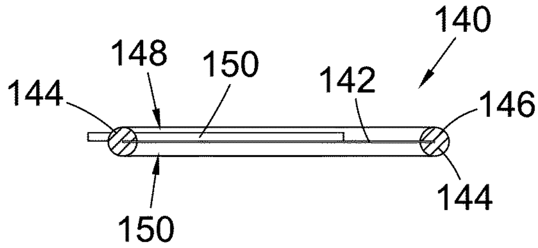


Fig. 10



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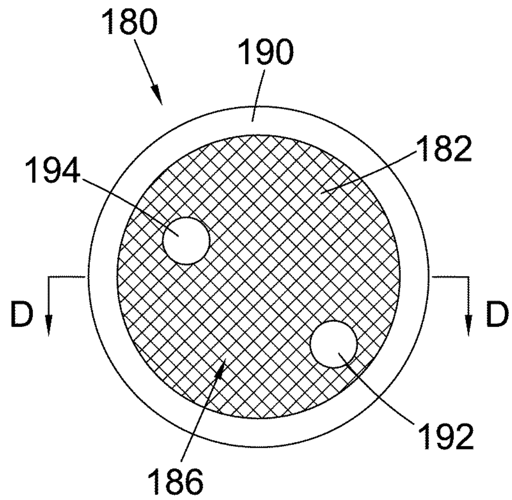

Fig. 12

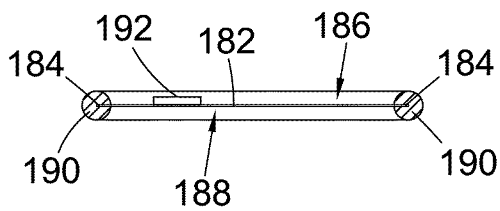

Fig. 13

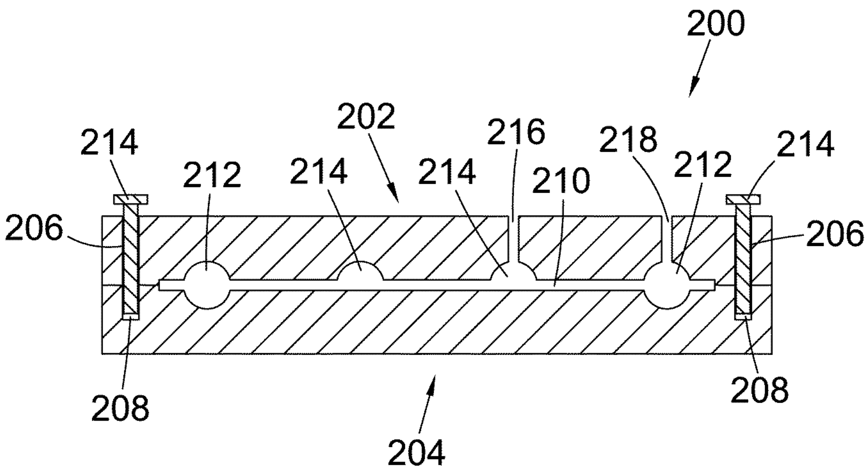
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Fig. 14

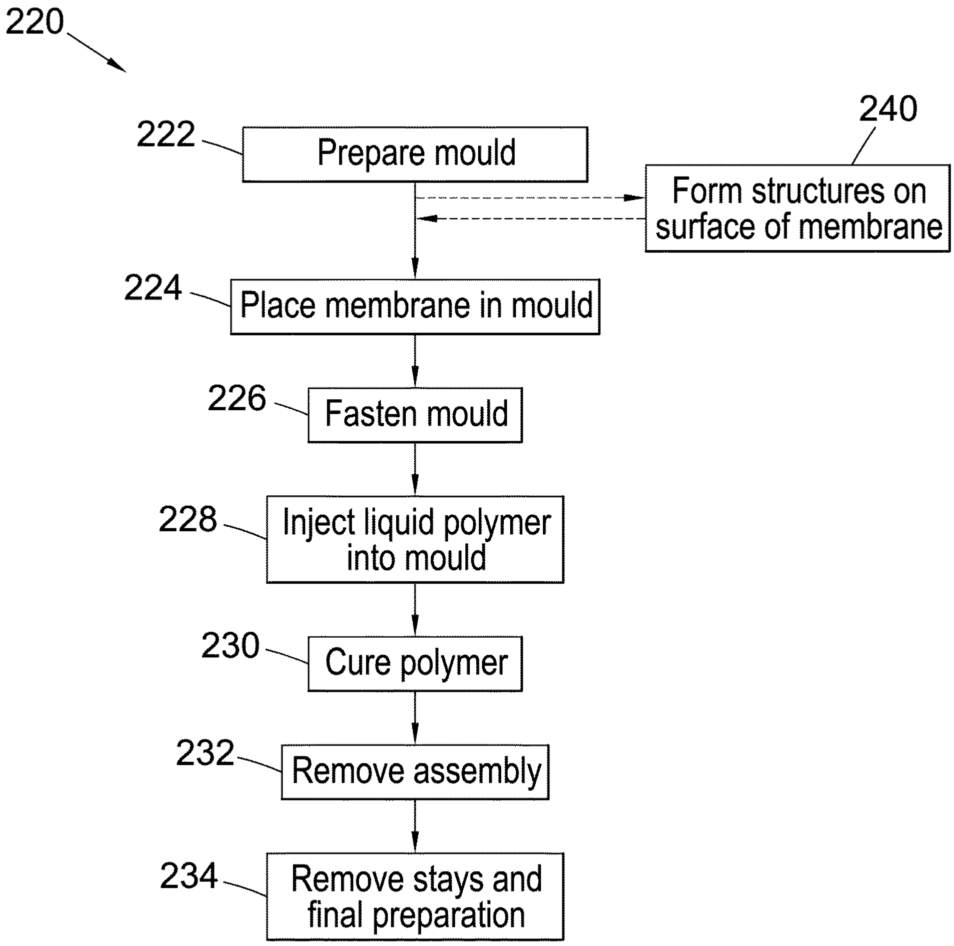
220
222
Prepare mould
240
Form structures on surface of membrane
224
Place membrane in mould
226
Fasten mould
228
Inject liquid polymer into mould
230
Cure polymer
232
Remove assembly
234
Remove stays and final preparation

Fig. 15

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/065718

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01D63/08 B01D69/06 C12M3/06
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)
B01D C12M B29C

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 practicable, search terms used)

EPO-Internal, WPI Data

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X	US 2002/100187 A1 (POLEGATO MARIO [IT]) 1 August 2002 (2002-08-01) paragraph [0063] - paragraph [0064]; figure 2	1,15

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

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

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

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"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
22 August 2013	03/09/2013

Name and mailing address of the ISA/	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Marti, Pedro

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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Information on patent family members

International application No
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