



A BIOSENSOR AND A METHOD FOR DETERMINING THE OHMIC RESISTANCE OF A SENSING CIRCUIT OF A BIOSENSOR

FIELD OF THE INVENTION

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Embodiments of the invention relate to the field of sensors. By way of example, embodiments of the invention relate to biosensors and methods for determining the ohmic resistance of a sensing circuit of a biosensor.

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BACKGROUND OF THE INVENTION

In the area of biotechnology and medical applications, specialized equipment is typically used in performing the detection and/or the analysis of
15 Deoxyribonucleic Acid (DNA) sequences in a given sample. It was only until the advent of DNA sensors and DNA sensor arrays (which includes a plurality of individual DNA sensors) in the last decade, before significant advances in DNA analysis appeared. This was because the DNA sensor arrays enabled simultaneous detection of multiple DNA sequences to be performed, thereby
20 significantly reducing analysis times as well as facilitating automatic sequencing.

In the above mentioned scenario, the DNA sensor arrays were used in a controlled laboratory environment. In order to change the use environment of
25 these DNA sensor arrays from the controlled laboratory environment to the mass market, for example, it is required to produce the DNA sensor array devices which are capable of high performance (particularly high selectivity and sensitivity), of sufficiently small size (for example, of a size suitable to be hand-held), of sufficiently small analysis time and of a low cost as well. In this
30 regard, new signal amplification methods are essential for achieving the high sensitivity requirement on unamplified samples (where there may be only a few DNA copies) and in genomic analysis of single cells.



Presently, commercially available state-of-the-art DNA array sensor systems on integrated circuit (IC) chips largely rely on optical techniques for DNA detection. The design of such a DNA array sensor system is challenging from the scaling point of view, due to the complexity of integrating different components of the system, such as optical components (for example, light sources and photo-detectors), which are bulky, and electronic components.

Further, the main limiting factor in developing DNA sensors and DNA sensor arrays (for all detection techniques, including optical detection) is the sensitivity of the sensing device. Presently, with typical optical detection techniques, it is only possible to obtain a sensitivity of about 10^{-15} M, i.e., 10^{-15} mol per liter (mol/L). Ideally, in DNA detection applications, a DNA sensor should be able to detect the presence of less than 1000 molecules, i.e., a detection sensitivity of about 10^{-21} M.

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A conventional technique to increase the sensitivity of optical based DNA sensors is by increasing the amount of DNA in a sample via the polymerase chain reaction (PCR) technique. However, the steps involved with the PCR technique are complicated, expensive, time consuming and prone to contamination. As such, while it may not be difficult to perform the PCR technique in the controlled laboratory environment, it would be nearly impossible to do so in the mass market environment. In this regard, the avoidance of the PCR technique may also simplify the design and the scaling of the design of such a DNA sensor or DNA sensor array system.

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SUMMARY OF THE INVENTION

In one embodiment of the invention, a biosensor is provided. The biosensor provided includes at least one sensing circuit arrangement having a sensing circuit having a sensing capacitance and a sensing ohmic resistance, and a transistor circuit having a gate capacitance and a gate ohmic resistance. The biosensor provided further includes at least one detecting circuit having a resistor having a predefined ohmic resistance, an operating mode switching

circuit being configured to, in a first operating mode, couple the sensing circuit and the transistor circuit in a parallel configuration, and the parallel configuration in series with the resistor, and in a second operating mode, couple the sensing circuit and the transistor circuit in a series configuration, and a control circuit being configured to determine a time constant of the parallel configuration in accordance with the first operating mode, determine a time constant of the series configuration in accordance with the second operating mode, and determine the sensing ohmic resistance.

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BRIEF DESCRIPTION OF THE DRAWINGS

In the drawings, like reference characters generally refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the invention. In the following description, various embodiments of the invention are described with reference to the following drawings, in which:

Figure 1 shows a photograph of a biosensor array and an enlarged photograph of a biosensor, according to an embodiment of the invention.

Figure 2 shows a block diagram of a biosensor array, according to one embodiment of the invention.

Figure 3 shows a cross-sectional view of the sensing circuit arrangement of the biosensor, according to one embodiment of the invention.

Figure 4 shows a circuit representation of the sensing circuit arrangement of the biosensor, according to one embodiment of the invention.

Figure 5 shows a circuit representation of the biosensor, according to one embodiment of the invention.

Figure 6 shows a circuit representation of the sensing circuit arrangement of the biosensor, when the switches are controlled in such a way that the sensing circuit is connected in parallel with the transistor circuit, according to one embodiment of the invention.

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Figure 7 shows a circuit representation of the sensing circuit arrangement of the biosensor, when the switches are controlled in such a way that the sensing circuit is connected in series with the transistor circuit, according to one embodiment of the invention.

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Figure 8 shows a block diagram with a system level implementation of the biosensor, according to one embodiment of the invention.

Figure 9 shows the time constant measurement results using the biosensor with the switches controlled in such a way that the sensing circuit is connected in parallel with the transistor circuit, according to an embodiment of the invention.

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Figure 10 shows the time constant measurement results using the biosensor with the switches controlled in such a way that the sensing circuit is connected in series with the transistor circuit, according to an embodiment of the invention.

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Figure 11 shows the sensing ohmic resistance and the sensing capacitance values computed from the measurement results shown in Figures 9 and 10, according to an embodiment of the invention.

