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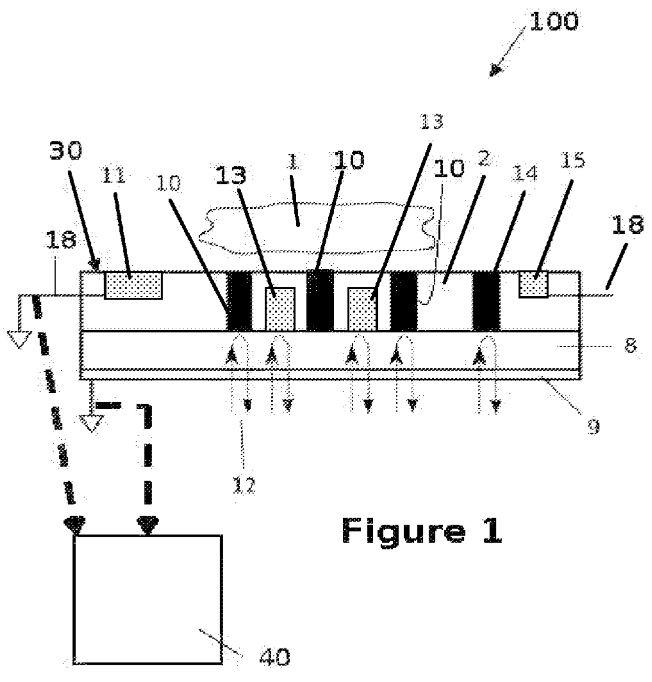

Figure 1

(57) Abstract: Disclosed is a system and method for obtaining an electrical recording data comprising: providing an object of interest which is at least partially located in a recording environment; providing at least one signal recording electrode or a transducer, which is adapted to conduct or transduce a signal data of interest from the object of interest; obtaining the signal data of interest; obtaining a noise data from a location within the recording environment; modulation of a signal to remove noise; and obtaining a noise cancelled data, the obtaining of the noise cancelled data including subtracting the noise data from the signal data of interest.

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Systems and methods for noise cancelation in recording systems

CROSS REFERENCE TO RELATED APPLICATION

[0001] The present application claims priority from Australian Provisional Patent Application No. 2023902596 filed on 15 August 2023, the contents of which are incorporated herein by reference in their entirety.

TECHNICAL FIELD

[0002] This disclosure relates to a method of noise cancellation and signal calibration, for example in the multi-channel or/and electro-optical acquisition of biopotentials.

BACKGROUND ART

[0003] Interference from ambient electromagnetic noise, internal Johnson–Nyquist noise, and movement artefacts are major challenges in the processing of recordings especially from excitable biological tissue, including those involved in neuroscience and cardiac electrophysiological recording systems. These recording systems are used in isolated tissue and organ laboratories (i.e. *ex vivo or in vitro*), but also in in vivo preparations for implantation in animals and humans.

[0004] This interference causes a reduction in signal to noise ratio, which is significant if the signal of interest is quite small in absolute terms, or relative to the background noise. For example, extracellular bio-electric signals are typically less than 1 millivolt (mV), commonly less than 100 microvolt (μV).

[0005] In traditional acquisition systems based on multi-electrode arrays (MEAs), the onus is on the user to try to reduce the interference from external electromagnetic noise, by grounding of equipment and electrical isolation of the recording rig. Some examples are the use of shielded cables, Faraday cages or Faraday rooms. Another method is the use of bioinstrumentation placed near the recording source.

[0006] A different aspect in which noise is conventionally dealt with is in the post-processing of the signal. For instance, some systems employ the modelling and reconstruction of noise, and then the removal of the reconstructed noise signal from the recorded signal, as their noise reduction strategy.

[0007] The Inventor(s) earlier developed an optical-electrode (optrode) for use in electrophysiological recordings. The noise interference issue presents itself in optical-electrodes (optrodes) as well. The reduction of noise is complicated by the fact in that in devices based on these electro-optical transducers, the output signal, i.e. a change in optical reflectance, is proportional to the input voltage but the scaling factor is unknown.

[0008] Any discussion of documents, acts, materials, devices, articles or the like which has been included in the present specification is solely for the purpose of providing a context for the present invention. It is not to be taken as an admission that any or all of these matters form part of the prior art base or were common general knowledge in the field relevant to the present invention as it existed before the priority date of each claim of this application.

SUMMARY

[0009] In a first aspect, the present disclosure provides a recording apparatus. The apparatus comprises a reference electrode, and a plurality of conductive devices. The plurality of conductive devices including at least one signal conduction device adapted to conduct a signal from an object of interest, for example biological tissue, cells, cell culture, or another biological or non-biological sample of interest, at least partially located in a recording environment, and at least one noise conduction device adapted to conduct a noise signal.

[0010] The at least one noise conduction devices can include one or more first noise conduction device which is, in use, adapted to be exposed in the recording environment. Furthermore, the first noise conduction device and the signal conduction device can be of substantially the same material and dimensions. In some cases, this means a half cell potential or electrode potential of the first noise conduction device is substantially the same as a half cell (or electrode) potential of the signal conduction device.

[0011] The at least one noise conduction device can include one or more second noise conduction device which is, in use, adapted to be isolated from the recording environment. In a further embodiment, at least some of the plurality of conductive devices can be provided in a substrate. The one or more second noise conduction devices can also be embedded within the substrate. The reference electrode can be provided in the substrate.

[0012] The plurality of conductive devices can be a multi-electrode array.

[0013] Alternatively, at least some of the conductive devices are transducers. In some embodiments, the one or more first noise conduction devices include at least one noise electrode and at least one noise sensing transducer.

[0014] A track for conduction with the at least one noise electrode can be of substantially the same material as a track for conduction with the reference electrode.

[0015] The transducers can be each adapted to transduce an optical signal into an electrical signal, sense a return electrical signal, and transmit an output optical signal which is transduced from the return electrical signal. The substrate can comprise liquid crystals.

[0016] The apparatus can further have a timer or controller adapted to time a switch between input to the signal conduction device and input to the noise conduction device.

[0017] The apparatus can further have a signal holding circuitry to periodically hold an output of the signal conduction device or the noise conduction device.

[0018] In a second aspect, the present disclosure provides measurement multi-channel recording apparatus. The apparatus comprises a reference electrode and a plurality of optical-electrical transducers embedded in a light transmitting substrate. The plurality of optical-electrical transducers include at least one signal recording transducer adapted to transduce an optical input into an electrical input to an object of interest. The plurality of optical-electrical transducers include at least one noise recording transducer adapted to receive a response signal from the object of interest and transduce it into an output optical signal. The apparatus further comprises a detector adapted to detect the output optical signal.

[0019] In a third aspect, the present disclosure provides an electrical measurement apparatus, comprising a reference electrode, and at least one signal recording device adapted to record a signal from an object of interest. The apparatus enables the provision of an input to the object of interest periodically, intermittently, or at such times as determined by the user.

[0020] The at least one signal measurement device can be at least one optical-electrical transducer, embedded in a light transmitting substrate, the at least one optical-electrical transducer being adapted to transduce an optical input into an electrical input to the object of interest.

[0021] The at least one optical-electrical transducer can be adapted to transduce an electrical signal from the object in response to the electrical input, into an output optical signal.

[0022] The optical input can be provided by, at user defined times: switching a light source on and off; interrupting a light transmission from a light source; moving the at least one optical-electrical transducer from a light receiving position.

[0023] In a fourth aspect, the present disclosure provides a recording system, comprising an electrophysiological recording apparatus mentioned in any of the aspects above.

[0024] In a fifth aspect, the present disclosure provides an signal recording method, comprising: providing an input signal to an object of interest at least partially located in a recording environment; obtaining a response signal from the object of interest, in response to the input signal, the response signal being transmitted or transduced by at least one signal recording electrode or a transducer obtaining a noise data from a location within the measurement chamber; and obtaining a noise cancelled data, the obtaining of the noise cancelled data including subtracting the noise signal from the response signal.

[0025] The method can include providing at least one noise recording electrode or transducer.

[0026] Obtaining the noise signal can include obtaining a first noise signal from at least one first noise electrode or transducer which is located to be isolated from the object of interest but exposed within the recording environment.

[0027] Obtaining the noise signal can include obtaining a second noise signal from at least one second noise electrode or transducer which is wholly embedded within a substrate located in the recording environment, so that it is not exposed within the recording environment.

[0028] The at least one first noise electrode or transducer can be at least one first noise electrode, and the noise signal includes a third noise signal from at least one noise transducer, which is located to be isolated from the object of interest but exposed within the recording environment.

[0029] The method can include obtaining a reference signal from a reference electrode.

[0030] The method can include obtaining a value of a voltage offset voltage, wherein the obtaining of the voltage offset voltage value includes calculating a difference between the reference signal and the first noise signal.

[0031] The method can include applying a compensation voltage to a substrate located within the recording environment, the compensation voltage being the voltage offset voltage with a reverse polarity.

[0032] The obtaining of the noise cancelled data can include subtracting the voltage offset value from the object signal data.

[0033] The method can include providing the input signal at a plurality of input values.

