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(71) Applicant: **PRESIDENT AND FELLOWS OF HARVARD COLLEGE** [US/US]; 17 Quincy Street, Cambridge, MA 02138 (US).

(72) Inventors: **AINLA, Alar**; 25 Webster Avenue, Apt. 406, Somerville, MA 02143 (US). **HAMEDI, Mahiar, Max**; 191 Parlmont Park, North Billerica, MA 01862 (US). **GUDER, Firat**; 13 Norseman Avenue, Watertown, MA 02472 (US). **WHITESIDES, George, M.**; 124 Grasmere Street, Newton, MA 02458 (US).

(74) Agents: **SCOZZAFAVA, Mary, Rose** et al.; Wilmer Cutler Pickering Hale and Dorr LLP, 60 State Street, Boston, MA 02109 (US).

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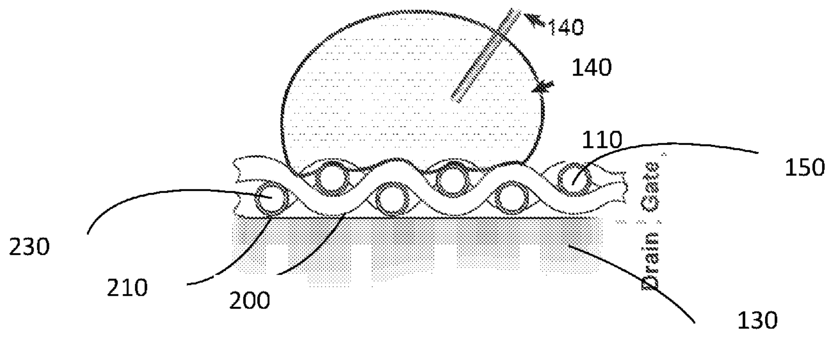
Figure 2A



(57) Abstract: A fluid gating valve includes a porous hydrophobic layer which acts a barrier for liquid flow; a liquid source on one side of the porous layer; a liquid drain on the opposing side of the porous hydrophobic layer; a source electrode in electrical connection with the liquid source; and a gate electrode electrically insulated from the liquid source, wherein the source electrode and the gate electrode are positioned and arranged to be connectable to a voltage source. And valve can be open by applying voltage between the gate and the source electrodes.

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ELECTRICAL VALVES INTEGRATED IN MICROFLUIDIC DEVICES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims the benefit of United States Patent Application No. 62/117,153, filed on February 17, 2015, the content of which is hereby incorporated by reference herein in its entirety.

INCORPORATION BY REFERENCE

[0002] All patents, patent applications and publications cited herein are hereby incorporated by reference in their entirety in order to more fully describe the state of the art as known to those skilled therein as of the date of the invention described herein

TECHNICAL FIELD

[0003] This technology relates generally to electronic valves. In particular, this invention relates to electronic valves integrated into paper devices.

BACKGROUND

[0004] Paper microfluidics is an emerging technology for low-cost assays in public health, veterinary medicine, food and water quality and environmental monitoring. Many common assays require multiple steps of reagent-addition and washing, and the quantitative value of the results they generate depend on the precise timing of each of these steps. A notable example is ELISA, which requires many separate, individually timed steps of binding, washing and amplification. Performing these steps manually is labor intensive (one assay may take from several minutes to hours) and human mistakes can lead to measurement errors. It would, therefore, be beneficial to have assays that could be fully automated.

[0005] Electrostatic devices driven by potential rather than electric currents are advantageous as the required energy to operate them can be very low. The notable example from the electronics world is the field effect transistor (FET). CMOS technology has enabled modern electronics, as we know it - with very large integration, compact size and low power consumption. In the realm of microfluidics, electrowetting-on-dielectric (EWOD) has given rise of wide variety of liquid handling techniques for multiple applications, such as “digital microfluidics” for moving, merging and splitting liquid droplets on surfaces, which enables creation of fully electrically configurable liquid circuits, displays and electronic paper, optical beam deflectors and trapping droplets on fibers. Electrowetting has been also applied in the context of material science to design textiles with variable wettability. Electrostatic principles for powering mechanical microvalves in elastomeric devices have been demonstrated.

[0006] A few valving concepts have been shown for paper devices based on mechanical pinching, sliding strip or mechanically moving cantilever. All these devices involve mechanical actuation making the system less robust and automatable. Alternatively chemical actuation has been used, exploiting surfactants to penetrate the hydrophobic barrier or electrochemical modulation of hydrophobicity. A carbon nanotube (CNT) loaded conductive paper has been used as substrate for droplet based digital-microfluidics, however this concept is not compatible with wicking based paper microfluidics. Chemical valving is more prone to interfere with assays compare to purely physical actuation.

SUMMARY

[0007] This disclosure describes a chemically robust electronic valve that can be integrated into microfluidic devices. The valves for microfluidic devices are electrically controlled, simple to manufacture, operate rapidly (switching starts instantly and completes within few seconds) and are chemically robust. The valves are actuated electrostatically and the control does not require any mechanical or moving parts.

[0008] In one aspect, a fluid gating valve includes a porous hydrophobic layer that acts a barrier to liquid flow; a liquid source on one side of the porous layer; a liquid drain on the opposing side of the porous hydrophobic layer; a source electrode in direct or indirect contact with the liquid source; and a gate electrode electrically insulated from the liquid source.

[0009] In one embodiment, the source electrode and the gate electrode are configured such that applying a voltage across the two electrodes creates a driving force of a liquid contained in the liquid source causing a liquid flow through the porous hydrophobic layer from the source side to the drain side.

[0010] In any of the preceding embodiments, the porous hydrophobic layer includes the gate electrode.

[0011] In any of the preceding embodiments, the porous hydrophobic layer includes a plurality of conductive threads coated with an insulating layer and the threads comprise at least a portion of the porous hydrophobic layer.

[0012] In any of the preceding embodiments, the conductive threads includes a non-conductive core having a conductive layer coated thereon.

[0013] In any of the preceding embodiments, the gate electrode includes a conductive trace disposed on the porous hydrophobic layer, and the conductive trace is coated with an insulating layer.

[0014] In any of the preceding embodiments, the porous hydrophobic layer includes insulating threads and conducting threads.

[0015] In any of the preceding embodiments, the conducting threads are individually addressable.

[0016] In any of the preceding embodiments, the porous hydrophobic layer contains at least two different electrical domains, which are electrically isolated from each other and one electrical domain acts as the source electrode and another electrical domain acts as the gate electrode.

[0017] In any of the preceding embodiments, the liquid drain is disposed between the porous hydrophobic layer and the gate electrode.

[0018] In any of the preceding embodiments, the gate electrode is disposed within the liquid drain.

[0019] In any of the preceding embodiments, the porous hydrophobic layer includes a nanostructured surface selected to enhance the hydrophobicity of the porous hydrophobic layer.

[0020] In any of the preceding embodiments, the porous hydrophobic layer includes a hydrophobic surface layer.

[0021] In any of the preceding embodiments, the hydrophobic surface layer includes fluorocarbon, perfluorocarbon, or hydrocarbon moieties covalently bound or adsorbed on the hydrophobic surface layer.

[0022] In any of the preceding embodiments, the porous hydrophobic layer includes a mesh, non-woven sheet or fabric or sheet with holes.

[0023] In any of the preceding embodiments, the source electrode is coated with an insulating layer.

[0024] In any of the preceding embodiments, the fluid source includes a channel, and optionally, the channel is filled with hydrophilic wicking material.

[0025] In any of the preceding embodiments, the fluid source is a channel of hydrophilic paper defined by a wax infused paper.

[0026] In any of the preceding embodiments, the valve further includes a voltage source.

[0027] In any of the preceding embodiments, the valve further includes a microcontroller to control the timing of voltage application.

[0028] In another aspect, a fluid control device is provided including a fluid flow valve as described herein.

[0029] In one or more embodiments, the valve is closed to fluid flow in the absence of a voltage and the valve is open to fluid flow on application of a voltage.

[0030] In any preceding device embodiment, the device further includes a microcontroller to control the timing a voltage application.

[0031] In any preceding embodiment, the device includes at least two valves and the valves are configured and arranged in parallel.

[0032] In any preceding embodiment, the device includes at least two valves and the valves are configured and arranged in series.

[0033] In any preceding embodiment, the device includes a plurality of valves and the valves are configured and arranged for one or both of series and parallel flow.

[0034] In any preceding embodiment, the device further includes a fluidoelectric switch, the switch configured and arranged to control voltage application to the valve.

[0035] In any preceding embodiment, the device includes plurality of fluidoelectric switches, configured and arranged to function as a logic state, wherein the presence of a liquid in the switch corresponds with an ON state and the absence of liquid in the switch corresponds to an OFF switch, and wherein the switches act as a logic circuit to control application of voltage to the valve.

[0036] In any preceding embodiment, the device includes a plurality of valves; and a plurality of fluidoelectric switches located at different positions along a fluid flow channel, each switch associated with a valve, wherein a conductive liquid introduced into the flow channel sequentially interacts with the plurality of switches to sequentially apply voltage to the plurality of valves.

[0037] In another aspect, a method of operating a fluid valve in provided and includes providing a fluid gating valve as described herein, and applying a voltage across the source and gate electrodes, wherein electrostatic forces generated on voltage application cause the liquid to penetrate through the porous layer from the source side to the drain side.

[0038] In one or more embodiment, the voltage is pulsed, and for example, the voltage pulse is in the range of 1ms to 1000 ms

[0039] In one or more embodiments, the applied voltage is in the range of 1V to 2 kV.

[0040] The valve for paper devices exhibits one or more desirable attributes such as i) simple and low-cost to manufacture (with a minimal number of components and process steps required for production); ii) integrates seamlessly with simple paper microfluidics based on wax printing technology; iii) rapid to operate (e.g. within <1s), so that it is suitable even for fast chemical processes; iv) electronically controlled (e.g. with no mechanical parts); v) available on demand, so that timing depends on feedback and sensory input; vi) independent (that is, different valves actuate independently of each other); and vii) applicable to wide range of different chemistries. Devices with these characteristics can be integrated readily into a wide variety of analytical systems. The devices further can include a source of electrical power and digital controllers, which are low-cost with long operating lifetimes.

[0041] These and other aspects and embodiments of the disclosure are illustrated and described below.

BRIEF DESCRIPTION OF THE DRAWINGS

[0042] The invention is described with reference to the following figures, which are presented for the purpose of illustration only and are not intended to be limiting.

[0043] In the Drawings:

[0044] **Figure 1A** is a schematic illustration of a valve system containing a liquid source, a porous hydrophobic layer (a mesh, also called a gate) and a drain channel, and source and gate electrodes, according to one or more embodiments.

[0045] **Figure 1B** is a schematic symbol for the circuit diagram of the integrated electronic valves containing a liquid source and drain separated by a hydrophobic layer (gate) and two electrodes according to one or more embodiments.

[0046] **Figure 2A** is a schematic illustration of an electronic valve including an insulator covered conductive textile or mesh (gate), which can be rendered hydrophilic by electrowetting (“Surface wetting”), in the closed state (gate is hydrophobic), according to one or more embodiments.

[0047] **Figure 2B** is a schematic illustration of an electronic valve including an insulator covered conductive textile, which can be rendered hydrophilic by electrowetting (“Surface wetting”), in the open state (gate is hydrophilic), according to one or more embodiments.

[0048] **Figure 2C** is a schematic illustration of the interfacial charging after applied voltage showing that the insulation layer of the gate material acts as a capacitor sandwiched between conductive layer and the liquid, according to one or more embodiments.

[0049] **Figure 3A** is schematic diagram illustrating the arrangement of source and gate electrodes in a surface wetting valve according to one or more embodiments.

[0050] **Figure 3B** is a schematic for the electrowetting valve of **Figure 3A** in which the gate electrode is coated with an insulating layer and the source electrode is in direct electrical contact with the liquid.

[0051] **Figure 3C** is a schematic diagram illustrating an electrowetting valve in which both the source and the gate electrodes are coated with an insulating layer.

[0052] **Figures 4A** and **4B** illustrate an electrowetting valve according to one or more embodiments, showing a configuration where either different fibers or different parts of the gate textile or mesh have two or more conductive parts or regions, which are isolated from each other by an insulator and outlets of the voltage source is connected to the two or more of the different regions; either one of the conductive parts or region is in direct contact with liquid and another one is separated by a thin insulating coating on the surface of the porous mesh (4A) or both conductive parts are covered by a thin insulating coating on the surface of the porous mesh (4B).

[0053] **Figure 4C** is an image of a woven mesh containing insulating plastic threads and conductive metallic threads, capable of being separately electrically addressed for use in one or more embodiments of the invention.

[0054] **Figure 5A** is a schematic illustration of an electronic valve including an insulating hydrophobic porous layer (gate) with electrodes positioned on opposing sides, (“Volume wetting”), in the closed state, according to one or more embodiments.

[0055] **Figure 5B** is a schematic illustration of an electronic valve including an insulator covered hydrophobic layer with electrodes positioned on opposing sides, (“Volume wetting”), in the open state, according to one or more embodiments.

[0056] **Figure 5C** is a schematic illustration of the charge formation on the interfaces of electrode and liquid after voltage is applied, according to one or more embodiments.

[0057] **Figure 6A** is a schematic illustration of a volume wetting valve having uncoated electrodes according to one or more embodiments.

[0058] **Figures 6B** is a schematic illustration of a valve having at least one insulator-coated electrodes according to one or more embodiments.

[0059] **Figures 7A** and **7B** illustrate the textiles or meshes used for both valves, in which **Figure 7A** is a photograph of conducting copper textile coated with insulating parylene layer and **Figure 7B** is a photograph of insulating lens paper, both materials have been rendered hydrophobic with Teflon® AF.

[0060] **Figures 7C** and **7D** illustrate the elementary operation of both (**C**) surface and (**D**) volume wetting based liquid penetration of the textile; in **Figure 7C** a constant voltage of 0.6kV was applied, while **Figure 7D** a second valve was actuated by short 10ms pulse of 2.7kV. In both cases, similarly to thyristors, the operation is bistable and valves remain open until the liquid source (here 20μL droplet of water) has been completely depleted.

[0061] **Figure 8A** is a circuit diagram of a device having two parallel valves.

[0062] **Figure 8B** is a schematic illustration of a surface wetting-based valve design, where the copper textile has been sandwiched between two paper layers. The upper layer is hosting a source pad and paper painted carbon electrodes together with interconnections, while the lower layer comprises a channel into which the solutions are injected.

[0063] **Figure 8C** illustrates the device assembly and shows the bottom and top view of the assembled device. For structural integrity different paper layers are bound together and sealed with thin layers of polyethylene film.

[0064] **Figure 8D** a time-sequenced series of photographs illustrating a fully computer controlled ("hands-off") valve actuation., in which a pulse diagram is shows the voltage-time plot for the experiment, and the Photo sequence below shows the timed release of colorful solutions (15μL) of acid red (V1) and brilliant green (V2). In order to match visual observations and electrical signals, a red LED has been used to indicate, when the voltage (0.85kV) is applied to the valves.

[0065] **Figure 9A** is a circuit diagram of two serial valves in which liquid view channels branching out from valves are used to visualize the operation, which is otherwise hindered by the compact stacked design.

[0066] **Figure 9B** is a schematics of a device where both valves are stacked on top of each other.

[0067] **Figure 9C** is a photograph of the printed structure on a single paper which can be then folded to form the final device together with separate gate meshes sandwich in between.