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DETAILED DESCRIPTION OF THE INVENTION

An improved solution to the problem of designing and fabricating a DNA sensor (or a DNA sensor array) which has a high detection sensitivity, may be the biosensors and the methods for determining the ohmic resistance of a sensing circuit of a biosensor, as defined in the respective independent claims of the present application.

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As used herewith, the term biosensor refers to a device for detecting an analyte that combines a biological component with a physicochemical detector component. A biosensor may be used to detect predetermined sensitive biological components, such as tissue, micro-organisms, organelles, cell receptors, enzymes, antibodies, nucleic acids (including DNA), for example.

Further, the term analyte refers to a substance or chemical constituent which may be determined in an analytical procedure. In relation to the present invention, the analyte may be DNA, or micro-Ribonucleic Acid (μ RNA), for example.

In this regard, it should be noted that an analyte itself cannot be measured; only measurable properties of the analyte can be measured. For example, one cannot measure glucose, but one can measure the glucose concentration. In this example, glucose is the analyte and the glucose concentration is the measurable property of glucose.

According to one embodiment of the invention, the biosensor provided includes a sensing circuit arrangement and a detection circuit. In more detail, the sensing circuit arrangement includes a sensing circuit and a transistor circuit. Further, the sensing circuit has a sensing ohmic resistance value and a sensing capacitance value.

The sensing circuit is in contact with a given sample, where DNA detection would be performed, for example. It may be assumed that the given sample has been earlier processed, for example, with appropriate DNA labeling methods (such as conductive polymer based labeling, for example), such that the appropriately labeled DNA strands may effect a measurable change in the resistance as well as the capacitance of the given sample, which in turn affects the sensing ohmic resistance and the sensing capacitance values.

The detection circuit includes a resistor of a predetermined ohmic resistance value, an operating mode switching circuit, and a control circuit. The resistor of a predetermined ohmic resistance value is used in conjunction with the operating mode switching circuit in order to obtain the necessary
5 measurements (which are made by the control circuit), which are then used to compute the sensing ohmic resistance and the sensing capacitance values.

In another embodiment of the invention, a biosensor is provided. The biosensor provided includes at least one sensing circuit arrangement having a
10 sensing circuit having a sensing capacitance and a sensing ohmic resistance, and a transistor circuit having a gate capacitance and a gate ohmic resistance. The biosensor provided further includes at least one detecting circuit having a resistor having a predefined ohmic resistance, an operating mode switching circuit being configured to, in a first switching state, couple
15 the sensing circuit and the transistor circuit in a parallel configuration, and the parallel configuration in series with the resistor having a predefined ohmic resistance, and in a second switching state, couple the sensing circuit and the transistor circuit in a series configuration, and a control circuit being configured to determine a time constant of the parallel configuration,
20 determine a time constant of the series configuration, and determine the sensing ohmic resistance using the determined time constants.

In one embodiment of the invention, a method for determining the ohmic resistance of a sensing circuit of a biosensor, wherein the biosensor includes
25 a sensing circuit arrangement, the arrangement including a sensing circuit and a transistor circuit, is provided. The method provided includes coupling, in a first operating mode, the sensing circuit and the transistor circuit in a parallel configuration, and the parallel configuration in series with a resistor having a predefined ohmic resistance, and determining a time constant of the
30 parallel configuration in accordance with the first operating mode. The method provided further includes coupling, in a second operating mode, the sensing circuit and the transistor circuit in a series configuration, determining a time constant of the series configuration in accordance with the second

operating mode, and determining the sensing ohmic resistance using the determined time constants and the resistor.

In another embodiment of the invention, a method for determining the ohmic resistance of a biosensor, wherein the biosensor includes a sensing circuit arrangement, the arrangement including a sensing circuit and a transistor circuit, is provided. The method provided includes coupling, in a first switching state, the sensing circuit and the transistor circuit in a parallel configuration, and the parallel configuration in series with a resistor having a predefined ohmic resistance, and determining a time constant of the parallel configuration. The method provided further includes coupling, in a second switching state, the sensing circuit and the transistor circuit in a series configuration, determining a time constant of the series configuration, and determining the sensing ohmic resistance using the determined time constants.

Embodiments of the invention emerge from the dependent claims.

According to one embodiment of the invention, the transistor circuit includes a field effect transistor. According to another embodiment of the invention, the gate capacitance includes the capacitance of the gate isolating region of the field effect transistor and wherein the gate ohmic resistance includes the ohmic resistance of the gate isolating region of the field effect transistor.

According to one embodiment of the invention, the at least one detecting circuit includes a comparator circuit.

According to one embodiment of the invention, the operating mode switching circuit includes a plurality of switches, wherein the switches are arranged such that in the first operating mode, a first switch of the plurality of switches couples the resistor to a first node of the sensing circuit, and a second switch of the plurality of switches couples a second node of the sensing circuit being located at the opposite side of the sensing circuit than the first node with a

reference potential, and in the second operating mode, a third switch of the plurality of switches couples the second node of the sensing circuit to an input voltage node.

- 5 As used herewith, the term plurality refers to two or more of the items referred to. For example, a plurality of switches means two or more switches.

According to another embodiment of the invention, in the second operating mode, a fourth switch of the plurality of switches to first couple the first node
10 of the sensing circuit with the reference potential, and then to decouple the first node of the sensing circuit from the reference potential.

