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(54) Title: CAPACITIVE BUBBLE DETECTION

(57) Abstract: A system and a method for detecting bubbles in an aqueous solution involve placing the solution onto a measurement area of a glass slide used for performing a life science experiment, the measurement area containing a plurality of electrodes. The slide includes a control unit that measures capacitance values associated with individual ones of the electrodes and/or pairs of the electrodes. A data processing unit receives and analyzes the measured capacitances to identify a presence and a location of a bubble in the solution. The system and the slide can optionally be used to adjust the pH level of the solution using at least some of the electrodes.

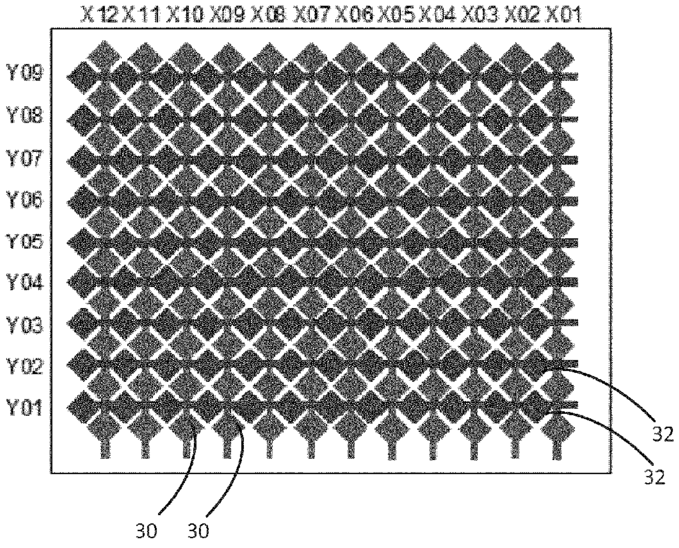

Fig. 2

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CAPACITIVE BUBBLE DETECTION

CROSS-REFERENCE TO RELATED APPLICATION

[0001] The present invention claims the benefit of United States Application Serial No. 61/939,396, filed on February 13, 2014. The contents of this application are incorporated herein by reference.

FIELD OF THE INVENTION

[01] The present invention relates to a method and corresponding devices and systems for detecting the presence of bubbles in an aqueous solution. The present invention also relates to glass slides for performing life science experiments, in which at least some of the processing of data measured at the slide is performed by a computer processor located on the slide or by a processor on a peripheral component connected to a body of, or wirelessly coupled to the slide. The present application relates to U.S. Pat. App. Ser. No. 13/543,300, entitled “Methods for generating pH/ionic concentration gradient near electrode surfaces for modulating biomolecular interactions,” the entire content of which is incorporated herein by reference.

BACKGROUND INFORMATION

[02] Many life science applications (proteomics, genomics, microfluidics, cell culture, etc.) use glass slides as a substrate for performing experiments. Examples of glass slides include protein microarrays, lysate arrays, DNA microarrays and cell culture platforms. One use of a protein microarray is to analyze biological substances (e.g., blood serum) from patients with a specific disease in comparison to corresponding substances from healthy or control subjects. The biological substances are applied to a microarray containing many (often thousands of) human proteins. Antibodies in diseased substances may react (bind) with certain antigens in the microarray, thereby identifying the antigens as disease-specific biomarkers. In addition to protein detection, other types of detection such as colorimetric, chemiluminescence and fluorescence detection are also possible with glass slides.

[03] Often the experiments are performed under aqueous conditions, in which a substance-of-interest is combined with water or a water-containing liquid and placed onto a slide for analysis. In many cases the presence of bubbles (formed of air or other gases) disturbs the experiment, adversely affecting the results. One example of an adverse effect is when a

bubble causes the test solution to dry out. This can create a false binding event where the substance-of-interest (e.g., a biomolecular analyte) fails to bind with a molecule with which the biomolecular analyte is supposed to interact. Another example is where the bubbles change the effective flow rate of the test solution and the flow rate is being measured as part of the experiment. Therefore, it is desirable to detect bubbles and to output an indication of their presence, so that experiment results can be interpreted correctly.

[04] One way to detect bubbles is to manually check each slide under a microscope. However, microscopy is not always practical because the field of view is typically limited to a small area of the slide, so that checking the entire slide is time-consuming. Additionally, the use of light to illuminate the slide under the microscope can sometimes have a destructive effect on the substance-of-interest.

SUMMARY

[05] Example embodiments of the present invention provide a system and method for detecting bubbles in an aqueous solution. The solution is placed onto a measurement area of a slide, the measurement area containing a plurality of electrodes configured to measure capacitance. According to example embodiments, the slide is configured to support measurements of at least one additional type of data in connection with an experiment involving a substance-of-interest contained in the solution. This allows the slide to be used for conventional testing purposes in addition to bubble detection. According to an example embodiment, one or more electrodes are configured for dual functioning so that the one or more electrodes helps facilitate both the conventional testing function and the bubble detection.

[06] According to example embodiments, the slide includes a control unit that measures capacitance values associated with individual ones of the electrodes and/or pairs of the electrodes. The control unit captures the capacitance value(s) for subsequent processing and allows for capturing of bubble detection relevant data, obviating the need to manually check the slide for bubbles.

[07] According to example embodiments, the system and method include analyzing measured capacitances to identify a location of a bubble in the solution. In an example, bubbles are detected based on comparing the value of the capacitances to a threshold value or to other measured capacitances. This allows the location of the bubbles to be determined without user input.

[08] According to example embodiments, the system and method involve displaying bubble locations graphically, preferably as a three-dimensional graph. This allows a user to quickly determine where bubbles are located, without having to manually interpret the measured capacitance values. The user can then determine, based on the bubble indications, whether to keep or discard additional data that is being measured as part of the experiment. In an example, the additional data is automatically invalidated by a computer processor in response to bubble detection, to further reduce user burden.

[09] According to example embodiments, the system and method involve using the slide to adjust the pH level of the solution using at least some of the same electrodes that are used for measuring capacitance in connection with bubble detection. This allows for more efficient usage of the electrodes and provides an additional level of functionality to the slide.

[10] According to example embodiments, the system and method include using a computer processor to perform at least some of the processing required by the system and method, prior to outputting the data to an external computer. The processor is powered by a small power source, on or connectable to the slide. The processor, in combination with the power source, allows routine processing to be performed in a power efficient manner.

BRIEF DESCRIPTION OF THE DRAWINGS

[11] Fig. 1 is a block diagram of a system for bubble detection, according to an example embodiment of the present invention.

[12] Fig. 2 is a top view of an example electrode array, according to an example embodiment of the present invention.

[13] Figs. 3 and 4 show different electrode shapes, according to example embodiments of the present invention.

[14] Figs. 5 and 6 show a simplified electrical model of a slide that provides bubble detection, according to an example embodiment of the present invention.

[15] Figs. 7 to 9 are graphs showing simulated capacitance values with and without the presence of a bubble.

[16] Fig. 10 is a graph showing actual measured capacitance values with and without the presence of a bubble.

[17] Fig. 11 is a flowchart of a method for detecting bubbles, according to an example embodiment of the present invention.

[18] Fig. 12 is a simplified schematic of a circuit for calculating capacitance, according to an example embodiment of the present invention.

[19] Fig. 13 is a flowchart of a method for pH modulation, according to an example embodiment of the present invention.

[20] Figs. 14 to 16 each shows a slide with data processing capability, according to an example embodiment of the present invention.

DETAILED DESCRIPTION

[21] Example embodiments of the present invention relate to the detection of bubbles in glass slides, on which slides an aqueous solution is placed for analysis. However, the example embodiments may also be applied towards other applications in which it is desirable to detect the presence of bubbles. In particular, although the capacitance based detection techniques are described herein in connection with the capacitive properties of water, these techniques may also be applied to other liquids for which the capacitive properties are known.

[22] Fig. 1 shows an example system 100 for detecting bubbles according to an example embodiment of the present invention. In the example shown in Fig. 1, the system 100 includes a slide 30 that includes an area 10 in which a test solution containing a substance-of-interest is placed for analysis, a control unit 12 and a power source 14. The slide 30 can be formed of any transparent and electrically insulating material. For example, glass would typically be used for this purpose and to serve as a substrate, on top of which the area 10, control unit 12 and power source 14 are formed. The glass can be formed, for example, of silicon dioxide (SiO_2), possibly with additives. Alternatively, other types of silicate glasses may be used.

[23] The area 10 includes an array of electrodes used for bubble detection. In an example embodiment, at least some of the electrodes in the area 10 are used for adjusting (also referred to herein as modulating) a pH level of the test solution. These pH modulating electrodes can be dedicated exclusively to adjusting the pH level or, alternatively, switched between pH modulating and bubble detecting modes of operation, as will subsequently be explained. (For example, U.S. Pat. App. Ser. No. 13/543,300, mentioned earlier, describes

the use of electrodes for pH modulation in a biosensor, which modulation can be performed using the electrodes discussed herein.)

[24] Fig. 2 shows a top view of an example electrode array, in which a set of column electrodes X01 to X12 are arranged at regularly spaced distances from each other. A set of row electrodes Y01 to Y09 are also arranged at regularly spaced distances and are separated from the column electrodes X01 to X12, e.g., by an intervening layer of glass. Each electrode includes one or more contact pads 30, 32 for use in bubble detection and/or pH modulation. The shape of the pads is variable and, in an example embodiment, is substantially square. Fig. 3 shows a close-up view of example square-shaped pads. Fig. 4 shows an alternative embodiment in which the pads form an interdigitated structure, and are therefore frame-shaped.

[25] In the example illustrated in Fig. 1, the control unit 12 is electrically connected to the electrode array 10 and controls the array 10 to perform bubble detection and pH modulation. The control unit 12 can be, for example, a microprocessor or an application specific integrated circuit (ASIC). In an example embodiment, the control unit 12 is located on an electronic circuit board that is detachably connected to the slide 30, e.g., using pogo pins. The control unit 12 can be located within a packaged chip bonded directly to a rigid glass substrate, e.g., using a chip-on-glass process. In an alternative example embodiment, the slide 30 is formed of a flexible foil-type substrate and the control unit 12 is glued to the slide 30 using a z-axis adhesive to form a chip-on-foil, in a manner similar to how chips are bonded in certain liquid crystal displays. The control unit 12 can include, for example, a non-transitory computer readable storage medium containing program code that implements the example bubble detection and pH modulation techniques described herein. In addition to bubble detection, the control unit 12 can control the electrodes to perform other types of sensing or to control other sensing structures, as is known in the art of biosensors.

[26] In an example embodiment, the control unit 12 transmits control signals that cause input pulses to be applied at specified electrodes. Capacitance values can be measured at the control unit 12 based on the responses of the electrodes to the input pulses. The measurement of capacitance is known in the art of touch screen displays, which utilize measurements of self-capacitance (e.g., a single electrode) or mutual capacitance (e.g., between two electrodes). To support bubble detection, the control unit 12 has a capacitance detection range that is greater than that of typical control units that measure capacitance in life science

experiments. Control signals can also be used to apply input pulses for pH modulation. Control signals for pH modulation can be initiated by the control unit 12, e.g., in accordance with a predefined program sequence designed for pH modulation. Alternatively, the control signals for pH modulation is initiated externally, e.g., in response to a command from a data processing unit 50. In an example, the control unit 12 includes hardware and/or software components that perform preliminary signal processing on the measured capacitance values, including converting the measurements from analog to digital format and/or filtering the measurements. In an example, the processed measurements are then output as raw data to the data acquisition unit 40.

[27] The power source 14 provides power to the control unit 12 and to the electrode array 10. For example, in an example embodiment, the power source 14 is a battery such as a coin-cell or a printed battery. In one example embodiment, the slide 30 is designed for one-time use and is disposable, the battery therefore being provided with a small energy capacity, e.g., sufficient for a single measurement, and the battery can be permanently attached to the slide, e.g., bonded or glued to the glass surface. In an example embodiment where the slide 30 is reusable, the battery can be rechargeable or user replaceable. Other forms of electric power delivery may alternatively be used. In one example embodiment, electrical power is delivered wirelessly through magnetic coupling between an external power supply (e.g., the data acquisition unit 40) and one or more resonant coils in the slide. As an alternative to magnetic coupling, but also using wireless power transfer, the external power supply may couple to the resonant coil using radio-frequency (RF) signals. In yet another example embodiment, the slide 30 receives power through a wired connection to the data acquisition unit 40.