[0034] The method can include obtaining a plurality of voltage offset values each at a corresponding input value, and calculating a baseline from the plurality of voltage offset values.

[0035] The method can include calibrating the response signal to remove the baseline and determine the gain.

[0036] The method can include conditioning the response signal and/or the noise signal.

[0037] The conditioning can include smoothing or filtering the response signal and/or the noise signal.

[0038] The input signal can be provided intermittently.

[0039] Obtaining the noise signal can include obtaining signal from the at least one signal electrode or transducer, when the input signal is not provided to the object of interest.

[0040] The input signal can be an optical input. The optical input can be provided by, at user defined times: switching a light source on and off; periodically interrupting a light transmission from a light source; moving the at least one signal electrode or transducer to and from a light receiving position.

[0041] In a sixth aspect, the present disclosure provides a computer programme, comprising instructions for controlling a computer or embedded processor to implement a method mentioned in the fifth aspect above.

[0042] In a seventh aspect, the present disclosure provides an apparatus for obtaining a functional measurement for an object of interest, comprising a computer having a processor and memory supporting computer processes, the computer implementing a method mentioned in the fifth aspect above.

[0043] In an eighth aspect, the present disclosure provides an electro-optical detection apparatus. The apparatus comprises a first optrode, configured to receive a first light signal and generate a first optrode signal, the first optrode configure to be in contact with a sample of interest, and a second optrode, configured to receive a second light signal and generate a second optrode signal. The second optrode is configured to be isolated from the sample of interest. The apparatus further comprises a receiver, configured to determine an output signal by applying an active noise cancellation algorithm to the first optrode signal and the second optrode signal.

[0044] In some embodiments, the apparatus further comprises a light source, configured to generate a light signal, and a light source splitter, configured to split the light signal into the first light signal and the second light signal.

[0045] In some embodiments, generating a first optrode signal comprises receiving, and reflecting, by the first optrode, the first light signal into a photodiode, generating, by the photodiode, an analogue electrical signal, and converting, by an analogue-to-digital converter, the analogue electrical signal to produce the first optrode signal.

[0046] In some embodiments, applying an active noise cancellation algorithm comprises subtracting the second optrode signal from the first optrode signal. In some embodiments, applying an active noise cancellation algorithm comprises applying a Wiener filter to the first optrode signal and the second optrode signal.

[0047] In some embodiments, applying an active noise cancellation algorithm comprises applying a one-tap adaptive filter to the first optrode signal. In some embodiments, applying an active noise cancellation algorithm comprises determining a cross-correlation of the first optrode signal and the second optrode signal. In some embodiments, applying an active noise cancellation algorithm comprises determining an auto-correlation of the second optrode signal. In some embodiments, applying an active noise cancellation algorithm comprises determining a filter coefficient based on the cross-correlation and the auto-correlation. In some embodiments, applying an active noise cancellation algorithm comprises applying a high-pass filter to the first optrode signal.

[0048] In some embodiments, the first optrode comprises one or more of, a polarisation-maintaining fibre, a liquid crystal layer, and a mirror.

[0049] In a ninth aspect, the present disclosure provides a method of detecting a nerve signal. The method comprises generating, by a light source, a light signal, and splitting the light signal into a first light signal and a second light signal. The method further comprises generating, based on the first light signal, by a first optrode, a first optrode signal, the first optrode configure to be in contact with a sample of interest, and generating, based on the second light signal, by a second optrode, a second optrode signal, the second optrode configure to be isolated from the sample of interest. The method further comprises determining an output signal by applying an active noise cancellation algorithm to the first optrode signal and the second optrode signal.

[0050] In some embodiments, generating the first optrode signal comprises receiving, and reflecting, by the first optrode, the first light signal into a photodiode, generating, by the photodiode, an analogue electrical signal, and converting, by an analogue-to-digital converter, the analogue electrical signal to produce the first optrode signal.

[0051] In some embodiments, applying an active noise cancellation algorithm comprises subtracting the second optrode signal from the first optrode signal.

[0052] In some embodiments, applying an active noise cancellation algorithm comprises applying a one-tap active filter to the first optrode signal and the second optrode signal.

[0053] In some embodiments, applying an active noise cancellation algorithm comprises applying a Wiener filter to the first optrode signal and the second optrode signal.

BRIEF DESCRIPTION OF THE DRAWINGS

[0054] Embodiments will now be described by way of example only, with reference to the accompanying drawings in which:

Figure 1 is a cross-section illustration of a multi-optrode array with added exposed and concealed optrodes and added exposed electrode for noise capture and signal calibration;

Figure 2 is a top-view illustration of a multi-optrode array with added exposed and concealed optrodes and added exposed electrode for noise capture and signal calibration;

Figure 3 is a cross-section illustration of a traditional MEA with added exposed and concealed electrodes for noise capture and baseline calibration;

Figure 4 is a top-view illustration of a traditional MEA with added exposed and concealed electrodes for noise capture and baseline calibration;

Figure 5 is a schematic view which conceptually depicts an arrangement for oversampling and sample-and-hold to isolate the signal and noise data series;

Figure 6-1 is a schematic view showing a time-based embodiment where the same electrode(s) or optrode(s) are used for signal sensing and for noise sensing;

Figure 6-2 is a representation of an oversampled data series obtained from a time-based embodiment;

Figure 6-3 shows the signal series and noise series isolated from the oversampled data series shown in Figure 6-2;

Figure 7-1 is a schematic view showing another time-based embodiment, where an input is alternatively provided to the signal sensing electrode(s) or optrode(s), and to the noise sensing electrode(s) or optrode(s);

Figure 7-2 is an example of an oversampled data series obtained from the time-based embodiment shown in Figure 7-1;

Figure 7-3 shows the signal series and noise series isolated from the oversampled data series shown in Figure 7-2;

Figure 8-1 is a schematic view showing another time based embodiment, where the substrate is positioned so that incident light is directed toward the signal sensing optrode(s);

Figure 8-2 depicts the embodiment shown in Figure 8-1, where the substrate is positioned so that incident light is directed toward the noise sensing optrode(s)

Figure 8-3 is an example of an oversampled data series obtained from the time-based embodiment shown in Figure 8-1;

Figure 9-1 is a schematic view showing a further time-based embodiment, where the substrate is positioned so that incident light is directed toward the signal sensing optrode(s);

Figure 9-2 depicts the embodiment shown in Figure 9-1, where the substrate is positioned so that incident light is directed toward the noise sensing optrode(s)

Figure 9-3 is an example of an oversampled data series obtained from the time-based embodiment shown in Figure 9-1;

Figure 10 schematically depicts an example of a calibration process to produce a noise-cancelled signal, where an optrode array is used to record the signals;

Figure 11 schematically depicts an example of a calibration process to produce a noise-cancelled signal, where a multi-electrode array is used to record the signals;

Figure 12 conceptually depicts an example of a general process for obtaining a final signal of interest;

Figure 13 illustrates the structure of an optrode, in accordance with an embodiment.

Figure 14 illustrates a design for an electro-optical detection system, in accordance with an embodiment.

Figure 15 is a block diagram of an Active Noise Cancelling (ANC) system 1500, in accordance with an embodiment.

Figure 16 illustrates the data flow in the system, in accordance with an embodiment.

Figure 17 illustrates Equations (a) to (e), in accordance with an embodiment.

Figure 18 is a schematic diagram of the light receiver board, in accordance with an embodiment.

Figure 19 shows a digital signal processing structure, in accordance with an embodiment.

Figure 20 is a graph illustrating a cross correlation of active optrode and inactive optrode channel at different light source power with no input signal at the active optrode, in accordance with an embodiment.

Figure 21 illustrates two pairs of graphs which illustrate the signals before (active optrode channel) and after (noise cancelling output channel) the noise-cancelling process, in accordance with embodiments.

Figure 22 is a graph illustrating the comparison between the RMS value for Channel1 input and DSP output at different light source current, when there is no input signal at the optrode, in accordance with an embodiment.

Figure 23 illustrates the signal-to-noise ratio and signal-to-noise ratio improvement before and after the active noise- cancelling process, for 200mV sinusoidal input, at different light source current, in accordance with an embodiment.

Figure 24 illustrates the signal-to-noise ratio and signal-to-noise ratio improvement before and after the active noise- cancelling process, for 10mV sinusoidal input, at different light source current, in accordance with an embodiment.

Figure 25 shows the comparison of active optrode channel (a) and noise cancelling output (b) at 500mA light current with 10mV 1 kHz sinusoidal input signal at the active optrode, in accordance with an embodiment.

Figure 26 shows active optrode experiment results with movement artefact, in accordance with an embodiment.

Figure 27 shows noise cancelling output experiment results with movement artefact reduction, in accordance with an embodiment.

DETAILED DESCRIPTION

[0055] In the following detailed description, reference is made to accompanying drawings which form a part of the detailed description. The illustrative embodiments described in the detailed description, depicted in the drawings and defined in the claims, are not intended to be limiting. Other embodiments may be utilised and other changes may be made without departing from the spirit or scope of the subject matter presented. It will be readily understood that the aspects of the present disclosure, as generally described herein and illustrated in the drawings can be arranged, substituted, combined, separated and designed in a wide variety of different configurations, all of which are contemplated in this disclosure.