According to another embodiment of the invention, the operating mode switching circuit includes a plurality of switches, wherein the switches are
15 arranged such that in the first operating mode, the third switch of the plurality of switches decouples the second node of the sensing circuit from the input voltage node, and the fourth switch of the plurality of switches decouples the node between a first node of the sensing circuit from the reference potential, and in the second operating mode, the first switch of the plurality of switches
20 decouples the resistor from a first node of the sensing circuit, and the second switch of the plurality of switches decouples the second node of the sensing circuit being from the reference potential.

According to another embodiment of the invention, the reference potential is a
25 ground potential.

According to one embodiment of the invention, the control circuit is configured such that the determining the time constant of the parallel configuration in accordance with the first operating mode includes applying a step input
30 voltage to the input voltage node and determining the step response.

According to another embodiment of the invention, the control circuit is configured such that the determining the time constant of the series

configuration in accordance with the second operating mode includes applying a step input voltage to the input voltage node and determining the step response.

- 5 According to another embodiment of the invention, the sensing ohmic resistance is determined using the time constant of the parallel configuration in accordance with the first operating mode, the time constant of the series configuration in accordance with the second operating mode and the predefined ohmic resistance of the resistor.

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According to one embodiment of the invention, wherein the transistor circuit includes a field effect transistor. According to another embodiment of the invention, the at least one detecting circuit includes a comparator circuit.

- 15 According to one embodiment of the invention, the switching circuit includes a plurality of switches, wherein the switches are arranged such that in the first switching state, a first switch of the plurality of switches couples the resistor to a first node of the sensing circuit, and a second switch of the plurality of switches couples a second node of the sensing circuit being located at the
- 20 opposite side of the sensing circuit than the first node with a reference potential, and in the second switching state, a third switch of the plurality of switches couples the second node of the sensing circuit to an input voltage node.

- 25 According to another embodiment of the invention, in the second switching state, a fourth switch of the plurality of switches to first couple the first node of the sensing circuit with the reference potential, and then to decouple the first node of the sensing circuit from the reference potential.

- 30 According to another embodiment of the invention, the switching circuit includes a plurality of switches, wherein the switches are arranged such that in the first switching state, the third switch of the plurality of switches decouples the second node of the sensing circuit from the input voltage node,

and the fourth switch of the plurality of switches decouples the first node of the sensing circuit from the reference potential, and in the second switching state, the first switch of the plurality of switches decouples the resistor from the first node of the sensing circuit, and the second switch of the plurality of switches decouples the second node of the sensing circuit from the reference potential.

According to one embodiment of the invention, the control circuit is configured such that the determining the time constant of the parallel configuration includes applying a step input voltage to the input voltage node and determining the step response.

According to another embodiment of the invention, the control circuit is configured such that the determining the time constant of the series configuration includes applying a step input voltage to the input voltage node and determining the step response.

According to another embodiment of the invention, the sensing ohmic resistance is determined using the time constant of the parallel configuration, the time constant of the series configuration and the predefined ohmic resistance of the resistor.

According to one embodiment of the invention, in the first operating mode, a first switch of a plurality of switches couples the resistor to a first node of the sensing circuit, and a second switch of the plurality of switches couples a second node of the sensing circuit being located at the opposite side of the sensing circuit than the first node with a reference potential, and in the second operating mode, a third switch of the plurality of switches couples the second node of the sensing circuit to an input voltage node, and a fourth switch of the plurality of switches to first couple the first node of the sensing circuit with the reference potential and then to decouple the first node of the sensing circuit and the detecting circuit from the reference potential.

According to another embodiment of the invention, in the first operating mode, the third switch of the plurality of switches decouples the second node of the sensing circuit from the input voltage node, and the fourth switch of the plurality of switches decouples the first node of the sensing circuit from the reference potential, and in the second operating mode, the first switch of the plurality of switches decouples the resistor from the first node of the sensing circuit, and the second switch of the plurality of switches decouples the second node of the sensing circuit being from the reference potential.

10 According to one embodiment of the invention, the determining the time constant of the parallel configuration in accordance with the first operating mode includes applying a step input voltage to the input voltage node and determining the step response.

15 According to another embodiment of the invention, the determining the time constant of the series configuration in accordance with the second operating mode includes applying a step input voltage to the input voltage node and determining the step response.

20 According to another embodiment of the invention, the sensing ohmic resistance is determined using the time constant of the parallel configuration in accordance with the first operating mode, the time constant of the series configuration in accordance with the second operating mode and the predefined ohmic resistance of the resistor.

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According to one embodiment of the invention, in the first switching state, a first switch of the plurality of switches couples the resistor to a first node of the sensing circuit, and a second switch of the plurality of switches couples a second node of the sensing circuit being located at the opposite side of the sensing circuit than the first node with a reference potential, and in the second switching state, a third switch of the plurality of switches couples the second node of the sensing circuit to an input voltage node, and a fourth switch of the plurality of switches to first couple the first node of the sensing circuit with the

reference potential and then to decouple the sensing circuit from the reference potential.

According to another embodiment of the invention, in the first switching state,
5 the third switch of the plurality of switches decouples the second node of the sensing circuit from the input voltage node, and the fourth switch of the plurality of switches decouples the first node of the sensing circuit from the reference potential, and in the second switching state, the first switch of the plurality of switches decouples the resistor from the first node of the sensing
10 circuit, and the second switch of the plurality of switches decouples the second node of the sensing circuit being from the reference potential.