[0068] **Figure 10A** demonstrates the bidirectional control from liquid to electricity and from electricity to liquid showing a circuit diagram of a device where liquid is first used to switch electricity, while the same electrical signal is directly couple to open a valve for a next liquid.

[0069] **Figure 10B** is a circuit diagram symbol for a fluidoelectric switch, which is formed by two disconnected electrodes that are separated by a liquid channel (inserted photo), at high voltage-low current conditions all aqueous solutions are good conductors and will close the circuit when reaching between the electrodes.

[0070] **Figure 10C** shows time lapse photos: at time=0 an input liquid (15μL of acid red) was pipetted to input pad (I), once the liquid reached the valve, an electric potential (2.7kV) opened the second source loaded with toluidine blue (15μL).

[0071] **Figures 11A-11D** illustrates a fluidic NAND device, in which the presence of liquid represents logical state '1' and lack of liquid represents state '0', in which **Figure 11A** shows the diagram symbol of the fluidic NAND device inspired by electronics NAND gate; **Figure 11B** shows the equivalent circuit of the fluidic NAND device; **Figure 11C** is a photograph of the fluidic NAND device and **FIGURE 11D** shows the operation sequence of the device.

[0072] **Figures 12A-12C** illustrate a fluidic timer, in which **Figure 12A** is a diagram symbol of the fluidic timer; **Figure 12B** is a phtoograph of the fluidic timer **and Figure 12C** is a series of photographs of a fluidic timer showing the operational sequence of the time and the timed release of three different fluids.

DETAILED DESCRIPTION

[0073] A system for electrostatic flow gating of liquids (a valve) for a microfluidic device is described. The valve includes a porous hydrophobic layer (e.g., textile or mesh) that acts as a barrier for liquids. The valve includes a liquid source on one side of the porous layer and liquid drain channel on the other side. The valve includes two electrodes positioned in the vicinity or in connection to the porous hydrophobic layer and/or the liquid. One or both of the two electrodes is at least initially (before the opening of the valve) separated from a liquid contained in the liquid source by an electrically insulating layer. When voltage is applied between the two electrodes, electrostatic forces cause the liquid to penetrate through the porous layer from the source side to the drain side. This actuation can be effected using electrowetting or electrostatic pressure as the fluid driving force. The valves are bi-stable, so once open, the valve remains open, as long as there is liquid supply even without further electrical supply.

[0074] The valve is illustrated schematically in **Figure 1A**. A valve **100** includes a liquid source **110**, a porous hydrophobic layer **120** and a drain channel **130**. Liquid source **110** is shown here as a droplet, however, it can be also a channel, either open such as tube or channel in a porous material, such as paper. In one or more embodiments, the liquid is electrically conductive and can be, for example, water or aqueous solutions. Porous hydrophobic layer **120** can be in the form of a mesh, fabric or textile or sheet with holes. The hydrophobic nature of the layer prevents wetting and transport of the liquid through the layer. In addition, the hydrophobic layer is fully or partially electrically insulating or has an insulating coating on portions of the layer. Drain channel **130** represents a structure that can accept a liquid after it passes through the porous hydrophobic layer. Drain channel **130** can be an open channel or channel defined into a porous material, such as paper. Valve **100** also includes electrode **140** positioned in the vicinity of liquid source **110** and electrode **150** positioned in the vicinity of mesh **120** and connectable to an electrical power source (not shown), to apply voltage between the two electrodes.

[0075] While not being bound or limited by any particular mode of operation, it is believed that the two electrode separated by an insulating layer generates a capacitance that can be used to regulate fluid flow. At given charge, the energy is lowered by the higher capacitance, providing a driving force in this direction. The capacitance can be increased either by enlarging the surface area of the capacitor plates or by reducing distance between them. Enlarged surface area occurs during electrowetting, when conductive liquid (e.g., all aqueous solutions) wets along conductive textile, increasing the area of the liquid-textile interface (capacitor). The distance between capacitor plates can be reduced when a liquid front penetrates through the textile towards the electrode on another side.

[0076] **Figure 1B** is a schematic illustration of a circuit diagram of the integrated electronic valves according to one or more embodiments. The source and gate electrodes are positioned across an insulating gap formed by the gate. Application of a voltage across the two electrodes alters the properties of the gate and allows passage of liquid from a source to a drain.

[0077] In one embodiment, the porous hydrophobic layer is fully or partially electrically conductive and one of the electrodes is the porous hydrophobic layer and the other is positioned within the liquid source. Because the capacitance is increase by electrowetting of the porous hydrophobic electrically conducting layer, the valve can be referred to as a "surface wetting" valve. With reference to **Figures 2A-2C,** a liquid droplet (representing the liquid source **110**, which can be a tube or channel or via and the like) is adjacent to the fully or partially electrically conductive layer **200**, which has a conductive core **230** that is coated with an insulating layer **210**. The insulating layer can be hydrophobic, or it can be further surface-treated with a hydrophobic surface so that is not wetted by aqueous solutions. Exemplary hydrophobic coatings include fluorocarbon, perfluorocarbon and hydrocarbon moieties. The coating can be covalently bound to the surface or adsorbed to the surface. In one or more embodiments, the fully or partially electrically conductive layer **200** is an insulator-covered conductive textile, so that the outer surface **210 is** an electric insulator and the inner textile **230** is conductive and serves as gate electrode **150**. An absorbent paper layer is disposed on the opposite side of the insulating layer to serve as liquid drain **130.** The liquid source is shown as a droplet, but it typically is in the form of a channel or tube. The liquid source can also be a channel in a liquid absorbent paper layer. Source electrode **140** is in direct or indirect electrical contact with the liquid source. In the closed state (no voltage applied), liquid in the liquid source is spaced apart from the liquid drain and there is no liquid flow (**Figure 2A**). The valve is opened by an electrical signal, that allows liquid to penetrate through the porous hydrophobic-coated medium (**Figure 2B**). **Figure 2C** illustrates the charge formation generated by the applied voltage between the liquid **110** and the conductive fiber **230** of the insulator-covered conductive textile **200**. The capacitance can be increased when conductive liquid (e.g. all aqueous solutions) wets along conductive textile, increasing the area of the liquid-textile interface (capacitor) and providing the driving force for liquid flow through the valve.

[0078] In one or more embodiments, the electrically conductive part of the porous hydrophobic layer is covered with a thin layer of insulator, in order to avoid or reduce the direct electrical conduct between the liquid and the electrode. **Figure 3A** is a schematic circuit diagram illustrating the valve showing the arrangement of electrodes, insulating layer and liquid according to one or more embodiments. The figure shows the porous hydrophobic layer ("mesh") covered with insulator, which has a further hydrophobic outer surface. One electrode is connected with the mesh and other with the liquid. In other embodiments, only the mesh electrode is covered with the insulator (and acts as a capacitor), or both electrodes are covered with the insulator (and both act as a capacitors). **Figure 3B** is an enlarged image of the schematic of **Figure 3A** in which only the mesh electrode acts as a capacitor. In one or more embodiments, the electrode inside the liquid source also is covered with a thin layer of insulator so that both the mesh electrode and the source electrode are covered with a thin layer of insulator, as shown in **Figure 3C**. Both electrodes function as capacitors when voltage is applied. For efficient operation, both capacitances can be matched. These capacitors can be charged, which results in electrowetting of the mesh, but they prevent the direct current and electrochemical reaction on the electrode surface, which would change/damage the liquid used.

[0079] In another embodiment, the porous hydrophobic layer contains at least two different electrical domains, which are electrically isolated from each other and one electrical domains acts as the source electrode and the one acts as the gate electrode. At least one of the domains is coated with a thin layer of insulator and the liquid is in either direct (liquid-conductor[electrode]) or indirect (liquid-thin layer of insulator-conductor[electrode]) contact with both electrodes. The arrangement of the electrical domains (electrodes) in the porous hydrophobic layer according to one or more embodiments are shown in **Figures 4A** and **4B**. In **Figure 4A**, fiber **400** includes a conducting, e.g., metallic, core **410** having an insulating coating **420,** having indirect electrical communication with the liquid. Fiber **450** is a conductive fiber in direct contact with the liquid. On voltage application, charge formation develops between liquid **460** and core **410**. Fibers which are fully insulating do not serve as an electrode, but fibers which are conductive and covered with layer of insulator can couple with conductive liquid capacitively (no direct current can flow through). The surface can charge and AC current can go through. Here both fibers are conductive, but one has an insulating coating.

[0080] In **Figure 4B**, the valve contains fibers **400** and **490**. Fiber **400** includes a conducting, e.g., metallic, core **410** having an insulating coating **420**. Fiber **460** also includes a conducting, e.g., metallic, core **470** having an insulating coating **480**. On voltage application, charge formation develops between liquid **495** and both electrodes, **410, 470**. **Figure 4C** shows a material containing insulating plastic threads **495** woven together with metallic threads **498** covered with a layer of thin insulator that can be used in the implementation of one or more embodiments.

[0081] In these embodiments, individual threads can be individually addressed as described above.

[0082] In yet another embodiment, the porous hydrophobic layer (mesh) is an electrical insulator and one electrode is positioned on the one side of the layer and another one is positioned to another side. Because the capacitance is increased when the liquid front penetrates through the mesh towards the electrode on another side, the valve can be referred to as a "volume wetting" valve. With reference to **Figures 5A-5C,** a liquid droplet (representing the liquid source **110**, which can be a tube or channel or via and the like) is adjacent to a porous hydrophobic insulating layer **500.** The hydrophobic insulating layer **500** is shown placed in direct contact with the liquid source on top; however, the liquid source can also be a channel in a liquid absorbent paper layer. The insulating layer can be inherently hydrophobic, or it can be further surface-treated with a hydrophobic surface so that is not wetted by aqueous solutions. An absorbent paper layer is disposed on the opposite side of the insulating layer to serve as liquid drain **130.** Gate electrode **510** is located in the drain channel or on the other side of liquid drain **130**. In one or more embodiments, the electrode in the drain channel is in close vicinity to the porous hydrophobic insulating layer **500**. For example, the electrode can be a part of the drain channel (in instances where the electrode is paper that has been rendered conductive), or it can be on the far side of the drain channel, in instances where the drain channel is thin. "Close vicinity" comes from the requirement of electrostatic pressure desired in this capacitive setting. Capacitance drops quickly with increasing distance between the electrodes. If the gate electrode is not sufficiently close, pressure is not sufficient to force the liquid through the mesh. It is readily apparent to one of skill in the art, how to position the electrode to attain the desired capacitance.

[0083] Source electrode **140** is in electrical contact with the liquid source. In the closed state (no voltage applied), liquid in the liquid source is spaced apart from the liquid drain by hydrophobic insulating layer **500** and there is no liquid flow (**Figure 5A)**. The valve is opened by an electrical signal, e.g., a high voltage pulse, applied across the source and gate electrodes, which causes electrostatic pressure on the liquid surface and pulls it through the hydrophobic layer into liquid drain **130** (**Figure 5B)**. **Figure 5C** illustrates the charge formation generated by the applied voltage between the source and the gate electrodes. The capacitance can be increased when conductive liquid (e.g., all aqueous solutions) flows through the hydrophobic layer into the drain, thereby reducing the distance between charges and providing the driving force for liquid flow through the valve.

[0084] In one or more embodiments, at least one of the electrodes is covered with a layer of insulation to prevent electrical shorting of the system. In one configuration, the voltage source contains a mechanism which limits the current between the electrodes, when liquid passes the mesh and comes in contact with both electrodes (valve is closed). This mechanism protects the liquid from electrochemical degradation. In one case the mechanism is high internal resistance, while in other embodiments, the voltage source includes a switch, switching off the voltage source, if current higher than a defined threshold is detected.

[0085] **Figure 6A** shows a two electrode configuration in which uncoated electrodes are initially separated from each other by the air in a dry drain channel. Once the valve is opened, e.g., by application of a voltage pulse across the electrodes, liquid wets through the mesh to the drain channel and contacts the drain electrode, forming an electrical contact and an increase in current. In this case current can be limited by a voltage cutoff switch on the voltage supply. **Figure 6B** shows a two electrode configuration in which both electrodes are covered with insulation layer. The high resistance of the insulating coatings limits current.

[0086] In any of the valve embodiments described herein, the porous hydrophobic layer can be provided in a range of formats. In one or more embodiments, the porous hydrophobic layer is woven from thread. In one or more embodiments, the threads can be made of metals, polymers, e.g., plastics, or natural polymers, e.g., cellulose, and combinations thereof. In one or more embodiments, the fabric threads are bonded to each other. In other embodiments, the porous hydrophobic layer can be a sheet of material with holes (which can be etched, drilled, punched or formed any other ways). These materials could be metal or from polymer covered with conductor.

[0087] In addition to conductive textiles described herein above, conductive textiles made out of plastic mesh covered with metallic layer can be used. Exemplary textiles include commercially available textiles composed of thin polyester fibers (57μm) covered by Zn, Ni, Cu, with excellent electrical conductivity (0.1 Ohm/sq). These textiles can be further coated with an insulator and optional hydrophobic treatment. In one exemplary embodiment, the textiles can be coated with a parylene based insulator and hydrophobic coating.

[0088] In one or more embodiments, the threads are conductive, or the threads are insulating and have a conductive coating. The conductive coating can be a metal, e.g., a plated metal, or it can be a conductive ink, e.g., carbon inks or conductive organic polymers, such as PEDOT (poly(3,4-ethylenedioxythiophene)). In one particular embodiment, Whatman Lens paper 105 can be used as the porous layer and the paper can be treated with CNT based conductive carbon inks as conductive porous substrates. Paper can be submerged in a conductive ink. The ink loading density can be chosen such that the ink covers the fibers without clogging the pores. These textiles can be further coated with an insulator and optional hydrophobic treatment. In one exemplary embodiment, the textiles can be coated parylene based insulator and hydrophobic coating.

[0089] In one or more embodiments, the porous layer can be a random mesh of fibers, such as cellulosic paper. The mesh can be made of conductive material or can be coated with conductive materials. These textiles can be further coated with an insulator and optional hydrophobic treatment. In one exemplary embodiment, the textiles can be coated with a parylene based insulator and hydrophobic coating.

[0090] In one or more embodiments, the conductive material includes an insulating coating and the insulating coating can be an organic or inorganic insulating material. Suitable insulating coatings include metal or metalloid oxides, and organic polymers, e.g., parylene. The polymers can be applied, for example, by dip coating or vapor or gas phase deposition. The coatings can be multicomponent.

[0091] In order to prevent liquid from passing through the porous layer in the closed state, the layer surface is hydrophobic. In some embodiments, the insulating layer can be sufficiently hydrophobic without further treatment. For example, a surface having a water contact angle larger than 90° can be considered hydrophobic. In other embodiments, a hydrophobic layer or coating can be applied to the layer. For example, a coating or surface treatment that provides a water contact angle larger than 90° can be considered a hydrophobic coating. The coating can be bonded, e.g., covalently bonded, to the insulating layer, or it can be applied as a separate layer. Methods known in the art to render surfaces hydrophobic can be used. For example, the porous layer can include a covalently functionalized surface made up of fluorinated, perfluorinated or hydrocarbon groups in an amount sufficient to provide a hydrophobic surface.

[0092] In one or more embodiments, the porous hydrophobic layer can include a nanostructured surface designed to enhance the hydrophobicity of the surface.

