

## PARTICLE SENSITIVE/RADIATION SENSITIVE DEVICES

### Background of the Invention

[0001] This invention relates generally to particle sensitive or radiation sensitive devices incorporating adjustable elastomeric materials containing adjustable elastomeric apertures, and methods for the fabrication of such adjustable elastomeric apertures and methods for the use of such adjustable elastomeric apertures for detecting, measuring or controlling particles and/or radiation.

[0002] Detecting, measuring or controlling matter and/or radiation are essential themes in both the natural world and in the world of invention. However, matter and radiation are thermodynamically compelled to dissipate and so the boundaries of vessels, membranes, and conduits provide a means for restraining and containing matter and/or radiation. Boundaries that limit the dissipation of matter and/or radiation are said to be substantially impervious, impermeable or opaque. Apertures are passages through impervious, impermeable or opaque media that allow for the passage of matter and/or radiation from one side of the boundary to the other side. Apertures can thus be used for detecting, measuring or controlling matter and/or radiation because they provide the focal point through which the passage of matter and/or radiation occurs and mechanisms for observing them are well known.

[0003] Moving particles that bear electrical charges can form an electric current and apertures can be used to detect, measure or control particles that are charged. Electrical measurement of the electrical path of ions through an electrolyte filled aperture was first disclosed in US 2656508 for use as a particle-sensing device called a Coulter counter, which comprises two substantially isolated reservoirs of electrically conductive ionic fluid. The two reservoirs are separated from each other by a substantially, electrically insulating barrier in which an aperture exists through which appropriately sized particles can pass between the reservoirs. Electrodes

placed in each reservoir provide a means to generate an electric current of ions through the aperture by the application of a potential difference, or voltage, across the electrodes. Particles caused to transiently occlude the aperture can thus be detected by monitoring of the electrical signal in a technique referred to as resistive pulse sensing. The transient partial occlusion of the aperture by appropriately sized particles causes blockades of the ionic flow that can be characterised by measuring the change in current amplitude and the duration of the blockade event. These parameters can be related to the hydrodynamic geometry and physical properties of both the aperture and the occluding particle and, together with the frequency of blockades, can be used for quantitative analysis (Bayley et al., "Resistive Pulse Sensing—From Microbes to Molecules" Chem. Rev., 100, 2575-2594, 2000). Particles smaller than 2% of the aperture volume cause blockade signals that are too small to be discriminated from the background electrical noise of the ionic current flow, while particles inappropriately matched to the aperture have a tendency to cause blockages. Coulter counters use a discrete number of solid-state apertures ranging in diameter from 20  $\mu\text{m}$  to 2 mm to detect a diversity of particle diameters ranging from 400 nm to 1 mm (Bayley et al., "Resistive Pulse Sensing—From Microbes to Molecules" Chem. Rev., 100, 2575-2594, 2000). Coulter-type analysis of molecular scale particles has been achieved using molecular-scale apertures of biological origin. Examples of such apertures are ion channels and transmembrane pores used by living cells for translocating molecules from one side of a lipid membrane to the other (Bayley et al., "Resistive Pulse Sensing—From Microbes to Molecules" Chem. Rev., 100, 2575-2594, 2000). One example is the toxin pore called alpha-hemolysin secreted by the bacterium *Staphylococcus aureus*, which assembles from a water-soluble monomer into the membrane bound heptamer and forms a ~2.0 nanometre diameter aperture within a lipid membrane. Application of the alpha-hemolysin pore for Coulter-type nucleic acid particle analysis has been published (Kasianowicz et al., "Characterization of individual polynucleotide molecules using a membrane channel" PNAS, 93, 13770-13773, 1996), such publication showing that an electric field applied across the aperture can drive single-stranded nucleic acid molecules through the alpha-hemolysin aperture singly whilst embedded in a lipid membrane. Because the diameter of the aperture can

accommodate only a single strand of nucleic acid macromolecule, the macromolecules must traverse the aperture individually as a linear chain. The detected resistive pulse of each macromolecule is proportional to the length of the macromolecule and so can be used to measure nucleic acid fragment length.

[0004] Not only can nanometre scale apertures be fabricated from naturally occurring biological nanopores, but they can be fabricated from or in solid-state materials such as inorganic nanotubes (Fan et al. "DNA translocation in inorganic nanotubes", Nano Letters, 5, 1633-1637, 2005) and track-etched polymer films (Mara et al., "An asymmetric polymer nanopore for single molecule detection", Nano Letters, 4, 497-501, 2004), from nanopipettes drawn from thin-walled quartz capillaries (Karhanek et al., "Single DNA molecule detection using nanopipettes and nanoparticles", Nano Letters, 5, 403-407, 2005), from pores lithographically sculpted in silicon-based membranes (Li et al., "DNA molecules and configurations in a solid-state nanopore microscope", Nature Materials, 2, 611-615, 2003) and from carbon nanotubes (Ito et al., "Simultaneous determination of the size and surface charge of individual nanoparticles using a carbon nanotube-based Coulter counter" Analytical Chemistry, 75, 2399-2406, 2003). Although apertures of a fixed or static geometry and mechanisms for observing them are known, only a few are capable of adjustable geometry.

[0005] Methods for regulating effective aperture geometry by controlling the degree of registry between objects of a fixed geometry have been disclosed. GB 2208611 discloses the use of apertures fabricated in two parallel sheets of polymer film where adjustment of the effective aperture size is made by controlling the degree of registry between the apertures in the parallel sheets. US 6706203 and US 2003/0080042 disclose an adjustable nanopore, nanotome and nanotweezer comprising two sliding solid-state crystalline or ceramic window apertures overlaid to create a single smaller aperture where adjustment of the effective aperture geometry is made by controlling the degree of registry between the windows. Piezoelectric actuation is utilized to achieve nanometre-scale mechanical actuation

that operates with dimensions of 1 to 10 nanometres. In US 4853618, a Coulter-type particle analysis apparatus with an aperture of variable size has been disclosed in which aperture geometry is adjusted by the precisely controlled insertion of an insert into a static aperture, thereby partially occluding the geometry of the static aperture and so adjusting the effective aperture geometry.

[0006] Methods for regulating effective aperture geometry by deforming the geometry of the aperture itself have been disclosed. GB 2337597 discloses a tapered orifice fabricated within a piezoelectric material or other such flexible material whereby adjustment of the orifice by the piezoelectric effect enables clearance of blockages by the concomitant adjustment of the aperture geometry. This provides a means for clearing blockages from Coulter-type particle sensors by applying ultrasonic vibration via the piezoelectric effect to a conical taper. US 3395344 discloses a deformable aperture comprising a material that is flexible (including elastic and rubber-like materials) which utilises its capacity to deform under hydrostatic pressure or vacuum to enable the dislodging of blockages, or partial blockages, in Coulter type devices using apertures fabricated by punching moulded diaphragms with a heated stylus. The hydrostatic pressure or vacuum exerts deformation pressure normal to the plane of the perforated membrane (i.e. parallel to the axis of the lumen aperture, but normal to all other points on the membrane plane) which causes the membrane to belly as it is deformed and so adjusts the aperture geometry to allow unblocking of the blockage. The deformable aperture of US 3395344 offers several advantages over the fixed geometry apertures of Coulter counters but lacks the capacity to be precisely opened to a specific level for the purposes of detecting, measuring or controlling particles and/or radiation.