According to one embodiment of the invention, the determining the time constant of the parallel configuration includes applying a step input voltage to
15 the input voltage node and determining the step response.

According to another embodiment of the invention, the determining the time constant of the series configuration includes applying a step input voltage to the input voltage node and determining the step response.
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According to another embodiment of the invention, the ohmic resistance of the sensing circuit is determined using the time constant of the parallel configuration, the time constant of the series configuration and a predefined ohmic resistance of a resistor.
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The embodiments which are described in the context of the biosensors provided are analogously valid for the methods for determining the ohmic resistance of a sensing circuit of a biosensor, and vice versa.

30 **Fig. 1** shows a photograph 100 of a biosensor array 101 and an enlarged photograph 105 of a biosensor 103, according to an embodiment of the invention.

The biosensor array 101 shown includes a plurality of biosensors 103. In the embodiment shown in **Fig. 1**, the plurality of biosensors 103 are arranged in a 10x10 manner (i.e., with 10 rows of biosensors 103, and 10 biosensors 103 in each row).

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Fig. 1 also shows an enlarged photograph 105 of a biosensor 103. The biosensor 103 includes a plurality of biosensor sites 107, where each biosensor site 107 includes or consists of an interdigitated electrode 109 and a nano-gap 111. For example, in one embodiment, the nano-gap is only 0.5 μm wide.

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Fig. 2 shows a block diagram of a biosensor array 200, according to an embodiment of the invention.

15 The biosensor array 200 includes or consists of a plurality of biosensors 201 arranged accordingly in rows and columns. The biosensor array 200 further includes or consists of logic circuitry including a row decoder 203, a plurality of column decoders 205, a plurality of column control lines 207 and a plurality of row control lines 209.

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Further, the biosensor 201 may be represented by a circuit 211. The circuit 211 will be discussed in more detail in relation to **Fig. 4** later.

Fig. 3 shows a cross-sectional view of the sensing circuit arrangement 300 of the biosensor, according to an embodiment of the invention.

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In one embodiment, the sensing circuit arrangement 300 of the biosensor includes a nano-gap based sensing circuit coupled to the gate of a transistor in a transistor circuit, as shown in **Fig. 3**. The nano-gap based sensing circuit includes or consists of two electrodes (301 and 303) and a nano-gap 305 between the two electrodes (301 and 303).

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As used herewith, the nano-gap 305 refers a small gap between the two electrodes, typically in the range of about 10 nanometers (nm) to 500 nm.

As mentioned earlier, the (nano-gap based) sensing circuit has a sensing
5 capacitance value as well as a sensing ohmic resistance value.

Further, it can be seen that the nano-gap 305 is thus small enough, such that a few suitably labeled bio-molecular structures 307 may be sufficient to effect a detectable change in the sensing capacitance and the sensing ohmic
10 resistance values of the (nano-gap based) sensing circuit, which may be considered as being measured across the nano-gap 305 (between the two electrodes 301 and 303). In this regard, with a nano-gap based sensing circuit, a high detection sensitivity may be achieved.

15 In one embodiment, the transistor circuit may include a field effect transistor.

The sensing circuit arrangement 300 may be fabricated on semiconductor, as shown in the illustration in **Fig. 3**.

20 **Fig. 4** shows a circuit representation of the sensing circuit arrangement 400 of the biosensor, according to an embodiment of the invention.

As shown in **Fig. 4**, the sensing circuit arrangement 400 of the biosensor includes a sensing circuit 401 and a transistor circuit 403, which are
25 connected in series. The sensing circuit 401 may be represented as a sensing capacitor C_S 405, and a sensing resistor R_S 407, which are connected in parallel.

Similar to the sensing circuit 401, the transistor circuit 403 may be
30 represented by a gate capacitor C_G 409, and a gate resistor R_G 411, which are connected in parallel. The transistor circuit 403 is represented in this manner, mainly due to the capacitance and the ohmic resistance values of the

gate of the transistor (to which the sensing component is connected, as described earlier in relation to Fig. 3).

Applying a step voltage, V_{STEP} , to the circuit shown in Fig. 3, the natural response of the circuit may be derived as equation (1) using Laplace Transform

$$V_{GATE}(t) = V_{STEP} \left[\frac{C_S}{C_S + C_G} e^{-pt} + \frac{R_G}{R_S + R_G} (1 - e^{-pt}) \right] \quad (1)$$

where the time constant p is given by

$$p = \frac{1}{(C_S + C_G)(R_S // R_G)} \quad (2)$$

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From equation (1), the resistance-capacitance (RC) time constant measurement may be used in order to determine the corresponding values of the sensing capacitor C_S 405 and the sensing resistor R_S 407.

15 Further, it can be seen that equation (1) has two terms, the first, an exponentially decaying term and the second, a rising term, with respect to time. In order to be able to observe the second term of equation (1), the following two criteria should be met.

20 Firstly, the gate leakage current must be negligible or kept very small. In other words, this means that the ohmic resistance value of the gate resistor is significantly greater than that of the sensing resistor (i.e., $R_G \gg R_S$). This may be achieved by having a thick silicon oxide (SiO_2) on the gate of the transistor.