[28] In an example, the data acquisition unit 40 is a device that communicates with the slide 30 to receive the measured capacitance values from the control unit 12, in the form of raw data. For example, in an example, the data acquisition unit 40 includes a wired communication interface 20 to a corresponding interface in the slide 30. In one example embodiment, the raw data is output from the control unit 12 in parallel. For example, in an example embodiment, the control unit 12 includes a plurality of output channels, with data from a single row or a single column being output on a corresponding channel. In this embodiment, the interface 20, for example, converts the parallel data into a format suitable for transmission to the data processing unit 50. The conversion may involve parallel-to-serial conversion using a Universal Asynchronous Receiver/Transmitter (UART) or other

conventional data conversion apparatus. In an alternative embodiment, the interface 20 communicates wirelessly with the slide 30, e.g., using RF signals.

[29] In an example embodiment, the data processing unit 50 receives the raw data from an output interface 22 of the data acquisition unit 40, e.g., from a transmitter portion of the UART. The output interface 22 can be a wired, serial interface such as a Universal Serial Bus (USB) interface. Alternatively, the output interface 22 can be wireless, e.g., a Bluetooth or WiFi interface. In an example, the interface is a Bluetooth low energy (LE) interface. The data processing unit 50 can be, for example, a general purpose computer in the form of a desktop, a laptop or tablet, and includes, for example, a processor and a memory storing instructions for further processing of the raw data. For example, in an example embodiment, the further processing includes normalizing the raw data to a predefined scale and using the normalized data to generate output images, such as two or three-dimensional graphs, for display at the display device 60. Where the data processing unit 50 is a laptop or tablet, the display device 60 can be integrated into a housing of the data processing unit 50 as a single unit. The display device 60 may alternatively be externally connected, e.g., where the data processing unit 50 is a desktop. The output images may be combined to form a video that shows changes in the data over time. In one embodiment, the output images, which represent the measured capacitance values, are displayed together with additional output images corresponding to other measured data. For example, the output images and the additional output images may be displayed in different portions of the same display screen or overlaid (superimposed) on the same portion of the display screen.

[30] In an example embodiment, the data processing unit 50 is also configured to issue commands to the control unit 12 for pH modulation. The commands may be automatically generated, e.g., when a processor of the data processing unit 50 determines that the pH level of the test solution should be adjusted. Alternatively or additionally, the commands may be user-initiated.

[31] According to an example embodiment, the slide 30 may include a layered structure in which one or more electrode layers are located on top of a glass substrate. The layered structure can be formed, for example, using a lamination technique in which two or more layers are formed separately and then laminated together, e.g., using adhesive or bonding. Alternatively, the layered structure can be monolithically formed as a single unit, using techniques known in the art of semiconductor device fabrication. The layered structure may

include one or more passivating layers formed, e.g., of SiO_2 (also referred to as oxide). However, it will be understood that the composition and size of passivating layers can vary, e.g., from an atomic layer of SiO_2 to several micrometers of SiO_2, and formed using various techniques such as low pressure chemical vapor deposition (LPCVD) or plasma-enhanced chemical vapor deposition (PECVD). Silicon nitride (Si_3N_4) is another example passivating material. Where the layered structure is formed using lamination, the passivating layer can be formed as a thin film that is laminated.

[32] The capacitance based bubble detection principles used in the example embodiments of the present invention will now be described with reference to Figs. 5 to 10. Fig. 5 shows a simplified electrical model of a slide including electrodes (ITOs 81 to 84) in an SiO_2 layer 73. The ITOs 81 and 82 represent electrode pads in a first layer, e.g., row electrode pads. The ITOs 83 and 84 represent electrode pads in a second layer beneath the first layer, e.g., column electrode pads. The ITOs 81 to 84 are formed above a glass substrate 79, with an optional ITO layer 89 that serves as a bottommost, passivating layer. For simplicity, the portion of the electrode array used for pH modulation in certain example embodiments is not shown. In this simplified model, the capacitance of the test solution is assumed to be equivalent to the capacitance of water (CW) since the test solution is, in practice, mostly water. When there is no bubble over the electrodes, the solution is in contact with the SiO_2 layer 73 and contributes to a series capacitance between ITOs 81 and 82. The SiO_2 layer 73 also contributes to the series capacitance, as represented by two capacitances $CSiO_2$.

[33] The pH modulating portion of the electrode array has been omitted for the sake of simplicity. One way to perform pH modulation is to separate the pads of adjacent electrodes so as to form channels that collect the test solution. The channels allow the test solution to come into contact with the electrodes, so that the pH level of the solution can be adjusted by sending a current between the adjacent electrodes. According to an example embodiment, the electrodes may be formed of any suitable conductive material, but are preferably indium tin oxide (ITO) because ITO is transparent and relatively colorless, making it suitable for experiments that involve optical measurements. This allows the entire measurement area 10 to be transparent. An oxide layer may be used as a passivating layer to cover the electrodes, similar to how the SiO_2 layer 73 covers the electrodes in Figs. 5 and 6. In fact, the same oxide layer may be used over the electrodes in both the bubble detecting and the pH modulation portions of the electrode array. Where the pH modulation is implemented using channels, in an example embodiment, the oxide layer does not completely fill the channels,

but instead a lateral portion of the electrodes is left exposed to allow for contact with the test solution.

[34] Fig. 6 shows additional details regarding the electrical model of Fig. 5 according to an example embodiment. In Fig. 6, the series capacitances are collectively represented as a mutual capacitance CL1,L1 between ITOs 81 and 82. Additionally, there exists a mutual capacitance between ITOs 81 and 83. In an example embodiment, bubbles are detected as a change in capacitance (e.g., in either of these mutual capacitances or in a self-capacitance) that results when the test solution is displaced by a bubble, which is typically formed of air. Since air has a much lower capacitance (the dielectric strength of air is approximately eighty times less than water), it is possible to detect a drop in capacitance associated with the presence of a bubble. This detection assumes that there is no electric field on top of the bubble which would minimally interfere with capacitance measurements. It also assumes that the size of the bubble is comparable to the pad, such that most of the surface of the pad is covered by the bubble, i.e., that no or almost no test solution is in contact with the pad. In practice, electromagnetic interference may create electric fields. Interference can be avoided through setup of an appropriate, low interference testing environment. As for bubble size, in practice the size will vary dramatically and it is unavoidable that sometimes a bubble will be smaller than the pad. To minimize the occurrence of bubbles that are smaller, each pad may be sized as small as possible while balancing performance parameters such as power consumption and maintaining inter-operative compatibility with the control unit 12. In one embodiment the pads are less than 2 millimeters wide, preferably 1 millimeter or less. This is substantially smaller than the size of electrodes typically used for conventional touch-screen applications or conventional bio-sensor applications.

[35] Fig. 7 is a simulated graph of self-capacitance along the x direction (from the top surface of the slide towards the glass substrate) when water covers a pad, in an example embodiment. The graph of Fig. 7 was generated based on a square pad of size 1 mm x 1 mm. As shown, the capacitance decreases continuously from a value of approximately 2 x 10^{-11} Farads at 10^{-6} meters down to approximately 7 x 10^{-14} Farads at 10^{-3} meters.

[36] Fig. 8 is a simulated graph of self-capacitance along the x direction when a bubble having a diameter of 1 millimeter is present on a 1 mm x 1 mm pad, in an example embodiment. As shown, the capacitance values are substantially smaller than the corresponding capacitance values from Fig. 7 between 10^{-6} and 10^{-3} meters. Specifically, the

capacitance starts at approximately 7.6 x 10^{-14} Farads and drops beginning around 3 x 10^{-5} meters to approximately 5 x 10^{-14} Farads. Therefore, the capacitance with water is several orders of magnitude greater for the majority of points between 10^{-6} and 10^{-3} meters. Accordingly, one way to detect bubbles, according to an example embodiment of the present invention, is based on an evaluation of the value or the magnitude of a capacitance at any given pad, e.g., by comparing the value or magnitude to a predefined threshold value. A bubble would then correspond to a capacitance that is less than the threshold. Figs. 7 and 8 are provided to illustrate basic electromagnetic principles by which example embodiments of the present invention detect bubbles based on changes in capacitance, and are not to be construed as restricting the range of capacitance detection techniques that may be applicable to a system or method of the present invention.

[37] Another way to detect bubbles is based on the percentage change in capacitance from water to a bubble. The simulated graph in Fig. 9, whose values were calculated using the values from Figs. 7 and 8, shows this difference in an example embodiment. In Fig. 9, the percentage change is initially small, but starts to increase at around 10^{-5} meters. Therefore, detection may be based on the percentage change if the pads are suitably located, e.g., at a distance of 10^{-5} meters or more from the top surface of the slide.

[38] In addition or as an alternative to evaluating the capacitance on an individual basis (e.g., for each pad when evaluating self-capacitance or for a pair of pads when evaluating mutual-capacitance), detection can be based on a comparison of capacitance values associated with a plurality of pads, according to an example embodiment. For example, according to an example embodiment, capacitance values from a group of neighboring pads are compared to determine whether any of the capacitance values is unusually small relative to the other capacitance values. This comparison is advantageous because it does not require the use of a threshold value, which may need to be adjusted based on the design of the slide, e.g., parameters such as pad size, shape or location.

[39] Fig. 10 is a graph showing actual test results from a prototype slide of an example embodiment. The graph shows mutual capacitance values between a column electrode and a row electrode. A bubble was manually introduced at the intersection of these electrodes, beginning at around 50 seconds. The bubble was then removed and another bubble introduced at around 75 seconds. This process was repeated again, with another bubble at

around 90 seconds. Each time a bubble was introduced, the capacitance dropped substantially.

[40] Control units exist for acquiring capacitance measurements in connection with touch-screen applications. However, these control units are generally unsuitable for use with the bubble detection according to the example embodiments of the present invention. These conventional control units are unsuitable because they tend to have a narrower detection range and lower sensitivity than what is required for the example embodiments. In contrast, bubble detection according to the example embodiments requires the ability to capture large capacitance swings (e.g., a 400 pF change in going from water to bubble) in addition to a high resolution in order to capture the low capacitance values associated with bubbles. A typical capacitance value range for when a bubble exists could be between 20 fF to 40 μF. The large range is due to the fact that many choices are available as to the size of the electrodes and the thickness of the passivation layer on top of the electrodes (e.g., SiO_2, TiO_2, nitride, or no passivation layer at all).

[41] Fig. 11 is a flowchart of a method 200 for detecting bubbles according to an example embodiment of the present invention. According to an example embodiment, the method 200 is performed using the system 100.

[42] At step 210, a capacitance (self or mutual) is measured at an electrode or between two electrodes to measure a capacitance value and the value is output as raw data. For example, in an example embodiment, the measurement is performed by outputting a control signal from the control unit 12, which control signal results in the application of an input pulse to an electrode being measured. The control unit 12 senses the electrical response of the electrode, e.g., by measuring a voltage or a current across the electrode, or between the electrode and another electrode, and calculates the capacitance as a function of this response. The calculation of self and mutual capacitances is known in the art of touch screen displays. Each measured capacitance can be output as a raw data value to the data processing unit 50 using the data acquisition unit 40.