[0093] In any of the valve embodiments described herein, the device is composed of three layers and includes a liquid input or source layer, a gate layer and a liquid outlet or drain layer.

[0094] In any of the valve embodiments described herein, a device can include more than one valve and the valves can be in the same or different layers. See **Figures 8A-8D** for an example of two valves in one layer.

[0095] In any of the valve embodiments described herein, the device is composed of 5 or more layers and includes a liquid input or source layer, a first gate layer and a first liquid outlet or drain layer, a second gate layer and a second liquid outlet or drain layer. In one or more embodiments, the valves can be actuated together or sequentially. See **Figures 9A-9C** for an example of two valves stacked one above another.

[0096] The device layers can be assembled by bonding using glue, lamination using meltable thermoplastics, tape, or by assembly in a case or housing that securely positions the layers.

[0097] In any of the valve embodiments described herein, one or both of the liquid source and the liquid drain can be a channel defined in a porous hydrophilic material that is capable of liquid wicking. In any of the valve embodiments described herein, one or both of the liquid source and the liquid drain can be an open channel (with a cavity) or can further include a liquid storing reservoir. In one or more embodiments, the gate porous hydrophobic layer is disposed between two hydrophilic liquid wicking layers.

[0098] The voltage required to open the valve can be in the form of an electrical pulse or AC voltage, although a constant voltage can also be applied. The electric signal required to open the valve can be short. For electrowetting valves, electric pulses in the range of a few hundreds of milliseconds are sufficient and can be for example 0.5-1kV for about 100ms. For volume wetting valves, electric pulses in the range of a few tens of milliseconds is sufficient and can be for example 2.5-3kV, or 1kV to 10kV, for <10ms. There is almost no current leakage in the device during the operation (operates with currents in the range of 10s to 100s of nA). Required voltage depends on the hydrophobicity of the coating, geometries of the mesh and most importantly on the thickness of the insulating coating and the dielectric permeability of the insulator material. The thicker is the layer and the lower is the dielectric permeability, the higher is the voltage, which is required. Too thin layers however may have more likely defect causing leak currents and dielectric breakdown. Length of applied pulse depends on the geometries of the mesh and liquid viscosity and internal resistances of the electrode and applied voltage. In some embodiment the length of the pulse could be chosen from the range of 1ms to 10ms, 10ms to 50ms, 50ms to 100ms, 100ms to 200ms, 200ms to

500ms, 500ms to 1000ms. The length of the pulse can have a range from 1 ms to 1000ms or can be any range bounded by the values included herein. In some embodiments the applied voltage could be chosen from the range of 1V to 10V, 10V to 50V, 50V to 100V, 100V to 500V, 500V to 1000V. The voltage can have a range from 1V to 1000V or can be any range bounded by the values included herein. In some embodiments, the applied voltage can be DC voltage, sequence of voltage pulses of AC voltage.

[0099] The valves are bi-stable, so once open, the valve remains open, as long as there is liquid supply even without further electrical supply. After a valve-opening pulse has been applied between the electrodes, liquid can propagate from the source to the drain, either by liquid pressure applied on the source side (e.g. liquid flow continues even into hydrophobic drain channel) or by capillary pressure (e.g. liquid is pulled by hydrophilic drain channel).

[0100] An inexpensive battery based unit can be used for controlling the valves. The control unit is based on miniature high-voltage converter and controlled by FET transistors.

[0101] In one or more embodiments, a device can incorporate one or more valves, for example, to regulate fluid flow. In some embodiments, the valves can be arranged to perform different functions. For example, the values can be arranged in parallel, for example, to allow parallel addition of liquids into a common channel. In other embodiments, the valves can be arranged in series, for example, to controllably pass the same liquid through a series of gates.

[0102] In other embodiments, the valves can be integrated into a device that functions as a fluidoelectric switch. The switch can include circuitry that regulates how voltage is applied to the valves. In one example, fluid flow along a channel can close a circuit to a voltage source that allows voltage to be applied to a valve. This system does not rely on a timer or microcontroller to trigger voltage. The fluidoelectric switches can be connected to a microcontroller or to electrical circuits containing fluidoelectric switches and resistive elements.

[0103] Any aqueous solution is sufficiently conductive to trigger the fluidoelectric switch. In some embodiments, the switches can differentiate between conductivities of the liquid. Conductivity differences can arise by having different salt concentrations or compositions.

[0104] In some embodiments, control gates or valves can be formed to control the liquid flow based on the presence or composition of the liquid in the fluidoelectric switches.

[0105] In some embodiments, the switches can be arranged such that the presence (ON) or absence (OFF) of a liquid allows the device to act as a large circuit.

A theoretical framework for the electrostatic valves

[0106] The valves can have two different types of actuation mechanisms, which are referred to as surface wetting (e.g., **Figures 2A-2C**) and volume wetting (e.g., **Figures 5A-5C**).

[0109] In both methods, the valve is actuated by penetration of liquid through the textile or other type of porous material. The pressure p required for the liquid to pass through a porous material is given by the Washburn equation (1)

[0107] $$p = -\frac{4\sigma cos\theta}{d_p}$$ **[0108]**

$$cos\theta = cos\theta_0 + \frac{\varepsilon\varepsilon_0 U^2}{2\sigma d_i} \quad (2)$$

[0110] Where σ is surface tension of the liquid, θ is contact angle of the porous material and d_p is the diameter of the pore. In case of the surface wetting design, the contact angle θ of the porous mesh is changed by voltage U according to the Lippmann-Young equation (2)

[0111] Where θ_0 is initial Young's contact angle, ε is the dielectric permeability of the insulator layer, and d_i is its thickness. A liquid pressure can be generated by various sources (3)

$$p = p_{ext} + p_g + p_s + p_e = \underbrace{p_{ext} + \rho gh + \frac{4\sigma}{r_l}}_{p_{ne}} + \frac{\varepsilon_0 U^2}{2d_t^2} \quad (3)$$

[0112] Where p_{ext} is external pressure (e.g. by gas), p_g is gravitational pressure by liquid column (of density ρ and height h), p_s is pressure by surface tension inside a liquid drop with radius r_l. These together constitute non-electric pressures p_{ne}. The electrostatic pressure p_e is determined by the voltage U and distance between the liquid and the electrode d_t. From these equations critical operation parameters, such as the activation voltage U_a can be derived. These parameters are summarized in Table 1.

Table 1. Comparison of theoretical operation parameters of both surface and volume wetting regimes

Parameter	**Surface wetting**	**Volume wetting**
Activation voltage U_a ($p_{ne} \approx 0$)	$\sqrt{-\frac{2\sigma d_i cos\theta_0}{\varepsilon\varepsilon_0}}$	$\sqrt{-\frac{8\sigma d_i^2 cos\theta_0}{d_p \varepsilon_0}}$
Liquid breakthrough pressure ($U = 0$) p_a	$-\frac{4\sigma cos\theta_0}{d_p}$	
Voltage induced decrease of breakthrough pressure $\Delta p_a(U)$	$-\frac{2\varepsilon\varepsilon_0}{d_p d_i}U^2$	$-\frac{\varepsilon_0}{2d_i^2}U^2$
Flow through Q conductance scaling with mesh dimensions r	$\propto r$	

[0113] As can be seen from Table 1, the properties of the system can be tuned by varying the pore size of the porous liquid insulation layer, while keeping other material parameters, which are harder to vary, the same (e.g., contact angle). The liquid breakthrough pressure p_a, determines the upper limit before spontaneous valve opening and its value can be optimized to design devices that cannot spontaneously open under liquid pressures in the storage cartridge, or during sudden changes because of handling (e.g. pressure changes during air transport, shock from dropping etc.). The activation voltage (U_a) determines the requirements for electronic control and insulation thickness and quality.

[0114] The invention is illustrated by the following examples, which are presented for the purpose of illustration only and are not intended to be limiting of the invention.

<u>Examples</u>

Example 1. Determination of actuation voltage

[0115] For experimental design we have tested several conductive and insulating textiles, exemplifying the flexibility of this technology. For the following demonstration we have chosen one conductive textile (**Figure 7A**) and one insulating paper (**Figure 7B**). The conductive textile was woven copper (wire diameter: 115μm rectangular opening size: 150μm thickness: 250μm) with 11μm Parylene-C ($\varepsilon = 3.15$). The insulating paper was Whatman™ lens paper 105 (thickness: 30μm, fiber diameter: $20 \pm 10\mu m$ opening size: $105 \pm 90\mu m$, characterized from optical images). Both materials were coated with Teflon AF for hydrophobicity ($\theta_0 = 105^\circ$). This resulted in a theoretical liquid breakdown pressure of 500Pa and 370-750Pa for the copper textile, and paper respectively. The copper textile has narrow pore size distribution (woven textile), while paper (non-woven) has statistical pore size distribution, where larger pores, with lower breakdown pressures are determining the overall pressure resistance. These pressures correspond to water column heights of 50 mm and 37-75 mm, which can be compared with the respective experimental results of 63-85mm and 15-201mm measured for different coating procedures.

[0116] We characterized the basic actuation mechanism of the materials using the simplest possible assembly of hydrophobically-treated paper (paper is a poor conductor and can serve as the insulator) as the porous liquid insulator (gate). The liquid was applied as a droplet onto the surface of porous liquid insulator (gate) and the voltage was varied to determine the required actuation voltage. The insulator-coated metal mesh provided actuation by surface wetting (**Figure 7C**) and the insulator-coated paper provided actuation by volume wetting (**Figure 7D**). The gate electrode was parylene coated copper mesh, that was pressed against the paper. However, any metal surface or conductive surface can be used. It was found that 0.5-0.6kV resulted in surface wetting with the metal mesh, and 2.5-2.7kV for volume wetting through papers.

[0117] Factors contributing to the actuation voltage include for the case of surface wetting, contact angle saturation, geometrical factors of the textile and the thickness of the Teflon coating. Factors contributing to the actuation voltage include for volume wetting include the field screening effect, which occurs since paper is not a complete isolator. Volume wetting favored quick pulses of HV over slow ramping, which means that the field is increasing faster than ionic currents in paper can compensate. Very short pulses (our experimental capability allowed testing of 1ms pulse) were sufficient to trigger the volume wetting through lens paper. In the case of 1ms pulses, the penetration was slower (67s) compare to longer pulses of 10ms (same 20μL droplet penetrated within 4s). Longer pulses did not cause faster penetration. This can be explained by other limiting factors of the flow - hydrodynamic resistance of the pores and formation mechanism of liquid flow through channels in paper, which stops after the liquid has penetrated through several ("weakest") points, as it screens the field and quenches further electrostatic force. In both cases the formed channels are stable and remain open even when the electric potential has been switched off. Also in all cases the entire liquid source was eventually depleted. This is similar to electronic thyristors, which also remain open as long as there is a forward bias between the main electrodes.

Example 2. Control system and energy source

[0118] Paper microfluidics is practical in settings where low-cost and portability are crucial. For this purpose we have developed an electronic device for controlling the valves, built using relatively low-cost (<200USD) off the shelf components, which can be portable and fully battery powered. The central component in this design is an IC sized miniature high voltage converter (EMCO AG), bringing 5Vdc to 3kVdc, with maximum current ratings of 470mA and 330μA respectively. The highest voltage rating compact and low-cost FET transistors we found were able to switch up to 4.5kV. Only the availability of these components limits the useful and practical voltage range for electrostatically actuated machinery, such as the valves presented here. Our device was fully powered from a USB port (5V, max 500mA and 2.5W) and a 9V battery. Other devices can provide different voltages and actuation ranges. For example, another power supply was built from the flash mechanism of disposable camera (<10USD including one AA battery), which could produce a max voltage 650V and max current 3mA.

[0119] The energy efficiency of electric field driven valving, can be calculated theoretically. For example, if we assume the diameter of the valve to be 5 mm and a dielectric thickness of 11μm, we would have capacitances ~150pF and ~50pF in case of surface (copper textile has about three times the fiber to sheet area ratio) and volume wetting designs. If the actuation voltages are 0.6kV and 2.7kV, the required energies would be 27μJ and 180μJ, respectively, which are extremely small energies. The experimental energy requirements are higher due to leak currents and losses, but still less than 1mJ/actuation. High voltage energy conversion efficiency of miniature energy converters is about 40%. As an example three AA batteries suitable to power this system would have an energy content of about 20kJ, enough to power about 8 million actuations. Even tiny fraction of this is suitable for most conceivable practical applications in portable settings.

Example 3. Device having valves in parallel

[0120] The valves provide a universal, reliable and stackable component that can be seamlessly integrated into numerous different circuits to serve in different paper device applications. Circuits of two terminal valves can be broken down into two elementary connections: parallel and serial.

[0121] A device having two or more valves integrated in parallel is described in **Figure 8A-8B**. **Figure 8A** is a schematic circuit diagram of the device showing two source pads S1 and S2 for connection to two source electrodes and two gate electrodes V1 and V2. The drain channels for the two valves meet to allow for mixing of fluids. The circled section is shown in a schematic illustration in **Figure 8B**. **Figure 8B** illustrates a first layer containing the liquid source in wax patterned paper to provide a channel that wicks liquid into a hydrophilic paper. A second layer is made up of a hydrophobically coated mesh having an outer insulating layer and an inner conductive thread. A third paper layer contains the liquid drain. Source electrode is positioned on the first paper layer in contact with a liquid loaded into the liquid reservoir and the conductive threads of the mesh form the gate electrode.

[0122] Assembly of an exemplary device is shown in **Figure 8C**. In order to assemble devices, plastic films from consumer ziplock bags (63μm thick polyethylene) were used, which were cut into suitable shapes with holes for liquids and electrodes and stacked with paper and metal net and hot pressed at 210°C for 1 min. This thin softened plastic formed strong adhesion with both wax printed and intrinsic paper, and did not delaminate under any deformation or when liquids were applied. Using plastics instead of glue is also favorable as plastics do not leak soluble compounds. Finally devices were enveloped using the same plastic film, for preventing drying and contamination.

[0123] The valve devices were loaded with liquid and connected to a computerized control unit, which performed the experiments without any human intervention. **Figure 8D** shows the voltage sequence used to actuate two valves at different times. The sync LED was used to synchronize the voltage pulses. In this experiment, parallel addition of liquids into a common channel is demonstrated. A voltage pulse at V1 occurs at 0.2 sec and subsequent images at 10 sec and 180 sec show fluid flow through the valve as evidenced by the growing dark spot that flows towards the second unactivated valve. At t= 180 sec, a voltage pulse at V2 occurs actuating the second valve as evidenced by a second growing spot. See arrows at t_5. This demonstrates that valves can be operated independently, without interfering with each other. This is a practical configuration, as it allows time-controlled addition of multiple solutions and reagents to an assay in a common channel. In this case, each valve would dose one portion of a reagent.