25 Secondly, the coefficient of the exponentially decaying term should be kept very small. In other words, this means that the capacitance value of the gate capacitor is significantly greater than that of the sensing capacitor (i.e., $C_G \gg C_S$). However, this may not be achievable in practice because the capacitance value of the sensing capacitor C_S 405 is typically in the range of about 1 nF to
30 10 nF (when conductive polymer based DNA labeling is used, for example),

whereas the capacitance value of the gate capacitor C_G 409 is typically in the range of about 5 pF to 10 pF.

Alternatively, the criteria $C_G \gg C_S$ may be achieved by connecting a capacitor of a large capacitance value (for example, in the range of about 10 μ F to 100 μ F) in parallel to the gate of the transistor. However, such a capacitor would result in the time constant ρ of $V_{GATE}(t)$ being increased by a factor of over a few hundred times, making this solution impractical in the mass market use scenario.

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Fig. 5 shows a circuit representation of the biosensor 500, according to an embodiment of the invention.

As mentioned earlier, the biosensor 500 includes the sensing circuit arrangement 501 and the detection circuit. As shown earlier in relation to **Fig. 4**, the sensing circuit arrangement 501 of the biosensor includes a sensing circuit and a transistor circuit, which are connected in series. The sensing circuit may be represented as a sensing capacitor C_S 503, and a sensing resistor R_S 505, which are connected in parallel. The transistor circuit may be represented as a resistor R_G 507 and a capacitor C_G 509, which are connected in parallel.

The detection circuit includes a comparator 511, a reference resistor of a predefined resistance value R_{REF} 513, a first switch (S_1) 515, a second switch (S_2) 517, a third switch (S_3) 519 and a fourth switch (S_4) 521.

The four switches (515, 517, 519 and 521) are controlled in such a way that the sensing circuit is either connected in series or in parallel with the transistor circuit (to which the sensing component is connected, as described earlier in relation to **Figs. 3 and 4**). This is done to make two measurements, which would then be used to determine the values of the sensing capacitor C_S 503 and the sensing resistor R_S 505. In one embodiment, the two measurements

made are resistance-capacitance (RC) time constant measurements, in response to a step voltage input.

5 A parallel connection between the sensing circuit and the transistor circuit may be implemented by closing the first switch S_1 515 and the second switch S_2 517 (or switched on), while leaving the other switches (519 and 521) open (or switched off). The resultant equivalent circuit is as shown in Fig. 6.

10 Similarly, a series connection between the sensing circuit and the transistor circuit may be implemented by switching on the third switch S_3 519, while leaving the other switches (515, 517 and 521) switched off. The resultant equivalent circuit is as shown in Fig. 7.

15 In this regard, in order to be able to perform the desired measurement, the fourth switch S_4 521 may also be switched on initially. This is to enable the sensing capacitor C_S 503 to be charged up fully, while at the same time, discharging the capacitor of transistor circuit C_G .

20 After a short period of time (say, for about 5 seconds to about 15 seconds, for example), the fourth switch S_4 521 is then switched off and the measurement of the time constant is initiated. It should be noted that when the fourth switch S_4 521 is switched off, the capacitor of the transistor circuit C_G begins to charge up.

25 With regard to the detection circuit, the comparator 511 of the detection circuit may be used to measure the time constant. In one embodiment, with a predetermined value of the reference voltage V_{REF} , the comparator 511 may be used to generate an output signal to indicate that the value of V_{GATE} has reached or exceeded the value of the reference voltage V_{REF} . In this regard,
30 the time taken for the value of V_{GATE} to reach or exceed the value of the reference voltage V_{REF} may be determined using the output signal generated by the comparator 511, together with a digital counter, for example.

Fig. 6 shows a circuit representation of the sensing circuit arrangement 600 of the biosensor; when the switches are controlled in such a way that the sensing circuit 601 is connected in parallel with the transistor circuit 603, according to an embodiment of the invention.

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As mentioned earlier, the sensing circuit 601 may be represented as a sensing capacitor C_S 605, and a sensing resistor R_S 607, which are connected in parallel. Similar to the sensing circuit 601, the transistor circuit 603 may also be represented as a gate capacitor C_G 609, and a gate resistor R_G 611, which are connected in parallel. As shown in **Fig. 6**, the sensing circuit 601 is connected in parallel with the transistor circuit 603, and this parallel configuration is connected in series with the reference resistor R_{REF} 613.

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Similar to the analysis performed in the discussion in relation to **Fig. 3**, the following equation may be obtained for the case of the parallel connection between the sensing circuit and the transistor circuit

$$V_{GATE}(t) = V_{STEP} \left[\frac{R_S // R_G}{R_{REF} + (R_S // R_G)} (1 - e^{-pt}) \right] \quad (3)$$

where the time constant p is given by

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$$p = \frac{1}{(C_S + C_G)(R_{REF} // (R_S // R_G))} \quad (4)$$

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As mentioned earlier, in practice, it is known that the ohmic resistance value of the gate resistor is significantly greater than that of the sensing resistor (i.e., $R_G \gg R_S$), and that ohmic resistance value of the sensing resistor is also significantly greater than that of the reference resistor (i.e., $R_S \gg R_{REF}$); or, in other words, $R_G \gg R_S \gg R_{REF}$. Further, it is also known that the capacitance value of the sensing capacitor is significantly greater than that of the gate capacitor (i.e., $C_S \gg C_G$). As such, equation (3) may be further simplified to

$$V_{GATE}(t) = V_{STEP} (1 - e^{-pt}) \quad (5)$$

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where the time constant p is given by

$$p = \frac{1}{C_S R_{REF}} \quad (6)$$

Therefore, the first time constant measured (i.e., as measured using this circuit), p_1 , is the time constant p of equation (6).

