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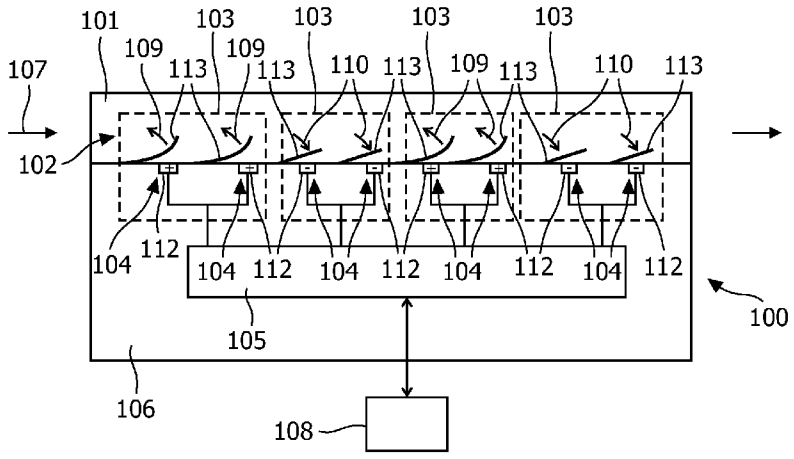

FIG. 1

(57) Abstract: A device (100) for handling a fluidic sample (101), the device (100) comprising a fluidic structure (102) being divided in a plurality of segments (103), a plurality of actuator units (104) arranged on and/or in the fluidic structure (102), wherein each of the plurality of segments (103) comprises at least two of the plurality of actuator units (104), and an activation unit (105) adapted to address each of the segments (103) individually or simultaneously to force the at least two actuator units (104) of the addressed segment (103) to move in a manner to mix a fluidic sample (101) located in the fluidic structure (102).

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A DEVICE FOR AND A METHOD OF HANDLING A FLUIDIC SAMPLE

FIELD OF THE INVENTION

The invention relates to a device for handling a fluidic sample.

Moreover, the invention relates to a method of handling a fluidic sample.

BACKGROUND OF THE INVENTION

Biochips for (bio)chemical analysis, such as molecular diagnostics, will become an important tool for a variety of clinical, forensic and food applications. Such biochips incorporate a variety of laboratory steps in one desktop machine.

Micro-fluidic chips are becoming a key foundation to many of today's fast-growing biotechnologies, such as rapid DNA separation and sizing, cell manipulation, sorting and molecule detection. In microfluidic devices, there is a basic need to control fluid flow, that is, fluids need to be transported, mixed, separated and directed through a microchannel system comprising channels with a typical width of 0.1 mm. Various actuation mechanisms have been developed and are used such as pressure-driven schemes, micro-fabricated mechanical valves and pumps, inkjet-type pumps, electrokinetically controlled flows, and surface-acoustic waves.

In many protocols that may be desired to be carried out on a lab-on-a-chip, the transportation of fluid and in particular of the biological particles within that fluid, is crucial. For example, in a fully integrated DNA lab-on-a-chip platform, the biological material has to be transported to a lyzing stage and then to PCR chambers, before being taken to an analysis stage. There are a variety of actuation methods available for the transportation of the bio-fluid. These include electrical actuation, electrophoresis and electroosmosis, capillary movement, pressure driving via MEMS, thermal gradients, etc. The technology of MEMS (micro-electro-mechanical systems) is related to devices comprising an electronic part and a micromechanical component.

Stroock et al. 2002, "Chaotic Mixer for Microchannels", Science, Vol. 295, pp. 647 to 651 disclose a solution to mix solutions in microchannels. Under typical operating conditions, flows in these channels are laminar - the spontaneous fluctuations of velocity that tend to homogenize fluids in turbulent flows are absent, and, at the same time, molecular

diffusion across the channels is slow. Stroock et al. 2002 present a passive method for mixing streams of steady pressure-driven flows in microchannels at low Reynolds number. This method uses bas-relief structures on the floor of the channel that are fabricated with commonly used methods of planar lithography.

However, the mixing performance of the devices proposed by Stroock et al. 2002 may be slow and require a minimal micro-channel length, so that it may occupy a significant amount of space on a micro-fluidic chip. Another disadvantage of their approach is, that the mixing effect cannot be switched on or off.

OBJECT AND SUMMARY OF THE INVENTION

It is an object of the invention to provide an efficient mixing system.

In order to achieve the object defined above, a device for handling a fluidic sample and a method of handling a fluidic sample according to the independent claims are provided.

According to an exemplary embodiment of the invention, a device for handling a fluidic sample is provided, the device comprising a fluidic structure being divided in a plurality of segments, a plurality of actuator units arranged on and/or in the fluidic structure, wherein each of the plurality of segments comprises at least two of the plurality of actuator units, and an activation unit adapted to address each of the segments individually or simultaneously, to force the at least two actuator units of the addressed segment to move in a manner to mix a fluidic sample located in the fluidic structure.

According to another exemplary embodiment of the invention, a method of handling a fluidic sample is provided, the method comprising individually or simultaneously addressing each of a plurality of segments of a fluidic structure to force at least two actuator units assigned to each of the addressed segments to move in a manner to mix a fluidic sample located in the fluidic structure.

In the context of this application, the term "fluidic structure" may particularly denote any structure through which a fluid may be guided. Such a fluid may be a liquid, a gas, or even a combination of these two phases. It is also possible that solid components are included in such a fluid. A fluidic structure may particularly be a well, a channel or another volume through which the fluid may flow.

The term "segments" may particularly denote spatially delimited portions of the fluidic structure. The fluidic structure is segmented or subdivided in these segments. The

segments may be defined as portions being individually or simultaneously addressable or controllable by an electronic control unit.

The term “actuator units” may particularly denote physical structures which can be moved in a controlled manner, for instance by applying electrical, magnetic, mechanical, thermally induced, or light-induced forces to the actuator units. Such actuator units may be blades, flaps, or rods which can be moved within a fluidic structure to thereby provide a flow resistance for a fluid flowing through the fluidic structure. In dependence of the correlation between the motion direction of the fluid and of the actuator units, the actuator units may accelerate the fluid or may force the fluid to flow in a modified direction, for instance in a reverse direction or in a direction perpendicular to a main flow.

The term “activation unit” may particularly denote any electric unit which can generate signals resulting in a motion of a corresponding actuator unit. Such signals may be supplied to individual segments or to individual actuator units of a segment, for instance via column lines and row lines.

The term “(fluidic) sample” may particularly denote any solid, liquid or gaseous substance to be analyzed, or a combination thereof. For instance, the substance may be a liquid or suspension, furthermore particularly a biological substance. Such a substance may comprise proteins, polypeptides, nucleic acids, lipids, carbohydrates, cells, etc.

A “substrate” may be made of any suitable material, like glass, plastics, or a semiconductor. The term "substrate" may be thus used to define generally the elements for layers that underlie and/or overlie a layer or portions of interest. Also, the "substrate" may be any other base on which a layer is formed, for example a glass or metal layer.

The term “sample chamber” may particularly denote a three-dimensional volume which is provided to accommodate a sample. This volume may be, for instance, in the order of magnitude of milliliters, microliters or nanoliters.

The term “actuator device” may particularly denote any device having a mechanically movable/bendable/turnable component which may be employed to handle (such as to mix or to transport) a fluid (such as a liquid, particularly an aqueous sample, or a gas). Such an actuator device may be in an inactive state, in which an actuator unit (such as an actuator beam) statically rests on a surface of a substrate or in defined relationship to a substrate. When the actuator unit is activated using an electrical signal applied to an electrode structure provided in the environment of the actuator unit, the actuator unit may be moved under the influence of an electric or magnetic force, or by thermally or optically induces forces.

The term "micro-electro-mechanical systems" (MEMS) may denote the technology of integrating mechanical elements, sensors, actuators, and electronics on a common substrate through microfabrication technologies. Micro-electro-mechanical systems may be devices and machines fabricated using techniques generally used in microelectronics, particularly to integrate mechanical or hydraulic functions, etc. with electrical functions. Micro-electro-mechanical systems may integrate mechanical structures with microelectronics. Applications include sample handling systems, medical devices, and microfluidic devices.

According to an exemplary embodiment of the invention, a fluid mixing apparatus for applications particularly in the field of life science may be provided in which a fluidic structure is divided in several segments. By allowing each segment to be individually controlled or activated separately from other segments, an efficient mixing scheme may be achieved, since adjacent segments may also be operated inversely to each other. This may allow to define even complex motion schemes in which, for example, a portion of segments move their assigned actuator units in a first direction, wherein other segments move their actuator units in a second direction which may be different (for instance opposite or orthogonal) to the first direction. This may allow for an intense mixture of components of the fluidic sample. This may also be achieved by arranging the geometrical lay-out of the actuator units differently for different segments, and addressing the segments simultaneously.