[0007] PCT/EP2005/053366 discloses an adjustable elastomeric aperture that can be adjusted for the purpose of detecting, measuring and controlling particles and/or electromagnetic radiation. The disclosed device is most typically fabricated by penetration of sheets of elastomeric material pre-cut into cruciform geometries.

[0008] The deformable apertures disclosed in PCT/EP2005053366 suffer from several disadvantages and limitations.

[0009] One disadvantage is that an adjustable elastomeric aperture fabricated in a deformable material of uniform cross-section requires the use of expensive, high-precision adjustment apparatus to achieve nanometre scale adjustment of the adjustable elastomeric aperture.

[0010] Other disadvantages are that (i) the use of sheets of deformable materials which must be cut into appropriate shapes for deployment introduces a waste component in the form of the excess trimmed material, (ii) sheet materials are most typically fabricated with rollers which introduce anisotropic line tensions, and (iii) the sheets of deformable materials are fabricated to have a specific thickness, within certain tolerances, requiring complex assembly procedures to be adopted to create architectures of varying thickness.

[0011] Another disadvantage is that fabrication of the apertures by penetration with a sharpened probe has limitations because the elastomeric nature of the deformable material causes the aperture to be fabricated uncontrollably as the probe penetrates the elastomeric material and the deformed elastomer elastically recoils following penetration.

[0012] Another disadvantage is that the deformation characteristics of elastomeric materials undergo significant structural changes upon deformation in a phenomenon known as the Mullins effect (Mullins L. "Softening of rubber by deformation" Rubber Chem. Tech. 42, 339-362, 1969) which require that devices and methods be adopted that accommodate, mitigate and utilise the Mullins effect in adjustable elastomeric apertures.

[0013] Another disadvantage is that fluid handling capabilities for adjustable elastomeric apertures have not been developed for analysing particles that are suspended in fluids and such fluid handling capabilities are required to facilitate fluid phase particle analysis.

[0014] Therefore it is desirable that a new type of improved adjustable elastomeric aperture is developed that is mechanically simple and allows the adjustable elastomeric aperture to be easily fabricated and characterised for the purpose of detecting, measuring or controlling particles and/or radiation over a plurality of scales.

[0015] It is an object of the present invention to provide an adjustable elastomeric aperture that is easily fabricated from inexpensive materials. The present invention relates generally to particle sensitive or radiation sensitive devices incorporating adjustable elastomeric materials containing adjustable elastomeric apertures, and methods for the fabrication of such adjustable elastomeric apertures, and methods for the use of such adjustable elastomeric apertures for detecting, measuring or controlling particles and/or radiation.

### **Summary of the invention**

[0016] According to one aspect of the present invention there is provided a particle sensitive and/or radiation sensitive device incorporating an adjustable elastomeric material containing an elastomeric septum portion adapted to be penetrated to form an aperture providing a path for particles and/or radiation, and adjustment means for adjusting the septum portion to change at least one of the parameters of the path provided by the aperture.

[0017] In a preferred embodiment of the invention the septum portion comprises a membrane portion of the material of greater or lesser thickness than a surrounding

portion of the material, the surrounding portion of the material advantageously being in the form of a raised rim enclosing the membrane portion so as to form a well.

[0018] It is also preferred that at least one hole extends through part of the material not containing the septum portion in order to provide a fluid path through the material prior to penetration of the septum portion. The or each hole may be surrounded by a raised rim enclosing the hole so as to form a well surrounding the hole.

[0019] Advantageously the adjustment means is detachably attachable to the adjustable elastomeric material to allow adjustment of the septum portion to change at least one of the parameters of the path provided by the aperture.

[0020] According to another aspect of the present invention there is provided a device for fabricating a deformable aperture in deformable material, the device comprising a probe for forcibly penetrating the deformable material to form a vacancy in the deformable material through which a continuous path extends from one side to another side of the deformable material, and an elastomer support component for supporting the deformable material to provide mechanical resistance antagonistic to the direction of the force exerted by the probe on penetration of the deformable material.

[0021] The unpenetrated blank membrane of adjustable elastomeric material is formed from elastomeric materials selected from the group, but not limited to: polymers; natural and synthetic rubbers; elastomeric materials; natural polymers, proteins, polypeptides, polysaccharides; plastics; doped conducting plastics; hydrocarbon plastics; perfluorocarbon plastics; latex materials; thermoplastic deformable materials; thermoplastic polyurethane (ethers and esters) deformable materials; olefin-based deformable materials including polypropylene, polyethylene, cyclic olefins; styrene-based deformable materials; polyamide-based deformable

materials; polyester-based deformable materials; nitril-based deformable materials; ethylene chloride copolymer cross-linked alloys; silicone deformable materials; semiconductor based materials; silicates; silicon; doped silicon; metals; or metal alloys; piezoelectric materials; piezoelectric ceramics. The deformable aperture can also be defined by composite deformable material made from a combination of one or more such materials.

**[0022]** The unpenetrated blank membrane of adjustable elastomeric material is formed into three-dimensional geometries by processes selected from the group, but not limited to: moulding; injection moulding; blow-moulding; compression moulding; compression-injection moulding; embossing; hot embossing; stamping; casting; etching, lithography; photolithography; carving; cutting; milling; ion milling; polymerising; epitaxial growth; or by any combination of the above described processes.

**[0023]** The unpenetrated blank membrane of adjustable elastomeric material can be of any general three-dimensional geometry selected from the group, but not limited to: cubic geometries; rhombic geometries; orthorhombic geometries; planar geometries; asymmetric planar geometries; symmetric planar geometries; planar geometries with two symmetry axes; planar geometries with three symmetry axes; symmetric planar geometries with four symmetry axes; symmetric planar geometries with five symmetry axes; geometries of variable cross-sectional thickness; planar geometries of variable cross-section thickness.

**[0024]** The unpenetrated blank membrane of adjustable elastomeric material can be of any general size in which one or more of the three spatial dimensions of the unpenetrated blank membrane of adjustable elastomeric material is less than 100 mm, or alternatively less than 10 mm, or alternatively less than 1 mm, or alternatively less than 0.1 mm.

[0025] The unpenetrated blank membrane of adjustable elastomeric material has structural features to facilitate attachment to instrumentation. The structural features are selected from the group, but not limited to: holes; eyelets; hooks; lugs; ridges; or by articles embedded into the elastomeric material from the group, but not limited to: rings; hooks; pins; rods, or by any combination of the above described features.

[0026] The unpenetrated blank membrane of adjustable elastomeric material has structural features to facilitate the controlled adjustment of the adjustable elastomeric material. The structural features are selected from the group, but not limited to: holes; ridges; rims; rings; walls; tubes; wells; reservoirs; regions of defined cross-section; layered regions, or by articles embedded into the elastomeric material from the group, but not limited to: fibres; ceramics; composites or by any combination of the above described features.