Example 4. Device having valves in series

[0124] A device having two or more valves integrated in series is described in **Figure 9A-9B**. **Figure 9A** is a schematic circuit diagram of the device showing a single source pad S1 for connection to a first source electrode and two gate electrodes V1 and V2. The first drain channel lies above the second gate electrode and actuation of the second valve is needed in order for the liquid to continue to flow through the system. In this device, liquid viewing channels (channels that branch off of the main fluid flow and are directed to a location that can be visually observed) are provided after both gate electrodes so that the progress of fluid flow can be monitored. **Figure 9B** illustrates a first layer containing the liquid source in wax patterned paper to provide a channel that wicks liquid into a hydrophilic paper. A second layer is made up of a first hydrophobically coated mesh having an outer insulating layer and an inner conductive thread. A second paper layer forms the first liquid drain and at the same time also becomes a liquid source for the second valve. A fourth layer is made up of a second hydrophobically coated mesh having an outer insulating layer and an inner conductive thread. A final paper layer forms the second liquid drain. Source electrodes are positioned on the first paper layer in contact with a liquid loaded into the liquid reservoir and on the second paper layer in contact with a liquid that flows through the first gated valve. Conductive threads of the mesh form the first and second gate electrodes. **Figure 9C** is an unfolded view of the device showing the location of the valve and microfluidic channel components and fold lines for its assembly. The separate mesh gate electrodes are positioned in the appropriate locations during assembly. Additional details regarding the design and fabrication of folded paper devices is found in USSN 62/142,204 filed April 1, 2015, the contents of which are incorporated in their entirety by reference.

[0125] The second, a serial circuit, could be used for stepwise motion of solutions, which could traffic through stages, where each could have, for example, specific pre-deposited compounds, which may require certain reaction or dilution time to function.

Example 5. Device having two-way communication

[0126] The design versatility is however not limited just to one-way communication, which allows electronics to trigger fluid flows. One can also integrate the transducer for the opposite direction and convey information from liquid to electricity. The simplest is a conductivity based fluidoelectric switch (**Figure 10B**) composed of two separated electrodes, where the presence of a liquid (conductive) would close the circuitry. These switches can be coupled to microcontrollers, but can also work as stand-alone devices actuating the valves directly as shown in **Figure 10A** and **10C** Figure 10C shows an exemplary operation of such a stand-alone device, containing one fluidoelectric switch, which triggers the valve, that adds another liquid into a common channel. This valve operates in volume wetting configuration, where constant voltage (2.7kV) is applied between the input electrodes V- and V+. **Figure 10C** shows the devices as seen from underneath. Initially one source liquid is deposited on the source area of the valve (S). This liquid is not visible on the photo. A second liquid is deposited on the liquid input (I). Liquid from the input I wicks towards the fluidoelectric switch. The valve does not trigger before the liquid has reached the switch (at 50s). Then the liquid connects the voltage to the Ψ shaped electrode painted under the paper layer with carbon ink. Voltage between the electrode and the liquid above creates electrostatic pressure, which forces the liquid through the hydrophobic barrier until it reaches the common paper channel underneath. At the end (100s) the liquid wicks into the common channel. In this case, the device operation would require only a single power supply, with no microcontrollers or voltage switching circuitry, while still providing synchronized timing functionality (adding another liquid certain amount of time after the first one has been applied).

Example 6. Fluidic NAND Gate

[0127] Other examples of electrofluidic devices, for example, where valves and electrofluidic switches are connected to each other such that one liquid can gate another one, can be prepared using the integrated valves described herein. We have implemented fluidic logic (fluidic NAND gate – fNAND), where presence of liquid is used to evaluate gating of another liquid. **Figure 11A-11D** illustrates this device.

[0128] A fluidic NAND gate is synchronous, meaning the input state is evaluated together with clock signal. OUT signal equals NOT (A AND B), where logical states are corresponding to the presence (true or '1') or lack (false or '0') of the liquid. **Figure 11A** is a suggested symbol of fluidic NAND gate inspired from electronics. **Figure 11B** shows the equivalent circuit for the device and **Figure 11C** is a photograph of the fNAND gate. **Figure 11D** shows the operation sequence of the device under a series of different instructions.

[0129] Initially one liquid is deposited on the source area of the valve (IN). Thereafter other liquids (logical inputs) are deposited on the logical inputs A and B (**Figure 11D** shows operation on all four different logical input state combinations that are possible in the two input NAND gate). Finally a third liquid is deposited on the clock input (CLK). Liquid in the clock input connects the voltage V to the source electrode of the valve, which is done through the resistor R (created using printed carbon pattern). The gate electrode is connected to the ground. Voltage becomes applied to the source electrode only if both A and B are not applied at the same time, otherwise the source electrode becomes grounded (potential will be similar to the gate electrode) and valve does not open, corresponding to logical output value false or '0'. In every other case voltage will be applied leading to valve opening and liquid injection into output (OUT) and corresponding to logical output value true or '1'.

Example 7. Fluidic Timer

[0130] In another application, the valve can be integrated into a device that can provide timed outputs, as shown in **Figures 12A-12C**. **Figure 12A** is a schematic showing the relationship of the fluidoelectric switches with the valves. **Figure 12B** is a photograph of a device made in a folded paper system. **Figure 12C** is a photo-series showing the operation of the timer. In this embodiment, one liquid (the orange one) is added to the input and it wicks along the paper channel where there are three fluidoelectric switches, that trigger additional three different liquids through three different valves into a common output channel. The timing of addition of these three liquids is defined by the wicking speed of the liquid in the control channel (orange) and the distance between fluidoelectric switches.

Experimental Details

[0131] **Device fabrication.** Paper devices were prepared using standard wax printing technology on Whatman™ Chromatography paper 1. Metallic textiles were obtained from McMaster-Carr and coated with 11μm thick layer of Parylen-C (Paratronix Inc., Attleboro, MA) and coated with Teflon® AF for hydrophobicity. Hydrophobic insulating mesh was prepared from Whatman™ 105 lens paper rendered hydrophobic by coating in Teflon® AF. Other examples of porous materials used in device fabrication include paper treated with carbon ink and Parylene-C (layer thickness about 10μm) and VeilShield™ commercial conductive textile (plastic covered with thin metal layer to render it conductive). Devices were assembled together using hot pressing with a PE film as a binder and envelope.

[0132] **Visualization.** All images and videos were recorded with a digital SLR camera Canon EOS550 with 28mm F2.8 objective and macro-adapters. Videos were recorded at frame rate of 30 or 50fps.

[0133] **Electrical measurements.** All electrical impedance measurements were performed with precision LCR meter Agilent E4980A.

[0134] **High voltage power supply**. A Keithly 2410 Source meter was used as a single channel voltage source up to voltages 1.1kV. The source meter was controlled manually or through serial port from MATLAB program. All two-channel measurement up to voltages 2.7kV were performed with in-house built high voltage control. High voltage measurements were performed with an 80K-40 high voltage probe (Fluke) with an attenuation ratio 1:1000 and an input resistance of 1GΩ with adjustments to be connected to 10MΩ DC voltage meter.

Preparation of Textiles

[0135] Materials. Metallic and polyester textiles were purchased from McMaster-Carr, materials tested have been listed in Table 2. Also few other paper types, such as Kimwipe and VWR cleanroom tissue were evaluated. Other materials include paper treated with carbon ink and Parylene-C (layer thickness about 10μm) and VeilShield™ commercial conductive textile (plastic covered with thin metal layer to render it conductive).

[0136] Parylene coating. For electrical insulation conductive textiles were coated with Parylene-C due to its excellent properties: high dielectric strength and conformal and pinhole free-coating, high mechanical strength and chemical resistance, low-cost. Parylene coating service was ordered from Paratronix Inc. (Attleboro, MA). Coating procedure according to Paratronix is following. Samples were cleaned with mixture of IPA:water (1:1) and primed with adhesion promoter Silquest A-17-NT silane (Chempoint, Bellevue, WA). Samples were loaded to deposition chamber, which was pump overnight followed by coating at rate about 5μm/h. During coating samples were rotated in the chamber in order to improve thickness uniformity. Though the dimer precursor of parylene is pyrolized at high temperatures (680°C) samples are not heated and stay at RT throughout the process. Thickness was estimated from deposition time and no online feedback was used. After completion thickness was measured on sample and was found to be 11μm (target was 10μm). Parylene coating would be compatible with low-cost manufacturing.

[0137] Table 2. List of tested conductive and insulated textiles.

Textile nr.	Source	Material	Thread diameter (μm)	Opening size (μm)	Period (μm)	Thickness (μm)
Conductive textiles	McMaste-Carr		Before/after parylene layer			
- Textile nr. 1	9224T819	Copper	114/136	152/130	279	300
- Textile nr. 2	9227T417	Aluminum	53/75	74/52	137	180

- Textile nr. 3	9228T617	Bronze	66/	104/82	180	150
- Textile nr. 4	9228T618	Bronze	53	74/52	131	150
Insulating textiles						
- Textile nr. 5	Whatman Lens paper 105	Paper	~20	statistical 0-200	--	45-40
- Textile nr. 6	McMaster-Carr 9218T73	Polyester	53	74	127	63

[0138] In addition to conductive textiles described in Table S2. We have used conductive textiles, made out of plastic mesh covered with metallic layer. These meshes were obtained commercially (Less EMF Inc. Latham NY). Particularly well suited material was VeilShield™, composed of thin polyester fibers (57μm) covered by Zn, Ni, Cu, with excellent electrical conductivity (0.1 Ohm/sq)

[0139] In another approach we have used Whatman Lens paper 105 treated with CNT based conductive carbon inks described above as conductive porous substrates. Paper was submerged to ink, which was diluted 50% (100% ink has too high solid content, which closes the pores). After this excess ink is removed with tissue paper and sample is dried (Conductance 1.5-2kOhm/sq). All these materials were covered with parylene based insulator and hydrophobic coating. Details of electrode fabrication is described below in the Electrode section.

[0140] Hydrophobic coating. Hydrophobic coatings were applied to surfaces using soluble fluoroplastic DuPont™ Teflon® AF. Teflon AF 2400 (powder) and fully fluorinated solvent 3M Fluorinert® FC-40 were purchased from Sigma-Aldrich. Solution was prepared in a small glass jar, into where powder (w/w 1%) and solvent were measured. The jar was placed to a +50°C water bath and the mixture was stirred with magnetic stirrer for about 24h until complete dissolution. 1% stock solution was further diluted into 0.1% - 0.2% solution in same solvent. Other concentrations could be used, so long as they do not clog pores. Coatings on textiles were created by tip coating samples into the solution. Wet samples were hanged with clips and dried first at ambient atmosphere for minimum 15min, followed by 3h baking in oven at 130°C. Coatings of Si wafers were created with spin-coating at 4000rpm for 1min followed by same baking procedure. This was used as a reference evaluation of electrowetting performance of coatings.

[0141] Contact angle measurements. For contact angle measurement were determined and the fraction of liquid f in contact with the material was estimated from Cassie-Baxter law for the wettability of porous surfaces,

$$\cos\theta = f(\cos\theta_0 + 1) - 1$$

where θ is contact angle of liquid on porous surface and θ_0 is Young's angle on flat surface. For Teflon AF θ_0 is 105°. f was found to correlate with the fraction of pore area.

[0142] Liquid breakthrough. In order to measure liquid breakthrough pressure p_a following experiment was performed. Textile piece was sandwiched between paper and transparent (300mm long) column sealed around with PDMS gasket. Through a syringe and a tube a blue liquid (weak solution of toluidine in water) was injected, gradually increasing the height of water column, until liquid breakthrough occurs. Critical pressure was determined and is given in Table 3. All uncertainties are statistical (A type) and given at 95% confidence interval.

[0143] Table 3. Contact angle measurements of hydrophobic textiles and liquid break through pressures.

Textile nr. and (Teflon % used in coating)	Advancing angle (°)	Receding angle (°)	Hysteresis (°)	f - fraction	Experimental liquid break through p_a (mm H_20)	Theoretical liquid break through p_a (mm H_20)
1 (1%)	144.6(24)	110(17)	35(17)	0.25	85	57
1 (0.1%)	131(11)	89.1(35)	42(12)	0.47	63	57
2 (1%)	141.4(44)	122.2(83)	19.2(93)	0.29	239	143
2 (0.1%)	142.0(44)	108.9(41)	33.1(65)	0.29	148	143
3 (1%)	135.2(46)	33.1(93)	102(10)	0.39	48	91
3 (0.1%)	138.13(54)	33(17)	105(17)	0.34	30	91
4 (1%)	134.2(92)	89.0(66)	45(11)	0.41	206	143
4 (0.1%)	133(20)	104.7(31)	28(21)	0.43	164	143
5 (1%)	139.8(36)	71(10)	69(11)	0.32	201	37
5 (0.1%)	137.4(67)	0	137.4(67)	0.36	15	37
6 (1%)	127.67(42)	19.6(47)	108.1(47)	0.52	65	101

6 (0.1%)	119.7(75)	0	119.6(75)	0.68	0	101

[0144] Electrowetting tests. Macroscopic electrowetting was tested on both smooth Si-Parylene-TeflonAF surfaces and on conductive textiles. 20μL droplet was placed on the surface and connected with voltage source and voltage was gradually ramped with Keithley Source Meter (5V/s), while videos of the droplets response was recorded. Interestingly experimental parabolic region of the contact angle curve correspond to much thicknesses of insulator (30μm instead of 11μm). It can be due to Teflon coating which has also lower ε = 1.9. Also voltage threshold between hydrophobic and hydrophilic surface was found to be ~200V, while actuation voltage U_a of the valve was about 500-600V. This is most likely explained by the effective hydrophobicity increase in the net due to porosity (in order to increase the contact area with hydrophilic surface, also contact area with hydrophobic air will increase, as described by Cassie-Baxter law, which reduces the effect).

[0145] Electrodes. In devices with integrated electrodes, electrodes were painted using conductive CNT ink, which was prepared in following way: 300mg multiwalled CNTs (Sigma-Aldrich) were measured into a test tube, into where 10mL CMC (Acros Organics) solution (10mg/mL, MW ~ 250'000) and 15mL of water was added. Mixture was stirred and in order to achieve homogeneous stable dispersion sonicated with high power tip sonicator (Duty cycle 50% of 400W power for 15min). Yielded ink was stored on the shelf and was found to be stable for several months. Electrodes were painted using injection of the ink through middle range or fine pipettor tip, after which devices were dried for >30min at 60°C oven. These electrodes are mechanically robust and insensitive to folding and have good conductivity (total circuit resistivity in devices presented here was found typically below 1kOhm). In one particular embodiment, after excess ink was removed with tissue paper and sample was dried, the conductivity was 1.5-2kOhm/sq. In order to create resistors with higher resistivities, ink can be diluted and wires can be made by wicking the dilute ink in the wax-printed paper channels.

[0146] Dilution of this ink was also used to render lens paper electrically conductive, such that it could be used as a gate material in surface wetting valve. A concentrated version was used to paint electrical wires. Also other carbon based inks could be used.

High voltage control unit.

[0147] We constructed high voltage (HV) control unit in order to automatically actuate multiple valves with high time resolution as well as to demonstrate a feasible design approach for low-cost portable instrumentation. The key components are a miniature HV converter (rendering 5V to 3kV) and high voltage transistors, enabling on-off switching of individual channels at voltages up to 4.5kV. This unit was based on microcontroller board Arduino Due, which was programmed in C and powered and controlled through computer USB port. The computer side software was created in Visual Studio .NET C++.

[0148] *High voltage at low-cost*. A low-cost high voltage power supply sufficient to actuate the valves was also fabricated. All essential components of the power supply from the flash mechanism of Fujifilm disposable camera were used. This circuitry was powered by a single AA battery (1.5V). Power supply contained following components: transformer (coil inductances 49μH, 100μH and 2H), NPN transistor (D2504), two diodes (1N4007), capacitors (C1, C2: 10μF), and resistors (R1: 220Ohm, R2: 2MOhm). These were arranged functionally into two parts oscillator with high-voltage transformer (Output: Vrms: 390V, 13kHz) and diode ladder/rectifier. Eventual power supply had maximum output voltage 650V and maximum current 3mA. Output voltage dropped linearly with current giving internal resistance about 217kOhm.