[43] Fig. 12 is a simplified schematic of a circuit 201 for measuring capacitance according to an example embodiment of the present invention, and is provided in support of the method 200. The circuit 201 includes a decoder 220, which may be included in the control unit 12 of Fig. 1. The decoder 220 is connected via a plurality of driving lines 203, over which the decoder 220 sends signals to activate switches 240. The switches 240 may be implemented

as thin-film transistors (TFTs) and are switched to connect to respective electrodes 242 that form the electrode array. The switches 240 are controlled by the decoder 220 to perform the capacitance measurements, e.g., by driving a specific line 203 simultaneously with an adjacent line 203. The switches 240 are further connected to sensing lines 205, which in this example, form the columns of the array. Each sensing line 205 is connected to a respective amplifier 230. The amplifiers 230 are in a negative feedback configuration with a sensing line 205 and a capacitor 99 being connected to a negative amplifier input, which is also connected to ground via a current source 235. A positive input of each amplifier 230 is connected to reference voltage 233, which may also be ground. The voltages on the sensing lines 205 are influenced by the capacitances at the electrodes, which capacitances depend on whether a bubble is present. Thus, the voltage outputs of the amplifiers 230 correspond to measured capacitances.

[44] Returning to Fig. 11, at step 212, the measured capacitance is compared to a threshold value. As mentioned above, the threshold value may vary depending on factors such as pad size, shape or location. However, given the design specifications of the slide, and in view of the above discussion on the bubble detection principles, one of ordinary skill in the art would be able to compute a suitable threshold value.

[45] Alternatively or additionally, at step 214 the measured capacitance is compared to other measured capacitances, e.g., from a group of neighboring electrodes or the entire set of electrodes in the array, to detect unusually low capacitances.

[46] At step 216, the results of the comparisons are evaluated at the data processing unit 60 to determine, based on the bubble detection principles described earlier, whether any bubbles exist, and if so, where the bubbles are located.

[47] At step 218, the results are output for display at the display device 60. According to an example embodiment, raw data values are displayed in the form of a two-dimensional table. Each table entry corresponds to a measured capacitance value obtained from a corresponding electrode pad. The raw data may be displayed as a three-dimensional graph, e.g., a 3-D mesh where the x and y values correspond to electrode locations and the z values correspond to measured capacitance values. To facilitate visual recognition, in an example embodiment, the graph is color coded, e.g., using a gradient scheme, e.g., a gray scale scheme or a heat map in which the color gradually changes until a bubble location is reached, at which point the color is changed to a color that contrasts the color(s) of non-bubble locations.

In another embodiment, color coding is used to show bubble locations on a two-dimensional graph in which the capacitance values are represented using changes in color. Alternatively or additionally to the display of raw data, the data processing unit 60, according to an example embodiment, processes the raw data by normalizing it to a predefined scale. The above described graphs can be displayed alone or together with additional values from other parameters that are the subject of the experiment, e.g., pH value, flow rate, etc. In one embodiment, the additional values are displayed on the same graph, e.g., using a different color scheme and superimposed onto the capacitance values.

[48] Advantageously, the graphical display of the capacitance values allows a user to quickly determine where bubbles are located, and to take appropriate corrective action in response to the presence of bubbles. The user may decide, for example, to keep those additional values (corresponding to one or more parameters being measured by the experiment) which are not associated with the locations of detected bubbles, while discarding values associated with bubble locations. Alternatively, the user may decide that the entire set of data should be discarded because there are too many bubbles, thus making the additional values unreliable as a whole.

[49] According to an example embodiment, the capacitance values are superimposed onto additional measurement data, which additional data is stored in association with layout data representing the physical configuration of the measurement area. The layout data may be stored in an electronic file in the form of an image (e.g., a scanned image of the measurement area) or text (e.g., a configuration file for a microarray spotter used to fabricate the array, or a GenePix Array List (GAL) file). The additional measurement data may also be image or text (e.g., measured pH values stored in a GAL file or measured pH values rendered in grayscale on a scanned image of the measurement area).

[50] According to an example embodiment in which the capacitance values are superimposed, a composite display may be generated in step 218, which display shows a graphical representation of the array together with the capacitance values superimposed onto the additional measurement values at corresponding locations in the array. The superimposition can be rendered as text-on-text, text-on-image or image-on-image. An example of text-on-text is displaying a capacitance value in one half of an array location and additional measurement data in the other half. An example of text-on-image is displaying the capacitances using a heat map while representing the additional measurement data as

numerical values on the heat map. An example of image-on-image is displaying the capacitances using a heat map while representing the additional measurement data using a 3-D mesh. Superimposed data may be stored in the electronic layout file, prior to or in conjunction with the superimposed display.

[51] According to an example embodiment, a processor on the slide or on an external computer is configured to automatically invalidate the additional measurement data (e.g., by replacing measurement values with null values) in response to detecting bubbles. For example, the processor on the slide may detect bubble locations and output an indication of where the bubbles are located to the external computer, which then performs the invalidating based on the indicated locations. This spares the user from having to manually review the capacitance values to decide whether to keep the additional measurement data.

[52] According to an example embodiment, bubble detection is combined with pH modulation. Fig. 13 is a flowchart of a method 300 for pH modulation according to an example embodiment of the present invention. According to an example embodiment, the method 300 is performed using the system 100.

[53] At step 310, a pair of electrodes that are not currently being used for bubble detection are switched to a pH modulation mode of operation by applying an input signal, e.g., a pulsed current between the electrodes. Preferably, the switches that control the mode of operation of the electrodes are implemented using TFTs, e.g., formed using amorphous silicon, polysilicon or indium gallium zinc oxide (IgZo). An advantage to using thin-film transistors is that the total capacitance of each electrode and its corresponding circuitry is reduced, thereby increasing the speed of measurement in addition to circumventing the need for thick oxides on the electrodes.

[54] To perform bubble detection, an input pulse can be applied, for example, to a single electrode. The input pulse for bubble detection may, but need not be identical in shape, magnitude or duration to the input pulse used for pH modulation. Changes in capacitance between water contact and bubble contact are detected by observing the electric response of the same electrode or in the case of mutual capacitance, the response of another electrode.

[55] The input signal applied at step 310 for pH modulation may be applied during a time in which the input pulse for the bubble detection is not being applied. As mentioned above, the input pulse for pH modulation is applied between a pair of electrodes. This produces a

current that, through oxidation and reduction of buffer components (e.g., quinones), changes the pH level of a test solution situated between the electrodes.

[56] At step 312, the input signal is ended before the electrodes are to be used again for bubble detection.

[57] At step 314, the pH level of the test solution is measured to determine whether additional adjustment is required. Where the slide is configured for pH level measurement, the pH level can be calculated at the control unit 12. Alternatively, the pH level can be measured using a separate testing device.

[58] At step 316, the input signal is reapplied by the control unit 12 in response to determining that further adjustment of the pH level is required. In one embodiment, the control unit 12 is configured to apply the input signal multiple times, as a plurality of pH modulating pulses, before determining whether further adjustment is required. The plurality of pH modulating pulses can be applied to the same pair of electrodes or to a different electrode pair. Similarly, the input signal may be reapplied at step 316 to the same or a different pair of electrodes. For example, the pH modulating pulses may be applied to different electrode pairs in a sequential manner so that the entire electrode array is triggered over time to perform pH modulation.

[59] According to an example embodiment, the electrodes can be used to perform functions in addition to bubble detection and pH modulation. For example, electrodes can be used for temperature modulation. As another example, the capacitance measurements can be used to estimate the dielectric constant of the test solution, which dielectric constant is then correlated to a rate of cell growth or a rate with which the substance-on-interest binds to a biomolecule.

[60] Example embodiments were described in which the electrodes were arranged in two layers (Figs. 5 and 6). However, it will be understood that the number of layers can be more or less. In fact, a single layer may be sufficient for both pH modulation and bubble detection. Additionally, not every electrode layer needs to be used for pH modulation or bubble detection. Instead, further electrode layers can be used for other purposes, in accordance with the usage of electrodes in conventional biosensors.

[61] Example embodiments of the present invention relate to glass slides with at least some of the processing of measurement data being performed on the slide itself or on a peripheral device connected to a body of the slide, rather than at an external computer

responsible for displaying the processed data. Such slides are referred to herein as an instrument-on-glass. Figs. 14 to 16 each shows an example embodiment of an instrument-on-glass.

[62] Fig. 14 shows a slide 400 according to an example embodiment of the present invention. The slide 400 includes a measurement area 405, a power source 410 and a processing circuit 420. The measurement area 405 may be formed of TFTs (for the switches) together with ITO (for the electrodes). Alternatively, the measurement area 405 may be formed using only ITO or ITO in combination with other metals. The power source 410 is analogous to the power source 14 in Fig. 1 and may be a battery or a passive power source powered, e.g., using magnetic or RF coupling.

[63] The processing circuit 420 is analogous to the control unit 12 in Fig. 1 and may perform preliminary signal processing. Additionally, the processing circuit 420 may perform some of the functions described earlier with respect to the data processing unit 50 (e.g., normalizing or scaling capacitance values or controlling pH modulation). The processing circuit 420 may include a processor (e.g., one or more CMOS chips) that processes the raw data obtained from measurement area 405. The processing circuit 420 may further include a memory storing instructions or data, used by the processor to process the raw data. The processing circuit 420 may be configured to arrange the raw data into a suitable format for output to an external computer, or to perform preliminary data analysis (e.g., bubble detection and invalidating data associated with bubbles). The processor may control the sensing operation of the measurement area 405 (e.g., driving and reading data out of the array), perform data compression, and perform wired or wireless transmission of the preliminarily processed data to an external computer. Post-processing and output of the data for display may be performed at the external computer.

[64] Fig. 15 shows a slide 500 according to an example embodiment of the present invention. The components 505, 510 and 520 are analogous to and perform the same functions as the components 405, 410 and 420, respectively, in Fig. 14. However, instead of being located on the body of the slide 500, the power source 510 and the processing circuit 520 are externally connected, e.g., on a peripheral circuit board 515 that fits into a hardware interface of the slide 500.

[65] Fig. 16 shows a slide 600 according to an example embodiment of the present invention. The components 605, 610 and 620 are analogous to and perform the same

functions as the components 405, 410 and 420, respectively, in Fig. 14. In the embodiment of Fig. 16, the power source 610 and the processing circuit are externally connected, similar to Fig. 15. However, the circuit board 615 includes a serial port connector for transmission of data and power between the board 615 and the external computer. Specifically, the serial port may be used to transfer measurement data to the external computer, and to supply power for operating the measurement area 605 or for recharging the power source 610.

[66] An example embodiment of the present invention is directed to one or more processors, which can be implemented using any conventional processing circuit and device or combination thereof, e.g., a Central Processing Unit (CPU) of a Personal Computer (PC) or other workstation processor, to execute code provided, e.g., on a non-transitory hardware computer-readable medium including any conventional memory device, to perform any of the methods described herein, alone or in combination, e.g., to output any one or more of the described graphical user interfaces. The memory device can include any conventional permanent and/or temporary memory circuits or combination thereof, a non-exhaustive list of which includes Random Access Memory (RAM), Read Only Memory (ROM), Compact Disks (CD), Digital Versatile Disk (DVD), flash memory and magnetic tape.

[67] An example embodiment of the present invention is directed to a non-transitory, hardware computer-readable medium, e.g., as described above, on which are stored instructions executable by a processor to perform any one or more of the methods described herein.

[68] An example embodiment of the present invention is directed to a method, e.g., of a hardware component or machine, of transmitting instructions executable by a processor to perform any one or more of the methods described herein.

[69] Example embodiments of the present invention are directed to one or more of the above-described methods, e.g., computer-implemented methods, alone or in combination.

[70] The above description is intended to be illustrative, and not restrictive. Those skilled in the art can appreciate from the foregoing description that the present invention may be implemented in a variety of forms, and that the various embodiments can be implemented alone or in combination. Therefore, while the embodiments of the present invention have been described in connection with particular examples thereof, the true scope of the embodiments and/or methods of the present invention should not be so limited since other modifications will become apparent to the skilled practitioner upon a study of the drawings,

specification, and the claims below. Further, steps illustrated in the flowcharts may be omitted and/or certain step sequences may be altered, and, in certain instances multiple illustrated steps may be simultaneously performed.

WHAT IS CLAIMED IS:

1. A slide arrangement for detecting bubbles in an aqueous solution, comprising:

a measurement area of a slide configured to receive the aqueous solution, the measurement area including a plurality of electrodes; and

a control unit configured to:

measure capacitance values associated with at least one of individual ones of the electrodes and pairs of the electrodes; and

determine, based on the measured capacitance values:

whether a bubble is present in the aqueous solution; and

where a bubble is present, a location of the bubble in the aqueous solution.