[0027] The unpenetrated blank membrane of adjustable elastomeric material has structural features to facilitate fluid handling. The structural features are selected from the group, but not limited to: holes; rims; walls; tubes; wells; reservoirs or by articles embedded into the elastomeric material from the group, but not limited to: tubes; connectors; wells; reservoirs; ridges, or by any combination of the above described features.

[0028] The unpenetrated blank membrane of adjustable elastomeric material has structural features to facilitate fluid handling that serve to dock to external hardware fluid handling devices. The structural features are selected from the group, but not limited to: holes; rims; walls; tubes; wells; reservoirs or by articles embedded into the elastomeric material from the group, but not limited to: tubes; connectors; wells; reservoirs; ridges, or by any combination of the above described features.

[0029] The unpenetrated blank membrane of adjustable elastomeric material has surface features to facilitate fluid handling. The surface features are selected from

the group, but not limited to: surface treatments to render the membrane of adjustable elastomeric material hydrophobic; surface treatments to render the membrane of adjustable elastomeric material hydrophilic; surface treatments to render the membrane of adjustable elastomeric material oleophilic; surface treatments to render the membrane of adjustable elastomeric material electrostatically charged; surface treatments to render the membrane of adjustable elastomeric material electrostatically neutral, or by any combination of the above described features.

[0030] According to another aspect of the present invention there is provided a device for fabricating one or more apertures in unpenetrated blank membranes of adjustable elastomeric material comprising a mechanism for penetrating the unpenetrated blank membrane of adjustable elastomeric material with a sharpened probe and a means for measuring one or more parameters of penetration process. Penetration of the unpenetrated blank membrane of adjustable elastomeric material using one or more pointed sharpened probes. Sharpened probes may be prepared by grinding and polishing processes, moulding processes, extrusion processes, electrochemical etching processes or lithographic processes. The probe may be of a type having a sharp point or a cutting tool with a defined shape or a scanning probe microscopy probe or a scanning tunnelling microscopy probe or an atomic force microscopy probe. The probe can be heated or cooled with respect to the deformable material and can be pushed through the deformable material, thereby cutting or separating or melting the fabric of the deformable material, or rotated or moved so as to drill out or otherwise create the aperture in the deformable material or by any combination of the above described methods.

[0031] Upon emerging from the opposing surface of the adjustable elastomeric material the probe is detected by a probe detection mechanism. The probe detection mechanism is selected from the group, but not limited to: optical detection; electrical detection; electrical detection by way of measured changes in capacitance; electrical detection by way of measured changes in electrical current; electrical detection by way of measured changes in electrical tunnelling current; electrical detection by way

of measured changes in electrical resistance; detection by way of measured changes in mechanical resistance; detection of the elastic recoil, or by any combination of the above described mechanisms.

**[0032]** According to another aspect of the present invention there is provided a device for preconditioning unpenetrated blank membranes of adjustable elastomeric material by way of mechanical adjustment comprising a mechanism for adjusting the unpenetrated blank membrane of adjustable elastomeric material and a means for measuring one or more parameters of unpenetrated blank membrane of adjustable elastomeric material. The measured parameters of the unpenetrated blank membrane of adjustable elastomeric material are selected from the group, but not limited to: optical detection; optical detection by way of polarising light; electrical detection; electrical detection by way of measured changes in capacitance; electrical detection by way of measured changes in electrical current; electrical detection by way of measured changes in electrical tunnelling current; electrical detection by way of measured changes in electrical ionic current; electrical detection by way of measured changes in electrical resistance; detection by way of measured changes in mechanical resistance; detection by way of measured changes in mechanical stress; detection by way of measured changes in mechanical strain, or by any combination of the above described parameters.

**[0033]** The elastic recoil of the adjustable elastomeric material following emergence of the sharpened probe from the opposing surface of the adjustable elastomeric material is substantially mitigated by providing a mechanical elastomer support component to the adjustable elastomeric material to provide mechanical resistance antagonistic to the direction of the force exerted by the sharpened probe prior to, during and following the emergence of the sharpened probe from the opposing side of the adjustable elastomeric material. The mechanical elastomer support component is selected from the group, but not limited to: a fluid; an electrolyte fluid; a solid; a metallic solid; a metallic electrode; a metallic electrode containing a cavity; a metallic electrode containing a fluid-filled cavity; a metallic

electrode containing an electrolyte fluid-filled cavity; a gold electrode containing an electrolyte fluid-filled cavity; a gel matrix; a gel matrix containing electrolyte, or by any combination of the above described features.

[0034] The cavity of the mechanical elastomer support component is any size, but is preferably of the same approximate dimensions as the sharpened probe so as to mitigate, as much as practically possible, the extent of deformation of the elastomeric material by force exerted by the sharpened probe prior to, during and following the emergence of the sharpened probe from the opposing side of the adjustable elastomeric material. The one or more of the three spatial dimensions of the cavity is less than 1000 $\mu\text{m}$ , or alternatively less than 100  $\mu\text{m}$ , or alternatively less than 10  $\mu\text{m}$ , or alternatively less than 1  $\mu\text{m}$ , or alternatively less than 0.1  $\mu\text{m}$ .

[0035] The cavity of the mechanical elastomer support component is any shape, selected from the group, but not limited to: notches; single notches; intersecting notches; depressions; tunnels or holes. The cavity of the mechanical elastomer support is fabricated by electrical discharge machining; milling; ion milling; drilling, penetration; indenting; indenting with the sharpened probe; indenting a gold billet with a sharpened probe, or by any combination of the above described methods.

[0036] The mechanical elastomer support component can be heated or cooled so as to heat or cool the adjustable elastomeric material. The heating or cooling can be achieved by methods selected from the group, but not limited to: conductive heating and/or cooling; convective heating and/or cooling; heating and/or cooling by way of Peltier devices, or by any combination of the above described methods.

[0037] The mechanical elastomer support component is positioned within the aperture fabrication device on the opposing side of the adjustable elastomeric material from that of the sharpened probe to prevent substantial deformation of the adjustable elastomeric material during penetration of the adjustable elastomeric

material by the sharpened probe. The position of the mechanical elastomer support component is preferably adjustable and can be in any general position selected from the group, but not limited to: less than 1 mm, or alternatively less than 100  $\mu\text{m}$ , or alternatively less than 10  $\mu\text{m}$ , or alternatively less than 1  $\mu\text{m}$ , or alternatively less than 0.1  $\mu\text{m}$ ; or alternatively in contact and with and less than 0.1  $\mu\text{m}$  applied deformation; or alternatively in contact and with and less than 1  $\mu\text{m}$  applied deformation; or alternatively in contact and with and less than 10  $\mu\text{m}$  applied deformation; or alternatively in contact and with and less than 100  $\mu\text{m}$  applied deformation; or alternatively in contact and with and less than 1 mm applied deformation; or alternatively in contact and with and less than 10 mm applied deformation.

[0038] According to another aspect of the present invention there is provided a method for fabricating one or more apertures in an unpenetrated blank membrane of adjustable elastomeric material comprising: providing an unpenetrated blank membrane of adjustable elastomeric material; providing an apparatus for penetrating the unpenetrated blank membrane of adjustable elastomeric material with a sharpened probe and a means for measuring one or more parameters of penetration process. The measured parameters of the penetration process are selected from the group, but not limited to: optical detection; optical detection by way of polarising light; electrical detection; electrical detection by way of measured changes in capacitance; electrical detection by way of measured changes in electrical current; electrical detection by way of measured changes in electrical tunnelling current; electrical detection by way of measured changes in electrical ionic current; electrical detection by way of measured changes in electrical resistance; detection by way of measured changes in mechanical resistance; detection by way of measured changes in mechanical stress; detection by way of measured changes in mechanical strain, or by any combination of the above described parameters.