[0149] Eventual device was characterized and had following features:

- Two high voltage digital outputs able to switch between 0 and set HV level U_{HV}
- Capability to deliver HV pulses with 1ms time resolution (but accuracy is significantly higher)
- Manually or automatically adjustable HV level U_{HV} between 300V to 2.7kV (no load)
- Maximum output current 33μA (short circuit)
- For instrument safety, full galvanic isolation between low (LV) and high voltage electronics (HV converter is isolated internally and control signals were coupled from LV to HV side through optocoupler. HV side control was powered with individual small battery)
- Computer communication was through USB emulated serial port
- Synchronization output to trigger any other instrument (e.g. camera) or LED, which can be incorporated into visual field in case of video recording of valve operation and enables easier analysis of response

[0150] Materials. HV converter was purchased from EMCO High Voltage Corporation (Sutter Creek, CA). High voltage transistors were purchased from Mouser Electronics (Mansfield, TX). All other standard electronic components were obtained from Mouser

Electronics, Digi-Key Corporation (Thief River Falls, MN) or were provided by Electronic Instrument Design Lab in Harvard University, Department of Physics.

[0151] Unless otherwise defined, used or characterized herein, terms that are used herein (including technical and scientific terms) are to be interpreted as having a meaning that is consistent with their accepted meaning in the context of the relevant art and are not to be interpreted in an idealized or overly formal sense unless expressly so defined herein. For example, if a particular composition is referenced, the composition may be substantially, though not perfectly pure, as practical and imperfect realities may apply; e.g., the potential presence of at least trace impurities (e.g., at less than 1 or 2%) can be understood as being within the scope of the description; likewise, if a particular shape is referenced, the shape is intended to include imperfect variations from ideal shapes, e.g., due to manufacturing tolerances. Percentages or concentrations expressed herein can represent either by weight or by volume.

[0152] Although the terms, first, second, third, etc., may be used herein to describe various elements, these elements are not to be limited by these terms. These terms are simply used to distinguish one element from another. Thus, a first element, discussed below, could be termed a second element without departing from the teachings of the exemplary embodiments. Spatially relative terms, such as “above,” “below,” “left,” “right,” “in front,” “behind,” and the like, may be used herein for ease of description to describe the relationship of one element to another element, as illustrated in the figures. It will be understood that the spatially relative terms, as well as the illustrated configurations, are intended to encompass different orientations of the apparatus in use or operation in addition to the orientations described herein and depicted in the figures. For example, if the apparatus in the figures is turned over, elements described as “below” or “beneath” other elements or features would then be oriented “above” the other elements or features. Thus, the exemplary term, “above,” may encompass both an orientation of above and below. The apparatus may be otherwise oriented (e.g., rotated 90 degrees or at other orientations) and the spatially relative descriptors used herein interpreted accordingly. Further still, in this disclosure, when an element is referred to as being “on,” “connected to,” “coupled to,” “in contact with,” etc., another element, it may be directly on, connected to, coupled to, or in contact with the other element or intervening elements may be present unless otherwise specified.

[0153] The terminology used herein is for the purpose of describing particular embodiments and is not intended to be limiting of exemplary embodiments. As used herein, singular forms, such as “a” and “an,” are intended to include the plural forms as well, unless the context indicates otherwise.

[0154] It will be appreciated that while a particular sequence of steps has been shown and described for purposes of explanation, the sequence may be varied in certain respects, or the steps may be combined, while still obtaining the desired configuration. Additionally, modifications to the disclosed embodiment and the invention as claimed are possible and within the scope of this disclosed invention.

CLAIMS

1. A fluid gating valve comprising:

    a porous hydrophobic layer that acts a barrier to liquid flow;
    a liquid source on one side of the porous layer;
    a liquid drain on the opposing side of the porous hydrophobic layer;
    a source electrode in direct or indirect contact with the liquid source; and
    a gate electrode electrically insulated from the liquid source.

2. The valve of claim 1, wherein the source electrode and the gate electrode are configured such that applying a voltage across the two electrodes creates a driving force of a liquid contained in the liquid source causing a liquid flow through the porous hydrophobic layer from the source side to the drain side.

3. The valve of claim 1, wherein the porous hydrophobic layer comprises the gate electrode.

4. The valve of claim 3, wherein the porous hydrophobic layer comprises a plurality of conductive threads coated with an insulating layer and the threads comprise at least a portion of the porous hydrophobic layer.

5. The valve of claim 4, wherein the conductive threads comprise a non-conductive core having a conductive layer coated thereon.

6. The valve of claim 1, wherein the gate electrode comprises a conductive trace disposed on the porous hydrophobic layer, and the conductive trace is coated with an insulating layer.

7. The valve of claim 1, wherein the porous hydrophobic layer comprises insulating threads and conducting threads.

8. The valve of claim 7, wherein the conducting threads are individually addressable.

9. The valve of claim 1, wherein the porous hydrophobic layer contains at least two different electrical domains, which are electrically isolated from each other and one electrical domain acts as the source electrode and another electrical domain acts as the gate electrode.

10. The valve of claim 1, wherein the liquid drain is disposed between the porous hydrophobic layer and the gate electrode.

11. The valve of claim 1, wherein the gate electrode is disposed within the liquid drain.

12. The valve of any preceding claim, wherein the porous hydrophobic layer comprises a nanostructured surface selected to enhance the hydrophobicity of the porous hydrophobic layer.

13. The valve of any preceding claim, wherein the porous hydrophobic layer comprises a hydrophobic surface layer.

14. The valve of claim 13, wherein the hydrophobic surface layer comprises fluorocarbon, perfluorocarbon, or hydrocarbon moieties covalently bound or adsorbed on the hydrophobic surface layer.

15. The valve of any preceding claim, wherein the porous hydrophobic layer comprises a mesh, non-woven sheet or fabric or sheet with holes.

16. The valve of any preceding claim, wherein the source electrode is coated with an insulating layer.

17. The valve of claim 1, wherein the fluid source comprises a channel.

18. The valve of claim 17, wherein the channel is filled with hydrophilic wicking material.

19. The valve of claim 18, wherein the fluid source is a channel of hydrophilic paper defined by a wax infused paper.

20. The valve of any preceding claim, further comprising a voltage source.

21. The valve of claim 20, further comprising a microcontroller to control the timing of voltage application.

22. A fluid control device comprising a valve according to any of claims 1-21.

23. The fluid control device of claim 22, wherein the valve is closed to fluid flow in the absence of a voltage

24. The fluid connection device of claim 23, wherein the valve is open to fluid flow on application of a voltage.

25. The fluid control device of claims 22, 23, or 24, further comprising a microcontroller to control the timing a voltage application.

26. The fluid control device of claim 20, wherein the device comprises at least two valves and the valves are configured and arranged in parallel.

27. The fluid control device of claim 20, wherein the device comprises at least two valves and the valves are configured and arranged in series.

28. The fluid control device of claim 20, wherein the device comprises a plurality of valves and the valves are configured and arranged for one or both of series and parallel flow.

29. The fluid control device of claim 20, wherein the device further comprises a fluidoelectric switch, the switch configured and arranged to control voltage application to the valve.

30. The fluid control device of claim 29, wherein the device comprises plurality of fluidoelectric switches, configured and arranged to function as a logic state, wherein the presence of a liquid in the switch corresponds with an ON state and the absence of liquid in the switch corresponds to an OFF switch, and

wherein the switches act as a logic circuit to control application of voltage to the valve.

31. The fluid control device of claim 29, wherein the device comprises:

a plurality of valves; and

a plurality of fluidoelectric switches located at different positions along a fluid flow channel, each switch associated with a valve,

wherein a conductive liquid introduced into the flow channel sequentially interacts with the plurality of switches to sequentially apply voltage to the plurality of valves.

32. A method of operating a fluid valve, comprising:

providing a fluid gating valve according to any of claims 1-21; and

applying a voltage across the source and gate electrodes,

wherein electrostatic forces generated on voltage application cause the liquid to penetrate through the porous layer from the source side to the drain side.

33. The method of claim 32, wherein the voltage is pulsed.

34. The method of claim 33, wherein the voltage pulse is in the range of 1 ms to 1000 ms

35. The method of claim 33, wherein the applied voltage is in the range of 1 V to 2 kV.

Figure 1A

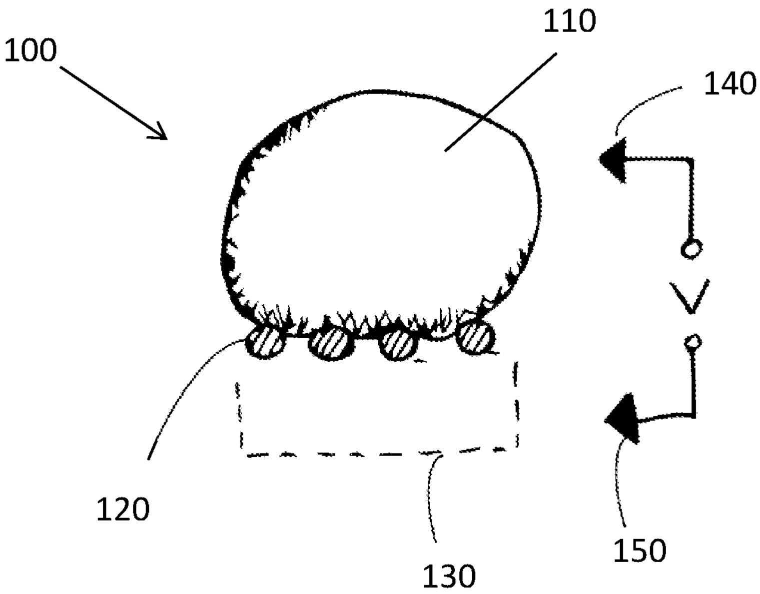


Figure 1B

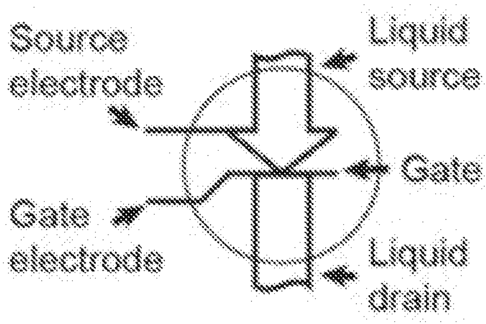


Figure 2A

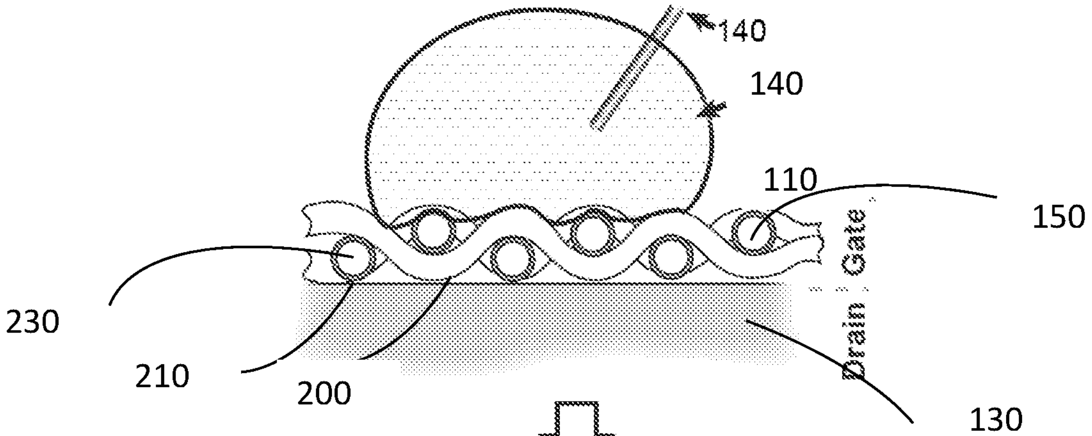


Figure 2B

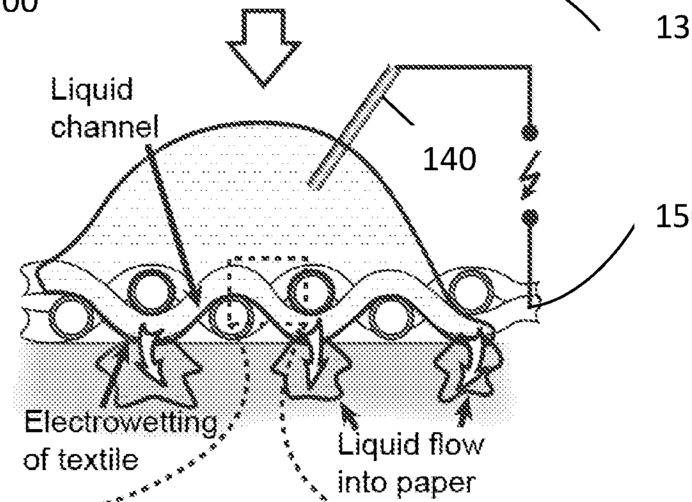


Figure 2C

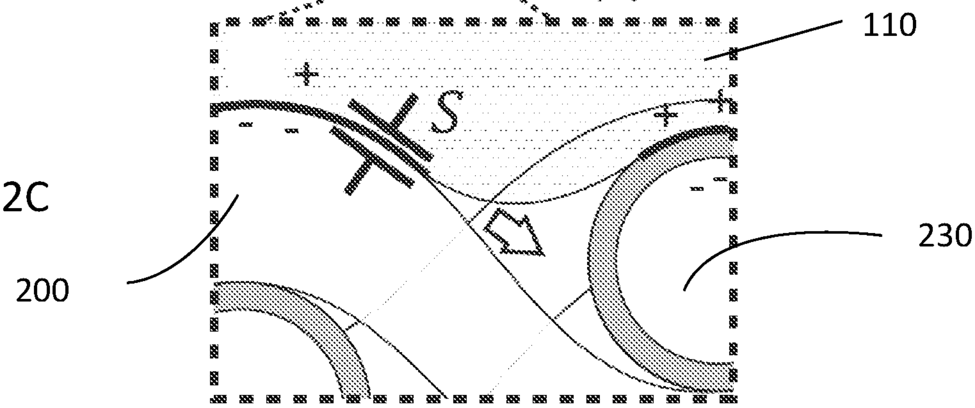
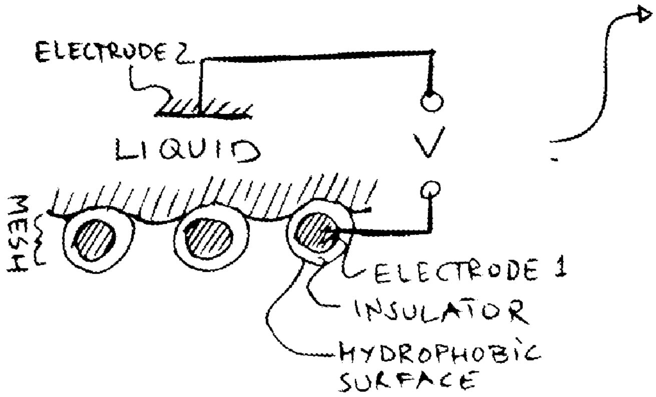
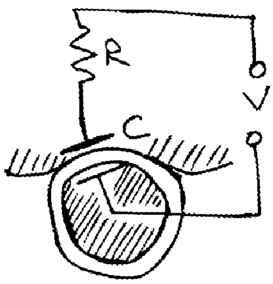