[0056] An optical-electrode or "optrode" is a device for detecting nerve signals. Figure 13 illustrates the structure of an optrode, in accordance with an embodiment. Light comes in from a polarisation-maintaining fibre 1302 and goes into a liquid crystal layer. The light is then reflected by a mirror and goes back to the fibre through the liquid crystal layer. The rotation angle of liquid crystal is controlled by the voltage across the layer (an example of which is shown in Reference [2]), which also is the voltage across the two metal pins. When passing through and back in the liquid crystal, the light power is reduced based on the rotation of the liquid crystal. Therefore, the higher the voltage across the metal pins, the higher the light power.

[0057] Figure 14 illustrates a design for an electro-optical detection system, in accordance with an embodiment. The optrode is used to convert nerve signals into light signals. A light source transmits light to an optrode transducer via a circulator. The light intensity is then changed by the liquid crystal layer in the optrode, based on the nerve signal voltage.

[0058] The light that comes out from the optrode is directed to a receiver board. A photodiode on the receiver board converts the light into an analogue signal and is then sampled by data acquisition equipment.

[0059] The design illustrated in Figure 14 may have lower electrical interference, low signal attenuation, and a compact size compared to conventional electrode detection systems. However, the output noise level of the current electro-optical system is significantly higher than that of conventional electrode systems. This means it may be harder to observe nerve activity, especially when the amplitude is small.

[0060] In some designs, most of the noise comes from the light source. Accordingly, a direct way to reduce noise from the system is to design a low-noise current source to power the light source. The example embodiment provided herein embodies another method to reduce noise, which is active-noise-cancelling.

[0061] Active-noise-cancelling technique is used in multiple applications such as noise-cancelling headphones, noise cancelling in cars, and RF signal noise cancelling. The basic principle of active-noise-cancelling for the sound wave is that when two waves with basically the same frequency and amplitude at inverted phases, they will cancel each other out.

[0062] With regard to optrode implementations, digital signal noise is produced. Accordingly, it is preferrable to apply filter technique rather than just subtracting the two signals. Wiener filters (as described in Reference [10]) may be used in the signal processing part of active-noise-cancelling applications. Since the nerve signal that the optrode system is detecting has a similar frequency range compared to audible sound frequency, active-noise-cancelling and the Wiener filter may be effective with regard to optrode systems.

[0063] Provided herein is a system that actively reduces the noise in an existing electro-optical detection system.

[0064] In one embodiment of the noise cancellation method provided by this disclosure, one or more extra channels are added to data-acquisition systems to record a noise signature simultaneously with the signal of interest. The position of extra recording channels will determine the noise signature (for example, but not limited to, inherent noise of device, noise of electrode-electrolyte bilayers, mechanical noise).

[0065] In traditional multichannel electrophysiology systems, the extra channels can be embedded in the holding substrate to capture a noise signature. In electro-optical (optrode) based electrophysiological recording systems, one of the electrodes can be insulated and this reflective optrode channel is used to capture a noise signature. Alternatively, or additionally, an extra electrode or optrode in contact with the external environment but not the object of interest can be added to capture a noise signature of a different origin.

[0066] In one aspect, the present disclosure provides a system for noise cancellation and signal calibration. It involves the separate acquisition of noise signatures, from the same channels that are used for acquiring the signal of interest (time-based embodiments), or from additional channels which are substantially collocated, or located in proximity, to the channels used for acquiring the signal of interest (extra channel based embodiments).

[0067] In an embodiment based on providing extra channels (e.g. see Figures 1-4), the recording system includes a sensing array, including one or more channels ("noise channels") for the recording of noise signals, in addition to the channels for the recording of electrophysiological signal of interest ("signal channels" or "signal probes"). The one or more noise channels are adapted to record noise signature(s) simultaneously with the signal of interest. The position of the extra electrodes or optrodes is adjustable, and will determine the components/origin of the noise signature (for example, but not limited to, inherent noise of device, noise of electrode-electrolyte bilayers, external electromagnetic noise, motion artefact).

[0068] In traditional MEA recording systems, some of the extra channels are electrodes embedded in the holding substrate, and insulated from the external environment by substrate material, to capture a noise signature.

[0069] The inventor(s) previously developed an optically based voltage sensing device and method, which can be used to obtain electrophysiological signals. These devices are referred to as "optrodes". They are described in the PCT publication WO2013/110141, the contents of which are incorporated herein. In electro-optical (i.e. optrode) based electrophysiology recording systems, extra optrodes are added with their metal VIAs insulated from the external environment preferably by the same material as the substrate, to capture a noise signature.

[0070] These noise signatures arise mainly from internal device noise.

[0071] This embodiment, when implemented as a retrofit to a system involving multi-electrode arrays or optrode arrays, involves adding one or more electrodes or optrodes to the system, e.g. a traditional multi-electrode array or optrode array, respectively.

[0072] In some examples involving optrode-based systems, an electrode (e.g. electrode 15 in Figure 1) can be embedded into the holding substrate such that it is exposed to the external environment and connected to the data acquisition system 40 via a wire/track. The electrode can be metal or it can be a non-metallic material, such as a conductive polymer. This electrode provides an extra recording channel which captures an additional noise signature. In doing so, the embedded electrode(s) allows the system to provide protection of the liquid crystal layer of the optrodes – which is sensitive to the direct current (DC) voltage by measuring and compensating for any DC offset across the optrodes.

[0073] In one example, the extra electrodes or optrodes are in contact with the external environment but not the sample of interest. Depending on the position of this or these extra electrodes, this signature could include the electrolyte-electrode bilayer noise as well as external electromagnetic noise. Thus, they are adapted to capture a different noise signature than noise electrodes provided in an alternative implementation, such as those which are positioned in correspondence to the location of the object of interest.

[0074] Thus, the extra channels (probes, being electrodes or optrodes in the examples), depending on their placement and choice of material in combination with the choice of material for the signal recording channels (probes, being electrodes or optrodes in the examples), can be used to produce noise signatures representing difference sources of noise. The noise signatures can be used to account for the noise components in the captured signature(s) of the signal of interest, and the signature of the reference signal capturing the measurement baseline. The true signal of interest, or a representation thereof, can be produced by comparing these different signatures, rather than by the application of more complex data processing techniques. The signatures of various noises and the baseline voltage level further can change with time. This also adds to the complexity of using post data processing of the overall recorded signal (rather than using separate channel signals as taught in this disclosure), to account for noise.

[0075] In the below, the channel-based embodiments are described with respect to the embodiments' application to two example systems, one having a recording arrangement using optical electrode transducers (optrodes), one having a recording arrangement using a multi-electrode array.

1. Optrodes

[0076] Figure 1 and Figure 2 depict a schematic representation of a multi-channel recording system 100 using optical electrodes or optrodes.

[0077] The multi-channel recording system 100, in some embodiments, is used to record electrical signals. For *in vivo* recording, the system 100 is adapted to be embedded in the recording area or object of interest 1, e.g., a tissue, cells, cell culture, or another sample of interest 1. Of course, the system 100 is also suitable for *in vitro* or *ex vivo* measurement of bio-potentials.

[0078] The system 100 includes a recording apparatus, here being an array of conductive devices 10, 13, 14, which are positioned separate from each other. The conductive devices 10, 13, 14 can be transducers. In this example, they are optical electrode transducers, or "optrodes".

[0079] The conductive electrodes 10, 13, 14 are each adapted to transmit a signal voltage, from the region being measured which is in proximity to the electrode. The conductive electrodes 10, 13, 14 are supported in a substrate 2. The electrodes 10, 13, 14 are arranged in, e.g. a matrix array, or any other configuration which suits the particular application. As will be explained later, the optrodes 10 are adapted to come into contact with the sample or object 1. They therefore are optrodes 10 which provide the signal. The other optrodes 13, 14 each provide noise signals attributable to different sources. As the optrodes 13 do not come into contact with the object 1 or the recording environment, they will measure noises and/or a baseline offset due to the optics or the system arrangements of the array. As the optrodes 14 are in contact with the external environment (measuring chamber) but not the tissue sample, they are adapted to capture noise signature(s) from sources external to the sample, either external to the array or included in the recording system itself. As will be mentioned below, they may also be useful for establishing whether a non-zero baseline exists in the potential in the measuring chamber.

[0080] The system 100 further includes a first reference electrode 11, which in use, is arranged to not come into contact with the sample 1, to provide a baseline voltage for the signals generated by the sensing electrodes. A first conductive track 18 for the first reference electrode 18 is provided. It is shown as being embedded in the substrate 2 in this example. The first conductive track 18 may be grounded.

[0081] However, in a different embodiment, the first reference electrode 11 can be placed away from the optrode array 10, 13, 14. In electrophysiological recording, if the first reference electrode 11 is placed away from the measurement chamber, it is preferred that it be placed somewhere on the measurement subject where there is minimal movement, or/and a location where the electrical continuity between the reference electrode 11 and the measurement chamber (i.e. optrode array 10, 13, 14) can be maintained. It is also preferred that in this case, the electrode 11 be made of an inert or substantially inert material, to further minimise the sources of baseline voltage outside of the measurement chamber.