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Fig. 7 shows a circuit representation of the sensing circuit arrangement 700 of the biosensor, when the switches are controlled in such a way that the sensing circuit 701 is connected in series with the transistor circuit 703, according to an embodiment of the invention.

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As mentioned earlier, the sensing circuit 701 may be represented as a sensing capacitor C_S 705, and a sensing resistor R_S 707, which are connected in parallel. Similar to the sensing circuit 701, the transistor circuit 703 may also be represented as a gate capacitor C_G 709, and a gate resistor R_G 711, which are connected in parallel. As shown in **Fig. 7**, the sensing circuit 701 is connected in series with the transistor circuit 703.

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As a side remark, it can be seen that this circuit representation is similar to that of **Fig. 4**.

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Similar to the analysis performed in the discussion in relation to **Fig. 3**, the following equation may be obtained for the case of the series connection between the sensing circuit and the transistor circuit

$$V_{GATE}(t) = V_{STEP} \left[\frac{R_G}{R_S + R_G} (1 - e^{-pt}) \right] \quad (7)$$

25 where the time constant p is given by

$$p = \frac{1}{(C_S + C_G)(R_S // R_G)} \quad (8)$$

As mentioned earlier, in practice, it is known that the ohmic resistance value of the gate resistor is significantly greater than that of the sensing resistor (i.e., $R_G \gg R_S$), and that the capacitance value of the sensing capacitor is

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significantly greater than that of the gate capacitor (i.e., $C_S \gg C_G$). As such, equation (7) may be further simplified to

$$V_{GATE}(t) = V_{STEP}(1 - e^{-pt}) \quad (9)$$

where the time constant p is given by

$$p = \frac{1}{C_S R_S} \quad (10)$$

Therefore, the second time constant measured (i.e., as measured using this circuit), p_2 , is the time constant p of equation (10).

10 In view of the earlier discussion in relation to **Fig. 6**, with the first time constant measured p_1 known, the capacitance value of the sensing capacitor C_S 701 may be determined from equation (6).

Similarly, with the second time constant measured p_2 and the capacitance
15 value of the sensing capacitor C_S 701 known (determined from equation (6)), the ohmic resistance value of the sensing resistor R_S 703 may then be determined from equation (10).

Fig. 8 shows a block diagram with a system level implementation of the
20 biosensor 800, according to an embodiment of the invention.

The biosensor 800 includes the sensing circuit arrangement 801, the reference resistor 803, the plurality of electronic switches 805 and the comparator 807. These components have been described in relation to **Fig.**
25 **5**, for example.

The biosensor 800 further includes a controller 809, a counter 811, a shift register 813, a digital-to-analog converter (DAC) 815, a voltage reference 817 and a ramp generator 819.

30 The controller 809 provides the control signals to other components in the system as well as receiving the measurements obtained for the time

constants. In one embodiment of the invention, the controller 809 may include control logic, which may be implemented as hard-wired control logic or as programmable control logic (e.g. a programmable processor, e.g., a microprocessor including complex instruction set computer (CISC) processor or reduced instruction set computer (RISC) processor).

The counter 811 measures the tripping time of the comparator 807, and stores the information in digital format. In the regard, the term tripping time refers to the number of counts that had passed before the comparator indicates that the value of gate voltage V_{GATE} described earlier has reached a predefined voltage value.

The shift register 813 performs the parallel shifting of digital data received from the counter 811 and then transmits the shifted data to the DAC 815.

The DAC 815 converts the shifted data received from the shift register 813 accordingly to an analog voltage, which would be used as a predefined reference voltage for the comparator 807.

The voltage reference 817 is used to provide accurate reference voltage values for use by analog components in the system, such as the DAC 815, for example.

The ramp generator 819 is used to perform calibration in order to provide offset compensation, caused by device mismatches which occurred during the manufacturing process, for example.

Fig. 9 shows the time constant measurement results using the biosensor with the switches are controlled in such a way that the sensing circuit is connected in parallel with the transistor circuit, according to an embodiment of the invention.

Fig. 10 shows the time constant measurement results using the biosensor with the switches are controlled in such a way that the sensing circuit is connected in series with the transistor circuit, according to an embodiment of the invention.

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Fig. 11 shows the sensing ohmic resistance and the sensing capacitance values computed from the measurement results shown in **Figs. 9** and **10**, according to an embodiment of the invention.

- 10 As mentioned earlier, the capacitance value of the sensing circuit may be first determined from equation (6). Subsequently, the ohmic resistance value of the sensing circuit may be then determined from equation (10).

- 15 It can be seen from **Fig. 11** that the capacitance value of the sensing circuit is proportional to the concentration of the DNA sample, while the ohmic resistance value of the sensing circuit is inversely proportional to the concentration of the DNA sample.

Embodiments of the invention have the following advantages.

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As shown by the embodiments of the invention described earlier, a high sensitivity of detection may be achieved using the biosensor provided by the present invention.