2. The slide arrangement of claim 1, wherein the control unit is configured to control at least some of the electrodes to adjust a pH level of the aqueous solution.

3. The slide arrangement of claim 2, wherein the control unit is configured to switch the at least some of the electrodes between a pH level adjusting mode and a bubble detection mode.

4. The slide arrangement of claim 2, wherein the control unit is configured to adjust the pH level by causing an input signal to be applied between two of the at least some of the electrodes, the input signal generating an electric current through the aqueous solution.

5. The slide arrangement of claim 1, wherein the slide includes a plurality of channels in which the at least some of the electrodes are exposed to the aqueous solution.

6. The slide arrangement of claim 5, wherein non-channel portions of the slide are isolated from the aqueous solution by a layer of passivating material.

7. The slide arrangement of claim 1, wherein the electrodes are arranged in a plurality of layers, each layer located at a different depth from a surface of the slide that contacts the aqueous solution.

8. The slide arrangement of claim 7, wherein the electrode layers are on top of a glass substrate, the electrode layers being one of laminated to and monolithic with the glass substrate.

9. The slide arrangement of claim 1, wherein the measurement area is transparent.

10. The slide arrangement of claim 9, wherein the electrodes are formed from a layer of indium tin oxide above a glass substrate.

11. The slide arrangement of claim 1, further comprising an output arrangement that is configured to transmit the measured capacitance values to an external data acquisition device.

12. The slide arrangement of claim 1, wherein the control unit is detachably connected to the slide.

13. The slide arrangement of claim 1, further comprising a power source that is configured to supply power to the electrodes and to the control unit.

14. The slide arrangement of claim 13, wherein the power source includes one of a battery and a resonant coil coupled to an external power supply through magnetic or radio frequency signals.

15. The slide arrangement of claim 1, wherein the control unit is configured to:
obtain additional data sensed by the electrodes; and
invalidate the additional data in response to determining that a bubble is present.

16. The slide arrangement of claim 1, wherein:

the control unit is one of located on a body of the slide and located on a peripheral device attached to the slide; and

the control unit processes the capacitance values before transmitting the processed capacitance values to an external computer.

17. A system for detecting bubbles in an aqueous solution, comprising:

a slide including a measurement area configured to receive the aqueous solution, the measurement area including a plurality of electrodes;

a control unit configured to:

measure capacitance values associated with at least one of individual ones of the electrodes and pairs of the electrodes;

determine, based on the measured capacitance values, whether a bubble is present in the aqueous solution; and

where a bubble is present, determine a location of the bubble in the aqueous solution; and

a data processing unit configured to generate output data from the measured capacitance values and transmit the output data for display at a display device.

18. The system of claim 0, wherein the data processing unit is configured to normalize the measured capacitance values to a predefined scale prior to generating the output data.

19. The system of claim 0, wherein the data processing unit is configured to generate the output data in the form of a graph in which two dimensions of the graph respectively represent row and column locations on the measurement area, the measured capacitance values being represented against the two dimensions.

20. The system of claim 19, wherein the graph is three-dimensional and the third dimension of the graph represents the measured capacitance values.

21. The system of claim 0, wherein the data processing unit is configured to transmit additional measurement data for simultaneous display with the output data at the display device.

22. The system of claim 21, wherein the data processing unit is configured to cause the additional measurement data to be superimposed on a single graph with the output data.

23. The system of claim 22, wherein the data processing unit stores the superimposed data together in an electronic file that describes a layout of the slide.

24. The system of claim 0, wherein the data processing unit is configured to identify bubble locations and format the output data so that the bubble locations are marked on the display device.

25. The system of claim 24, wherein the data processing unit is configured to mark the bubble locations by applying a color scheme to the measured capacitance values, according to which scheme the bubble locations are displayed in a different color than non-bubble locations.

26. The system of claim 0, wherein the data processing unit is configured to generate the output data over a period of time so that the output data is displayed as a series of video images that show changes in the measured capacitance values over the period of time.

27. The system of claim 0, wherein:

the control unit is configured to obtain additional data sensed by the electrodes; and

one of the control unit and the data processing unit invalidates the additional data in response to a determining, by the control unit, that a bubble is present.

28. The system of claim 0, wherein:

the control unit is one of located on a body of the slide and located on a peripheral device attached to the slide; and

the control unit processes the capacitance values before transmitting the processed capacitance values to the data processing unit.

29. A computer-implemented method for detecting bubbles in an aqueous solution, comprising:

receiving, by a computer processor, a plurality of measured capacitance values obtained using electrodes arranged along a surface to which the aqueous solution is applied, the measured capacitances associated with at least one of individual ones of the electrodes and pairs of the electrodes; and

analyzing, by the processer, the measured capacitances to identify a presence and a location of a bubble in the aqueous solution.

30. The method of claim 29, further comprising:

identifying the location of the bubble based on a measured value that is less than a predefined threshold capacitance value associated with the presence of water.

31. The method of claim 29, further comprising:

identifying the location of the bubble based on a measured value for which the difference between the measured value and a capacitance value associated with the presence of water is greater than a predefined percentage.

32. The method of claim 29, further comprising:

identifying the location of the bubble based on a measured value that is substantially lower compared to measured capacitances obtained from a group of neighboring electrodes.

33. The method of claim 29, further comprising:

outputting the measured capacitances for display such that the bubble location is marked on a display.

34. The method of claim 33, wherein the bubble location is marked by applying a color scheme to the measured capacitance values, according to which scheme the bubble locations are displayed in a different color than non-bubble locations.

35. The method of claim 33, further comprising:

outputting additional measurement data for simultaneous display with the output data.

36. The method of claim 35, wherein the additional measurement data is superimposed on a single graph with the output data.

37. The method of claim 36, further comprising:

storing the superimposed data together in an electronic file that describes a layout of the electrodes.

38. The method of claim 29, further comprising:

controlling at least some of the electrodes to adjust a pH level of the aqueous solution.

39. The method of claim 38, further comprising:

switching the at least some of the electrodes between a pH level adjusting mode and a bubble detection mode.

40. The method of claim 38, wherein the controlling includes adjusting the pH level by causing an input signal to be applied between two of the at least some of the electrodes, the input signal generating an electric current through the aqueous solution.

41. The method of claim 29, further comprising:

obtaining additional data sensed by the electrodes; and

invalidating the additional data in response to a determining that a bubble is present.

42. A data processing unit for detecting bubbles in an aqueous solution, the data processing unit comprising:

an arrangement configured to receive a plurality of measured capacitance values obtained using electrodes arranged along a surface to which the aqueous solution is applied, the measured capacitances associated with at least one of individual ones of the electrodes and pairs of the electrodes; and

a computer processor configured to analyze the measured capacitances to identify a presence and location of a bubble in the aqueous solution.

43. The data processing unit of claim 42, wherein the processor is configured to identify the location of the bubble as corresponding to a measured value that is less than a predefined threshold capacitance value associated with the presence of water.

44. The data processing unit of claim 42, wherein the processor is configured to identify the location of the bubble as corresponding to a measured value for which the difference between the measured value and a capacitance value associated with the presence of water is greater than a predefined percentage.

45. The data processing unit of claim 42, wherein the processor is configured to identify the location of the bubble as corresponding to a measured value that is substantially lower compared to measured capacitances obtained from a group of neighboring electrodes.

46. The data processing unit of claim 42, wherein the processor is configured to output the measured capacitances for display such that the bubble location is marked on a display.

47. The data processing unit of claim 46, wherein the processor is configured to mark the bubble location by applying a color scheme to the measured capacitance values, according to which scheme the bubble locations are displayed in a different color than non-bubble locations.

48. The data processing unit of claim 46, wherein the processor is configured to output additional measurement data for simultaneous display with the output data.

49. The data processing unit of claim 48, wherein the processor is configured to invalidate the additional measurement data in response to determining that a bubble is present.

50. The data processing unit of claim 48, wherein the processor is configured to superimpose the additional measurement data on a single graph with the output data.

51. The data processing unit of claim 50, wherein the processor is configured to store the superimposed data together in an electronic file that describes a layout of the electrodes.

52. The data processing unit of claim 42, wherein the processor is configured to control at least some of the electrodes to adjust a pH level of the aqueous solution.

53. The data processing unit of claim 52, wherein the processor is configured to cause the at least some of the electrodes to be switched between a pH level adjusting mode and a bubble detection mode.

54. The data processing unit of claim 52, wherein the processor is configured to adjust the pH level by causing an input signal to be applied between two of the at least some of the electrodes, the input signal generating an electric current through the aqueous solution.

55. A non-transitory computer readable medium storing program code that, when executed by a computer processor, causes the processor to perform a method for detecting bubbles in an aqueous solution, the method comprising:

receiving a plurality of measured capacitance values obtained using electrodes arranged along a surface to which the aqueous solution is applied, the measured capacitances associated with at least one of individual ones of the electrodes and pairs of the electrodes; and

analyzing the measured capacitances to identify a presence and a location of a bubble in the aqueous solution.

AMENDED CLAIMS
received by the International Bureau on 24 June 2015 (24.06.2015)

What is claimed is:

1. A slide arrangement for detecting bubbles in an aqueous solution, comprising:

a measurement area of a slide configured to receive the aqueous solution, the measurement area including a plurality of electrodes;

a power source that is configured to supply power to the electrodes and to the control unit,

wherein the power source includes one of a battery and a resonant coil coupled to an external power supply through magnetic or radio frequency signals; and

a control unit configured to:

measure capacitance values associated with at least one of individual ones of the electrodes and pairs of the electrodes; and

determine, based on the measured capacitance values:

whether a bubble is present in the aqueous solution; and

where a bubble is present, a location of the bubble in the aqueous solution.

2. The slide arrangement of claim 1, wherein the control unit is configured to control at least some of the electrodes to adjust a pH level of the aqueous solution.

3. The slide arrangement of claim 2, wherein the control unit is configured to switch the at least some of the electrodes between a pH level adjusting mode and a bubble detection mode.

4. The slide arrangement of claim 2, wherein the control unit is configured to adjust the pH level by causing an input signal to be applied between two of the at least some of the electrodes, the input signal generating an electric current through the aqueous solution.

5. The slide arrangement of claim 1, wherein the slide includes a plurality of channels in which the at least some of the electrodes are exposed to the aqueous solution.

6. The slide arrangement of claim 5, wherein non-channel portions of the slide are isolated from the aqueous solution by a layer of passivating material.

7. The slide arrangement of claim 1, wherein the electrodes are arranged in a plurality of layers, each layer located at a different depth from a surface of the slide that contacts the aqueous solution.

8. The slide arrangement of claim 7, wherein the electrode layers are on top of a glass substrate, the electrode layers being one of laminated to and monolithic with the glass substrate.

9. The slide arrangement of claim 1, wherein the measurement area is transparent.

10. The slide arrangement of claim 9, wherein the electrodes are formed from a layer of indium tin oxide above a glass substrate.

11. The slide arrangement of claim 1, further comprising an output arrangement that is configured to transmit the measured capacitance values to an external data acquisition device.

12. The slide arrangement of claim 1, wherein the control unit is detachably connected to the slide.

13. (Canceled)

14. (Canceled)

15. The slide arrangement of claim 1, wherein the control unit is configured to:
obtain additional data sensed by the electrodes; and
invalidate the additional data in response to determining that a bubble is present.

16. The slide arrangement of claim 1, wherein:

the control unit is one of located on a body of the slide and located on a peripheral device attached to the slide; and

the control unit processes the capacitance values before transmitting the processed capacitance values to an external computer.

17. A system for detecting bubbles in an aqueous solution, comprising:

a slide including a measurement area configured to receive the aqueous solution, the measurement area including a plurality of electrodes;

a control unit configured to:

measure capacitance values associated with at least one of individual ones of the electrodes and pairs of the electrodes;

determine, based on the measured capacitance values, whether a bubble is present in the aqueous solution; and

where a bubble is present, determine a location of the bubble in the aqueous solution;

a power source that is configured to supply power to the electrodes and to the control unit,

wherein the power source includes one of a battery and a resonant coil coupled to an external power supply through magnetic or radio frequency signals; and

a data processing unit configured to generate output data from the measured capacitance values and transmit the output data for display at a display device.