Figure 3B

Figure 3A





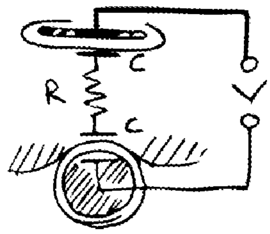


Figure 3C

Figure 4A

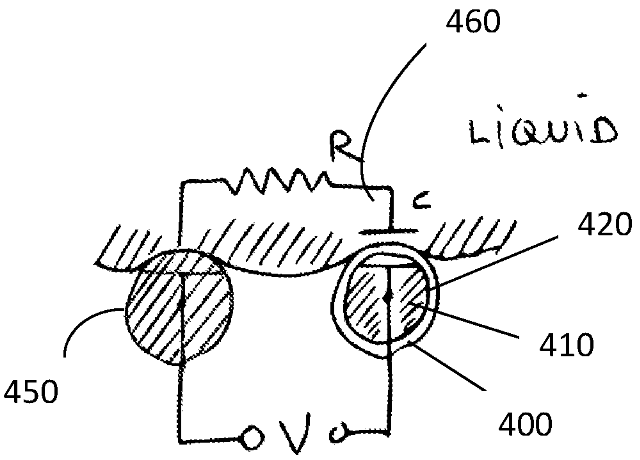


Figure 4B

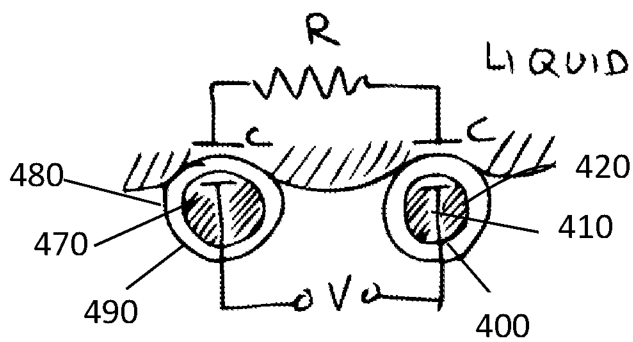


Figure 4C

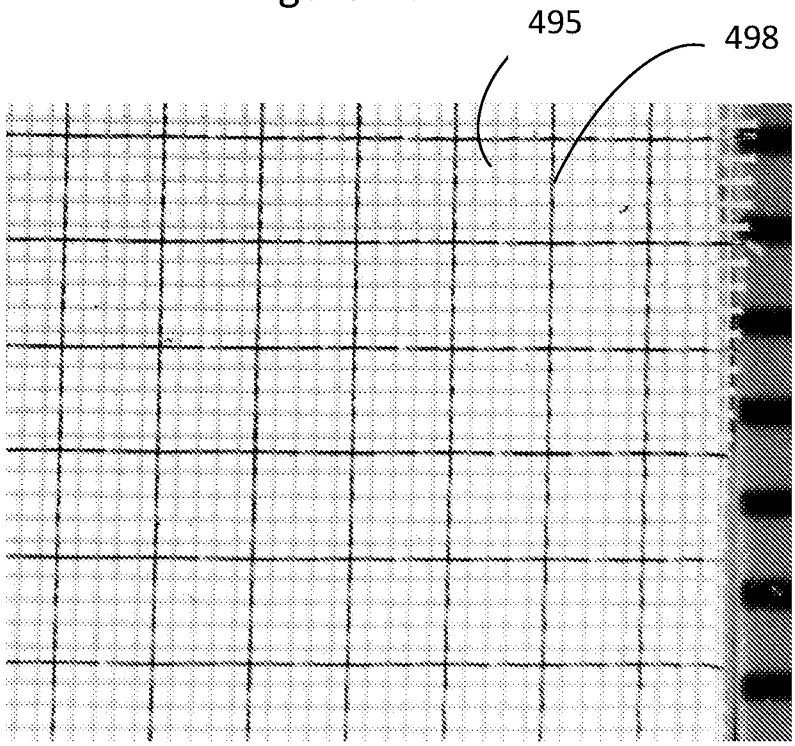


Figure 5A

Figure 5B

Figure 5C

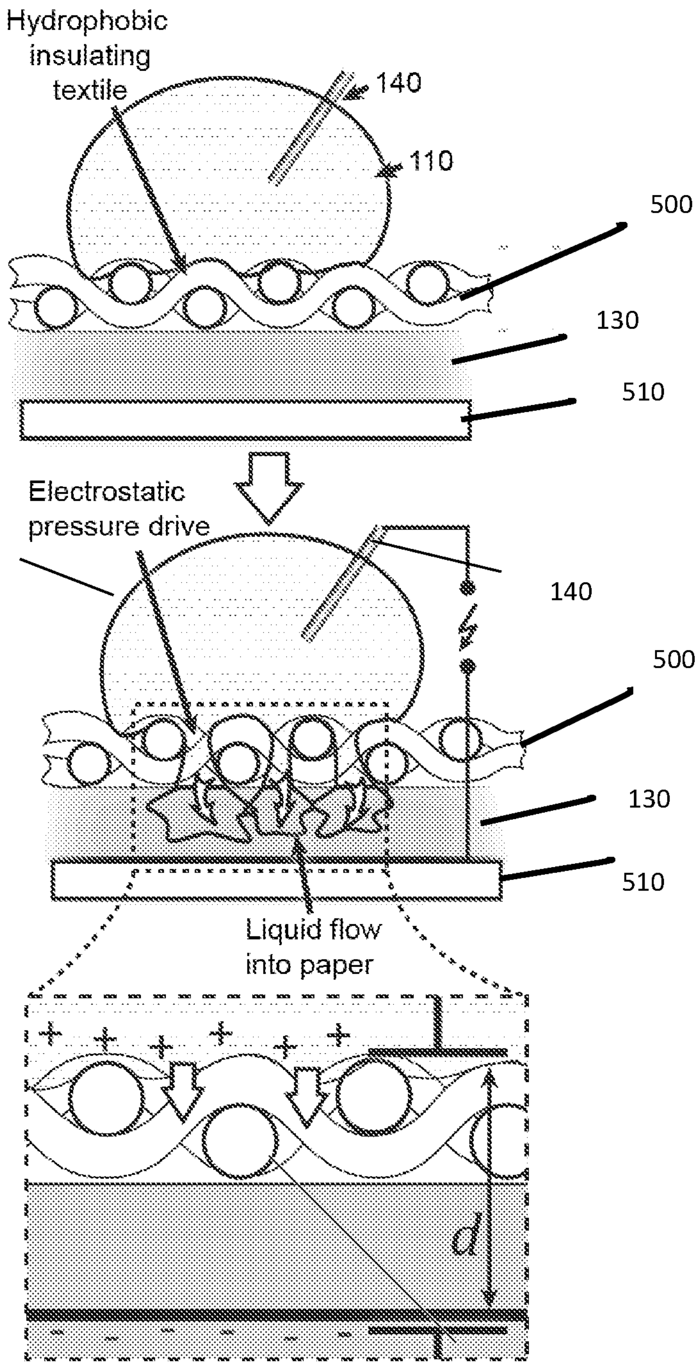


Figure 6A

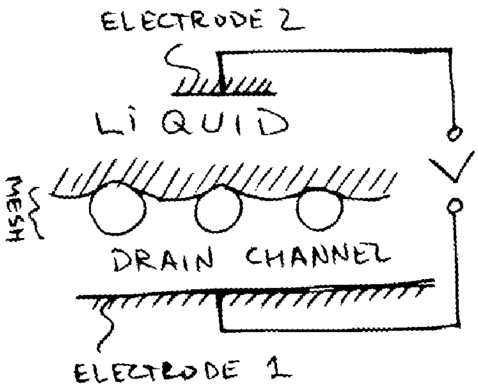


Figure 6B

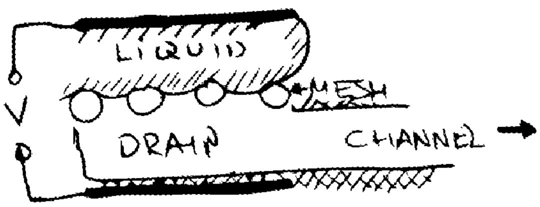
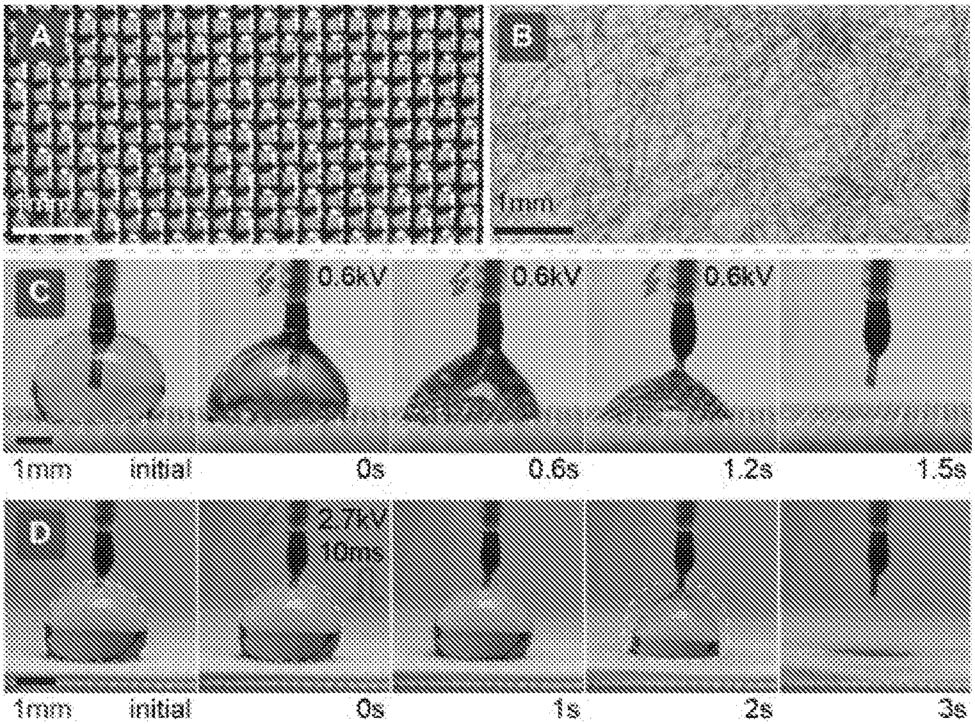