[0039] According to another aspect of the present invention there is provided a method of using one or more of the measured penetration parameters recorded during

the aperture fabrication process to determine the quality and thereby the utility of the said formed aperture. The measured penetration parameters are selected from the group, but not limited to: optical detection; optical detection by way of polarising light; electrical detection; electrical detection by way of measured changes in capacitance; electrical detection by way of measured changes in electrical current; electrical detection by way of measured changes in electrical tunnelling current; electrical detection by way of measured changes in electrical ionic current; electrical detection by way of measured changes in electrical resistance; detection by way of measured changes in mechanical resistance; detection by way of measured changes in mechanical stress; detection by way of measured changes in mechanical strain, or by any combination of the above described parameters.

[0040] According to another aspect of the present invention there is provided a method of using one or more of the measured parameters of the adjustable elastomeric aperture to determine the quality and thereby the utility of the said formed aperture. The measured parameters are selected from the group, but not limited to: optical parameters; optical polarising light parameters; optical diffraction parameters; electrical parameters; electrical capacitance; electrical current; electrical tunnelling current; electrical ionic current; electrical conductivity; electrical resistance; electrical membrane resistance; electrical access resistance; electrical current rectification; mechanical resistance; mechanical stress; mechanical strain, or by any combination of the above described parameters.

[0041] According to another aspect of the present invention there is provided a method of microscopic examination of the adjustable elastomeric aperture to determine the quality and thereby the utility of the said formed aperture. The microscopic examination methods are selected from the group, but not limited to: optical microscopy; polarising light microscopy; confocal microscopy; scanning confocal microscopy; probe microscopy, scanning probe microscopy; atomic force microscopy; scanning electrochemical microscopy; electron microscopy; scanning electron microscopy; transmission electron microscopy.

[0042] According to another aspect of the present invention there is provided a method for preconditioning the unpenetrated blank membrane of adjustable elastomeric material prior to aperture fabrication comprising: providing the unpenetrated blank membrane of adjustable elastomeric material; providing an apparatus for adjusting the unpenetrated blank membrane of adjustable elastomeric material and a means for measuring one or more parameters of unpenetrated blank membrane of adjustable elastomeric material. The preconditioning is selected from the group, but not limited to: preconditioning by way of curing; preconditioning by way of chemical curing; preconditioning by way of thermal curing; preconditioning by way of curing with electromagnetic radiation; preconditioning by way of mechanical adjustment, from the group, but not limited to compression; tensioning; stretching; bending or twisting; preconditioning by way of zero or more cycles of mechanical adjustment; preconditioning by way of one or more cycles of mechanical adjustment until a mechanical equilibrium is established; or by any combination of the above described features. The measured parameters of the unpenetrated blank membrane of adjustable elastomeric material are selected from the group, but not limited to: optical detection; optical detection by way of polarising light; electrical detection; electrical detection by way of measured changes in capacitance; electrical detection by way of measured changes in electrical current; electrical detection by way of measured changes in electrical resistance; detection by way of measured changes in mechanical resistance; detection by way of measured changes in mechanical stress; detection by way of measured changes in mechanical strain, or by any combination of the above described parameters.

[0043] According to another aspect of the present invention there is provided a device for conditioning an adjustable elastomeric aperture in an adjustable elastomeric material by way of mechanical adjustment comprising an apparatus for adjusting the adjustable elastomeric aperture and a means for measuring one or more parameters of adjustable elastomeric aperture and/or the adjustable elastomeric material in which the aperture is fabricated. The measured parameters of the

adjustable elastomeric aperture and/or the adjustable elastomeric material in which the aperture is fabricated are selected from the group, but not limited to: optical detection; optical detection by way of polarising light; electrical detection; electrical detection by way of measured changes in capacitance; electrical detection by way of measured changes in electrical current; electrical detection by way of measured changes in electrical resistance; detection by way of measured changes in mechanical resistance; detection by way of measured changes in mechanical stress; detection by way of measured changes in mechanical strain, or by any combination of the above described parameters.

[0044] According to another aspect of the present invention there is provided a method of conditioning an adjustable elastomeric aperture in adjustable elastomeric material comprising: providing an adjustable elastomeric aperture; providing an apparatus for adjusting the adjustable elastomeric aperture and a means for measuring one or more parameters of the adjustable elastomeric aperture. The conditioning is selected from the group, but not limited to: conditioning by way of curing; conditioning by way of chemical curing; conditioning by way of thermal curing; conditioning by way of curing with electromagnetic radiation; conditioning by way of mechanical adjustment, from the group, but not limited to compression; tensioning; stretching; bending or twisting; conditioning by way of zero or more cycles of mechanical adjustment; conditioning by way of one or more cycles of mechanical adjustment until a mechanical equilibrium is established, or by any combination of the above described features. The measured parameters of adjustable elastomeric aperture in adjustable elastomeric material are selected from the group, but not limited to: optical detection; optical detection by way of polarising light; electrical detection; electrical detection by way of measured changes in capacitance; electrical detection by way of measured changes in electrical current; electrical detection by way of measured changes in electrical ionic current; electrical detection by way of measured changes in electrical resistance; detection by way of measured changes in mechanical resistance; detection by way of measured changes in mechanical stress; detection by way of measured changes in mechanical strain, or by any combination of the above described parameters.

[0045] According to another aspect of the present invention there is provided a device for detecting, measuring or controlling particles and/or radiation comprising: an adjustable elastomeric aperture fabricated in an adjustable elastomeric material; a device for adjusting the adjustable elastomeric aperture by way of mechanical adjustment of the adjustable elastomeric material in which the aperture is fabricated and a means for measuring one or more parameters of adjustable elastomeric aperture and/or the adjustable elastomeric material in which the aperture is fabricated.

[0046] According to another aspect of the present invention there is provided a method for detecting, measuring or controlling particles and/or radiation the method comprising providing an adjustable elastomeric material containing an adjustable elastomeric aperture defining a path for particles and/or radiation; adjusting the adjustable elastomeric aperture to a prescribed geometry and/or size by adjusting the adjustable elastomeric material to change at least one of the parameters of the path defined by the adjustable elastomeric aperture; and causing the particle or radiation to be detected, measured or controlled to enter the adjustable elastomeric aperture.