18. The system of claim 17 wherein the data processing unit is configured to normalize the measured capacitance values to a predefined scale prior to generating the output data.

19. The system of claim 17, wherein the data processing unit is configured to generate the output data in the form of a graph in which two dimensions of the graph respectively represent row and column locations on the measurement area, the measured capacitance values being represented against the two dimensions.

20. The system of claim 19, wherein the graph is three-dimensional and the third dimension of the graph represents the measured capacitance values.

21. The system of claim 17, wherein the data processing unit is configured to transmit additional measurement data for simultaneous display with the output data at the display device.

22. The system of claim 21, wherein the data processing unit is configured to cause the additional measurement data to be superimposed on a single graph with the output data.

23. The system of claim 22, wherein the data processing unit stores the superimposed data together in an electronic file that describes a layout of the slide.

24. The system of claim 17, wherein the data processing unit is configured to identify bubble locations and format the output data so that the bubble locations are marked on the display device.

25. The system of claim 24, wherein the data processing unit is configured to mark the bubble locations by applying a color scheme to the measured capacitance values, according to which scheme the bubble locations are displayed in a different color than non-bubble locations.

26. The system of claim 17, wherein the data processing unit is configured to generate the output data over a period of time so that the output data is displayed as a series of video images that show changes in the measured capacitance values over the period of time.

27. The system of claim 17, wherein:

the control unit is configured to obtain additional data sensed by the electrodes; and

one of the control unit and the data processing unit invalidates the additional data in response to a determining, by the control unit, that a bubble is present.

28. The system of claim 17, wherein:

the control unit is one of located on a body of the slide and located on a peripheral device attached to the slide; and

the control unit processes the capacitance values before transmitting the processed capacitance values to the data processing unit.

29. A computer-implemented method for detecting bubbles in an aqueous solution, comprising:

receiving, by a computer processor, a plurality of measured capacitance values obtained using electrodes arranged along a surface to which the aqueous solution is applied, the measured capacitances associated with at least one of individual ones of the electrodes and pairs of the electrodes; and

analyzing, by the processer, the measured capacitances to identify a presence and a location of a bubble in the aqueous solution.

30. The method of claim 29, further comprising:

identifying the location of the bubble based on a measured value that is less than a predefined threshold capacitance value associated with the presence of water.

31. The method of claim 29, further comprising:

identifying the location of the bubble based on a measured value for which the difference between the measured value and a capacitance value associated with the presence of water is greater than a predefined percentage.

32. The method of claim 29, further comprising:

identifying the location of the bubble based on a measured value that is substantially lower compared to measured capacitances obtained from a group of neighboring electrodes.

33. The method of claim 29, further comprising:

outputting the measured capacitances for display such that the bubble location is marked on a display.

34. The method of claim 33, wherein the bubble location is marked by applying a color scheme to the measured capacitance values, according to which scheme the bubble locations are displayed in a different color than non-bubble locations.

35. The method of claim 33, further comprising:

outputting additional measurement data for simultaneous display with the output data.

36. The method of claim 35, wherein the additional measurement data is superimposed on a single graph with the output data.

37. The method of claim 36, further comprising:

storing the superimposed data together in an electronic file that describes a layout of the electrodes.

38. The method of claim 29, further comprising:

controlling at least some of the electrodes to adjust a pH level of the aqueous solution.

39. The method of claim 38, further comprising:

switching the at least some of the electrodes between a pH level adjusting mode and a bubble detection mode.

40. The method of claim 38, wherein the controlling includes adjusting the pH level by causing an input signal to be applied between two of the at least some of the electrodes, the input signal generating an electric current through the aqueous solution.

41. The method of claim 29, further comprising:

obtaining additional data sensed by the electrodes; and

invalidating the additional data in response to a determining that a bubble is present.

42. A data processing unit for detecting bubbles in an aqueous solution, the data processing unit comprising:

an arrangement configured to receive a plurality of measured capacitance values obtained using electrodes arranged along a surface to which the aqueous solution is applied, the measured capacitances associated with at least one of individual ones of the electrodes and pairs of the electrodes; and

a computer processor configured to analyze the measured capacitances to identify a presence and location of a bubble in the aqueous solution.

43. The data processing unit of claim 42, wherein the processor is configured to identify the location of the bubble as corresponding to a measured value that is less than a predefined threshold capacitance value associated with the presence of water.

44. The data processing unit of claim 42, wherein the processor is configured to identify the location of the bubble as corresponding to a measured value for which the difference between the measured value and a capacitance value associated with the presence of water is greater than a predefined percentage.

45. The data processing unit of claim 42, wherein the processor is configured to identify the location of the bubble as corresponding to a measured value that is substantially lower compared to measured capacitances obtained from a group of neighboring electrodes.

46. The data processing unit of claim 42, wherein the processor is configured to output the measured capacitances for display such that the bubble location is marked on a display.

47. The data processing unit of claim 46, wherein the processor is configured to mark the bubble location by applying a color scheme to the measured capacitance values, according to which scheme the bubble locations are displayed in a different color than non-bubble locations.

48. The data processing unit of claim 46, wherein the processor is configured to output additional measurement data for simultaneous display with the output data.

49. The data processing unit of claim 48, wherein the processor is configured to invalidate the additional measurement data in response to determining that a bubble is present.

50. The data processing unit of claim 48, wherein the processor is configured to superimpose the additional measurement data on a single graph with the output data.

51. The data processing unit of claim 50, wherein the processor is configured to store the superimposed data together in an electronic file that describes a layout of the electrodes.

52. The data processing unit of claim 42, wherein the processor is configured to control at least some of the electrodes to adjust a pH level of the aqueous solution.

53. The data processing unit of claim 52, wherein the processor is configured to cause the at least some of the electrodes to be switched between a pH level adjusting mode and a bubble detection mode.

54. The data processing unit of claim 52, wherein the processor is configured to adjust the pH level by causing an input signal to be applied between two of the at least some of the electrodes, the input signal generating an electric current through the aqueous solution.

55. A non-transitory computer readable medium storing program code that, when executed by a computer processor, causes the processor to perform a method for detecting bubbles in an aqueous solution, the method comprising:

receiving a plurality of measured capacitance values obtained using electrodes arranged along a surface to which the aqueous solution is applied, the measured capacitances associated with at least one of individual ones of the electrodes and pairs of the electrodes; and

analyzing the measured capacitances to identify a presence and a location of a bubble in the aqueous solution.

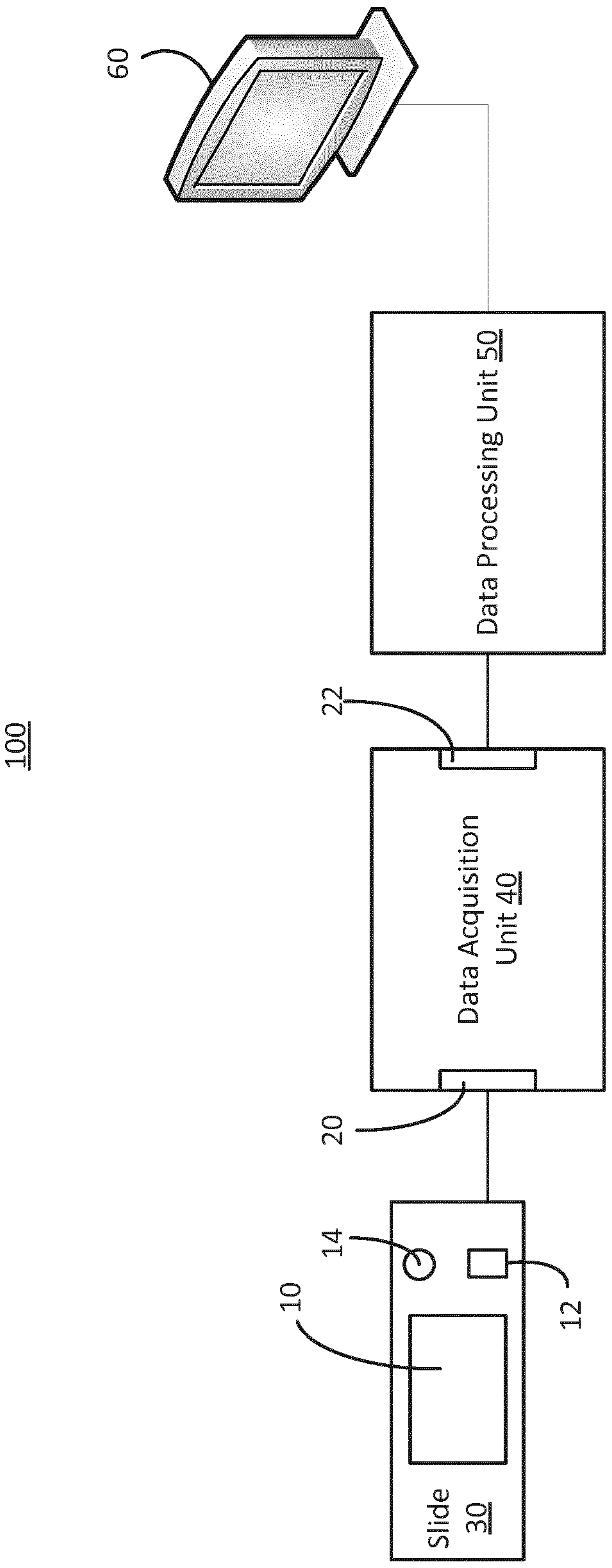
100
Slide 30
10
14
12
20
Data Acquisition Unit 40
22
Data Processing Unit 50
60

Fig. 1

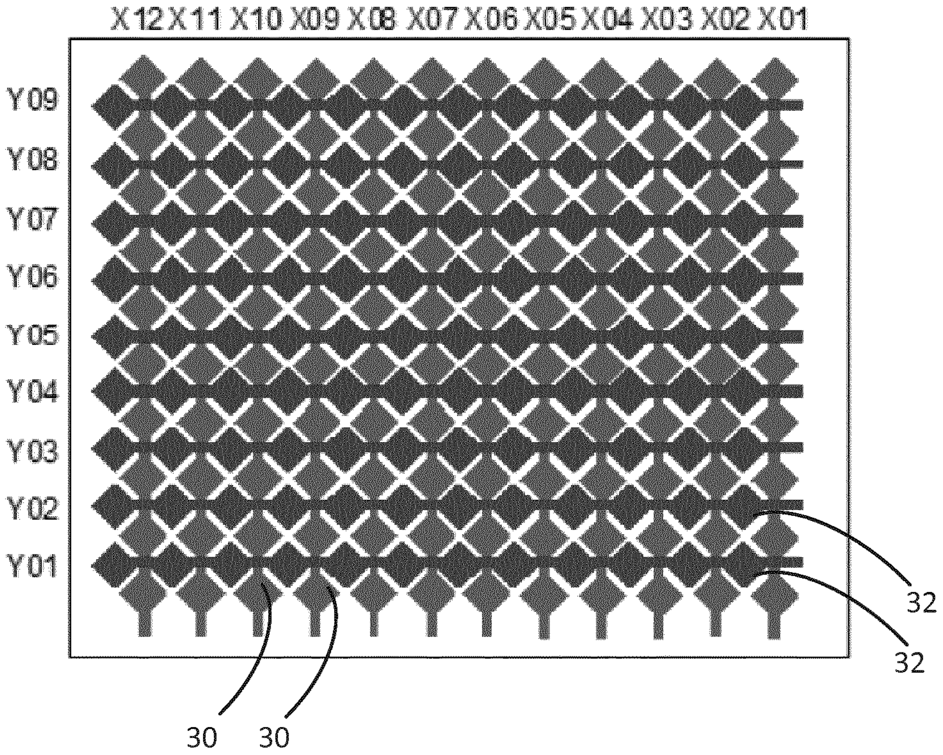
X12
X11
X10
X09
X08
X07
X06
X05
X04
X03
X02
X01
Y09
Y08
Y07
Y06
Y05
Y04
Y03
Y02
Y01
32
32
30
30