[0082] Referring back to the embodiment shown in Figure 1 and Figure 2, the system 100 optionally further includes a noise sensing electrode 15, arranged so that it also does not come into contact with the sample during use. In the example shown in Figure 1, only one noise sensing electrode 15 is included. However more noise electrodes 15 can be included in the system 100 at various locations. A second conductive track 20 is provided for each noise sensing electrode 15. In this example the noise electrode conductive track 20 is also embedded in the substrate 2.

[0083] Depending on the placement of the noise sensing electrode 15, it will have a baseline voltage contributed by different sources, such as the ambient noise, instrumentation noise, and movement noise (e.g. from a breathing subject). In the example shown in Figure 1, the noise sensing electrode 15 is placed within the measurement chamber, but without contact to the sample of interest. Thus, the noise sensing electrode 15 will capture the baseline voltage attributed to the junction potential of the electrode, the inherent instrumentation noise, and where applicable, a movement noise (e.g. if the substrate is embedded in a moving sample).

1.1. Noise Cancellation

[0084] In the example shown in Figure 1 and Figure 2, the optrodes 10, 13, 14 are provided in an optrode array 30. Each optrode is a layered structure including the sensing electrode which is embedded in a substrate layer 2, a liquid crystal layer which transduces the optical-electrical signals, and an output conduction layer 9 made from a transparent conductive material. The optrode array 30 is arranged so that the optrodes 10, 13, 14 share the layered structure, but have separate sensing electrodes.

[0085] The array of optrodes includes one or more signal recording optrodes 10 for recording the signals from the sample of interest. The array also includes one or more noise-sensing optrode(s) 13 which are embedded in the substrate 2. They are embedded within the substrate 2, and are insulated by the substrate 2 from the external environment, and from the neighbouring optrodes 10, 14. The substrate 2 can be either a rigid structure or a flexible construct. Using a flexible substrate would provide conformal object/sample contact and better signal transmission from sample to exposed electrodes, and improve the comfort of the subject from whom the recordings are being taken.

[0086] A single noise-sensing optrode 13 can be used for the entire multi-optrode array. That is, the entire array includes only one noise sensing optrode 13, with the rest being signal sensing optrodes 10. The other approach is to provide one noise-sensing optrode 13 to be paired with each signal recording optrode 10. An intermediate arrangement, is to provide multiple noise-sensing optrodes 13, but fewer than the signal recording optrodes 10.

[0087] In a preferred embodiment, the noise-sensing optrode 13 is located in between the signal recording optrodes. However other placements are possible.

[0088] Light 12 is projected toward each of the noise-sensing electrodes 13, for a noise signature to be generated by each noise-sensing electrodes 13. The noise signature(s) is attributable to optical sources or noise within the optrode device, arising from, e.g., refraction, wiring noises, movement artefacts, inherent noise, or random noise. Electrical signals are transduced by the optrodes 10, 13, 14, into light signals which are then detected and processed.

[0089] In the example shown in Figure 1, a second noise-sensing optrode(s) 14 is embedded in the substrate 2. Unlike the insulated noise-sensing optrodes 13, these optrodes 14 are exposed to the recording environment, i.e. the measurement chamber. They are also arranged so that in use they will be located at a distance from the sample of interest 1. The exposed noise-sensing optrode (s) 14 are of the same, or substantially the same, construction, to the signal recording optrodes 10, albeit not in contact with the tissue or sample of interest 1. Because the noise-sensing optrode (s) 14 are exposed to the external environment, they will provide a different noise signature, compared to the noise signature captured by the insulated noise-sensing optrode (s) 13. As will be mentioned, having these noise channels enables the determination of the amount of noise attributable to specific sources, by manipulating the noise levels recorded from the different noise channels.

[0090] In this example, the optrode array includes a liquid crystal layer 8 to polarise the incident light to help optimise the operation of the optrode array. It is located between the substrate layer 2 holding the sensing electrodes 11, 13, 14, and a layer of transparent conducting material 9 (e.g. indium tin oxide). The layer of transparent conducting material 9 allows transmission of the output of the optrode array to the data acquisition system 40.

[0091] The liquid crystal layer 8 will have inherent liquid crystal noise. The system 100 in this example includes an additional noise-sensing electrode 15. But more noise-sensing electrodes 15 can be provided. The noise sensing electrode 15 is exposed to the external environment. For instance the noise sensing electrode 15 will be in direct contact with a solution (e.g. a saline solution) added to the tissue or sample being measured. The noise-sensing electrode(s) 15 are of the same or substantially the same material and size to the VIAs (vertical interconnected access) of the signal recording optrodes 10, but insulated from the liquid crystal and the optrode array by the substrate 2. The noise sensing electrode 15 is connected to the data acquisition system (conceptually shown by reference 40) via a track in the substrate 2. If two or more noise sensing electrodes 15 are provided, each will be connected to the data acquisition system 40 by a separate track. Due to their placement, the noise sensing electrodes 15 provide an additional noise signature, which includes the electrolyte-electrode bilayer noise, but not inherent liquid crystal noise. The additional noise signature can be processed and used in noise cancellation. The data acquisition system 40 can be located in the same or a separate processing system, as a control system which controls the optical instrumentation, i.e. light source for the optrode array.

[0092] Thus, given the arrangement described above, the system 100 is adapted for the recording of noise signatures from the noise-sensing optrodes 13, 14 and/or electrodes 15. These signatures, associated with different noise sources, are processed and subtracted from signals of interest recorded by the signal recording optrodes 10. They are thus useful in improving signal quality.

[0093] The improvement in signal quality produced by embodiments of technology described herein could increase the information elucidated from electrophysiological experiments and recordings, and also increase the sensitivity of clinical diagnostic electrophysiology systems. For example, when applied to electrophysiological measurements involving the brain, the improved signal quality can improve the controllers for brain machine interfaces, and for the feedback circuits in neuro prostheses.

[0094] In one embodiment of the system for electro-optical recording, the embodiments of the technology described herein can improve the sensitivity of the transducers. The improved sensitivity allows for the detection and recording of ultra-low voltage signals.

[0095] Thus, in a further aspect, the technology presently disclosed includes a method for recording noise signatures, and real-time and offline analysis of captured noise signatures, as well as device calibration. Software embodying methods described herein is a further aspect of the present disclosure.

1.2. Signal Calibration

[0096] The noise signatures from the insulated noise-sensing optrodes 13 can be used to build a "baseline" for the optical signal acquired using the recording optrode 10. This allows a calibration of the reflectance signal from the signal recording optrodes 10, so that the reflectance noise component can be removed from the measurement obtained using the signal recording optrodes 10.

[0097] In electro-optical transducers (i.e. optrodes), the change of reflectance is proportional to the sensed electric potential. However, the offset (e.g. caused by a non-zero baseline voltage) and scale (e.g. caused by optical gain in the optrode) of the outputted signal relative to input is unknown. By applying a series of known potentials across the device (to optrodes 10) and measuring the signatures of the noise-sensing 13, and 14 as well as the signal of signal recording optrodes 10, a calibration curve can be constructed for each of the recording optrodes 10.

1.3. Protection of Liquid Crystals

[0098] The liquid crystals in optrode devices can be damaged by a DC potential applied across the device. Referring back to Figure 1, the noise-sensing electrode 15 provides a mechanism to protect the liquid crystal 8 by detecting and offsetting any DC voltage generated across the device.

[0099] As the noise-sensing electrode 15 will be in direct contact with the solution, or surrounding fluid in the case of an in vivo preparation, a half-cell potential (junction potential) is generated. This electrode 15 is of identical or substantially identical material and size to the VIAs of recording optrodes 10, which are also in contact with the same external solution. Therefore it can reasonably be assumed that the half-cell potential of the noise-sensing electrode 15 approximates the half-cell potential of the VIAs of recording optrodes 10. Thus, in the embodiment shown in Figure 1, the difference between the half-cell potentials of the reference electrode 11 and the noise-sensing electrode 15 is comparable to the difference in the half-cell potentials between the ground electrode 11 and the recording optrodes 10, which can generate a potential difference across the liquid crystal layer that as mentioned can damage the liquid crystal layer 8. Therefore, if the two half-cell potentials are not the same, a compensatory potential of the required amplitude and polarity is applied to the ground/reference electrode, to offset the difference between the half-cell potentials.

[0100] An example calibration process 300 to produce a noise-cancelled signal 316 is shown in Figure 10. A data signature 302 is recorded from the signal recording optrodes 10. A first noise signature 304 is generated by the substrate- insulated optrodes 13. The first noise signature 304 is attributable from, e.g. inherent instrumentation noise (e.g. due to optical gain), movement artefacts, random noise, wiring noise, reflectance, electromagnetic noise, etc. A second noise signature 306 is generated by the exposed noise recording optrode(s) 14. The second noise signature 306 is attributable to external noise and e.g. the junction potential which preferably will theoretically match the junction potential of the signal recording optrodes 10. Removal of the noise signals 304, 306 from the signal 302 from the recording optrode, will yield a calibrated tissue signal 314.