The implementation of active mixing units in a fluid channel according to an exemplary embodiment of the invention may provide a significantly improved mixing performance as compared to passive solutions in which the actuators cannot be actively controlled or regulated. Therefore, particularly biological samples may be efficiently mixed, for instance to promote biological or chemical reactions or interactions between components in the fluid or to improve homogeneity of a multi-component sample. Therefore, embodiments of the invention may allow to efficiently mix even samples of a very small volume in the order of magnitude of microliters or less.

Mixing over short distances (for instance less than 1 cm) in microchannels is difficult. According to an exemplary embodiment of the invention, active mixing in a micro-channel is made possible. Specific patterns of rollable devices may be attached to the microchannel wall enabling a controlled flow perpendicular (or in another desired direction) to a horizontal main flow.

Advantages according to an exemplary embodiment of the invention are that a substantially enhanced mixing speed is obtainable compared to conventional purely passive

micro-mixers, that the effect can be switched on or off, and that the driving of the actuators can be adjusted to the specific needs in the system (for instance depending on the viscosity of the liquid the frequency of the actuation can be changed, for instance between 1 Hz and 500 Hz).

According to an exemplary embodiment of the invention, a mixing channel design using polymer actuator elements is provided. Configurations are disclosed that lead to mixing.

Previous studies have worked on mixing using passive structures present in micro-channels, such as grooves or ridges. Such a passive system is described in Stroock et al. 2002. A fluid is pumped through a micro-channel by external means, for example by an external pump. The channel is divided in segments of a certain length, and each segment contains a pattern on the surface that causes a secondary flow. Since the pattern is different for consecutive segments, different secondary flow patterns are generated in the different segments. The changing flow patterns, when designed in a proper way, lead to mixing of the fluid as it travels through the channel. According to an exemplary embodiment of the invention, the passive mixing grooves may be replaced by actively controllable actuator structures such as polymer actuators. The active nature of such an embodiment may lead to enhanced mixing, while the effect can also be switched off and on at will.

Exemplary embodiments may be implemented in microfluidic systems, biosensors, and a lab-on-chip. For example, exemplary embodiments of the invention may be applied in biotechnological or biomedical applications such as biosensors, rapid DNA separation and sizing, cell manipulation and sorting. Other fields of applications are pharmaceutical applications, in particular high-throughput combinatorial testing where local mixing is essential. Microchannel cooling systems in microelectronics applications are an other field of application of exemplary embodiments.

Next, further exemplary embodiments of the device will be explained. However, these embodiments also apply to the method.

The fluidic structure may comprise at least one of the group consisting of a channel and a well. Through such a microfluidic structure, a fluid may flow and can be mixed by means of an actuation of the actuator units which disturb intentionally the fluid flow characteristics of the fluidic sample flowing through the channel or well. Such a superpositioned influence may force a laminar flow or may even initiate a chaotic flow.

The device may further comprise a substrate, wherein the fluidic structure may be formed in and/or on the substrate. Thus, the device may be manufactured as a

monolithically integrated device thereby allowing to manufacture the device in very small dimensions, for example to treat samples in the order of magnitude of microliters to nanoliters. Such a substrate may be a semiconductor substrate, a glass substrate, etc. and may be treated with an etching procedure to thereby form channels.

The plurality of actuator units may be arranged on at least a part of a wall of the fluidic structure, particularly on a bottom wall and/or a top wall and/or a lateral wall of the fluidic structure. By aligning an inner wall of the fluidic structure with actuator units, the influence of the movable actuator structures on the fluidic sample may be further refined, thereby allowing to introduce even very complex mixing schemes.

The actuation unit may be adapted to force a first part of the actuator units to move along a first (for instance forward) direction and to force a second part of the actuator units to move along a second (for instance backward) direction, wherein the first direction may be different from the second direction, particularly may be opposite to the second direction. By operating the actuator units with a phase shift relative to one another, for instance with a phase shift of 180° or π, a part of the actuator units may induce a backflow and another part of the actuator units may induce a forward flow of portions of the fluidic sample, thereby bringing particles or components of the fluidic sample in functional contact to one another.

Particularly, the device may comprise a fluid transport unit (such as a pump, for instance a peristaltic pump, a syringe pump, or pressurized air) for transporting a fluidic sample along a flowing direction through the fluidic structure, wherein the activation unit may be adapted to force at least a part of the actuator units to move opposite to the flowing direction, or in a direction not parallel to the flowing direction of the fluidic sample, for example perpendicular to it, through the fluidic structure to thereby promote mixing of the fluidic sample. Thus, the function of the fluid transport unit may be coordinated with the function of the activation unit, so that a main transport direction of the fluid may differ from a fluid flow direction forced or promoted by the activation unit. By taking such a measure, a transport of the fluid may be sufficiently combined and harmonized with a selective mixing, wherein the (chaotic) mixing forces may be significantly lower than the transport forces to allow for a simultaneous mixing and transporting.

The segments may be arranged as an alternating sequence of first segments and second segments, wherein the activation unit may be adapted to address the first segments in common and to separately address the second segments in common. For example, when the first segments are denoted with A and the second segments are denoted

with B, a sequence ABAB... can be generated. By such a one-dimensional or a two-dimensional (chessboard-like) architecture, it is possible to provide only two (or any other number) of control signals being applied to the segments in a groupwise manner, so that an efficient mixing can be combined with a low effort for regulating or addressing the segments. This may further contribute to the miniaturization of the device.

Alternatively, the geometrical arrangement of the actuator units may be different in the different segments, for example in an ABAB... sequence, such that the direction or nature of the movement of the actuator units in the different segments is different, even when addressing the segments simultaneously. This may lead to a mixing effect even when the segments are addressed simultaneously.

The at least two actuator units assigned exclusively to one of the plurality of segments may be arranged in rows and/or columns. By such a one-dimensional or two-dimensional array of actuator units, the mixing performance may be further improved.

The activation unit may be adapted to address the segments depending on a present operation parameter of the device, particularly depending on a viscosity of a fluidic sample. Thus, a parameter characterizing an assay or an experiment, such as a viscosity of a presently investigated or treated fluidic sample, may be measured, for instance by a sensor. Based on the sensor result, the fluid flow and mixing performance may be improved or even optimized by a corresponding addressing of the segments.

At least a part of the plurality of actuator units may be configured as a polymeric micro-actuator. Such a polymeric micro-actuator in a configuration as an electrostatically activatible polymer composition structure is shown, for instance, in Fig. 2. In the non-actuated state, the micro-actuator is bending away from the substrate. Such a configuration may include a layer structure of an electrically conductive layer and a dielectric (for instance polymer) layer, wherein the generation of an electrostatic force by applying an electrical potential difference between an electrode (which may be integrated in the substrate) and the conductive layer of the structure may force such a micro-actuator to roll out to thereby efficiently generate mixing forces.

The activation unit may be adapted to individually address each of the segments to force the at least two actuator units of the addressed segment to move relative to each other in a manner to mix a fluidic sample located in the fluidic structure. Such a motion relative to each other may include a configuration in which adjacent actuator units approach each other in one operation state, whereas, in another operation state, both adjacent actuators are simultaneously departing from one another. In other words, a first half of the duty cycle

of both actuator units is characterized by an approaching of the actuator units, whereas the other half of the duty cycle, the distance between tips of the actuator units is increased.

The actuator device may be adapted as a microfluidic device, that is to say as a device dimensioned, designed (for instance regarding materials), capable or adapted to treat or handle microfluidic samples.

The actuator device may be a micro-electro-mechanical system (MEMS), for instance a micro-electro-mechanical fluid mixer. When the actuator unit is provided in a sample chamber in which two or more components shall be mixed together, oscillation of the actuator unit by generating alternating attracting and repulsive forces may mix the individual components.

The actuator device may be a sensor device (particularly a biosensor device), a biochip, a lab-on-chip, an electrophoresis device, a sample transport device, a sample mix device, a cell lyzing device, a sample washing device, a sample purification device, a sample amplification device, a polymerase chain reaction (PCR) device, a sample extraction device or a hybridization analysis device. Particularly, the microfluidic device may be implemented in any kind of life science or diagnostic apparatus.

The aspects defined above and further aspects of the invention are apparent from the examples of embodiment to be described hereinafter and are explained with reference to these examples of embodiment.