Figure 7B

Figure 7A

Figure 7C

Figure 7D



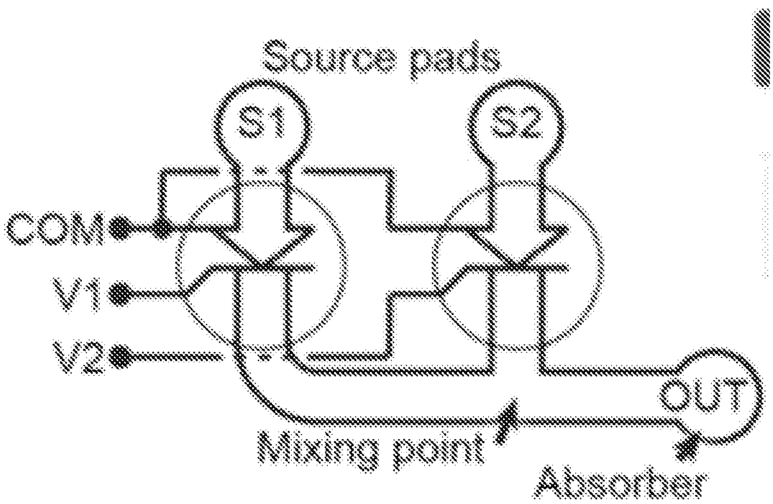


Figure 8A

Figure 8B

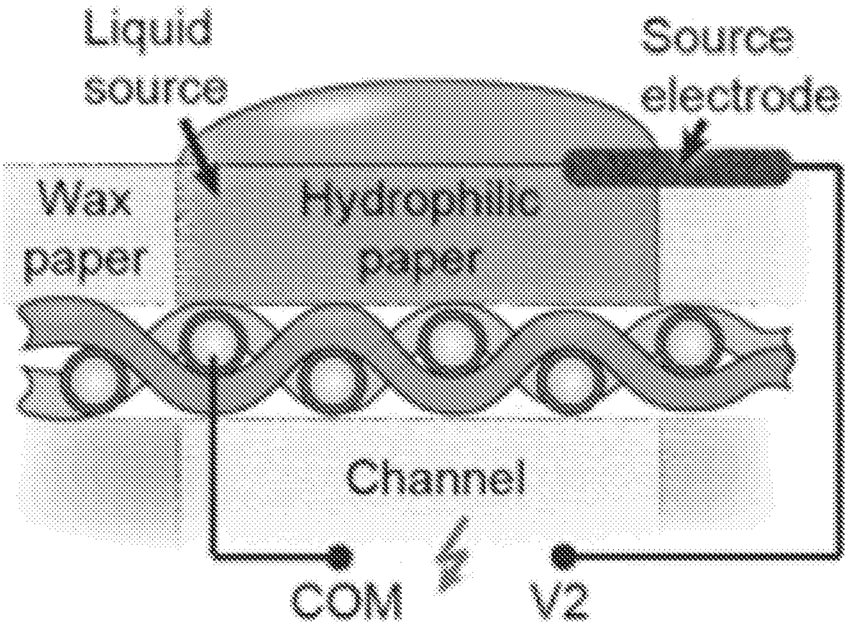

Liquid
source
Source
electrode
Wax
paper
Hydrophilic
paper
Channel
COM
V2

Figure 8C

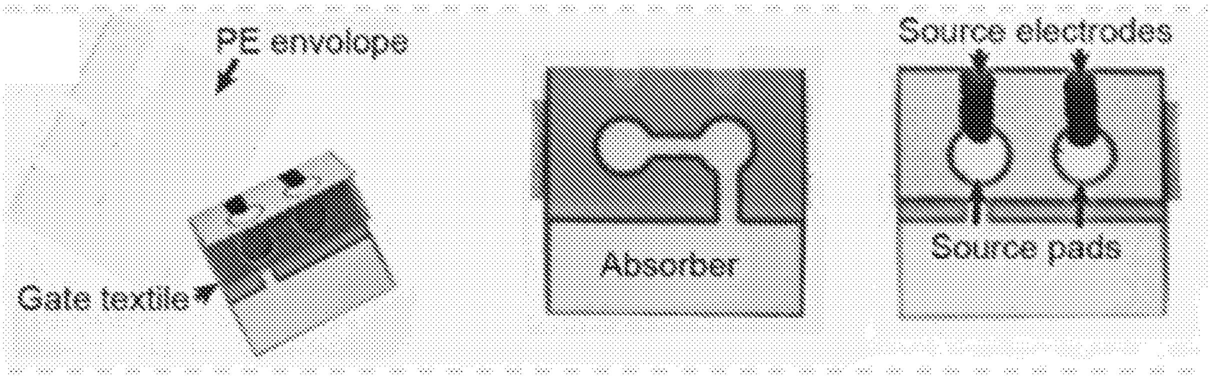


Figure 8D

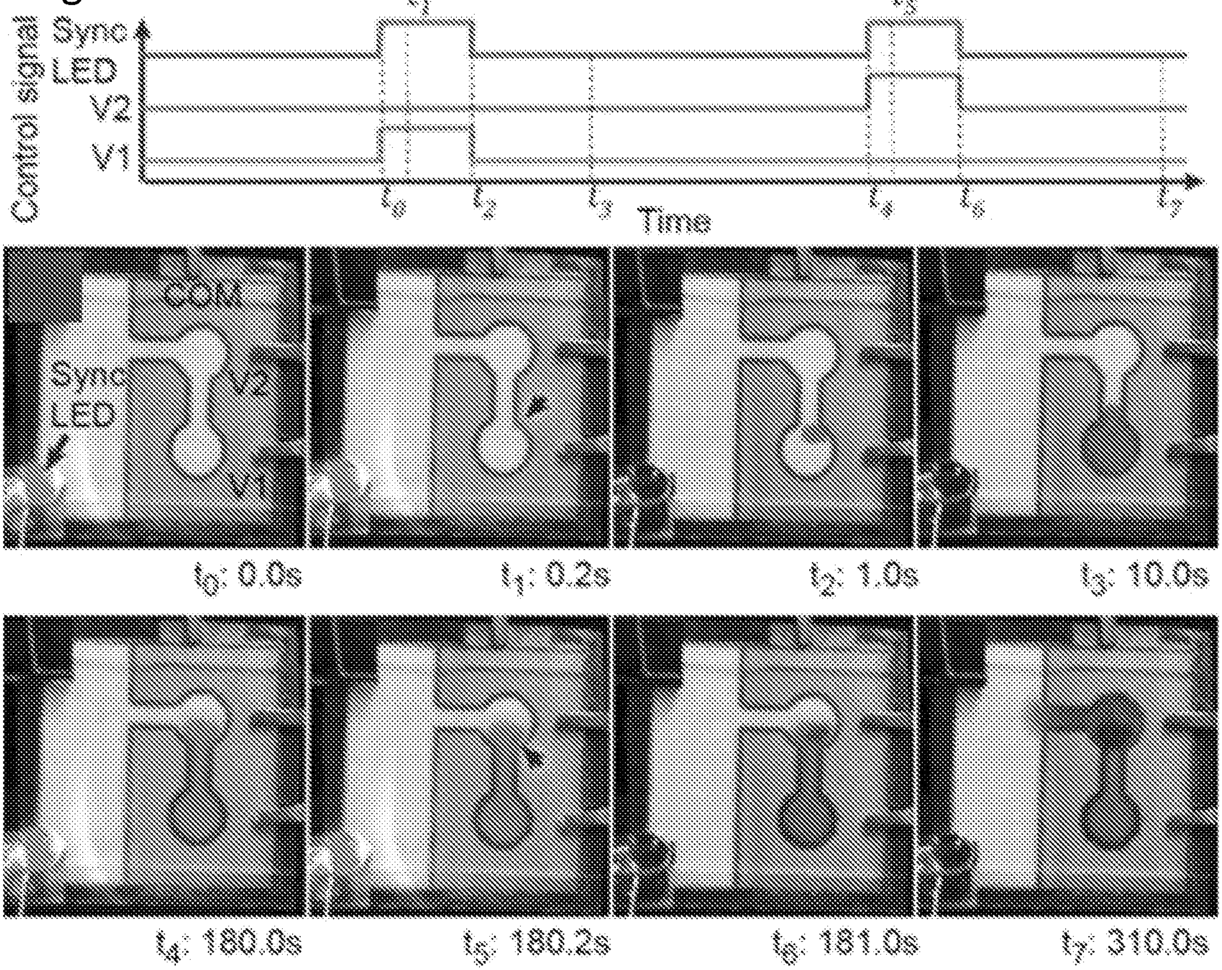


Figure 9A

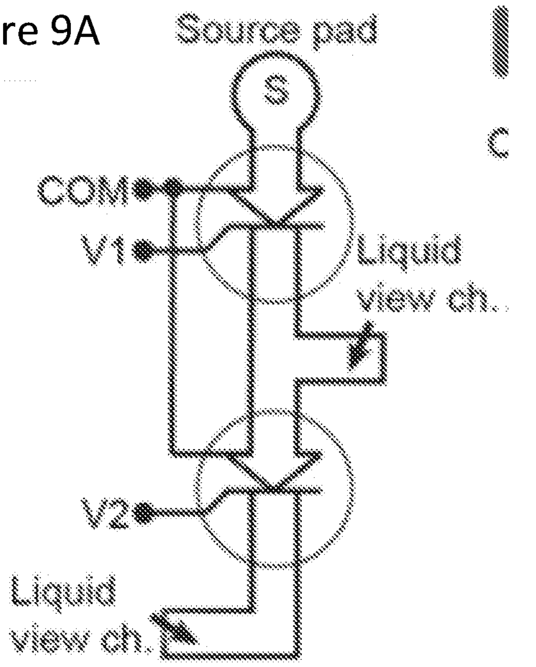


Figure 9B

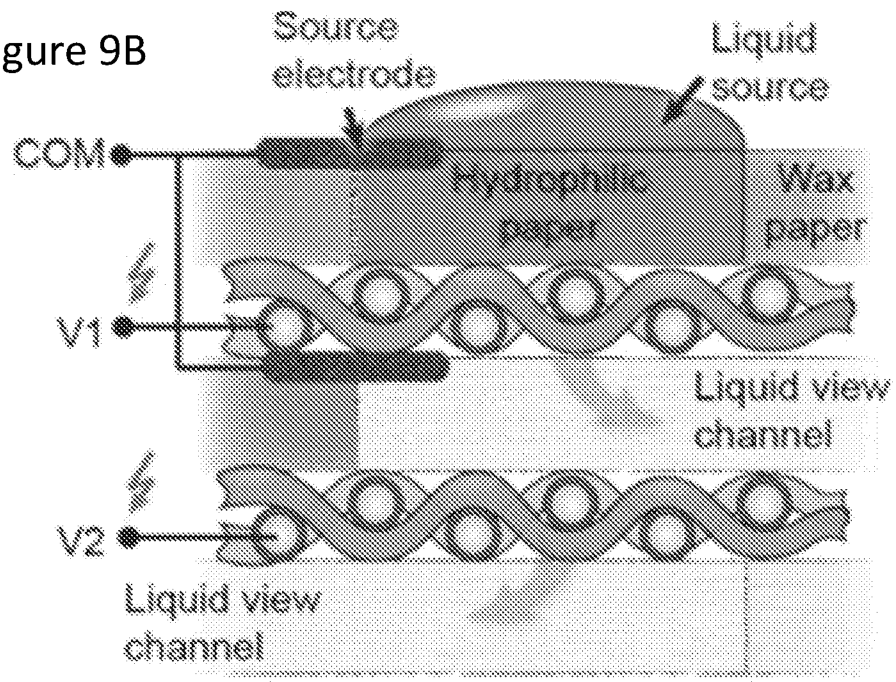


Figure 9C

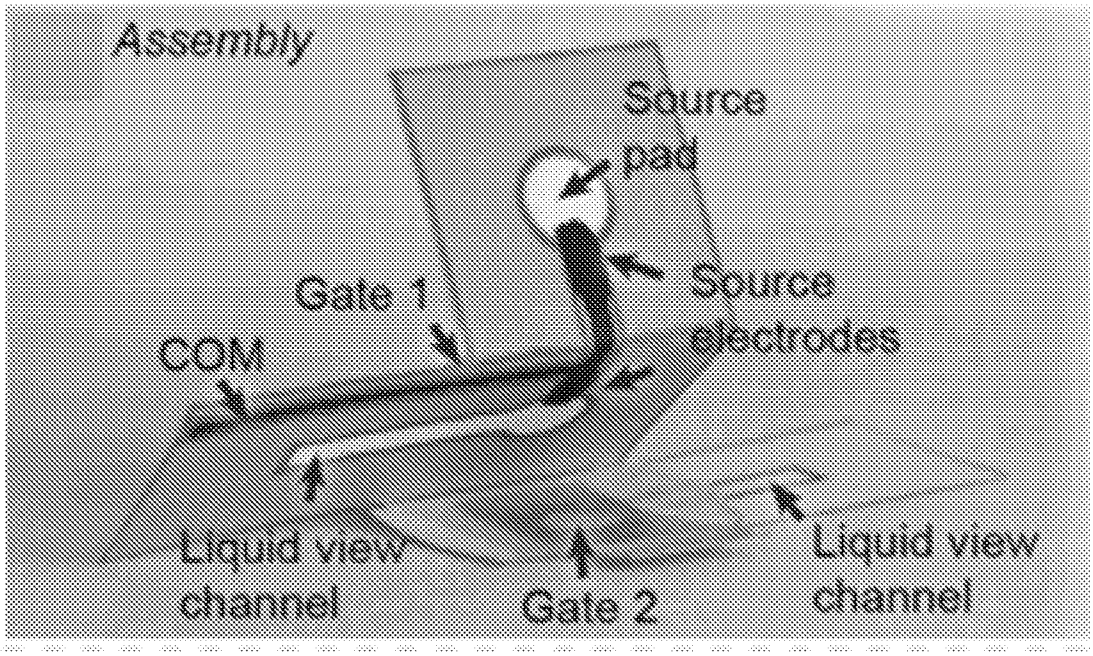


Figure 10A

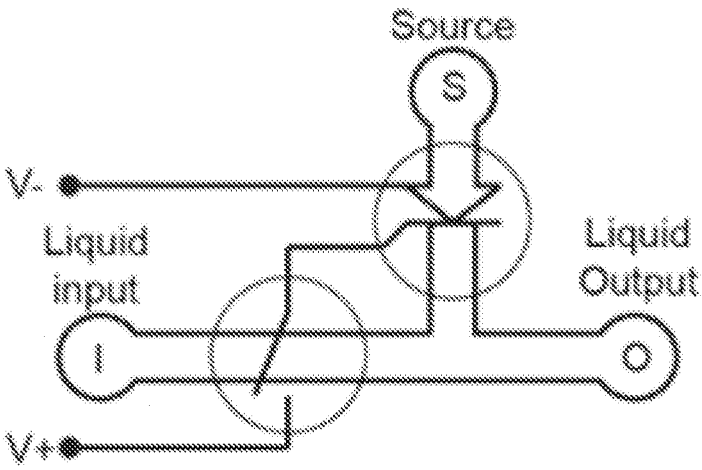


Figure 10B

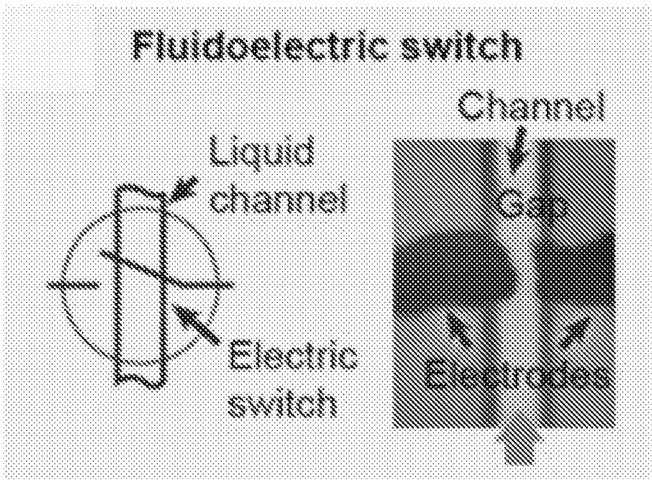


Figure 10C

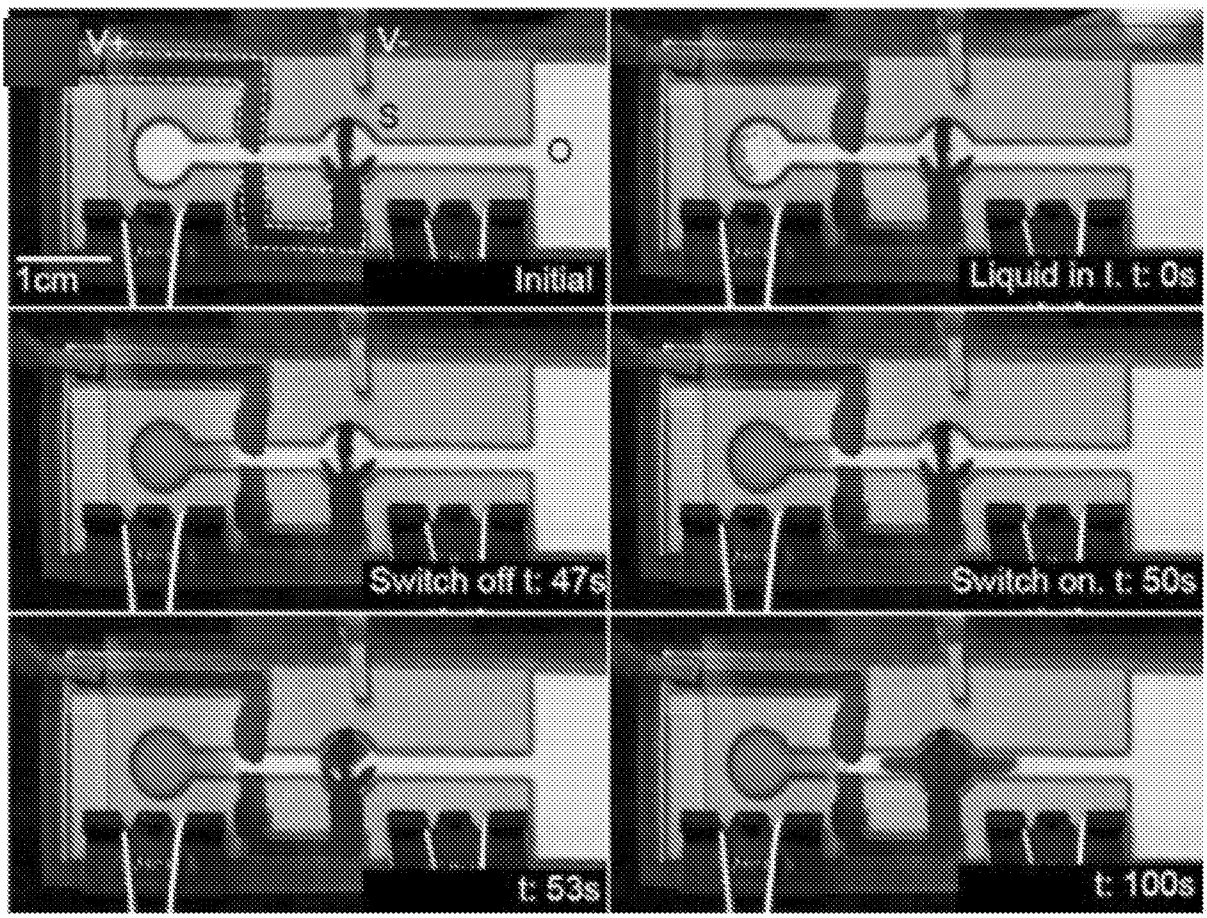


Figure 11A

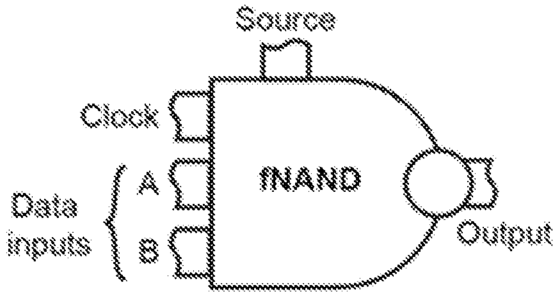


Figure 11B

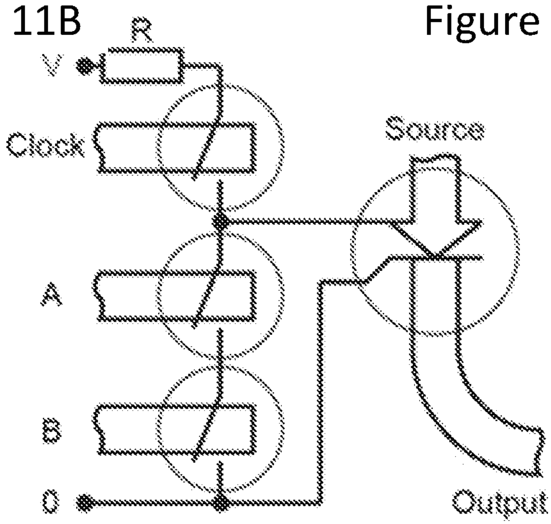


Figure 11C

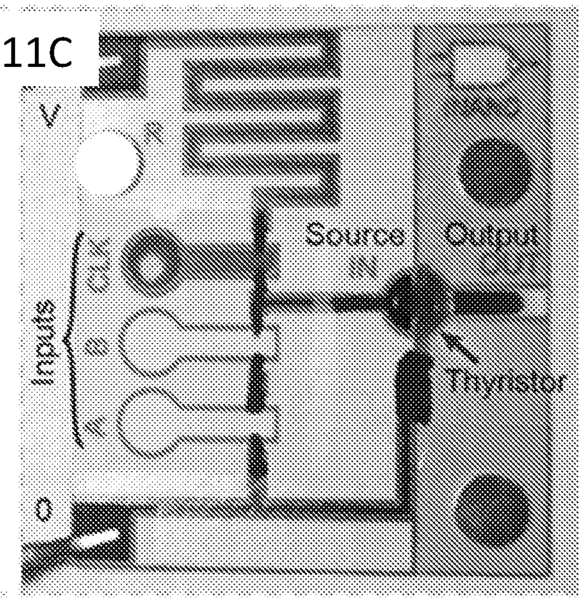


Figure 11D

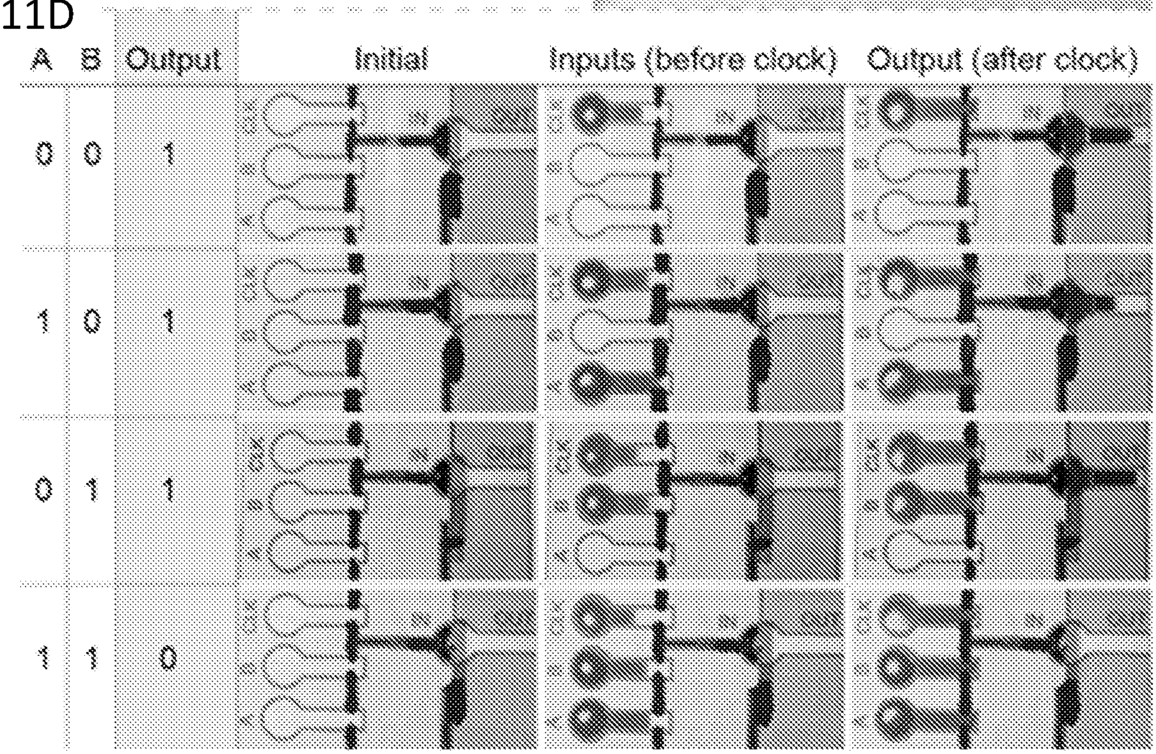


Figure 12A

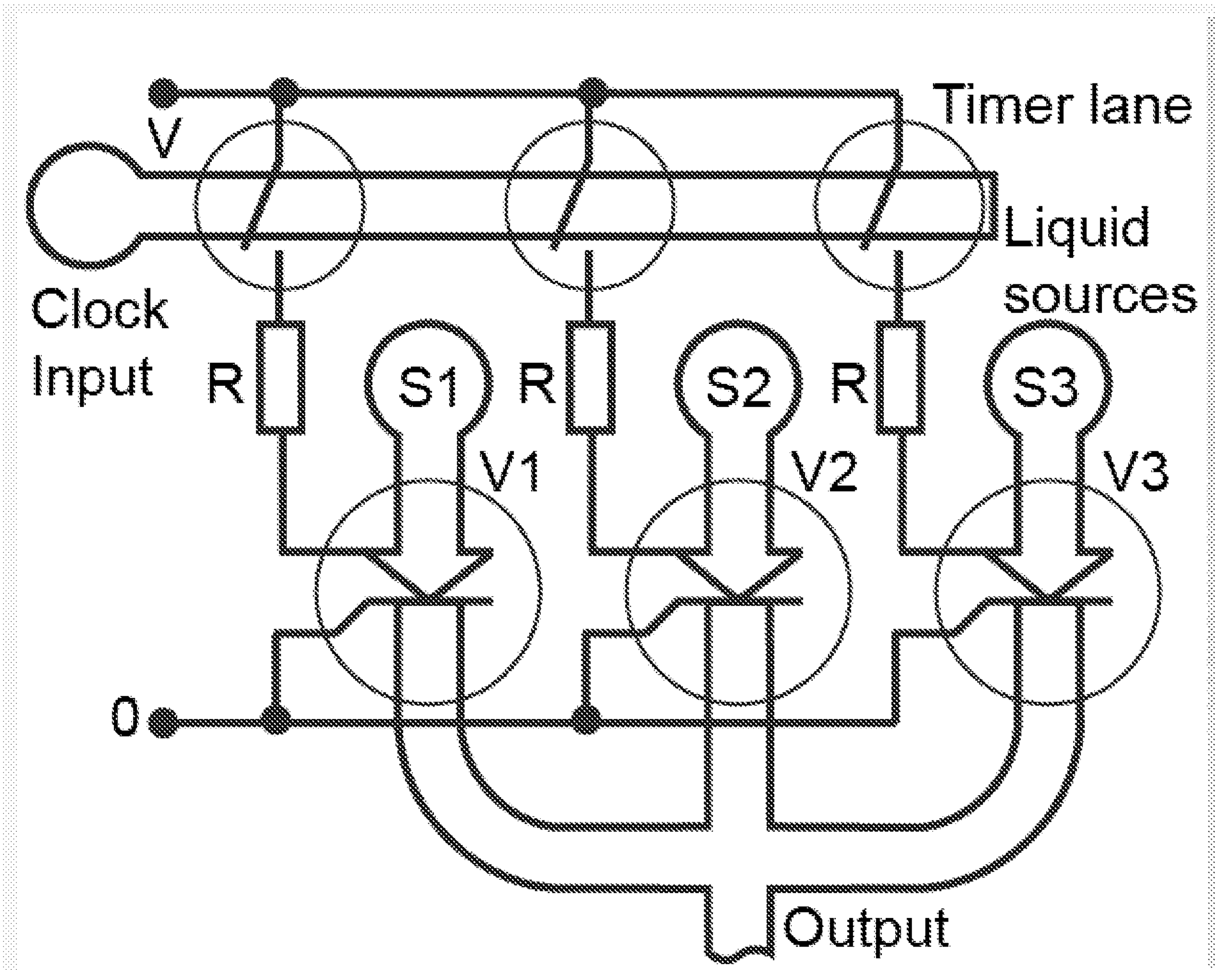

Timer lane
V
Liquid
sources
Clock
Input
R
S1
R
S2
R
S3
V1
V2
V3
0
Output

Figure 12B

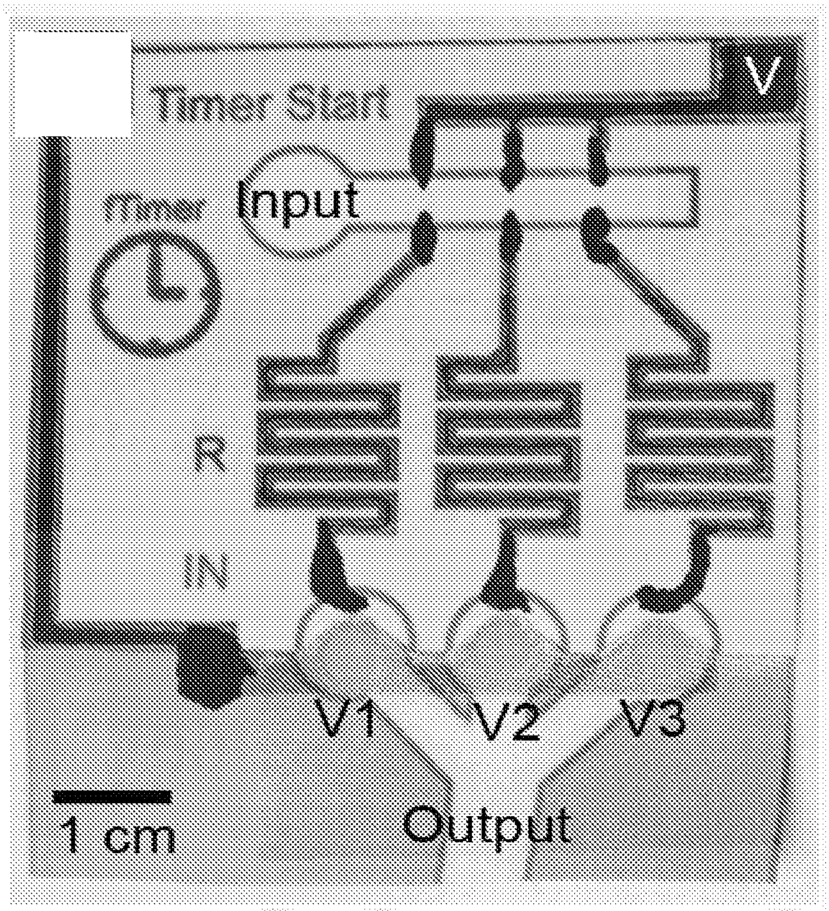
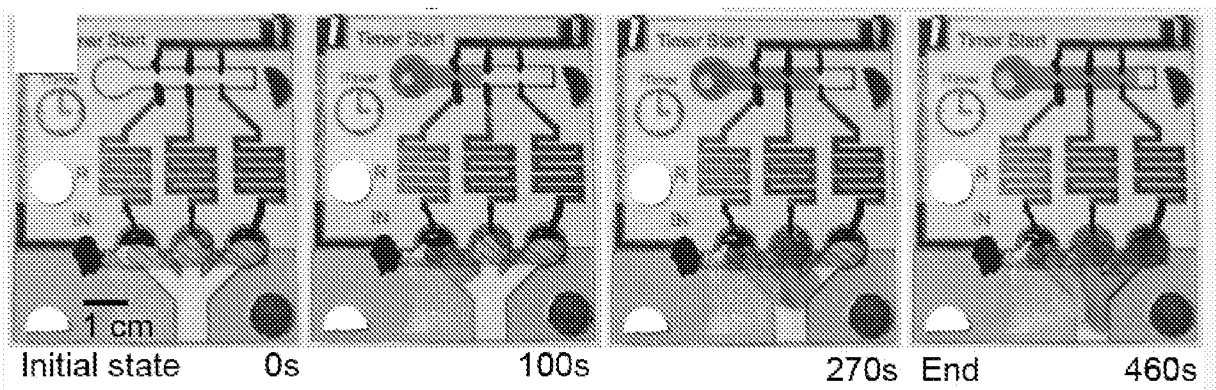


Figure 12C



INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/18336

A. CLASSIFICATION OF SUBJECT MATTER
IPC(8) - F16K 99/00; B81B 1/00 (2016.01)
CPC - F16K 99/0017, 99/0051
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)
IPC(8) - F16K 99/00; B81B 1/00 (2016.01)
CPC - F16K 99/0017, 99/0051

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
CPC - F16K 99/00, 99/0001, 99/0015, 99/0021, 2099/0084; B01L 3/50273, 3/502738, 2400/0415, 2400/0427, 2400/06; B81B 1/00; F15C 1/02, 1/06