[0101] The half-cell potential 308 of the noise-sensing electrode 15 is compared to the half-cell potential 310 of the ground/reference electrode 11, to produce an offset measurement 312. The offset measurement 312 can be used to produce a voltage which counteracts the DC offset produced due to the non-equal half-cell potentials between the ground electrode 11 and the recording optrodes 10. Application of the counteracting voltage can help to protect the liquid crystal layer.

[0102] Furthermore, the measurement also provides a baseline of the electrode measurement by the recording electrode 4, compared with the reference electrode 11.

[0103] The calibrated signal data 314 and the offset measurement 312 can thus be used in a comparison process to produce a calibrated electrical measurement 316.

2. Multi-Electrode Arrays (MEAs)

[0104] Embodiments of technology escribed herein are also applicable to recording systems 200 using MEAs. Each electrode in the system 200 will have a separate track 3 linking to the data acquisition system 40.

2.1. Noise Cancellation

[0105] In the embodiment shown in Figure 3 and Figure 4, the recording arrangement 200 includes a multi-electrode array (MEA) 50 which includes a plurality of electrodes 4, 5, 6, and 7 which are embedded in a substrate 2. The electrodes 4, 7, 6 include one or more signal recording electrodes 4 for recording the signal from the tissue or sample of interest 1. The electrodes 4, 7, 6 includes one or more first noise-sensing electrode 6 which are completely embedded in the substrate 2. Each of the first noise-sensing electrodes 6 are insulated by the substrate 2 from the external environment and from the neighbouring electrodes 4, 7. As in the case for the embodiments involving optrodes (i.e. optrode based embodiments), the substrate 2 can be either a rigid structure, or a flexible structure which is more conformal for the subject.

[0106] One first noise-sensing electrode 6 can be used for the entire MEA 50. Or, one noise-sensing electrode 6 can be paired with each signal recording electrode 4. A compromise between these two approaches, such that there are more than one noise-sensing electrode but fewer than the number of the standard recording electrodes, can instead be adopted. In a preferred embodiment, the noise-sensing electrodes 6 are located in between the standard signal recording electrodes 4, but other placements are permitted.

[0107] Additionally, in this example, second noise-sensing electrode(s) 7 are also embedded in substrate 2. However, the second noise sensing electrodes 7, unlike the insulated noise sensing electrodes 6, are exposed to the external environment. The second noise sensing electrodes 7 are each located at a distance from the tissue or sample of interest 1. The second, or "exposed" noise sensing electrodes 7 are of the same or substantially the same construct (material, size), as the signal recording electrodes 4. As it is exposed to the external environment, the exposed noise-sensing electrode(s) 4 will provide a different noise signature compared to insulated noise-sensing electrodes 6.

[0108] Each electrode will have a separate track 3 to conduct signal to the data acquisition system 40 (see Figure 3). The noise signatures from the noise-sensing electrodes 6, 7 are processed and subtracted from signals of interest recorded by the standard recording electrodes 4.

2.2. Signal Calibration

[0109] Signals from the exposed noise-sensing electrodes 7, which are distal from the sample of interest 1, can be used to calibrate a baseline of the recording arrangement 200.

[0110] The baseline level of the signal recorded by each signal recording electrode 4 is at least partially attributable to the difference in the half-cell potentials of the signal recording electrode 4 and the reference/ground electrode 5. It is also attributable to any background bio-electric signal from tissue distal to the region of interest which is directly probed by the signal recording electrode 4.

[0111] As the exposed noise-sensing electrode 7 is not in contact with the biological material or the sample or interest 1, the baseline of the signal captured by the exposed noise-sensing electrode 7 is instrumentation-based, attributed mainly to the difference in half-cell potentials of noise sensing electrode 7 and ground/reference electrode 5.

[0112] The exposed noise-sensing electrode 7 has identical or substantially identical material and size as the signal recording electrodes 4. Therefore its half-cell potential (i.e. junction potential) is approximately equal to the half-cell potential (i.e. junction potential) of the standard recording electrode 4. Any difference between the two recorded half-cell potentials will be mainly be attributable to an instrumentation based direct current offset (DC). This offset will affect the baseline of the recording by the signal recording electrodes 4.

[0113] Figure 11 depicts an example of a calibration process, which utilises signals measured using the channels provided in the arrangement shown in Figure 3 (i.e. measurement using a multi-electrode array). A subtraction of the baseline 404 of the distal noise-sensing electrode 7 signal, from the baseline 402 of the signal acquired by each standard recording electrodes 4, will yield an estimate of the background noise (e.g. due to electrophysiology activity) 406. A subtraction of the baseline 404 of the distal noise-sensing electrode 7 from a baseline 408 of the reference electrode 5, will yield any instrumentation based DC offset 410 in the recording electrodes 4. Therefore, having the electrode channels in the arrangement shown in Figure 3 enables separating the instrumentation DC offset 410, from a baseline electrophysiology signal level 406. The DC offset 410 and the baseline electrophysiological signal 406 can be used to build the baseline 412 for the signal of interest as recorded by the recording electrodes 4. The baseline 412 can thus be subtracted from the physiological recordings to produce a noise-adjusted signal.

3. Common features

[0114] In the examples discussed above, both the optrode based and the traditional multi-electrode based recording configurations require a reference or ground electrode 5, 11. The reference electrode 5, 11 records a signal from the ambient external noise. The electrode also has a junction (i.e. half-cell) potential.

[0115] Real-time or offline signal processing can be applied, to subtract noise signature(s), from the signal(s) of interest. This process involves minimal distortion to the signal(s) of interest. The processing can involve time-domain and/or Fourier-domain subtraction of noise signatures.

[0116] The real-time or offline processing can also calibrate the signal outputted by the signal recording optrodes (in the arrangement 100 as shown in Figure 1). It can also allow for the measurement and resulting adjustment for the DC offset in both MEA and multi-optrode array based systems.

[0117] In some embodiments, the signal processing is implemented in hardware. For example, as shown in Figure 5, the system will include a differential amplifier, a sample-and-hold circuitry, and other hardware processing units to process main and reference signals or a software equivalent of such systems.

[0118] Figure 5 further shows an example where a sample and hold circuity 508 will hold the sample points taken during the oversampling period (or the sample points taken during the recording period). A subtraction circuit 510, such as one including a differential amplifier, can then be used to output a noise-cancelled output 512, being the difference between the optrode output during the oversampling period 514 and the optrode output during the object of interest signal recording period 516.

[0119] The comparison between the noise acquired during the oversampling period, with the single of interest collected during the 'true sample' or 'recording period', can instead be performed via signal processing using software.

[0120] In the below, several examples of how time-based embodiments can be implemented are provided. However it will be appreciated that these are not exhaustive. The time-based method, for example in a system using optrodes positioned to sense the data of interest, involves oversampling and sample-and-hold. The data acquisition and digital-to-analogue converters of the system will oversample, that is, the system will acquire data samples at a rate which is higher than the actual rate of sampling the signal of interest. During the oversampling period, for each 'true' sample point (i.e. a sample point from the signal of interest), at least one other “noise” sample point will be taken, where light transmission is interrupted and no light reaches the object of interest.

[0121] For example, as shown in Figure 6-1, shutter 506 can be placed between the light source 502 and the optical components 532 (e.g. mirrors, pinholes, collimators, optic fibres, circulators, etc) which direct the light to the optrodes 536, to interrupt light incidence to the optrodes 536. Alternatively, or in addition a shutter 506 is placed between the optical components 532 which directs the output from the optrode 536 to the photodetector 534 which detects the output, to interrupt the detection of the output from the optrodes 536. The interruption of light transmission can be done using other mechanisms, such as switching the light source on and off, or having a resonating mirror that will intermittently (e.g. periodically) deviate the incident light away from its set path onto the optrodes). Alternative to the shutter, the voltage supply to the optrode cell used in the arrangement can be turned on and off.

[0122] The samples collected, during the oversampling intervals when no light is incident on the optrodes, will contain noise information but not the signal of interest. The noise collected during the oversampling interval will include information about the system.

[0123] Depending on the placement of the shutter or resonating mirror in the optical pathway, or depending on whether the light is periodically switched off at the source, the noise signal will contain information about noise originating from the system up to the shutter or resonating mirror insertion point. If the light transmission between the light source and the optrodes 536 is interrupted, then the noise data will include noise contributed by system components which are downstream from the light source 502. If the light transmission between the optrodes 536 and the photodetector 534 is interrupted, then the noise data will include noise contribution from the photodetector and the downstream instrumentation.

[0124] The28versamplingg (i.e. sampling at a rate higher than the sample rate needed for the true data) results in a data series 538 (see Figure 6-2) where the black circles represent the data from the signal optrodes, and the grey circles represent the data from the noise-sensing optrodes. The data series 538 can then be separated into a signal data series 542 and a noise data series 540 (see Figure 6-3) using software or hardware, e.g., a shutter timer or a counter. The signal and noise data series 542, 540 will then be processed for the various functions discussed herein, such as noise cancellation to get noise cancelled data, and the establishment of various baselines. The data series 538, 542, 540 shown are for illustrative purposes only, and do not in any way restrict the scope of the invention.