[0047] In operation of the devices and methods used to detect and/or measure and/or control the flux of matter and/or radiation in accordance with the present invention, control of the adjustment of the adjustable elastomeric aperture may be effected on the basis of parameters selected from the group comprising, but not limited to: the flux of particles traversing the adjustable elastomeric aperture, the flux of atomic particles traversing the adjustable elastomeric aperture; the flux of molecular particles traversing the adjustable elastomeric aperture; the flux of ionic particles traversing the adjustable elastomeric aperture; the flux of ionic particles in solution traversing the adjustable elastomeric aperture; the flux of electrical current traversing the adjustable elastomeric aperture, the flux of electrical tunnelling current traversing the adjustable elastomeric aperture; and the flux of electromagnetic radiation traversing the adjustable elastomeric aperture. Measurable parameters of

the adjustable elastomeric material in which the adjustable elastomeric aperture is fabricated may be selected from the group comprising, but not limited to: capacitance; resistance; conductivity; opacity; transparency; length; width; height; volume; thermal conductivity; and dielectric properties. Measurable parameters linked to the actuation mechanism by which the adjustable elastomeric aperture is adjusted may be selected from the group comprising, but not limited to: capacitance; conductivity; actuator displacement; actuator position; stepper motor position; inductance; motor coil inductance; resistance; and motor coil resistance.

### **Brief description of the drawings**

[0048] In order that the invention may be more fully understood, a preferred embodiment of the invention will now be described, by way of example, with reference to the accompanying drawings, in which:

Figures 1a and 1b show an adjustable diaphragm for use in the preferred embodiment;

Figure 2a and 2b show the diaphragm attached to actuators in the preferred embodiment, Figures 3a and 3b showing the actuators in different positions;

Figure 4a schematically shows preferred aperture fabrication apparatus, Figure 4b being a graph of a recorded aperture fabrication event;

Figure 5 shows a scanning confocal microscopy image of the adjustable aperture produced by such apparatus;

Figure 6 schematically shows the aperture adjustment arrangement in the preferred embodiment;

Figures 7 to 10 are graphs that can be used to characterise the performance capabilities of the adjustable aperture in the preferred embodiment; and

Figure 11 is a flow chart depicting one possible mode of operation of the preferred embodiment of Figures 2a & 2b, Figures 3a & 3b, Figure 4a and Figure 6.

### **Detailed description of the drawings**

[0049] The following description is given by way of example with reference to a preferred embodiment of the invention utilizing polyurethane as an adjustable elastomeric material. One preferred example of polyurethane is the polyether type Elastollan® 1100 series from BASF Corporation, Wyandotte Michigan, USA. However, materials that may be used for the adjustable elastomeric material in other embodiments of the invention include, but are not limited to: polymers, natural and synthetic rubbers, elastomeric materials, natural polymers, proteins polypeptides, polysaccharides, plastics, doped conducting plastics; hydrocarbon plastics, perfluorocarbon plastics, latex materials, thermoplastic deformable materials, thermoplastic polyurethane (ethers and esters) deformable materials, olefin-based deformable materials including polypropylene, polyethylene, cyclic olefins, styrene-based deformable materials, polyamide-based deformable materials, polyester-based deformable materials, nitril-based deformable materials, ethylene chloride copolymer cross-linked alloys, silicone deformable materials, semiconductor based materials, silicates, silicon, doped silicon, metals or metal alloys, piezoelectric materials, and piezoelectric ceramics. The deformable aperture can also be defined by composite deformable material made from a combination of one or more such materials.

[0050] Furthermore, modifications can be made to the adjustable elastomeric aperture by treatment of the surface of the adjustable elastomeric material. The surface treatment may be selected from the group comprising, but not limited to:

surface treatment to render the membrane of adjustable elastomeric material hydrophobic, surface treatment to render the membrane of adjustable elastomeric material hydrophilic, surface treatment to render the membrane of adjustable elastomeric material oleophilic, surface treatment to render the membrane of adjustable elastomeric material electrostatically charged, surface treatment to render the membrane of adjustable elastomeric material electrostatically neutral, and any combination of the above described surface treatments.

[0051] Figures 1a and 1b show an adjustable diaphragm 100 in the form of an injection moulded elastomeric sheet 101 of cruciform shape made of polyurethane incorporating at least one adjustable aperture fabricated by penetration in the sheet for use in the preferred embodiment of the invention. In a non-illustrated variant embodiment Figure 1a schematically illustrates in plan view the diaphragm 100 having an isometric planar cruciform geometry. The polyurethane sheet 101 is formed from polyurethane being shaped by injection moulding in an appropriately shaped cavity. The cruciform shape of the polyurethane sheet 101 comprises four equal arms 102. At the ends of each of the four arms 102 eyelets 103 are formed that pass through the polyurethane sheet 101. At the centre of the polyurethane sheet 101 there is formed a raised circular rim 104, and centrally within the raised rim 104 there is formed a septum 105 which is a disk of planar cross-section. The septum 105 is joined to the raised rim 104 by a tapering zone 106 of variable cross-section. In the central region of each arm 102 there is a raised rim 107 that encircles a formed porthole 108 that passes through the polyurethane sheet 101. In this respect, the above described features for each arm 102 of the polyurethane sheet 101 are identical, with each arm 102 having identically arranged eyelets 103, raised rim 107 and porthole 108. Actuators 204, as will be described in more detail below with reference to Figures 2a and 2b, are provided to effect deformation of the diaphragm 100 and are movable to and fro in the direction indicated by the double-headed arrows in Figures 2a and 2b. The actuators 204 can move independently in the same or opposite directions or in unison in the same or opposite directions. Figure 1b shows a transverse cross-section through the diaphragm 100 along the dashed line (A-A) 109 in Figure 1a.

[0052] Figure 2a schematically shows the diaphragm 200 of Figure 1a with each of the four arms of the polyurethane sheet 201 individually attached to actuators 204. The eyelets 203 in the polyurethane sheet 201 facilitate attachment to the actuators 204 that contain pins 205 which match the size and placement of the eyelets 203 formed in the polyurethane sheet 201. The pins 205 pass through the eyelets 203. Figure 2b shows a transverse cross-section through the diaphragm 200 along the dashed line (A-A) 209 in Figure 2a.

[0053] Figures 3a and 3b show photographs of the injection moulded polyurethane sheet 301 positioned on an adjustment apparatus 302 and attached through the eyelets 303 to the actuators 304 by the actuator pins 305. Figure 3a shows the polyurethane sheet 301 in an unadjusted configuration. Figure 3b shows the polyurethane sheet 301 with applied isotropic biaxial extension caused by the equal and opposite displacement of opposing actuators 304, which are connected to the four arms of the cruciform by the pins 305. The ruler 306 indicates the displacement of one of the sets of actuator pins 305 as between the position of Figure 3a and the position of Figure 3b by a distance of approximately 5 millimetres (mm). The total isotropic biaxial displacement is thus 10 mm per axis and is given the symbolic representation  $\Delta X$ .