Fig. 2

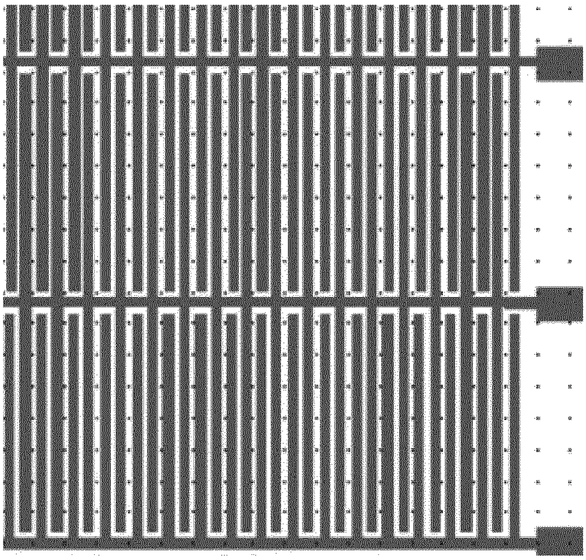

Fig. 4

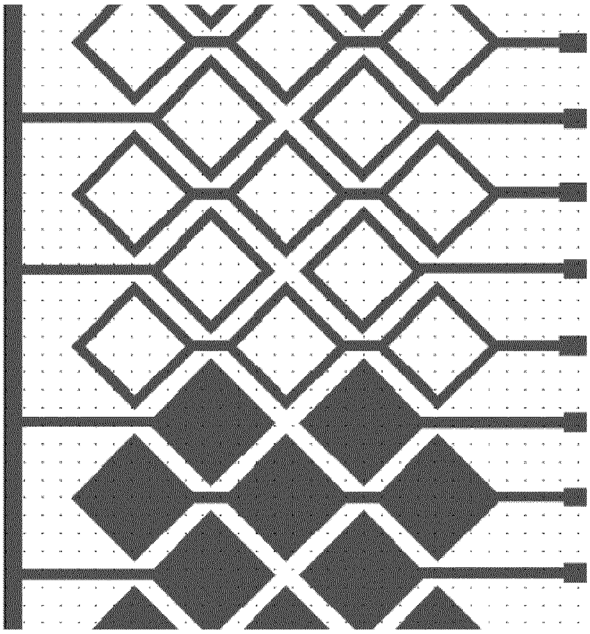

Fig. 3

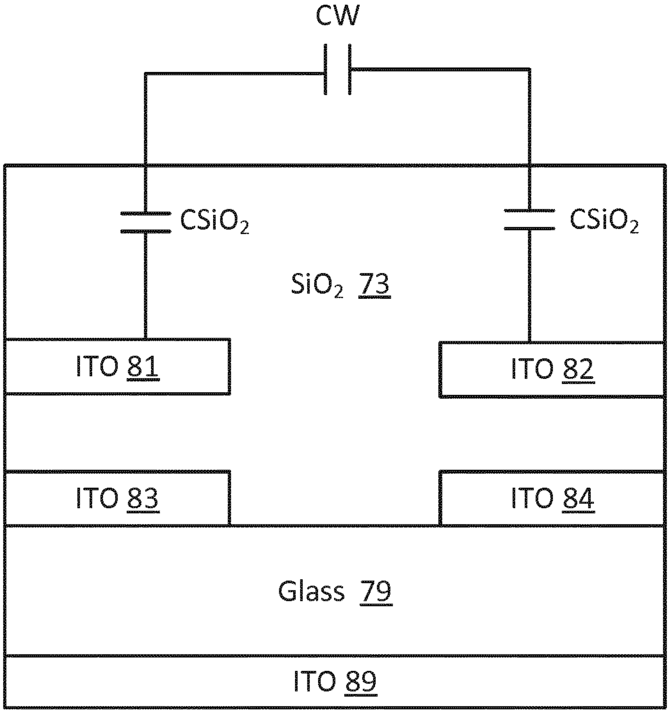
CW
CSiO₂
CSiO₂
SiO₂ 73
ITO 81
ITO 82
ITO 83
ITO 84
Glass 79
ITO 89

Fig. 5

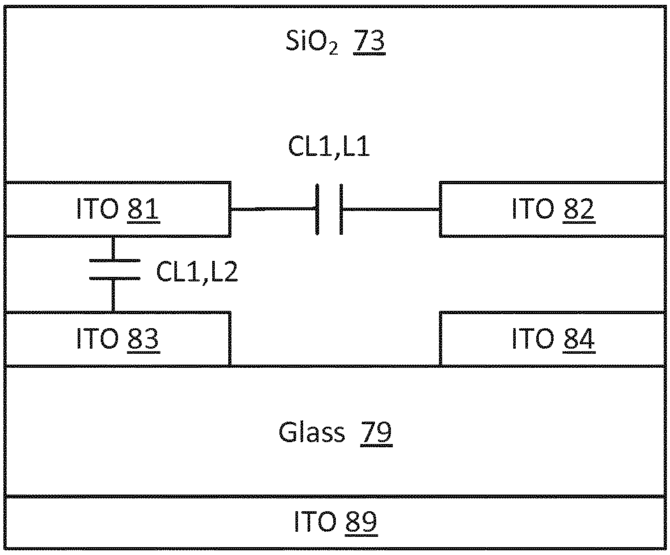
SiO₂ 73
CL1,L1
ITO 81
ITO 82
CL1,L2
ITO 83
ITO 84
Glass 79
ITO 89

Fig. 6

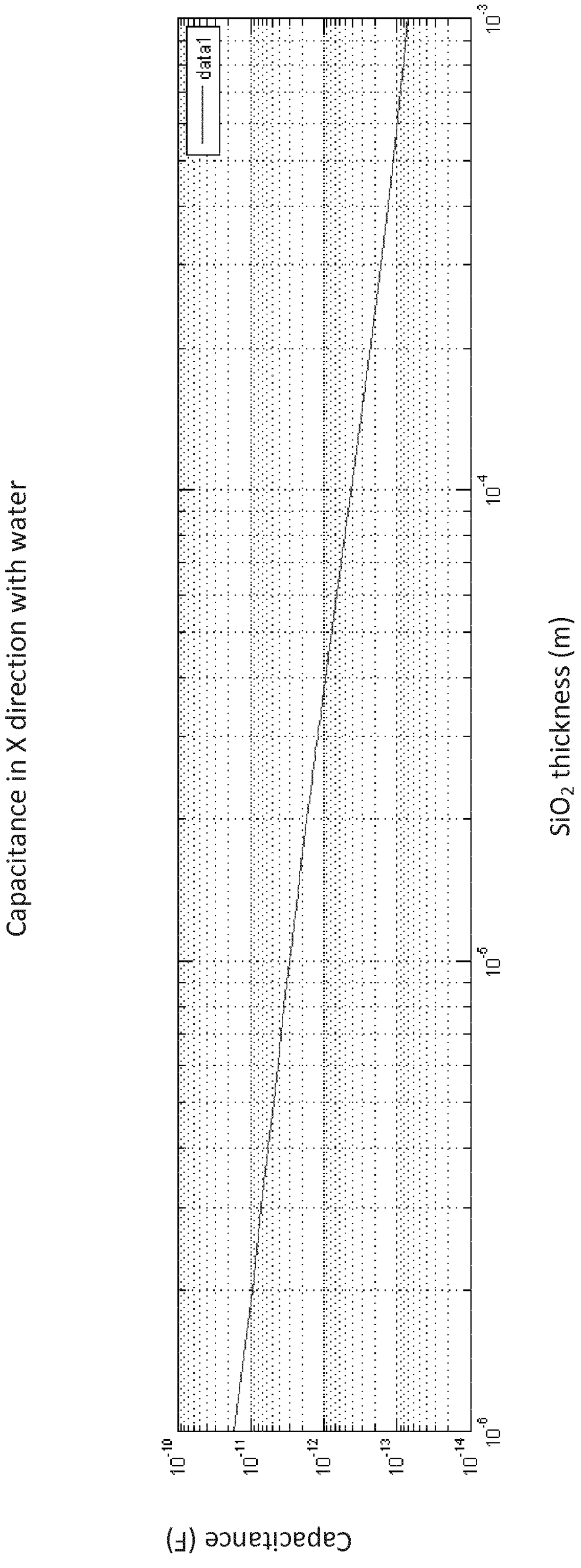
Capacitance in X direction with water
data1
Capacitance (F)
10^{-10}
10^{-11}
10^{-12}
10^{-13}
10^{-14}
10^{-6}
10^{-5}
10^{-4}
10^{-3}
SiO$_2$ thickness (m)

Fig. 7

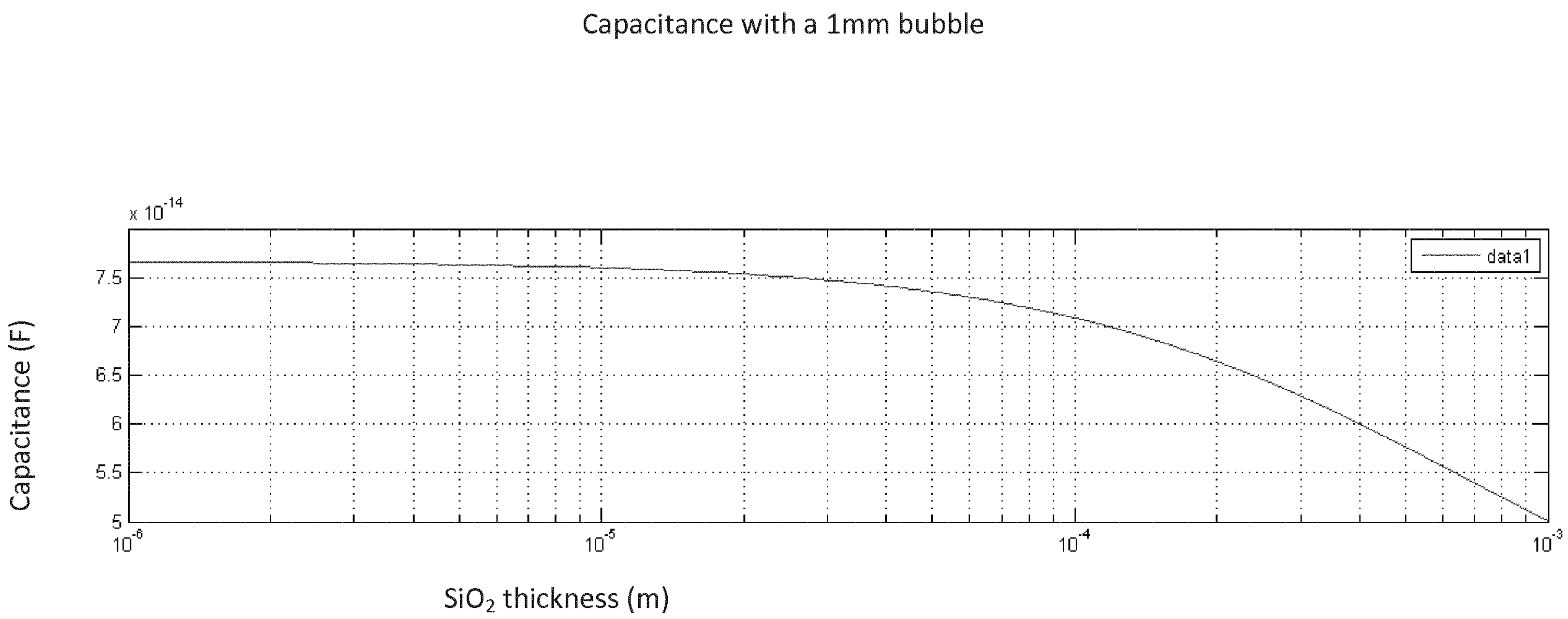
Capacitance with a 1mm bubble
x 10^{-14}
7.5
7
6.5
6
5.5
5
Capacitance (F)
10^{-6}
10^{-5}
10^{-4}
10^{-3}
SiO_2 thickness (m)
data1