BRIEF DESCRIPTION OF THE DRAWINGS

The invention will be described in more detail hereinafter with reference to examples of embodiment but to which the invention is not limited.

Fig. 1 shows a mixing device according to an exemplary embodiment of the invention.

Fig. 2 illustrates an electrostatically actuatable polymer composite structure in a schematic view.

Fig. 3 shows an electrostatically actuated polymer composite structure in a practical realization.

Fig. 4 shows a mixing configuration according to an exemplary embodiment of the invention, wherein a view of the channel wall divided into square segments containing different actuator layouts is shown.

Fig. 5 shows another mixing configuration according to an exemplary embodiment of the invention, wherein a view of the channel wall divided into square segments containing different actuator layouts is shown.

Fig. 6 illustrates further actuator layouts for mixing according to exemplary embodiments of the invention.

Fig. 7 and Fig. 8 show a proof of principle device for active mixing by polymer actuators.

Fig. 9 and Fig. 10 illustrate a visualization experiment showing mixing, wherein Fig. 9 shows actuators switched off (no mixing), and Fig. 10 shows actuators switched on (mixing).

Fig. 11 is a cross-sectional view of the channel (made using OCT, optical coherence tomography) showing that a secondary flow is induced due to the actuators (that are placed in the bottom of the channel).

Fig. 12 shows a mixing device according to an exemplary embodiment of the invention.

Fig. 13 Results of particle tracking experiments: (A) Top view of the actuator layout. (B) and (C) show the estimated flow speeds as a function of switching frequency and applied voltage.

Fig. 14: (a) Top view of the "basic flow creating element" (BFCE), consisting of four polymer micro-actuators oriented in four different directions, that can be addressed individually; (b) Top view of an array of the "basic flow creating elements" (BFCE's).

Fig. 15 Two examples of flows created by a specific addressing of the arrays of BFCE's in a micro-fluidic device.

DESCRIPTION OF EMBODIMENTS

The illustration in the drawing is schematical. In different drawings, similar or identical elements are provided with the same reference signs.

In the following, referring to Fig. 1, a device 100 for handling a fluidic sample 101 according to an exemplary embodiment of the invention will be explained.

The device 100 comprises a fluidic structure 102, configured as a channel, being spatially divided in a plurality of segments 103. In Fig. 1, four segments 103 are shown, however a larger or smaller number of segments 103 is possible.

Each of the segments 103 has assigned (in the present embodiment) two actuator units 104 which will be explained in more detail referring to Fig. 2. The actuator units 104 are arranged on and in the fluidic structure 102, more specifically on a bottom wall of the channel 102. Each of the segments 103 has assigned two actuator units 104. However, the number of actuator units 104 per segment 103 may be larger than two.

Moreover, an activation unit 105 is provided and is realized as a monolithically integrated semiconductor circuit integrated in the silicon substrate 106 and adapted to individually address each of the segments 103 to force the two actuator units 104, respectively assigned to a selected/addressed one of the segments 103, to move in a manner to mix the fluidic sample 101 located in the fluidic structure 102. The fluidic sample 101 may be a biological sample such as a mixture of different protein components, a body fluid such as blood or urine, etc.

It may happen that, in the context of a biochemical assay, different components of the fluidic sample 101 have to be brought in functional interaction to one another. For this purpose, the activation unit 105 may drive the actuator units 104 to generate a mixing force, as will be described below in more detail.

The activation unit 105 may be realized by a processing unit such as a central processing unit (CPU) or a microprocessor. Furthermore, Fig. 1 shows an input/output unit 108 which is bidirectionally coupled to the activation unit 105. The input/output unit 108 is a user interface via which a human user may control operation of the device 100. The input/output unit 108 may comprise an input element such as a keypad, a joystick, or a button. Furthermore, the user interface 108 may comprise an output unit such as an LCD display. The input/output unit 108 is bidirectionally coupled to the processor 105 to thereby allow a user to provide control commands to or to perceive results of a performance of the device 100.

The device 100 comprises the semiconductor substrate 106, for instance a semiconductor chip or wafer, but can also be manufactured from other materials such as glass or plastic. The channel 102 is etched in the substrate 106, or established by other means such as powderblasting or by a construction using a patterned layer e.g. from a photopatternable material, and is therefore formed as a recess in the substrate 106.

The activation unit 105 is adapted to force the actuator units 104 of the first segment 103 and of the third segment 103 (counted from left to right) in a first direction 109 whereas a second segment 103and a forth segment 103 (counted from left to right) have motion directions of their actuator units 104 which are indicated with reference numeral 110.

As can be taken from the arrows 109, 110 shown in Fig. 1, the first motion direction 109 is different from the second motion direction 110 so as to provide an efficient mixing within the channel 102.

In the embodiment of Fig. 1, the actuator units 104 are arranged linearly, that is to say as a one-dimensional row. Alternatively, a two-dimensional matrix-like arrangement with rows and columns is possible as well.

The motion of the actuator units 104 is performed by applying electrical signals to electrode structures 112 assigned to each of the actuator units 104. As indicated schematically in Fig. 1 by the signs "+" and "-", the electric signals provided by the CPU 105 to the electrodes 112 are different for the different segments 103. Therefore, the sign/polarity of the electric forces acting on the polymer composite structures 113 may vary for the different segments 103, resulting in a different motion (opposite motion) of the actuators 104 in the first and third segment 103 as compared to the second and fourth segment 103.

In the following, referring to Fig. 2, construction and operation of an actuator unit 104 will be described in more detail.

The actuator unit 104 comprises an electrode 112 integrated in the substrate 106. Furthermore, an dielectric layer 200 is provided as a isolation structure. This can be made from any isolating material, for example poly-acrylate, poly-imide, silicon-oxide, silicon-nitride, or other materials or combinations thereof. Moreover, an electrically conductive structure 202 is formed as a first part of a double layer 203, and may be a thin chromium layer. Other conductive materials are also possible, such as titanium, aluminum, copper, gold, etc. Furthermore, a further polymer layer 201 is provided as the second part of the double layer structure 203 forming an actuator beam. This polymer material may be made from a wide range of materials or combinations thereof, such as elastomers like silicone rubbers or poly-urethane, (semi-crystalline) or glassy polymers, for example poly-imide, poly-acrylate, and also liquid-crystal elastomers, or liquid-crystal networks. In the configuration of Fig. 2, an electric signal is applied to the electrode 112 that the actuator beam 203 formed by the components 201, 202 is rolled up. It is also possible to roll down the double layer 201, 202 so that an essentially planar structure is obtained.

An example of an electrostatically polymer actuator 300 that can be used in this application is shown in Fig. 3. Fig. 3 is a practical realization of the concept of Fig. 2

The actuator 104 is formed by a double-layer composite structure 203 consisting of a polymer film 201 and a conductive film 202. When a voltage difference is applied between the electrode 112 underneath the actuator beam 203 and the conductive film

202 that is part of the actuating structure 203, an electrostatic force will pull the structure 203 towards the substrate 106. Consequently, the structure 203 will roll out and flatten out on the substrate 106. When the voltage is removed, the slab will return to its original curled shape by elastic recovery.

A mixing flow in a micro-channel 102 may be obtained by placing the actuators 104 in the channel 102 according to a specific geometrical configuration. According to exemplary embodiments of the invention, solutions are provided how to design this arrangement to get good mixing.

The channel 102 may be divided into various segments 103 along its length. The size of the segments 103 is naturally of the order of magnitude of the channel width, which can be from about 10 microns (or less) to about a millimeter (or more). Each segment 103 contains multiple polymer actuators 104, such as the one in Fig. 2 and Fig. 3, arranged in such a way that, when actuated, a specific flow pattern is generated in the segment. This is a secondary flow superposed on the main flow that is driven, for example, by an external pump.

The actuator configuration in consecutive segments 103 is different, typically in an A-B-A-B-… sequence (or in an A-B-C-A-B-C-… sequence), so that different secondary flows are generated in different segments 103. The sequence of different flow patterns will lead to mixing of the fluid 101 as it is pumped through the channel 102.

More specific, an example of an arrangement 400 of polymer actuators 104 is shown in Fig. 4.

Fig. 4 depicts segments 401, 402 in an A-B-A manner, containing rows of electrostatic polymer actuators 104, viewed from the top (the actuators 104 are curled upwards in Fig. 4 and are visible as small rectangles). The segments 401, 402 are present on the bottom of a micro-channel 102 with a width equal to the segment size, through which a fluid is pumped causing a main flow. When actuated, the polymer actuators 104 will all roll out in one direction, perpendicular to the main flow, in segment A 401, and in the opposite direction in segment B 402. This will cause opposite secondary (or transverse) flows to be generated that will lead to mixing.