- 25 Additionally, by using only electronic devices in the biosensor provided by the present invention (and without other devices, such as optical devices, for example), the fabrication process of a biosensor array based on the biosensor provided by the present invention is less complex.

- 30 While the invention has been particularly shown and described with reference to specific embodiments, it should be understood by those skilled in the art that various changes in form and detail may be made therein without departing from the spirit and scope of the invention as defined by the

appended claims. The scope of the invention is thus indicated by the appended claims and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced.

CLAIMS

What is claimed is:

- 5 1. A biosensor, comprising:
at least one sensing circuit arrangement having
a sensing circuit having a sensing capacitance and a sensing
ohmic resistance; and
a transistor circuit having a gate capacitance and a gate ohmic
10 resistance; and
at least one detecting circuit having
a resistor having a predefined ohmic resistance;
an operating mode switching circuit being configured to,
in a first operating mode, couple the sensing circuit and
15 the transistor circuit in a parallel configuration, and the parallel configuration in
series with the resistor; and
in a second operating mode, couple the sensing circuit
and the transistor circuit in a series configuration; and
a control circuit being configured to
20 determine a time constant of the parallel configuration in
accordance with the first operating mode;
determine a time constant of the series configuration in
accordance with the second operating mode; and
determine the sensing ohmic resistance.
- 25 2. The biosensor of claim 1,
wherein the transistor circuit comprises a field effect transistor.
3. The biosensor of claim 2,
30 wherein the gate capacitance comprises the capacitance of the gate
isolating region of the field effect transistor and wherein the gate ohmic
resistance comprises the ohmic resistance of the gate isolating region of the
field effect transistor.

4. The biosensor of claim 1,
wherein the at least one detecting circuit comprises a comparator
circuit.

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5. The biosensor of claim 1,
wherein the operating mode switching circuit comprises a plurality of
switches, wherein the switches are arranged such that

in the first operating mode, a first switch of the plurality of
10 switches couples the resistor to a first node of the sensing circuit, and a
second switch of the plurality of switches couples a second node of the
sensing circuit being located at the opposite side of the sensing circuit than
the first node with a reference potential; and

in the second operating mode, a third switch of the plurality of
15 switches couples the second node of the sensing circuit to an input voltage
node.

6. The biosensor of claim 5,

wherein in the second operating mode, a fourth switch of the plurality of
20 switches to first couple the first node of the sensing circuit with the reference
potential, and then to decouple the first node of the sensing circuit from the
reference potential.

7. The biosensor of claim 6,

25 wherein the operating mode switching circuit comprises a plurality of
switches, wherein the switches are arranged such that

in the first operating mode, the third switch of the plurality of
switches decouples the second node of the sensing circuit from the input
voltage node, and the fourth switch of the plurality of switches decouples the
30 node between a first node of the sensing circuit from the reference potential;

in the second operating mode, the first switch of the plurality of
switches decouples the resistor from a first node of the sensing circuit, and

the second switch of the plurality of switches decouples the second node of the sensing circuit being from the reference potential.

8. The biosensor of any one of claims 5, 6 or 7,
5 wherein the reference potential is a ground potential.
9. The biosensor of claim 1,
wherein the control circuit is configured such that the determining the
time constant of the parallel configuration in accordance with the first
10 operating mode comprises applying a step input voltage to the input voltage
node and determining the step response.
10. The biosensor of claim 1,
wherein the control circuit is configured such that the determining the
15 time constant of the series configuration in accordance with the second
operating mode comprises applying a step input voltage to the input voltage
node and determining the step response.
11. The biosensor of claim 1,
20 wherein the sensing ohmic resistance is determined using the time
constant of the parallel configuration in accordance with the first operating
mode, the time constant of the series configuration in accordance with the
second operating mode and the predefined ohmic resistance of the resistor.
- 25 12. A biosensor, comprising:
at least one sensing circuit arrangement having
a sensing circuit having a sensing capacitance and a sensing
ohmic resistance; and
a transistor circuit having a gate capacitance and a gate ohmic
30 resistance; and
at least one detecting circuit having
a resistor having a predefined ohmic resistance;
an operating mode switching circuit being configured to,

in a first switching state, couple the sensing circuit and the transistor circuit in a parallel configuration, and the parallel configuration in series with the resistor having a predefined ohmic resistance; and

in a second switching state, couple the sensing circuit
5 and the transistor circuit in a series configuration; and

a control circuit being configured to
determine a time constant of the parallel configuration;
determine a time constant of the series configuration; and
determine the ohmic resistance of the sensing circuit
10 using the determined time constants.

13. The biosensor of claim 12,
wherein the transistor circuit comprises a field effect transistor.

15 14. The biosensor of claim 12,
wherein the at least one detecting circuit comprises a comparator circuit.

15. The biosensor of claim 12,
20 wherein the switching circuit comprises a plurality of switches, wherein the switches are arranged such that

in the first switching state, a first switch of the plurality of switches couples the resistor to a first node of the sensing circuit, and a second switch of the plurality of switches couples a second node of the sensing circuit being located at the opposite side of the sensing circuit than the first node with a reference potential;
25

in the second switching state, a third switch of the plurality of switches couples the second node of the sensing circuit to an input voltage node.
30

16. The biosensor of claim 15,
wherein in the second switching state, a fourth switch of the plurality of switches to first couple the first node of the sensing circuit with the reference

potential, and then to decouple the first node of the sensing circuit from the reference potential.