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Patbase; Google Patents; Google Scholar; Google Web; Espacenet; Search Terms: address*, cloth*, conduct*, electrode*, electrowet*, fabrc*, filament*, film*, fluid*, gate, hydrophil*, hydrophob*, infus*, layer*, liquid*, mesh*, metal*, microfluid*, paper*, porous*, sheet*, source*, strand*, textilc*, thread*, trace*, valv*, volt*, wax*, wire*

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X --- Y	US 2009/0188794 A1 (Simon et al.) 30 July 2009 (30.07.2009), Figs. 4A-4B, para [0047]-[0054]	1-5, 11, 12/(1-5 and 11) --- 6-9, 12/(6-10) and 17-19
X --- Y	US 2011/0303531 A1 (Hunter et al.) 15 December 2011 (15.12.2011), Fig. 3a, para [0020]-[0023]	1-2 and 10 --- 12/(10)
Y	US 2008/0251383 A1 (Sobek et al.) 16 October 2008 (16.10.2008), para [0080]-[0081]	6 and 12/(6)
Y	US 2003/0119391 A1 (Swallow et al.) 26 June 2003 (26.06.2003), Figs. 3 and 12, para [0093]	7-8 and 12/(7-8)
Y	US 2007/0039832 A1 (Heikenfeld et al.) 22 February 2007 (22.02.2007), Figs. 5C-5D; para [0069]	9 and 12/(9)
Y	US 2012/0198684 A1 (Carrilho et al.) 09 August 2012 (09.08.2012), para [0023]-[0024]	17-19
A	US 2014/0016176 A1 (Kodani et al.) 16 January 2014 (16.01.2014), para [0124]-[0130]	1-12 and 17-19

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

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"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
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 April 2016 (14.04.2016)	06 MAY 2016

Name and mailing address of the ISA/US	Authorized officer:
Mail Stop PCT, Attn: ISA/US, Commissioner for Patents P.O. Box 1450, Alexandria, Virginia 22313-1450 Facsimile No. 571-273-8300	Lee W. Young PCT Helpdesk: 571-272-4300 PCT OSP: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 16/18336

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claims Nos.: 13-16 and 20-35
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

☐ No protest accompanied the payment of additional search fees.