Fig. 4 is just one specific example of an arrangement 400 of polymer actuators 104 in the segments 401, 402.

Another embodiment 500 is shown in Fig. 5.

Here, each of segments 501, 502 contain rows of actuators 104 with mixed roll-out directions. In segment 501 C, three of five rows are rolling out in a specific direction

perpendicular to the main flow, and the other two are rolling out in the other direction. In segment 502 D, the asymmetry in rolling out direction is reversed. Therefore, in each segment 501, 502 two secondary, asymmetric flow patterns are generated of which the asymmetry plane is shifting between segments 501, 502.

Many other arrangements are possible. A common characteristic of embodiments of the invention is: consecutive segments with different arrangements, leading to different secondary flow patterns (having at least a velocity component perpendicular to the main flow).

Fig. 6 shows several other possible layouts 600.

Also, the actuators can be placed on any wall of the channel (bottom-top-sides), or combinations of walls. Each segment may be addressed individually.

A proof-of-principle device 800 for active mixing by polymer actuators is shown in Fig. 7 and Fig. 8.

To test the concept, a Y-shaped mixing channel 700 has been designed and fabricated. The actuators are manufactured on a glass plate. A polydimethylsiloxane (PDMS) cap, containing the Y-shaped channel structure, is mounted on top of the glass plate. The two inlets are connected to syringe pumps.

The bottom channel wall is covered with actuator arrangements in sixteen segments of 1 by 1 mm, containing various actuator lay-outs, typically in an A-B-A-B-… sequence. The layout shown in Fig. 4 has been used. Each individual segment can be individually addressed. The main flow is driven by the syringe pumps, the movement of the actuators induces a transverse flow.

Flow visualization experiments using silicone oil (viscosity 9.3 mPas) have been carried out. In one type of test, the fluid entering though the two inlets was colored with a red and a blue dye, respectively. The main flow speed was about 3 mm/s. After switching on the artificial actuators with a frequency of 20 Hz, the mixing is clearly enhanced by their movement, as can be seen in Fig. 9 and Fig. 10.

Optical coherence tomography (OCT) has been used to look at perpendicular cross sections of the channel. The fluid entering through one of the inlets was seeded with TiO_2 particles. Upon switching on the actuators, a transversal vortex is generated causing mixing over the total cross section. The induced transversal velocity is typically 300 μm/s.

Fig. 11 is a cross-sectional view of the channel (made using OCT, optical coherence tomography) showing that a secondary flow is induced due to the actuators (that are placed in the bottom of the channel).

Thus, active mixing may be obtained in a micro-channel.

Fig. 12 shows a mixing device 1200 according to an exemplary embodiment of the invention.

The embodiment of Fig. 12 is similar to the embodiment of Fig. 1. However, the orientation of the polymer actuators 113 is oriented oppositely in consecutive segments 103. Thus, the actuator units 104 may be oriented in different directions for different segments 103, as shown in Fig. 12, so that they move in different directions when actuated (even simultaneously with the same (electrical) signal). The induced fluid flows are also oriented differently, which may lead to efficient mixing within the channel 102.

According to exemplary embodiments of the invention, one electrode 112 may be shared by more than one, or even all moving structures 113. This is, effectively, what happened in the mixing experiments shown in Fig. 9 to Fig. 11.

The electrostatic actuators shown in Fig. 2 and Fig. 3 can induce significant fluid velocities. The induced flow velocities were estimated by carrying out particle tracking experiments in silicone oil. The actuators were arranged on a substrate in square segments of 1 mm^2, as shown in a top view in Fig. 13A. The segment contains five columns of twenty actuators, visible in Fig. 13A as black rectangles since they are in the curled state. The surface was covered with a 0.5 mm thick silicone oil film (viscosity 9.3 mPa s), so that the actuators were completely immersed. To visualize the flow two kinds of particles were dispersed in the fluid, namely titaniumdioxide (TiO_2) particles with a mean diameter of 0.5 micron and hollow glass spheres with an average diameter of 12 micron.

The actuators were actuated with different switching frequencies and actuation voltages, and the movement of the tracer particles was recorded at 30 frames per second. Particle tracking was done manually from the obtained movies, and the induced flow velocities were estimated.

Fig. 13 (B) shows the induced velocity as a function of switching frequency, estimated from tracking of TiO_2 particles (solid lines) and hollow glass spheres (broken lines). The applied AC voltage was 75V/1kHz.

Fig. 13 (C) shows the effect of applied AC voltage (always 1 kHz) on the induced velocity, measured using hollow glass spheres. The switching frequency was here fixed at 50 Hz. The lines are drawn as a guide to the eye.

Flow speeds up to 0.6 mm/s were generated. The flow direction is determined by the rolling-out direction of the micro-actuators. The induced velocity increases with both the

switching frequency and the actuation voltage, and the agreement between the two types of particles is good. The electrostatic actuators turn out to be very effective in producing fluid flow.

The actuators can be integrated into a micro-fluidic device in a particular manner, such that by changing the driving scheme, the induced flow direction and speed can be varied at will. Fig. 14 shows an advantageous embodiment. The "basic flow-creating element" (BFCE) is shown in 14 (a). It consists of four micro-actuators, acting in four different directions. These can be the electrostatically actuated polymer MEMS, shown in Fig. 2 and Fig. 3, of which the rolling-out direction, and hence the induced direction of flow, is indicated by the arrows in Fig. 14 (a). For example, the actuator "R" will roll out to the right, and hence it will create a fluid velocity to the right (of which the magnitude depends on the applied voltage and frequency, as illustrated in Fig. 13). The under-electrode of the BFCE is divided into four segments that can be addressed individually, so that any of the polymer actuators can be driven separately. In the micro-fluidic device, arrays of many BFCE's are combined, as shown schematically in Fig. 14 (b). This structure can be integrated in a channel or in a micro-chamber of a micro-fluidic device.
The configuration shown in Fig. 14(b) offers the possibility of versatile flow creation in micro-fluidic devices.

Fig. 15 shows two examples of flows created by a specific addressing of the arrays of BFCE's. In Fig. 15 (a), all segments "R" of the BFCE's are addressed, while the other segments are inactive. In each BFCE, a flow to the right is therefore induced, and thus in the whole flow system a uniform flow to the right occurs. By activating different segments in different BFCE's, more complicated overall flow patterns can be generated. Figure 15 (b) shows an example in which a global eddy or vortex is induced by a particular driving scheme.

A wide variety of flow patterns can be created depending on the addressing scheme. In addition, the flow speed can be controlled by varying the applied voltage and switching frequency. This makes this concept extremely versatile.

The basic concept applies to any micro-actuator that can be addressed individually and generates a flow in a particular direction (such as the magnetic, temperature-sensitive and optically actuated actuators described above). Also, the BFCE shown in Fig. 14 (a) is just

one example; other BFCE's (for instance with only 3 independent directions of roll-out, or with different particular orientations), can be applied.

Finally, it should be noted that the above-mentioned embodiments illustrate rather than limit the invention, and that those skilled in the art will be capable of designing many alternative embodiments without departing from the scope of the invention as defined by the appended claims. In the claims, any reference signs placed in parentheses shall not be construed as limiting the claims. The word "comprising" and "comprises", and the like, does not exclude the presence of elements or steps other than those listed in any claim or the specification as a whole. The singular reference of an element does not exclude the plural reference of such elements and vice-versa. In a device claim enumerating several means, several of these means may be embodied by one and the same item of software or hardware. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage.

CLAIMS:

1. A device (100) for handling a fluidic sample (101), the device (100) comprising:

- a fluidic structure (102) being divided in a plurality of segments (103);
- a plurality of actuator units (104) arranged on and/or in the fluidic structure (102), wherein each of the plurality of segments (103) comprises at least two of the plurality of actuator units (104);
- an activation unit (105) adapted to address each of the segments (103) individually or simultaneously to force the at least two actuator units (104) of each addressed segment (103) to move in a manner to mix a fluidic sample (101) located in the fluidic structure (102).

2. The device (100) according to claim 1, wherein the fluidic structure (102) comprises at least one of the group consisting of a channel and a well.

3. The device (100) according to claim 1, comprising a substrate (106), wherein the fluidic structure (102) is formed in and/or on the substrate (106).