[0125] Referring to Figure 7 an alternative to the light interruption shown in Figure 6 is to operate a switch 520. The switch 520 switches between the signal lines 3 from the signal electrodes 522 and the noise-sensing electrodes 524. The switching results in an oversampled data series 526 where the black circles represent the data from the signal electrodes, and the patterned (dotted) circles represent the data from the noise-sensing electrodes. The data series 526 can then be separated into a signal data series 528 and a noise data series 530 using hardware or software processing. For instance, a timer or a counter can be used. The signal and noise data series 528, 530 will then be processed for the various functions discussed herein, such as noise cancellation, and the establishment of various baselines. The data series 526, 528, 530 shown are for illustrative purposes only, and do not in any way restrict the scope of the invention.

[0126] Figure 8-1 and Figure 8-2 depict an alternative, mechanical, embodiment. In this embodiment, the substrate 2 in which the optrodes 522, 524 are embedded is moved periodically. In Figure 8-1, the substrate 2 is positioned so that the light incident from the light source 502 and redirected by the optical components 532 reaches the signal optrode(s) 522. In Figure 8-2, the substrate 2 is positioned so that the redirected light reaches the noise sensing optrode(s) 524 at another spot on the substrate 2. The position is changed at a rate dictated by the oversampling rate, to obtain the oversampled data series 550, which can be separated into a noise data series 551 and a signal of interest data series 552 (Figure 8-3) on the basis of the position of the substrate 2 at the time each data point is taken. The movement of the substrate will induce a noise in the signal, however this noise can be recorded and removed from the signal. A variation of this embodiment is one where the substrate is fixed in place but the optical components directing the light input are moved periodically.

[0127] A further alternative time-based embodiment is shown in Figure 9-1 and Figure 9-2. In this embodiment, the optical components include a redirecting part 552. The redirecting part is a component which is movable between multiple positions. In one position, it directs the light from the light source 502 toward the signal optrode(s) 522 as shown in Figure 9-1. In another position, it directs the light from the light source 502 toward the noise sensing optrode(s) 524 as shown in Figure 9-2. The movable part 552 moves at the "oversampling rate" (shown in Figure 9-3), to obtain an oversampled data series 560 which comprises both the signal data and the noise data. The data series 560 can be separated into a signal of interest series 562 and a noise series 564 by software or hardware processing. In a variation of this embodiment, the redirecting part can be a resonator (such as a resonating crystal) which oscillates between different positions when excited by certain frequency or frequencies. This can be done, for instance, using standard components in scanning microscopy systems.

[0128] Figure 12 depicts a general conceptualisation of the process 600 to obtain a final signal of interest 602, in accordance with one embodiment. Measurements or recordings 604 from the signal electrode(s) or optrode(s) provides an overall signal which incorporates the signal of interest and noise signals. The measurements or recordings 606 from the noise sensing electrode(s) or optrode(s) which are not in contact with the recording chamber or the object of interest will capture the noise from the measurement system (and optical noise, in the case of optrodes). These measurements 606 can be used to determine a noise and/or a baseline offset due to the system itself.

[0129] The measurements or recordings 608 from noise sensing electrodes which are in contact with the recording chamber but not in contact with the object of interest, will capture at least some of the noise attributable to the electronics (e.g. noises induced by the junction potential as discussed above). These measurements 608 can be used to determine a noise and/or a baseline offset due to the electronics. For instance, the baseline component may exist if there is non-zero difference in the junction potentials in the electrodes or optrodes used.

[0130] Thus, the measurements 606 and/or 608 from the noise sensing electrodes will be used, in an offset determination step 612, to determine a signal offset.

[0131] The measurements 604, 606, 608 are optionally processed or conditioned in a conditioning step 610, using software or hardware processing. This involves, e.g., the smoothing out or filtering of the signals. Next, in a noise subtraction step 614, the conditioned signals are then processed so as to isolate and subtract the noise component from the signal component, to obtain a noise-subtracted signal of interest. The order of performing the condition step 610 and the noise subtraction step 614 can be reversed.

[0132] From the overall signal. In an offset compensation step 616, the baseline calculated using the noise electrode (or optrode) measurements 606, 608 is subtracted from the noise-subtracted signal of interest, to obtain the final signal of interest 602.

[0133] An advantage of embodiments of the technology described herein, involving separately acquiring the noise signature from one or more sources, using the same channel(s) as the acquisition channel(s) for the signal of interest or using separate channels which are located in close proximity to the acquisition channels, is that the electro-physiological recording can be made in vivo by embedding the recording arrangement into any excitable tissue of interest.

[0134] For instance, in recording electro-physiological signals from the heart to account for the movement of the heart, existing methods involves injecting the heart tissue with a chemical compound to induce an interruption in the beating of the heart. This method is not suitable for in vivo recordings. However, with noise acquisition using the signal channels, or channels essentially collocated with the signal channels, the movement artefact affect the noise acquisition and the signal acquisition substantially in the same way. That is, the noise signatures will be affected by the movement artefacts to a similar or the same extent as the signal of interest. Thus, the effects of the movement artefact will be substantially cancelled out by the processing of the noise and signal signatures. Of course, the advantage whereby the effects of the movement artefact are cancelled or minimised, also exists in cases where the sample is nonbiological or non-physiological.

[0135] Embodiments described herein enable noise cancellation, output signal calibration, or both. Embodiments of the present disclosure can be applied not just for electrophysiology recording systems, but in any application/field where single or multiple channel recordings of ultra-low voltage signals is desired.

[0136] It will be appreciated that the drawing figures are not to scale. The arrangement depicted in the drawing figures is for illustrative purposes only.

[0137] Variations and modifications may be made to the parts previously described without departing from the spirit or ambit of the disclosure.

[0138] For example, the electrodes/optrodes can be laid out in any configuration, and not only in the layout shown in the examples depicted in the drawing figures.

[0139] It further will be appreciated that the optrode or electrode materials can be chosen to suit the arrangement for particular applications. However, as mentioned above, for the purpose of baseline calibration, in optrode-based systems, the extra noise-sensing optrodes are preferably made with the same or substantially the same material as the standard recording optrodes. The extra noise sensing electrodes are preferably made with the same or substantially the same materials as that of the ground electrode VIA, so that the half-cell potentials of the extra noise sensing electrodes and the ground electrode are substantially the same or are similar. Ideally the conductive track and connection to the data acquisition system 40 should be the same or substantially the same materials to that used for the reference electrode.

[0140] In MEA systems, the extra noise sensing electrodes are preferably made with the same or substantially the same materials as the standard recording electrodes. The conductive tracks and connections to data acquisitions system 40 for these extra electrodes are preferably also of the same or substantially the same material as the standard recording electrodes.

[0141] While embodiments are disclosed in relation to examples involving optrode recording or multi-electrode recording, it is applicable to different recording systems where a physical signal (reflectance, sound, or another signal) from the tissue or sample of interest is converted to an electrical signal. The sample can be biological or it may not be biological.

[0142] In the above, the term “measurement chamber” refers to the location or space in which the recording apparatus is located, so as to obtain both the signal from the recording area (i.e. sample or tissue of interest), and one or more noise signals. It can be more generally referenced by the term “recording environment”, which is understood not to be limited by a specific “chamber”, as in the case of e.g., ex vivo or in vitro recordings.

[0143] Thus, generalising from the above, the system can include one or more transducer units which are not insulated within a holding substrate, but rather, sensing the signal(s) of interest. The transducer units are provided along with one or more first noise transducer unit that is insulated from the signal(s) of interest and which may be provided in the substrate. The extra channels, provided by the first noise transducer unit(s), capture a first noise signature. Further in some embodiment, the system includes one or more second transducer unit which capture a second noise signature. The sum of the first and second noise signatures is subtracted from the recorded signal of interest, to determine a calibrated signal, where at least some of the noise associated with the recorded signal has been removed.

4. Example embodiment

[0144] An example embodiment is described in relation to Figures 13 to 26. Figure 17 illustrates Equations (a) to (e), in accordance with an embodiment.

4.1 Active Noise Cancelling (ANC) System

[0145] In some implementations, the light source contributes the majority of the output signal's noise. By placing a light splitter at the light source's output, it is possible to obtain two light output channels with nearly identical noise levels. The two light channels may then be linked to an active optrode, an inactive optrode, and two channels from the photodiode receiver. With this setup, one message channel contains nerve signal and system noise, while the other noise channel contains only system noise. By transferring the signals from the two channels to an active noise cancellation algorithm, the noise in the message channel can be substantially reduced based on the information contained in the noise channel.

[0146] Figure 15 is a block diagram of an Active Noise Cancelling (ANC) system 1500, in accordance with an embodiment. The ANC system consists of two boards: a receiver board and an FPGA development board. Two channels of light signals are received by the receiver board, amplified by a maximum gain of 140 dBΩ, and converted into digital signals. Two channels of digital signals are then processed by noise cancelling algorithm on the FPGA development board which outputs a clean signal.