Fig. 8

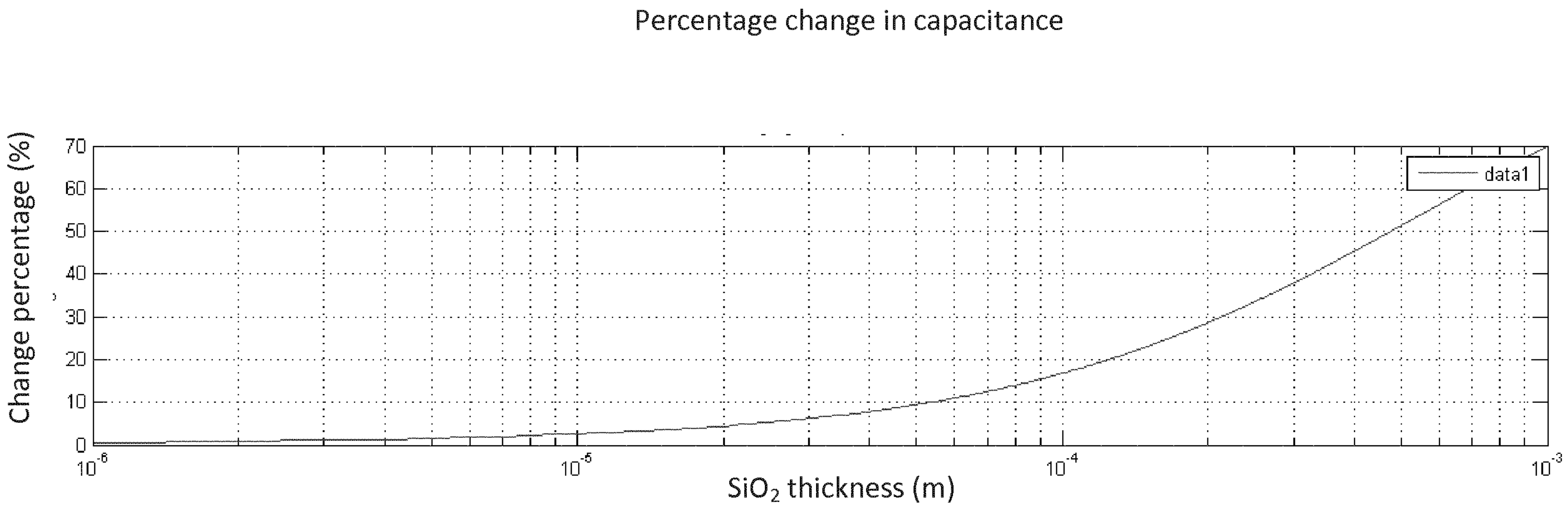
Percentage change in capacitance
data1
Change percentage (%)
70
60
50
40
30
20
10
0
10^{-6}
10^{-5}
10^{-4}
10^{-3}
SiO_2 thickness (m)

Fig. 9

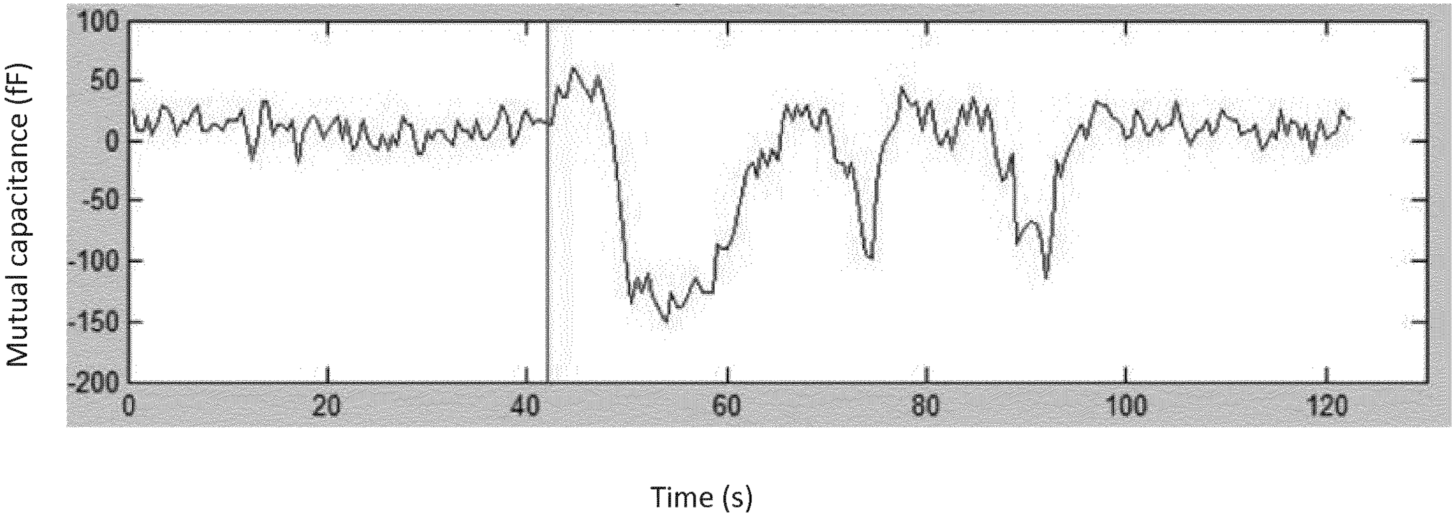
Mutual capacitance (fF)
100
50
0
-50
-100
-150
-200
0
20
40
60
80
100
120
Time (s)

Fig. 10

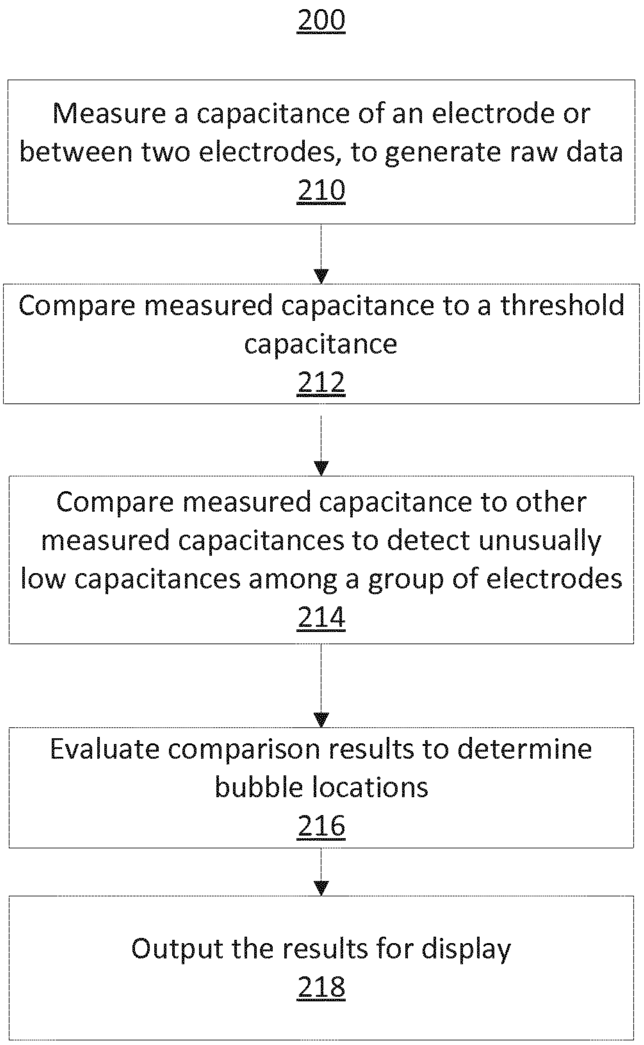
200
Measure a capacitance of an electrode or between two electrodes, to generate raw data
210
Compare measured capacitance to a threshold capacitance
212
Compare measured capacitance to other measured capacitances to detect unusually low capacitances among a group of electrodes
214
Evaluate comparison results to determine bubble locations
216
Output the results for display
218

Fig. 11

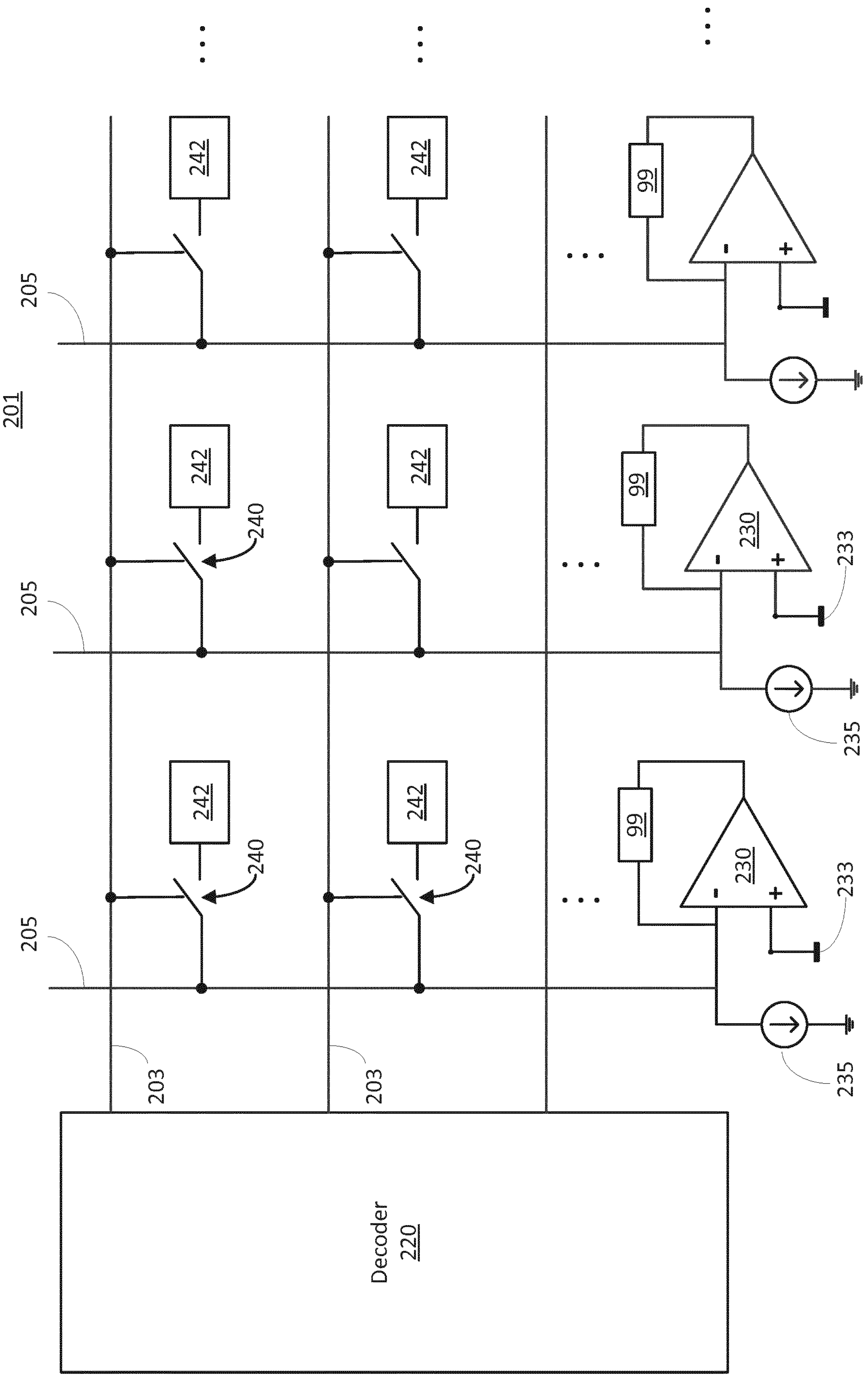
201
205
205
205
203
203
242
242
242
242
242
242
240
240
240
99
99
99
230
230
233
233
235
235
-
+
Decoder
220