4. The device (100) according to claim 1, wherein the plurality of actuator units (104) are arranged on and/or in a wall of the fluidic structure (102), particularly on and/or in one of the group consisting of a bottom wall, a top wall and a lateral wall of the fluidic structure (102).

5. The device (100) according to claim 1, wherein the activation unit (105) is adapted to force a first part of the actuator units (104) to move along a first direction and to simultaneously force a second part of the actuator units (104) to move along a second direction, wherein the first direction is different from the second direction, particularly is opposite to the second direction.

6. The device (100) according to claim 1, comprising a fluid transport unit (107) adapted for transporting a fluidic sample (101) along a flowing direction through the fluidic structure (102), wherein the activation unit (105) is adapted to force at least a part of the actuator units (104) to move opposite to the flowing direction of a fluidic sample (101) through the fluidic structure (102) to thereby promote mixing of the fluidic sample (101).

7. The device (400) according to claim 1, wherein the segments are arranged as an alternating sequence of first segments (401) and second segments (402), wherein the activation unit (105) is adapted to address the first segments (401) in common and to separately address the second segments (402) in common.

8. The device (400) according to claim 1, wherein the segments are arranged as an alternating sequence of first segments (401) and second segments (402), wherein a geometrical layout of the actuator units (104) is different for the first segments (401) and second segments (402).

9. The device (400) according to claim 8, wherein the activation unit (105) is adapted such that all segments (401, 402) are addressed in common.

10. The device (100) according to claim 1, wherein the plurality of actuator units (104) are arranged in rows and/or columns.

11. The device (100) according to claim 1, wherein the activation unit (105) is adapted to address the segments (103) in dependence of a present operation parameter of the device (100), particularly in dependence of a viscosity of a fluidic sample (101).

12. The device (100) according to claim 1, wherein at least a part of the plurality of actuator units (104) is configured as a polymeric micro-actuator.

13. The device (100) according to claim 1, wherein at least a part of the plurality of actuator units (104) is an electrostatic activatable polymer composition structure.

14. The device (100) of claim 1, wherein the activation unit (105) is adapted to individually address each of the segments (103) to force the at least two actuator units (100)

assigned to the addressed segment (103) to move relative to each other in a manner to mix a fluidic sample (101) located in the fluidic structure (102).

15. The device (100) of claim 1, adapted as a microfluidic device.

16. The device (100) of claim 1, wherein the plurality of actuator units (104) are adapted as a micro-electro-mechanical system, particularly as a micro-electro-mechanical fluid mixer.

17. The device (100) of claim 1, adapted as at least one of the group consisting of a sensor device, a biosensor device, a biochip, a lab-on-chip, an electrophoresis device, a sample transport device, a sample mix device, a cell lyzing device, a sample washing device, a sample purification device, a sample amplification device, a polymerase chain reaction device, a sample extraction device, and a hybridization analysis device.

18. A method of handling a fluidic sample (101), the method comprising:

- addressing each of a plurality of segments (103) of a fluidic structure (102) individually or simultaneously to force at least two actuator units (104) assigned to each of the addressed segments (103) to move in a manner to mix a fluidic sample (101) located in the fluidic structure (102).