[0054] Figure 4a is a simplified schematic illustration of the preferred aperture fabrication apparatus 401 for fabricating at least one adjustable elastomeric aperture in the polyurethane sheet 402. In Figure 4a the aperture fabrication apparatus 401 comprises the injection-moulded polyurethane sheet 402 (shown in cross-section). The arms 403 of the polyurethane sheet 402 containing the eyelets 404 facilitate attachment of the sheet 402 to the aperture fabrication apparatus 401 via the pins 405. The sharpened probe 407 is attached to a mechanical actuator 408 held within the aperture fabrication apparatus 401. An elastomer support component 409 is connected to a mechanical actuator 410 of the aperture fabrication apparatus 401 and is positioned directly opposite to the sharpened probe 407 on the opposite side of the

polyurethane sheet 402 at the site of the cruciform septum 412. The elastomer support component 409 comprises a metallic rod of stainless steel bearing a cavity 411 filled with an electrolyte fluid 413. The mechanical actuator 408 is configured to enable precise mechanical actuation of the sharpened probe 407 to and fro perpendicular to the plane of the polyurethane sheet 402 at the site of the cruciform septum 412. Likewise the mechanical actuator 410 is configured to enable precise mechanical actuation of the elastomer support component 409 to and fro perpendicular to the plane of the polyurethane sheet 402 at the site of the cruciform septum 412. Connected to each actuator 408 and 410 is an actuator controller 414 that is in turn connected to and controlled by a computer 415. The actuators 408, 410 can be caused to independently move the attached sharpened probe 407 and/or the elastomer support component 409 to and fro perpendicular to the plane of the polyurethane sheet 402 in the directions indicated by the double-headed arrows. The sharpened probe 407 and the elastomer support component 409 are both connected to a voltage clamping current signal detector 416. One such type of voltage clamping current signal detector 416 is the voltage-clamping amplifier (Axopatch 200B with CV203BU preamplifier from Molecular Devices Corporation, Sunnyvale CA, USA) connected via a shielded preamplifier to electrodes 407, 409 as shown in Figure 4a. Analogue current signals are acquired using the amplifier in the resistive feedback mode with a 10 kHz low pass Bessel filter, digitized with a Digidata 1322A (also from Molecular Devices Corporation) and recorded to computer hard disk using the program, pCLAMP version 9, supplied with the amplifier.

[0055] In the fabrication of an aperture as described above the adjustment of the elastomer support component 409 is used to modulate the degree of elastic recoil of the polyurethane sheet 402 at the site of the cruciform septum 412. The elastomer support component 409 can be adjusted to be in any general position selected from the group comprising, but not limited to: less than 1 mm, or alternatively less than 100  $\mu\text{m}$ , or alternatively less than 10  $\mu\text{m}$ , or alternatively less than 1  $\mu\text{m}$ , or alternatively less than 0.1  $\mu\text{m}$ , or alternatively in contact and with and less than 0.1  $\mu\text{m}$  applied deformation, or alternatively in contact and with and less than 1  $\mu\text{m}$  applied deformation, or alternatively in contact and with and less than 10  $\mu\text{m}$  applied

deformation, or alternatively in contact and with and less than 100  $\mu\text{m}$  applied deformation, or alternatively in contact and with and less than 1 mm applied deformation, or alternatively in contact and with and less than 10 mm applied deformation. The position of the elastomer support component 409 can be adjusted one or more times to one or more prescribed positions to achieve a mechanical conditioning prior to, during or post fabrication of the aperture. The method of aperture fabrication can also be inverted so that the probe 407 penetrates the cruciform septum 412 from the reverse side of the cruciform septum.

[0056] The elastomer support component 409 and/or the sharpened probe 407 can also be temperature controlled.

[0057] In the fabrication of the aperture as described above the electrolyte fluid 413 filling the cavity 411 of the elastomer support component 409 was 1M KCL, 10mM Tris-HCL pH 8.0, 1mM EDTA, 0.1%, Triton X-100, filter sterilised through a 0.22  $\mu\text{m}$  Millipore filter and stored as frozen aliquots. All reagents were AR grade.

[0058] In the fabrication of the aperture as described above the sharpened probe 407 is a conically shaped probe prepared by AC electrochemical etching of polycrystalline tungsten rod (0.51 mm diameter from Midwest Tungsten Service Inc., Willowbrook IL, USA) in 4M NaOH.

[0059] Figure 4b shows the graph 417 of the recorded current trace 418 of an aperture fabrication event as described above. The y axis 419 shows the current level in pico amperes (pA). The x axis 420 shows the time in seconds (s). Features of the current trace 418 are indicative of the process of aperture fabrication. These features include a period representing the open circuit state prior to penetration by a recorded current value of 0 pA 421. Following the initiation of penetration a short period of elevated current response 422 is recorded that precedes the rapid rise 423 indicating completion of the electrical circuit. The circuit is completed by the establishment of

electrical continuity between the tip of the sharpened probe 407 and the electrolyte fluid 413 held within the cavity 411 of the elastomer support component 409. As the probe 407 progresses through the adjustable elastomer septum the recorded current trace 418 increases until a set-point value 424 is reached, whereupon the probe 407 reverses its direction and the recorded current trace 418 is observed to decrease rapidly at 425. Prior to the breakage of electrical continuity between the probe 407 and the electrolyte fluid 413 shown by a decrease in the recorded current trace to 0 pA 427, a secondary spike 426 is recorded in the current trace as the probe 407 is withdrawn from the newly formed aperture (not shown).

[0060] The trace features 421-427 show characteristics indicative of the aperture fabrication process caused by interactions between the sharpened probe 407, the cruciform septum 412 and the electrolyte fluid 413 held within the cavity 411 of the elastomer support component 409. Variations in the sharpened probe 407, the cruciform septum 412, the electrolyte fluid 413 held within the cavity 411 of the elastomer support component 409, the position of the elastomer support component 409, the temperature of the probe 407, the temperature of the elastomer support component 409, the temperature of the cruciform septum 412, or any other parameter of the aperture fabrication process will be manifest themselves as variations in the recorded trace features 421-427. The variations in the fabricated apertures of the present invention can be correlated to the performance capabilities of the adjustable elastomeric aperture. The trace features 421-427 can thus be used to characterise the performance capabilities of adjustable elastomeric apertures. Thus, for example, the presence of a well defined step feature 422 produced by the pre-tunnelling current as the probe 407 initially begins to pass through the septum 412 tends to indicate a suitable aperture in the preferred embodiment of the invention, as also does the presence of the shoulder feature 426 indicative of the initial flow of electrolyte fluid 413 into the aperture after the probe has begun to emerge from the opposite side of the septum 412, and the presence of the feature 427 at substantially the same level as the feature 418 indicating that the aperture has substantially completely resealed (to leave a residual hole smaller than an ion) on withdrawal of the probe 407 from the septum 412.

[0061] Figure 5 shows a scanning confocal microscopy image 500 with a scale bar 501 representing 500 micrometres. In the image 500 the site 502 caused by the fabrication of an aperture in the septum of an injection moulded polyurethane article by the controlled penetration of the sharpened tungsten probe comprises a cavity 503 encircled by a raised mound 504. Features 502-504 observed in micrographic images can thus be used to characterise the performance capabilities of the adjustable elastomeric aperture.