Fig. 12

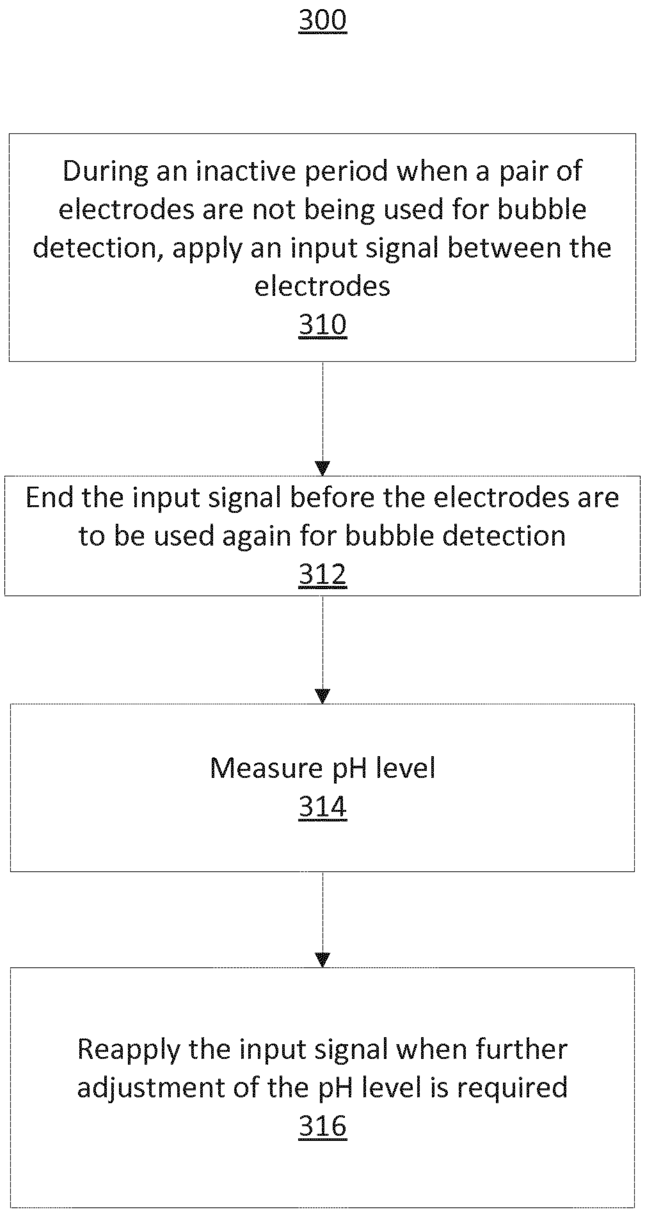
300
During an inactive period when a pair of electrodes are not being used for bubble detection, apply an input signal between the electrodes
310
End the input signal before the electrodes are to be used again for bubble detection
312
Measure pH level
314
Reapply the input signal when further adjustment of the pH level is required
316

Fig. 13

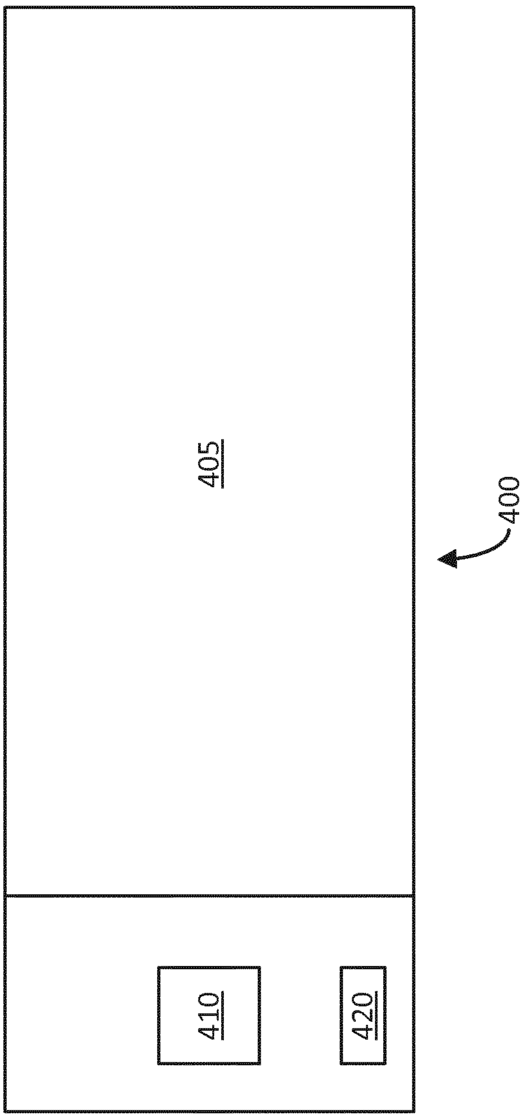

Fig. 14

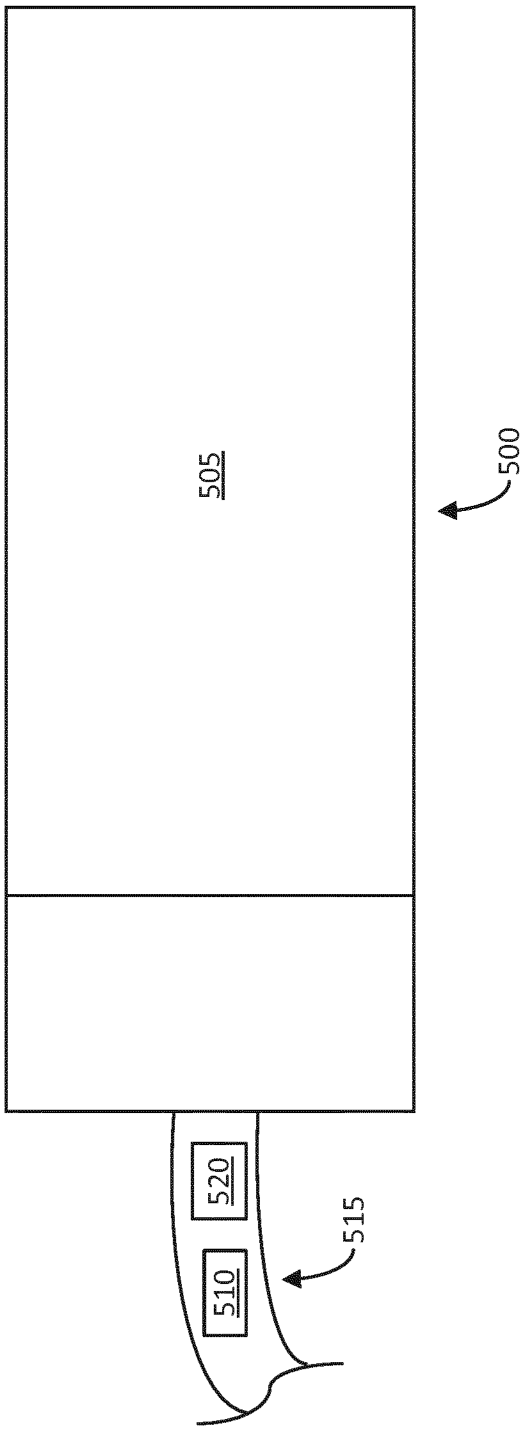

Fig. 15

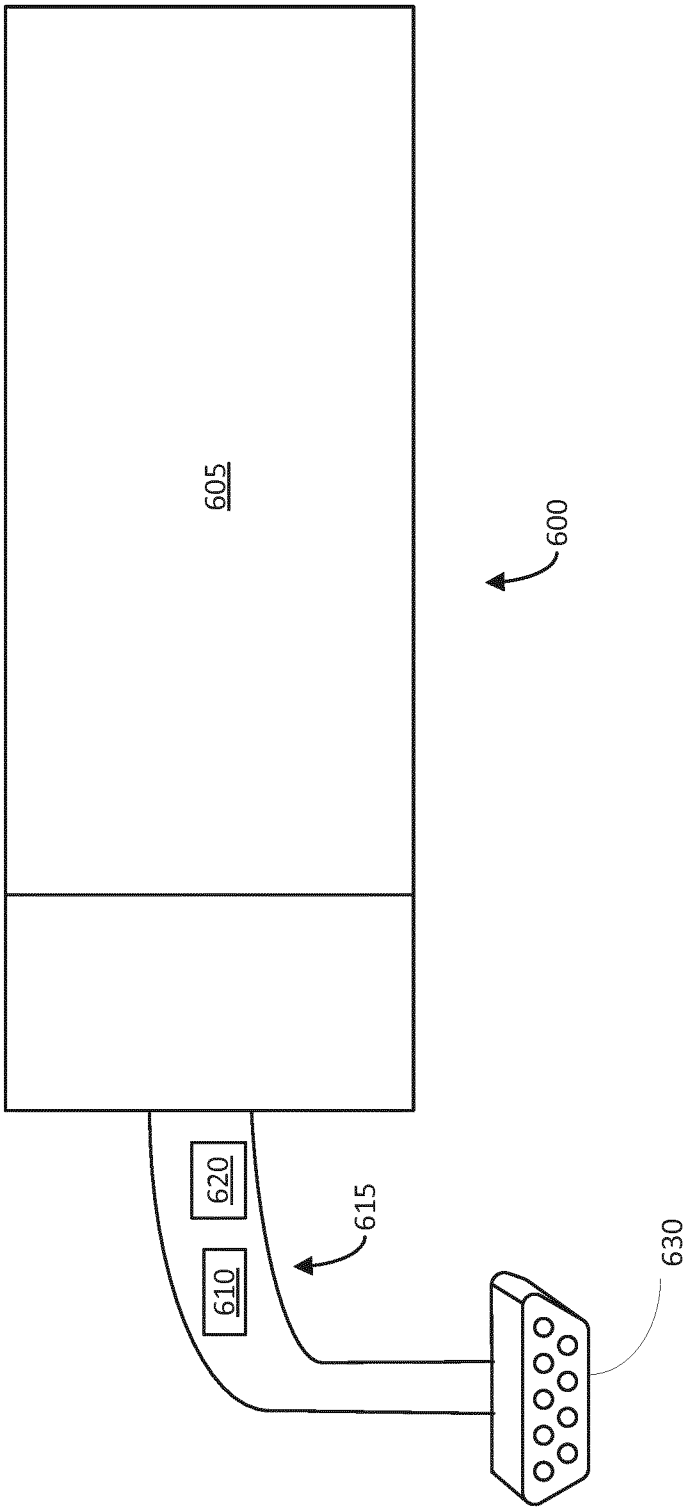

Fig. 16

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/052661

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N27/22
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G01N

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

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

EPO-Internal, WPI Data, INSPEC, COMPENDEX

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2012/055809 A1 (GLEZER ELI N [US] ET AL) 8 March 2012 (2012-03-08)	1,5-37, 41-51,55
Y	paragraphs [0057], [0105], [0140] - [0144], [0151], [0175], [0248], [0255] - [0257]; figures 1-23 ----- -/--	2-4, 38-40, 52-54

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

☒ See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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

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

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

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

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Date of the actual completion of the international search
14 April 2015

Date of mailing of the international search report
24/04/2015

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Authorized officer
Gangl, Martin

International application No
PCT/EP2015/052661

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2012/068055 A2 (ADVANCED LIQUID LOGIC INC [US]; POLLACK MICHAEL [US]; STURMER RYAN [US) 24 May 2012 (2012-05-24)	1,6-14, 16-26, 28-37, 42-48, 50,51,55
A	figures 1-8 page 14, line 10 - line 11 page 15, line 26 page 23, line 14 - line 16 page 24, line 3 - line 8 page 25, line 13 page 27, line 23 - line 24 page 29, line 18 - line 20 page 36, line 12 - line 18 page 37, line 8 - line 9 page 38, line 17 - line 20 -----	2-5,15, 27, 38-41, 49,52-54
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A	figures 1-8 paragraphs [0007] - [0010], [0071] - [0075] -----	1,5-37, 41-51,55
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Information on patent family members

International application No
PCT/EP2015/052661

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