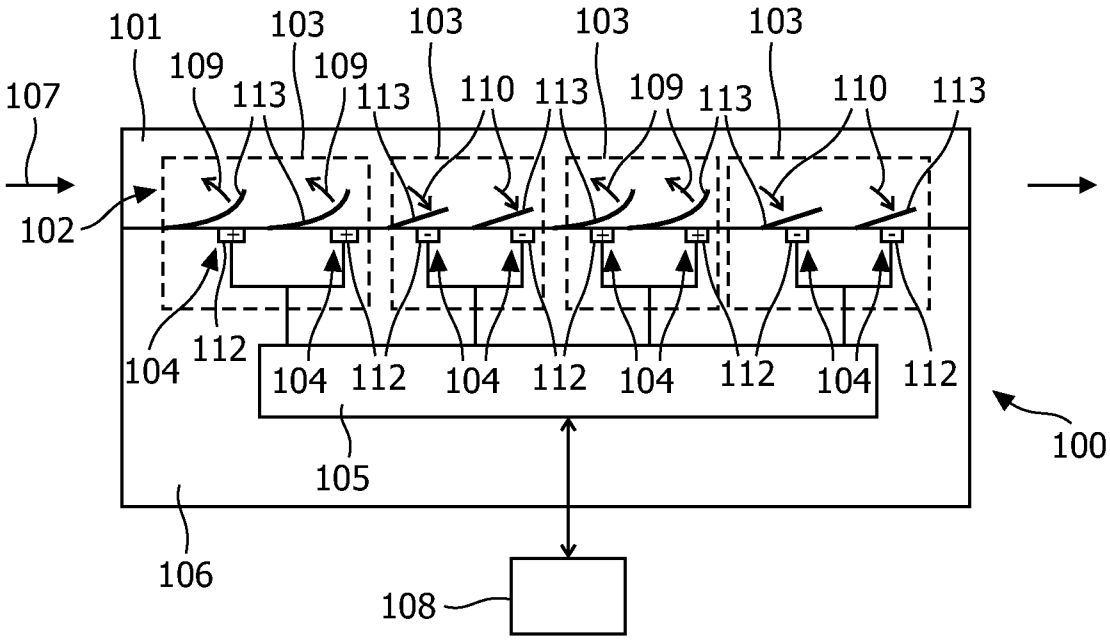


FIG. 1

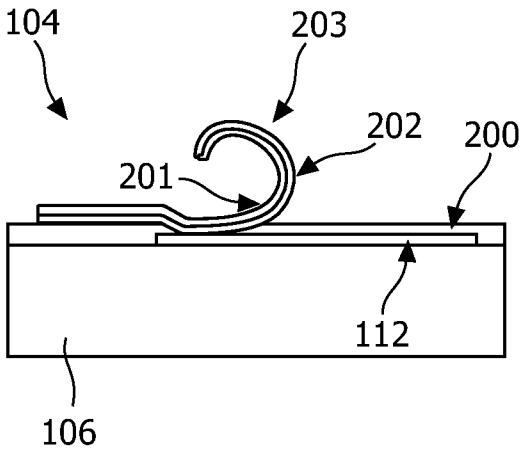


FIG. 2

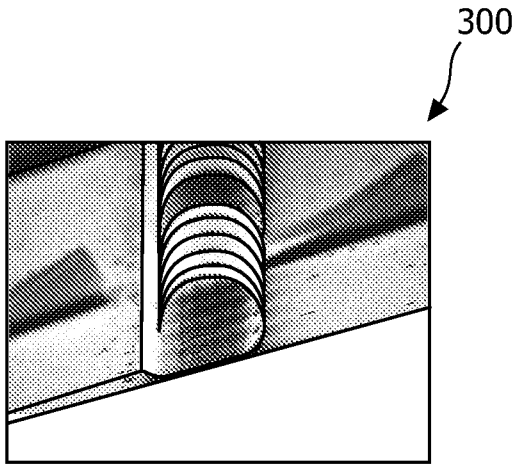


FIG. 3

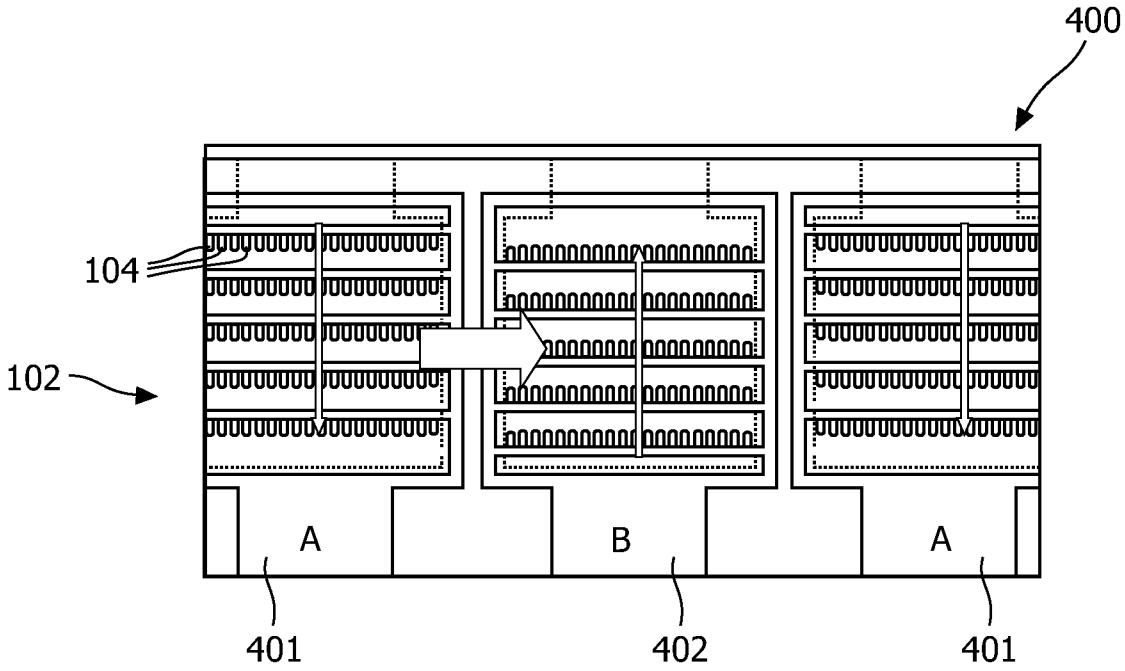


FIG. 4

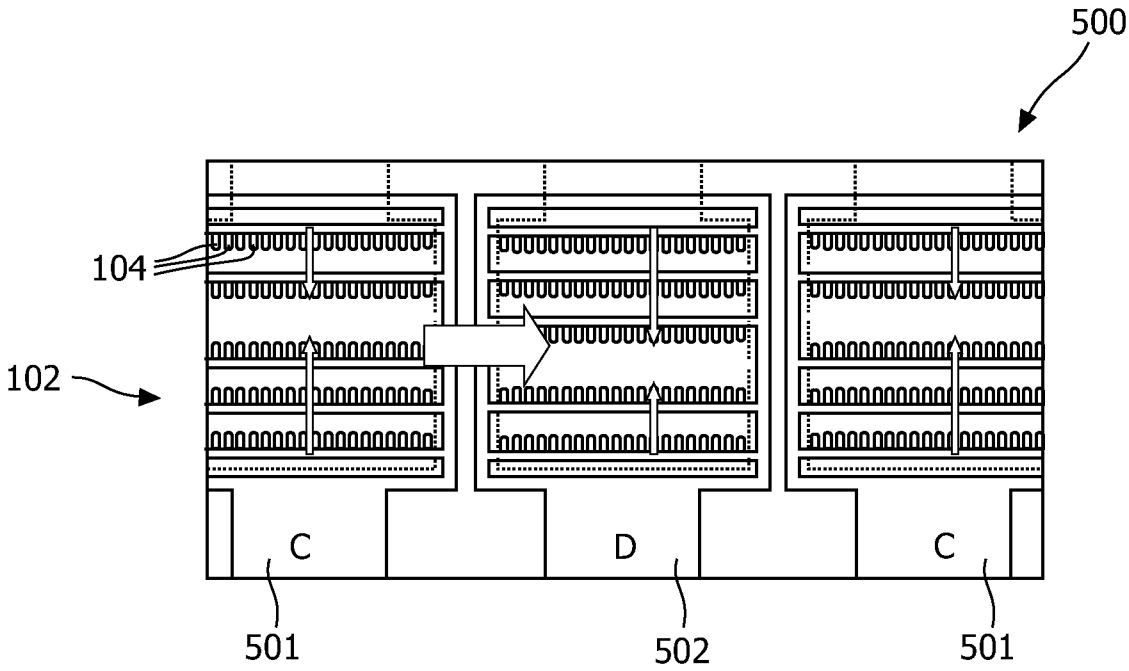


FIG. 5

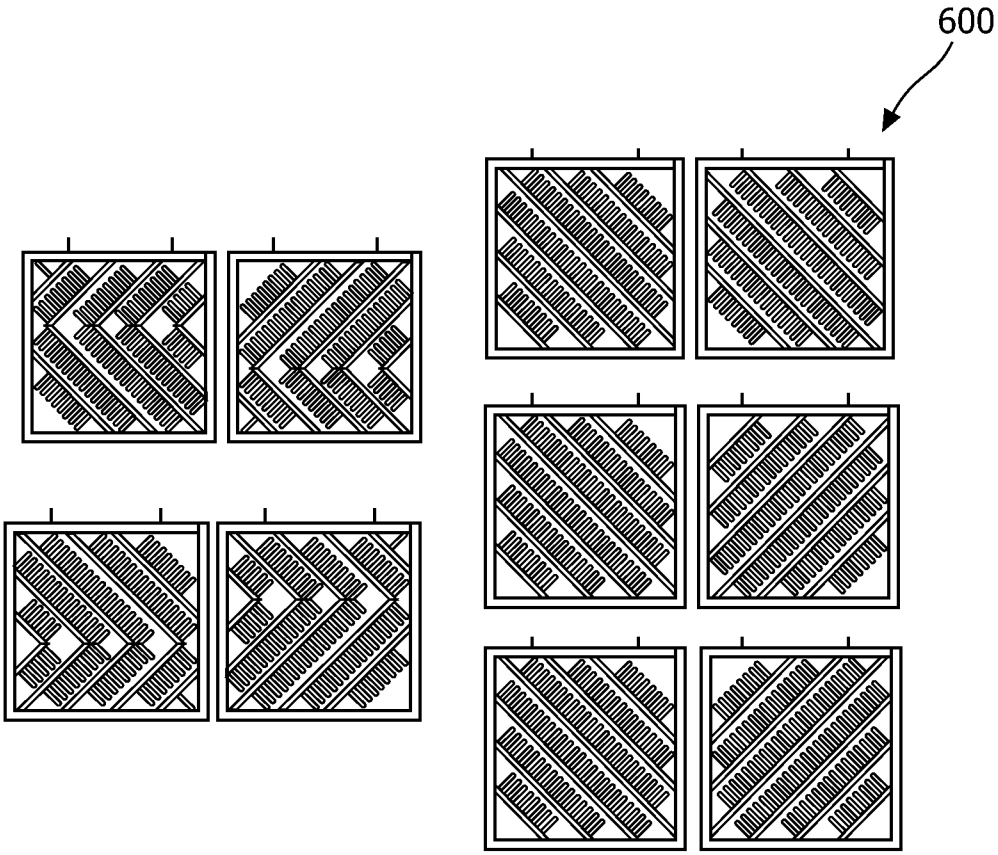


FIG. 6

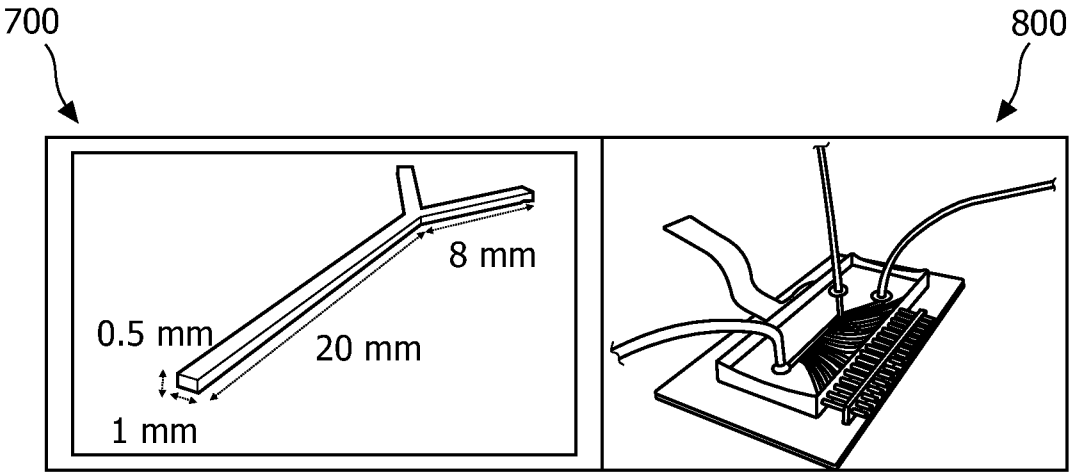


FIG. 7

FIG. 8

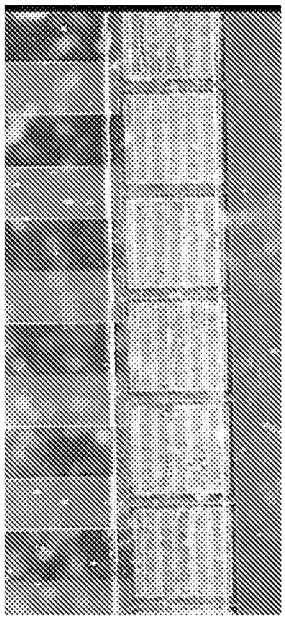


FIG. 10

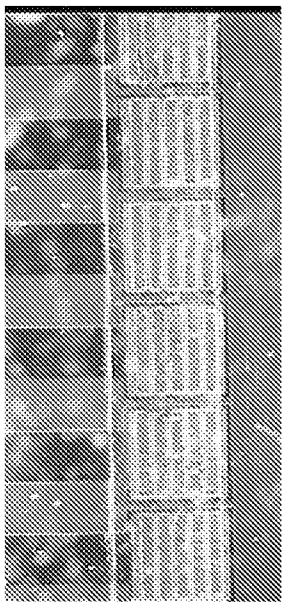
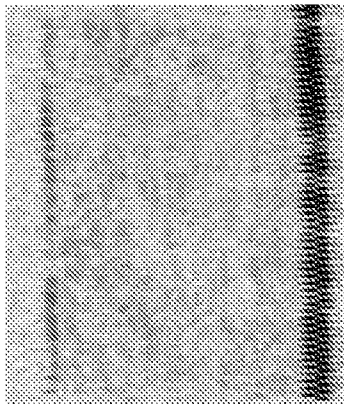