[0062] Figure 6 is a simplified schematic illustration of a preferred aperture adjustment apparatus 600 for utilising an adjustable elastomeric aperture in the polyurethane sheet 602. In Figure 6, the aperture adjustment apparatus 600 comprises the polyurethane sheet 602 (shown in cross-section) containing a single adjustable elastomeric aperture 603. The arms 604 of the cruciform containing the eyelets 605 facilitate attachment of the polyurethane sheet 602 to the aperture adjustment apparatus 601. For electrical measurements of the septum, the aperture adjustment apparatus 601 is equipped with an electrolyte reservoir 607 in contact with the surface of the septum. A second electrolyte reservoir 608 is formed by the moulded rim 609 on the opposing *cis* surface of the polyurethane sheet 602. The portholes 610 in the polyurethane sheet 602 allow electrolyte 611 in the electrolyte reservoir 607 to be accessible to a first Ag/AgCl electrode 612. A second Ag/AgCl electrode 613 is immersed in the electrolyte 611 in the second electrolyte reservoir 608. A voltage bias applied across the two electrodes 612 and 613 by a voltage clamping current signal detector 614 allows the ionic current caused to flow through the aperture 603 in the polyurethane sheet 602 to be measured by the voltage clamping current signal detector 614.

[0063] The aperture adjustment apparatus 601 serves to adjust the adjustable elastomeric aperture in operation by means of the actuators 615 connected to the eyelets 605 in the polyurethane sheet 602 by pins 617 that match the size and placement of the eyelets 605 in the polyurethane sheet 602. The actuators 615 are

operated by one or more actuator controllers 616 connected to a computer 618 or alternatively can be operated manually.

[0064] In operation to effect adjustment of the adjustable elastomeric aperture the computer 618 controls the aperture adjustment apparatus 601 in dependence on feedback received from the voltage clamping current signal detector 614. The computer 618 allows for algorithms of aperture adjustment to be programmed, recorded and utilised, and algorithms for data acquisition to be programmed, recorded and utilised to enable fully automated and precise operation of the adjustable elastomeric aperture.

[0065] Figure 7 is a composite graph 700 of the primary wetting of an adjustable elastomeric aperture fabricated in an injection moulded polyurethane sheet polyurethane article as described above. The lower trace 701 depicts the amount of isotropic biaxial adjustment applied to the injection moulded polyurethane sheet. The y axis 702 is the adjustment ( $\Delta X$ ) in millimetres (mm) between the eyelet-to-eyelet distance measured from the internal outer eyelet surface of the unadjusted polyurethane article (41.5 mm) subtracted from the measured value after adjustment. The x axis 703 is time in seconds (s). The upper trace 704 depicts the current flowing between the two electrodes immersed in electrolyte in contact with the opposing sides of the injection moulded cruciform septum ( $I_m$ ). The y axis 705 is the measured current in nano amperes (nA). The x axis 706 is time in seconds (s). The voltage bias was held at 50 mV throughout the duration of the recording and the data acquired at 500  $\mu$ s sampling intervals. It can be seen from the graph 700 that the lower x axis 703 time and the upper x axis 706 time represent the same time course and that the lower  $\Delta X$  trace 701 is linked to the upper  $I_m$  trace 704. The graph 700 shows the initial current level ( $I_m = 0$  pA) of the penetrated cruciform septum and the lack of observed change in  $I_m$  as  $\Delta X$  was increased from 0 to 5 mm and then maintained at that level. At 624 s the current trace abruptly increased and rapidly reached a steady state ( $I_m \sim 4$  nA). Upon subsequent reduction of  $\Delta X$  to 1.8 mm,  $I_m$  returned to the initial open circuit value ( $I_m = 0$  pA). The onset of electrical activity

could be detected only after 624 s of simultaneous exposure to electrolyte and biaxial isotropic extension ( $\Delta X = 5$  mm). Once initiated, the trans-septum ionic current rapidly increased to  $\sim 4$  nA. Upon relaxation of  $\Delta X$  to  $\leq 1.5$  mm,  $I_m$  dropped to an undetectable level. This sequence of events shows that apertures of this nature are thus effectively self-sealing. The traces 701 and 704 can thus be used to characterise the performance capabilities of the adjustable elastomeric aperture.

[0066] Figure 8 is a composite graph 800 of the opening and closing of an adjustable elastomeric aperture fabricated in an injection moulded polyurethane sheet following primary wetting. The lower trace 801 depicts the amount of isotropic biaxial adjustment applied to the injection moulded polyurethane sheet. The y axis 802 is the adjustment ( $\Delta X$ ) in millimetres (mm) between the eyelet-to-eyelet distance measured from the internal outer eyelet surface of the unadjusted moulded polyurethane sheet (41.5 mm) subtracted from the measured value after adjustment. The x axis 803 is time in seconds (s). The upper trace 804 depicts the current flowing between the two electrodes immersed in electrolyte in contact with the opposing sides of the injection moulded cruciform septum ( $I_m$ ). The y axis 805 is the measured current in nano amperes (nA). The x axis 806 is time in seconds (s). It can be seen from the graph 800 that the lower x axis 803 time and the upper x axis 806 time represent the same time course and that the lower  $\Delta X$  trace 801 is linked to the upper  $I_m$  trace 804. The voltage bias was held at 50 mV throughout the duration of the recording and the data acquired at 1000  $\mu$ s sampling intervals. The graph 800 shows that, with careful adjustment of  $\Delta X$ , a transition zone can be encountered that enables repeated observation of the onset and breakage of electrical continuity. Successive stepwise increases in  $\Delta X$  initially result in no significant change in  $I_m$ . Towards the end of the transition zone ( $\Delta X \sim 0.8$  mm) an abrupt increase in  $I_m$  (to  $\sim 40$  pA) is observed. By contrast, in the reverse direction of adjustment,  $I_m$  can be incrementally decreased until no longer detectable due to electrical disconnection and shows that adjustable elastomeric apertures can repeatedly self-seal upon relaxation. The traces 801 and 804 can thus be used to characterise the performance capabilities of the adjustable elastomeric aperture.

[0067] Figure 9a is a composite graph 900 of the opening and closing of an adjustable elastomeric aperture fabricated in the injection moulded polyurethane sheet following primary wetting. The lower trace 901 depicts the amount of isotropic biaxial adjustment applied to the injection moulded polyurethane sheet. The y axis 902 is the adjustment ( $\Delta X$ ) in millimetres (mm) between the eyelet-to-eyelet distance measured from the internal outer eyelet surface of the unadjusted moulded cruciform (41.5 mm) subtracted from the measured value after adjustment. The x axis 903 is time in seconds (s). The upper trace 904 depicts the current flowing between the two electrodes immersed in electrolyte in contact with the opposing sides of the injection moulded cruciform septum ( $I_m$ ). The y axis 905 is the measured current in nano amperes (nA). The x axis 906 is time in seconds (s). It can be seen from the graph 900 that the lower x axis 903 time and the upper x axis 906 time represent the same time course and that the lower  $\Delta X$  trace 901 is linked to the upper  $I_m$  trace 904. The voltage bias was held at 50 mV throughout the duration of the recording and the data acquired at 1000  $\mu$ s sampling intervals. The graph 900 shows step adjustment of  $\Delta X$  and the corresponding  $I_m$  response during one complete cycle of aperture opening and closing within the practical  $I_m$  current measurement range (0 to 10 nA) of the current amplifier. The dynamic range of the aperture under these conditions corresponded to  $\Delta X \sim 0.8$  mm (5.3 G $\Omega$ ) to  $\Delta X \sim 3.2$  mm (30.5 M $\Omega$ ). The traces 901 and 904 can be acquired one or more times and used to demonstrate the elastomer softening Mullins effect. The traces 901 and 904 can be acquired one or more times and used to condition the aperture. The traces 901 and 904 can be thus be used to characterise the performance capabilities of the adjustable elastomeric aperture.