4.2 Receiver Board

[0147] Figure 18 is a schematic diagram of the light receiver board, in accordance with an embodiment. The light receiver board has two stages of power supplies. The first stage low drop-out (LDO) regulator (LT3045EMSE) converts an external voltage supply with a range of 7V to 20V down to 6.2V. To reduce interference and noise on the board, there are three second-stage LDOs (LT3045EMSE), two for analogue supply and one for digital supply, that all convert 6.2V to 3.3V.

[0148] Light is reflected at different reflection rates at the optrode, the reflection rate is decided by the angle of the liquid crystal being rotated by the nerve signal voltage. The added AC nerve signal portion is less than 10% of the whole light intensity. Since only the nerve signal part of the light is of interest, and the signal needs to be amplified at least 120dB, the DC part of the light must be removed before amplification. Therefore, the amplifiers are AC coupled by a large capacitor right after the photodiode. When the photodiode is configured to reverse-biasing, the system suffers from 1/f noise that comes from the LDO. Therefore, the photodiode D1 is configured in “zero-mode” (an example of which is described in Reference [13]). In this mode, the sensitivity is reduced because of no DC biasing, but the noise from the DC biasing power supply is also removed, which makes the overall signal-to-noise ratio a lot better.

[0149] Referring again to Figure 18, U1 and U2 are two stages of amplifiers. A large capacitor C1 makes sure only AC current is sent to op-amp U1, which is configured to a transimpedance amplifier. The gain of the transimpedance amplifier is set by a variable resistor R1. Op-amp U2 along with R2 and R3 forms an inverting amplifier and the gain is controlled by variable resistor R3. The resistance of R1 and R3 both come from a digital potentiometer with the lowest resistance of 390Ω and largest resistance of 10 000 kΩ, which gives the two-stage amplifier a total gain from 43.6 dBΩ to 140 dBΩ. The op-amps U1 and U2 (ADA4896) are chosen to have very low noise. The op-amps U1 and U2 have an input-referred voltage noise of 2.3 nV/√Hz and an input-referred current noise of 11 pA/ √Hz at 10 Hz. However, the op-amps also introduce −11 uA input bias current, which can be undesirable in the even that huge gains are present. With R1 set to 10 000 kΩ, −11 uA input bias current will result in −1.1V output voltage. Therefore, Vref is set to be 2.1V to have about 2V peak-peak signal range and also 1.1V bottom gap room. The maximum input current from the photo-diode is 2V/140dBΩ = 200nA.

[0150] The output voltage Vx from the two-stage amplifier is then put through an active fourth-order anti-aliasing low-pass filter, consisting of U3 and U4 (LT6233).

The cut-off frequency is set to 12 kHz for the balance of retaining signal up to 10 kHz and anti-aliasing at ADC sampling frequency of 64 kHz.

[0151] Finally, a 24-bit 64 kHz Analogue to Digital Converter (MAX11254) converts the amplified analogue signal into a digital signal, which is sent to the FPGA board (Arty Z7) via an SPI port.

4.2 Digital Signal Processor (DSP)

[0152] A brain-machine interface may utilise an array of hundreds of optrodes working together. It is desirable that the processing of the signals produced by the optrodes occurs in real-time.

[0153] The Wiener filter (described in Reference [10]) was tested effective for actively cancelling the noise using signals recorded from an existing setup. However, the Wiener filter processes part of the signal in a bin at a time and requires a huge amount of computation resources when the bin size gets very large. From experimental data, the optrode system showed little correlation between data streams beyond 3 samples from zero lag. Conversely, a one tap filter showed significant noise reduction, but increasing the number of taps showed little improvement. Also, to fit an algorithm that can process hundreds of channels all at the same time, the algorithm for each channel has to be small in size and consume little power. Therefore, a one-tap adaptive filter algorithm that is based on the Wiener filter was designed and implemented in the FPGA board.

[0154] Figure 19 shows a digital signal processing structure, in accordance with an embodiment. Assume the transfer functions H1 are removed from the system, and the transfer functions H2 are integrators. The system has two inputs $x_1(i)$ and $x_2(i)$, and an output y. Signal $x_1(i)$ is the noisy message signal and $x_2(i)$ is the noise signal. The system is trying to remove the part of the noise in $x_1(i)$ that is correlated to part of the noise in $x_2(i)$. The value of signal $x_1(i)$ may be determined in accordance with Equation 17(a), where n is the noise in both $x_1(i)$ and $x_2(i)$, s is signal plus other noise in $x_1(i)$, m is other noise in $x_2(i)$, and k is the scale factor. s, n, and m are random signals and are uncorrelated to each other.

[0155] Let N be the total number of samples in $x_1(i)$ and $x_2(i)$. Take $x(cc)$, the cross-correlation of $x_1(i)$ and $x_2(i)$; and $x(ac)$, the auto-correlation of $x_2(i)$. $x(cc)$ may be determined in accordance with Equation 17(b).

[0156] The filter coefficient may be determined by dividing the cross-correlation by auto-correlation, in accordance with Equation 17(c). Since s, n, and m are uncorrelated, their cross-correlation should be equal to zero, in accordance with Equation 17(d).

[0157] In some embodiments, experiment result shows kn is the dominant noise in x_2, as shown in Equation 17(e). Therefore, Equation 17(c) may be reduced in accordance with Equation 17(f).

[0158] Output signal y may be determined in accordance with Equation 17(g).

[0159] Since $kn \gg m$, the noise level in y is largely improved compared to $x_1(i)$.

[0160] To make the system more practical, a high-pass filter H_1 is implemented to remove DC offset in the signals to improve cross-correlation and auto-correlation results. A leaky integrator H_2 is used so the system has a moving average to track the most recent signal, for about half a second. This leaky integrator compensates for the change of different noise gain in $x_1(i)$ and $x_2(i)$ caused by temperature change or physical movement.

[0161] Figure 16 illustrates the data flow in the system, in accordance with an embodiment. Light comes out of a light source and splits into two identical lights at the light splitter. Then one light goes into the active optrode where it carries a nerve signal, and the other light goes into the inactive optrode and carries no extra information. Both lights are converted into current by the photodiode, then converted into voltage by the amplifier, and finally converted into digital signals by the ADC, all happen on the light receiver board.

[0162] Then the digital signals are transmitted to the FPGA for digital signal processing. The light source is a Super-Luminescent Diode with a 1550nm wavelength, and a variable current of up to 800mA, running at a constant temperature of 20 ◦C. The frequency range of the nerve signal is 10 Hz to 10 kHz.

[0163] The USB serial port embedded in the FPGA board can only stream the data to a PC at 300Hz, which does not meet the requirement. However, it is capable to stream out real-time data at 64 kHz with suitable peripherals.

5. Experimental Results

5.2 Cross correlation

[0164] Preferably, for the digital signal processing algorithm to function well, the noise in the two light channels must be very similar. By directly taking measurements from the two receiver channels without any processing algorithm, with the light source turned on and no input to the optrode, the crosscorrelation of the two receiver channels may be calculated. Figure 20 is a graph illustrating a cross correlation of active optrode and inactive optrode channel at different light source power with no input signal at the active optrode, in accordance with an embodiment.

[0165] At lower light source power, the noise on the optrode and light receiver board is quite large compared to the noise from the light source. The nerve signal and light source noise increase proportionally to the increase of light power, while the light receiver board noise stays the same. When the light source current exceeds 500mA, the light source noise dominates the whole noise in the system, and the normalised cross-correlation stays at a steady 0.8. This suggests the possibility of active-noise-cancelling in this optrode system.

5.2 Noise comparison

[0166] Figure 21 shows two pairs of graphs illustrating the signals before (active optrode channel) and after (noise cancelling output channel) the noise-cancelling process, in accordance with embodiments.

[0167] Graphs (a) and (b) illustrate noise signals coming from the light source that is powered with 500mA current. The active optrode channel signal, illustrated in graph (a), has a much larger amplitude range than the noise cancelling output signal, illustrated in graph (b), which means the noise in the noise cancelling output channel has been reduced. However, these two signals, in graphs (a) and (b), still have a normalised cross-correlation of 0.4, which implies there is still room to improve the performance.

[0168] Graph (c) in Figure 21 illustrates an active optrode signal with 500mA current at the light source. Graph (d) illustrates the corresponding noise cancelling output channel, in which a 200mV sinusoidal signal input has been applied to the active optrode signal illustrated in graph (c). Advantageously, the signal in the noise cancelling output channel, graph (d), is more smooth and standard than the signal in the active optrode channel, graph (c).

[0169] Figure 22 is a graph illustrating the comparison between the RMS value for Channel1 input and DSP output at different light source current, when there is no input signal at the optrode, in accordance with an embodiment. The blue bar shows the Channel1 input before the signal processing algorithm. The RMS value of the blue bar raises when the light source current goes up, which confirms that the noise in the light source is proportional to the light source current. The red bar shows the RMS value of the digital signal processing output. At lower light source current, the noise reduction from the blue to the red bar is quite small, and it is improving with larger light source current, and stays at around 50% when light source current is above 500mA, which is matching the cross-correlation result.