FIG. 9



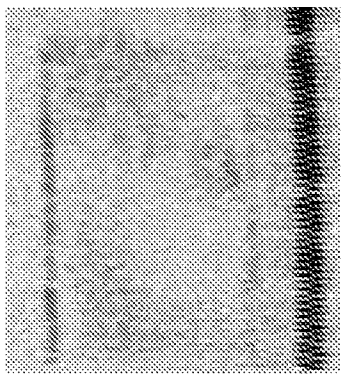
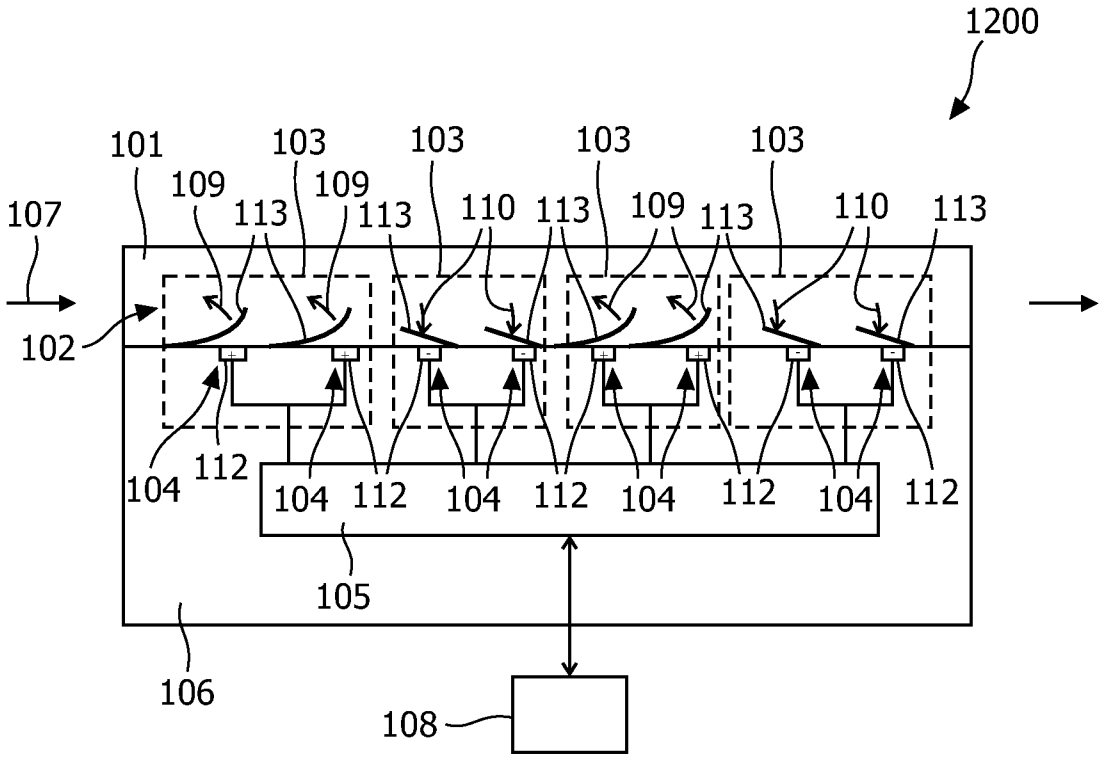


FIG. 11


1200
101
103
103
103
103
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113
113
110
113
109
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107
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112
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112
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112
105
106
108