[0068] Figure 9b is a graph 907 illustrating the relationship between  $\Delta X$  and  $I_m$ . The trace 908 depicts the  $I_m$  response following step adjustment of  $\Delta X$  during one complete cycle of aperture opening and closing within the practical  $I_m$  current measurement range (0 to 10 nA) of the current amplifier. The x axis 909 is the change adjustment ( $\Delta X$ ) in millimetres (mm) between the eyelet-to-eyelet distance

measured from the internal outer eyelet surface of the unadjusted moulded polyurethane sheet (41.5 mm) subtracted from the measured value after adjustment. The y axis 910 is the measured current in nano amperes (nA). The trace 908 can thus be used to characterise the performance capabilities of the adjustable elastomeric aperture.

[0069] Figure 10 is a composite graph 1000 of the adjustment of an adjustable elastomeric aperture fabricated in an injection moulded polyurethane sheet following primary wetting. DNA molecules are included in the electrolyte. The lower trace 1001 depicts the amount of isotropic biaxial adjustment applied to the injection moulded polyurethane sheet. The y axis 1002 is the adjustment ( $\Delta X$ ) in millimetres (mm) between the eyelet-to-eyelet distance measured from the internal outer eyelet surface of the unadjusted moulded polyurethane sheet (41.5 mm) subtracted from the measured value after adjustment. The x axis 1003 is time in seconds (s). The upper trace 904 depicts the current flowing between the two electrodes immersed in electrolyte in contact with the opposing sides of the injection moulded polyurethane sheet ( $I_m$ ). The y axis 1005 is the measured current in nano amperes (nA). The x axis 1006 is time in seconds (s). It can be seen from the graph 900 that the lower x axis 1003 time and the upper x axis 1006 time represent the same time course and that the lower  $\Delta X$  trace 1001 is linked to the upper  $I_m$  trace 1004. The voltage bias was held at 200 mV throughout the duration of the recording and the data acquired at 10  $\mu$ s sampling intervals. The graph 1000 shows step adjustment of  $\Delta X$  and the corresponding  $I_m$ . The electrolyte reservoir on the *cis* side of the septum contained pUC DNA at 2 ng/ $\mu$ l. Zones I-V marked on the current trace are delineated by abrupt baseline shifts as  $\Delta X$  was adjusted. The current trace 1004 shows downward pointing transients in zones I, III and V that were not apparent prior to the addition of DNA. The transients are typical of DNA current blockades (See Mara et al., "An asymmetric polymer nanopore for single molecule detection", *Nano Letters*, 4, 497-501, 2004; Karhanek et al., "Single DNA molecule detection using nanopipettes and nanoparticles", *Nano Letters*, 5, 403-407, 2005; Li et al., "DNA molecules and configurations in a solid-state nanopore microscope", *Nature Materials*, 2, 611-615, 2003; Ito et al., "Simultaneous determination of the size and surface charge of

individual nanoparticles using a carbon nanotube-based Coulter counter" Analytical Chemistry, 75. 2399-2406, 2003), where each isolated event is caused by single molecule occlusion of the aperture. Regions II and IV at reduced  $\Delta X$  (1.92 -1.95 mm) and lowered baseline  $I_m$  (2.1-2.3 nA) exhibit no such transients, indicating that reduction of the aperture introduces an entropic barrier to DNA translocation. The graph 1000 shows that the effect was reversible because the appearance and disappearance of the transients is observed to coincide with increase and reduction of  $\Delta X$ . Adjustment of the aperture thus provides a mechanism for the controlled gating of DNA molecules and the traces 1001 and 1004 can thus be used to characterise the performance capabilities of the adjustable elastomeric aperture. The electrolyte was 1M KCL, 10mM Tris-HCL pH 8.0, 1mM EDTA, 0.1%, Triton X-100, filter sterilised through a 0.22  $\mu$ m Millipore filter and stored as frozen aliquots. All reagents were AR grade. The DNA sample was the 2686 base pair plasmid pUC 19 (from Sigma-Aldrich, St Louis, MO, USA), linearised with *Sma* 1, dephosphorylated with calf intestinal phosphatase, purified using a QIAquick spin column and used at a concentration of 2 ng/ $\mu$ l.

[0070] Figure 11 is a flow chart depicting one exemplary generic mode of operation of the embodiments of the invention illustrated in Figures 2a & 2b, Figures 3a & 3b, Figure 4a and Figure 6. For each embodiment illustrated in Figures 2a & 2b, Figures 3a & 3b, Figure 4a and Figure 6, the exemplary mode of operation is to intended to achieve a mechanical equilibrium of the elastomeric material by comparing a measured parameter prior to and following a mechanical adjustment. Mechanical equilibration indicates mitigation of the Mullins effect in the elastomeric material of the septum, either prior to fabrication of the aperture, or post fabrication of the aperture, and is achieved when the change in the measured parameter is within specified tolerances.

[0071] The measured parameters of the unpenetrated blank membrane or the penetrated membrane are selected from the group comprising, but not limited to: optical detection, optical detection by way of polarising light, electrical detection,

electrical detection by way of measured changes in capacitance, electrical detection by way of measured changes in electrical current, electrical detection by way of measured changes in electrical resistance, detection by way of measured changes in mechanical resistance, detection by way of measured changes in mechanical stress; detection by way of measured changes in mechanical strain, or by any combination of the above described parameters.

**CLAIMS:**

1. A device for fabricating a deformable aperture in deformable material, the device comprising a probe for forcibly penetrating the deformable material to form a vacancy in the deformable material through which a continuous path extends from one side of the deformable material to another side of the deformable material, and an elastomer support component for supporting the deformable material to provide mechanical resistance antagonistic to the direction of the force exerted by the probe on penetration of the deformable material, wherein the support component comprises a metallic electrode and an electrolyte fluid-filled cavity for receiving a tip of the probe on penetration of the deformable material by the probe, the device further comprising monitoring means for monitoring the quality of the formed aperture.
2. A device according to claim 1, wherein monitoring means is provided for monitoring one or more parameters of the penetration of the deformable material by the probe.
3. A device according to claim 1 or 2, wherein control means is provided for monitoring the extent of penetration of the deformable material by the probe and controlling the adjustment of the extent of penetration of the deformable material by the probe in response to such monitoring.
4. A device according to claim 3, wherein control means is arranged to monitor the extent of penetration of the deformable material by the probe by monitoring an electrical current and/or electrical tunnelling current passing through the deformable material between the probe and an electrically conducting medium on the other side of the deformable material.

5. A device according to any one of claims 1 to 4, wherein adjustment means is provided for adjusting the position of the support component relative to the probe.
6. A device according to any one of claims 1 to 5, wherein the support component incorporates a fluid-filled cavity for receiving a tip of the probe on penetration of the deformable material by the probe.
7. A device according to any one of claims 1 to 6, wherein means are provided for heating or cooling the support component.
8. A device according to any one of claims 1 to 7, wherein means are provided for heating or cooling the probe.
9. A device according to claim 1, wherein the device is arranged to use the results of the monitoring to characterize the quality and/or utility of the aperture.