17. The biosensor of claim 16,

5 wherein the switching circuit comprises a plurality of switches, wherein the switches are arranged such that

in the first switching state, the third switch of the plurality of switches decouples the second node of the sensing circuit from the input voltage node, and the fourth switch of the plurality of switches decouples the
10 first node of the sensing circuit from the reference potential;

in the second switching state, the first switch of the plurality of switches decouples the resistor from the first node of the sensing circuit, and the second switch of the plurality of switches decouples the second node of the sensing circuit from the reference potential.

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18. The biosensor of claim 12,

wherein the control circuit is configured such that the determining the time constant of the parallel configuration comprises applying a step input voltage to the input voltage node and determining the step response.

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19. The biosensor of claim 12,

wherein the control circuit is configured such that the determining the time constant of the series configuration comprises applying a step input voltage to the input voltage node and determining the step response.

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20. The biosensor of claim 12,

wherein the sensing ohmic resistance is determined using the time constant of the parallel configuration, the time constant of the series configuration and the predefined ohmic resistance of the resistor.

30

21. A method for determining the ohmic resistance of a sensing circuit of a biosensor, wherein the biosensor comprises a sensing circuit arrangement,

the arrangement comprising a sensing circuit and a transistor circuit, the method comprising:

coupling, in a first operating mode, the sensing circuit and the transistor circuit in a parallel configuration, and the parallel configuration in series with a resistor having a predefined ohmic resistance;

determining a time constant of the parallel configuration in accordance with the first operating mode;

coupling, in a second operating mode, the sensing circuit and the transistor circuit in a series configuration;

determining a time constant of the series configuration in accordance with the second operating mode; and

determining the sensing ohmic resistance using the determined time constants and the resistor.

22. The method of claim 21,

wherein, in the first operating mode, a first switch of a plurality of switches couples the resistor to a first node of the sensing circuit, and a second switch of the plurality of switches couples a second node of the sensing circuit being located at the opposite side of the sensing circuit than the first node with a reference potential;

wherein, in the second operating mode, a third switch of the plurality of switches couples the second node of the sensing circuit to an input voltage node, and a fourth switch of the plurality of switches to first couple the first node of the sensing circuit with the reference potential and then to decouple the first node of the sensing circuit and the detecting circuit from the reference potential.

23. The method of claim 22,

wherein, in the first operating mode, the third switch of the plurality of switches decouples the second node of the sensing circuit from the input voltage node, and the fourth switch of the plurality of switches decouples the first node of the sensing circuit from the reference potential;

wherein, in the second operating mode, the first switch of the plurality of switches decouples the resistor from the first node of the sensing circuit, and the second switch of the plurality of switches decouples the second node of the sensing circuit being from the reference potential.

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24. The method of claim 21,

wherein the determining the time constant of the parallel configuration in accordance with the first operating mode comprises applying a step input voltage to the input voltage node and determining the step response.

10

25. The method of claim 21,

wherein the determining the time constant of the series configuration in accordance with the second operating mode comprises applying a step input voltage to the input voltage node and determining the step response.

15

26. The method of claim 21,

wherein the sensing ohmic resistance is determined using the time constant of the parallel configuration in accordance with the first operating mode, the time constant of the series configuration in accordance with the second operating mode and the predefined ohmic resistance of the resistor.

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27. A method for determining the ohmic resistance of a sensing circuit of a biosensor, wherein the biosensor comprises a sensing circuit arrangement, the arrangement comprising a sensing circuit and a transistor circuit, the method comprising:

25

coupling, in a first switching state, the sensing circuit and the transistor circuit in a parallel configuration, and the parallel configuration in series with a resistor having a predefined ohmic resistance;

determining a time constant of the parallel configuration;

30

coupling, in a second switching state, the sensing circuit and the transistor circuit in a series configuration;

determining a time constant of the series configuration;

determining the sensing ohmic resistance using the determined time constants.

28. The method of claim 27,

5 wherein, in the first switching state, a first switch of the plurality of switches couples the resistor to a first node of the sensing circuit, and a second switch of the plurality of switches couples a second node of the sensing circuit being located at the opposite side of the sensing circuit than the first node with a reference potential;

10 wherein, in the second switching state, a third switch of the plurality of switches couples the second node of the sensing circuit to an input voltage node, and a fourth switch of the plurality of switches to first couple the first node of the sensing circuit with the reference potential and then to decouple the sensing circuit from the reference potential.

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29. The method of claim 26,

wherein, in the first switching state, the third switch of the plurality of switches decouples the second node of the sensing circuit from the input voltage node, and the fourth switch of the plurality of switches decouples the first node of the sensing circuit from the reference potential;

20

wherein, in the second switching state, the first switch of the plurality of switches decouples the resistor from the first node of the sensing circuit, and the second switch of the plurality of switches decouples the second node of the sensing circuit being from the reference potential.

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30. The method of claim 25,

wherein the determining the time constant of the parallel configuration comprises applying a step input voltage to the input voltage node and determining the step response.

30

31. The method of claim 25,

wherein the determining the time constant of the series configuration comprises applying a step input voltage to the input voltage node and determining the step response.

5 32. The method of claim 25,

wherein the sensing ohmic resistance is determined using the time constant of the parallel configuration, the time constant of the series configuration and a predefined ohmic resistance of a resistor.