FIG. 12

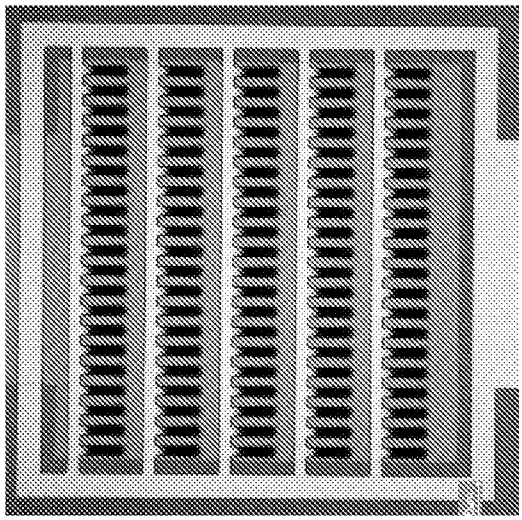

FIG. 13A

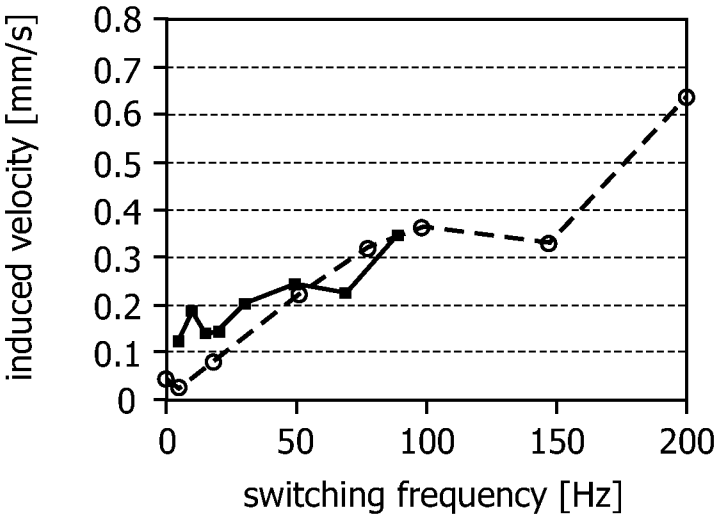

FIG. 13B

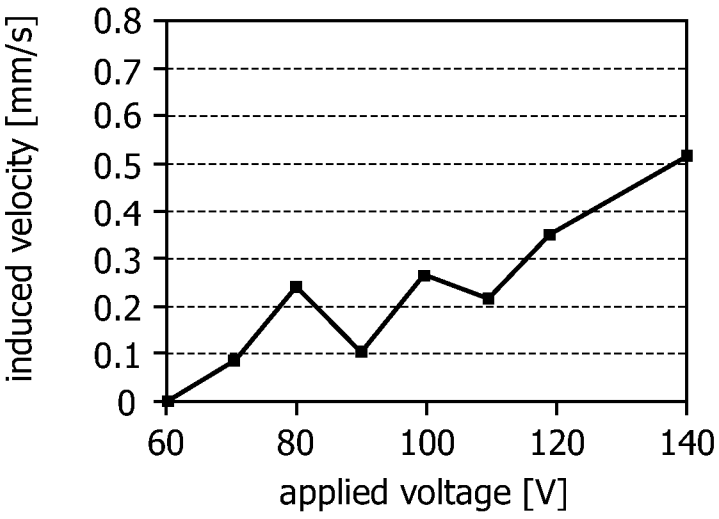

FIG. 13C

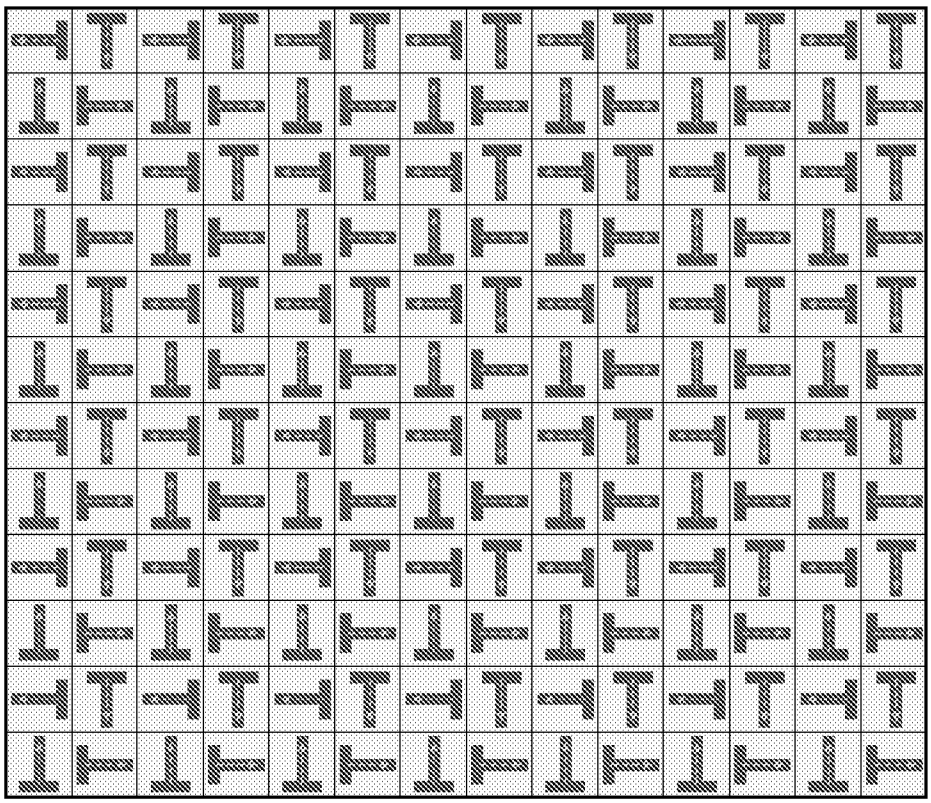

FIG. 14b

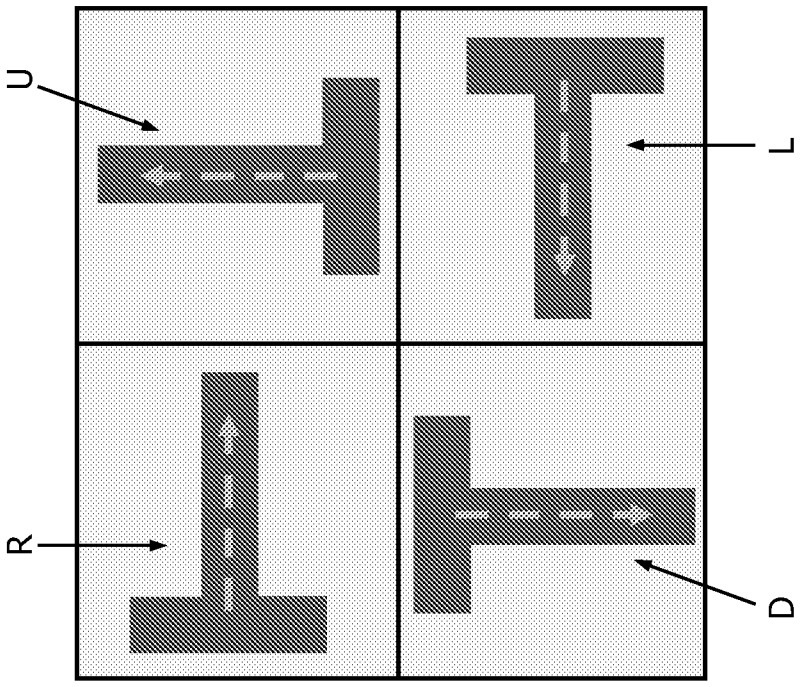

FIG. 14a

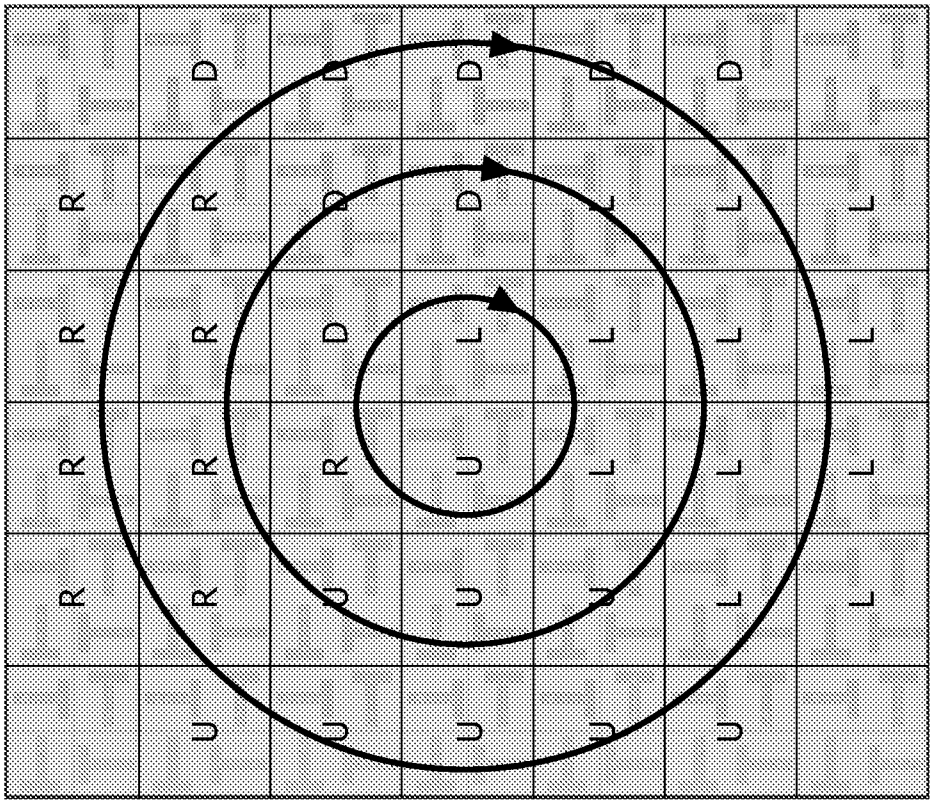

FIG. 15b

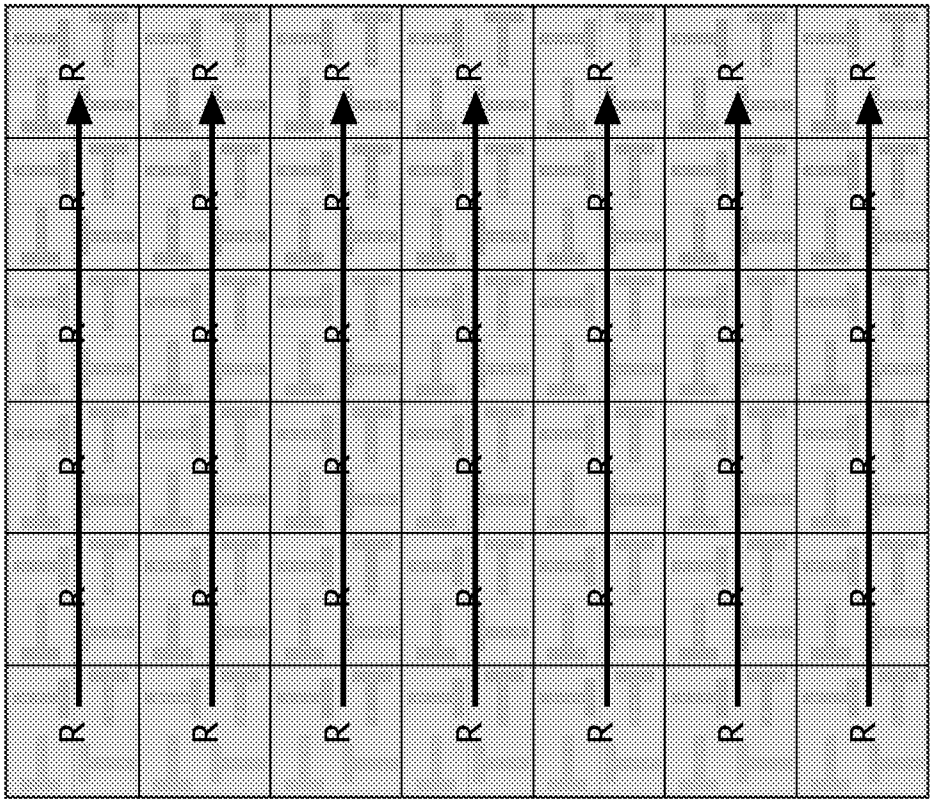

FIG. 15a