5.3 Optical input test with sin signal

[0170] Figure 23 illustrates the signal-to-noise ratio and signal-to-noise ratio improvement before and after the active noise- cancelling process, for 200mV sinusoidal input, at different light source current, in accordance with an embodiment.

[0171] Figure 24 illustrates the signal-to-noise ratio and signal-to-noise ratio (SNR) improvement before and after the active noise-cancelling process, for 10mV sinusoidal input, at different light source current, in accordance with an embodiment.

[0172] There is an outstanding data point at 300mA input, but overall it matches the previous results that at lower light source current the signal-to-noise ratio improvement is quite small and it gets larger as the light source current increases, then gets steady at higher light source current.

[0173] Figure 25 shows the comparison of active optrode channel (a) and noise cancelling output (b) at 500mA light current with 10mV 1 kHz sinusoidal input signal at the active optrode, in accordance with an embodiment. The 1 kHz signal level in both graphs stays the same, while everywhere else the magnitude drops by 5 dB to 10 dB, which matches the results from above reading.

5.4 Cancel Physical Movement

[0174] When mounting the nerve signal detection device onto a human body, the system will incur some physical movement artifacts. Figures 26 and 27 illustrate corresponding experimental results graphs, in accordance with an embodiment. Figure 26 shows active optrode experiment results with movement artefact, in accordance with an embodiment. Figure 27 shows noise cancelling output experiment results, corresponding to the experimental results of Figure 26, with movement artefact reduction, in accordance with an embodiment.

[0175] Although there is still some low frequency noise left in the DSP channel, those spikes caused by the movement have been largely removed, which shows that this system embodiment is effective in removing physical movement artifacts.

[0176] It will be appreciated by persons skilled in the art that numerous variations and/or modifications may be made to the above-described embodiments, without departing from the broad general scope of the present disclosure. Furthermore, it will be appreciated by persons skilled in the art that embodiments disclosed herein can be combined with one or more other embodiment disclosed herein, without departing from the broad general scope of the present disclosure. The present embodiments are, therefore, to be considered in all respects as illustrative and not restrictive.

[0177] It will be appreciated by persons skilled in the art that any suitable distribution of functionality between different functional units may be used without detracting from the invention. For example, functionality illustrated to be performed by separate devices may be performed by the same device. Likewise, functionality illustrated to be performed by a single device may be distributed amongst several devices. Hence, references to specific functional units are only to be seen as references to suitable means for providing the described functionality, rather than indicative of a strict logical or physical structure or organization.

[0178] It will be appreciated by persons skilled in the art that, for processes and methods disclosed herein, the operations performed in the processes and methods may be implemented in differing order. Furthermore, the outlined steps and operations are only provided as examples, and some of the steps and operations can be optional, combined into fewer steps and operations, or expanded into additional steps and operations without detracting from the essence of the disclosed embodiments.

[0179] Throughout this specification the word ‘comprise’, or variations such as ‘comprises’ or ‘comprising’, will be understood to imply the inclusion of a stated element, integer or step, or group of elements, integers or steps, but not the exclusion of any other element, integer or step, or group of elements, integers or steps.

[0180] As used herein, any reference to “one embodiment” or “an embodiment” means that a particular element, feature, structure, or characteristic described in connection with the embodiment is included in at least one embodiment. The appearances of the phrase “in one embodiment” in various places in the specification are not necessarily all referring to the same embodiment. Similarly, use of “a” or “an” preceding an element or component is done merely for convenience. This description should be understood to mean that one or more of the element or component is present unless it is obvious that it is meant otherwise.

[0181] Unless expressly stated to the contrary, "or" refers to an inclusive or and not to an exclusive or. For example, a condition A or B is satisfied by any one of the following: A is true (or present) and B is false (or not present), A is false (or not present) and B is true (or present), and both A and B are true (or present).

References

[0182] The following references are incorporated herein:

[2] E. Scherschener, C. D. Perciante, E. A. Dalchiele, E. M. Frins, M. Korn, and J. A. Ferrari, "Polymer-dispersed liquid-crystal voltage sensor," Applied Optics, vol. 45, no. 15, p. 3482, 2006.

[10] N. Benvenuto, S. Tomasin, and G. Cherubini, Algorithms for communications systems and their applications. Wiley, 2021.

13] Y. Wei, T. Lehmann, L. Silvestri, H. Wang, and F. Ladouceur, "Photodiode working in zero-mode: Detecting light power change with dc rejection and ac amplification," Optics Express, vol. 29, no. 12, p. 18915, 2021.

CLAIMS

1. A recording apparatus, comprising:

a reference electrode;

a plurality of conductive devices;

the plurality of conductive devices including at least one signal conduction device adapted to conduct a signal from an object of interest at least partially located in a recording environment, and at least one noise conduction device adapted to conduct a noise signal.

2. The apparatus of claim 1, wherein the at least one noise conduction device includes one or more first noise conduction device which is, in use, adapted to be exposed in the recording environment.

3. The apparatus of claim 2, wherein the first noise conduction device and the signal conduction device are of substantially the same material and dimension.

4. The apparatus of any of claims 1 to 3, wherein the at least one noise conduction device includes one or more second noise conduction device which is, in use, adapted to be isolated from the recording environment.

5. The apparatus of claim 4, wherein at least some of the plurality of conductive devices are provided in a substrate.

6. The apparatus of claim 5, wherein the one or more second noise conduction device is embedded within the substrate.

7. The apparatus of claim 5 or claim 6, wherein the reference electrode is provided in the substrate.

8. The apparatus of any of claims 1 to 7, wherein the plurality of conductive devices are a multi-electrode array.

9. The apparatus of any of claims 1 to 7, wherein at least some of the conductive devices are transducers.

10. The apparatus of claim 9, when directly or indirectly dependent on claim 2, wherein the one or more first noise conduction devices include at least one noise electrode and at least one noise sensing transducer.

11. The apparatus of claim 10, wherein a track for conduction with the at least one noise electrode is of substantially the same material as a track for conduction with the reference electrode.

12. The apparatus of any of claims 9 to 11, wherein the transducers are each adapted to transduce an optical signal into an electrical signal, receive a return electrical signal, and transmit an output optical signal which is transduced from the return electrical signal.

13. The apparatus of any of claims 1 to 12, further comprising a timer or controller adapted to time a switch between input to the signal conduction device and input to the noise conduction device.

14. The apparatus of claim 13 further comprising a signal holding circuitry to periodically hold an output of the signal conduction device or the noise conduction device.

15. A multi-channel recording apparatus, comprising:

a reference electrode;

a plurality of optical-electrical transducers, embedded in a light transmitting substrate;

the plurality of optical-electrical transducers including at least one signal recording transducer adapted to transduce an optical input into an electrical input to an object of interest;

the plurality of optical-electrical transducers including at least one noise recording transducer adapted to receive a response signal from the object of interest and transduce it into an output optical signal;

a detector adapted to detect the output optical signal.

16. An electrical measurement apparatus, comprising:

a reference electrode;

at least one signal recording device, adapted to record a signal from a object of interest;

an input device adapted to simulate the object at user defined times.

17. The apparatus of claim 16, wherein the at least one signal recording device is at least one optical-electrical transducer, embedded in a light transmitting substrate, the at least one optical-electrical transducer being adapted to transduce an optical input into an electrical input to the object of interest.

18. The apparatus of claim 17, the at least one optical-electrical transducer being adapted to transduce an electrical signal from the object of interest in response to the electrical input, into an output optical signal.

19. The apparatus of claim 18, wherein the optical input is provided by, at user defined times: switching a light source on and off; interrupting a light transmission from a light source at the user defined times; moving the at least one optical-electrical transducer from a light receiving position.

20. A recording system, comprising a recording apparatus of any of claims 1 to 19.

21. A signal recording method, comprising:

providing an input signal to an object of interest which is at least partially located in a recording environment;

obtaining a response signal from the object of interest, in response to the input signal; the response signal being transmitted or transduced by at least one signal recording electrode or transducer;

obtaining a noise data from a location within the measurement environment;

obtaining a noise cancelled data, the obtaining of the noise cancelled data including subtracting the noise signal from the response signal.

22. The method of claim 21, including providing at least one noise recording electrode or transducer.

23. The method of claim 22, wherein obtaining the noise signal includes obtaining a first noise signal from at least one first noise electrode or transducer which is located to be isolated from the object of interest but exposed within the measurement environment.

24. The method of claim 22 or claim 23, wherein obtaining the noise signal includes obtaining a second noise signal from at least one second noise electrode or transducer which is wholly embedded within a substrate located in the recording environment, so that it is not exposed within the recording environment.

25. The method of any of claims 21 to 24, wherein the at least one first noise electrode or transducer is at least one first noise electrode, and the noise signal includes a third noise signal from at least one noise transducer,

which is located to be isolated from the object of interest but exposed within the recording environment.

26. The method of any of claims 21 to 25, further comprising obtaining a reference signal from a reference electrode.

27. The method of claim 26, when directly or indirectly dependent on claim 23, further comprising obtaining a value of a voltage offset voltage, wherein the obtaining of the voltage offset voltage value includes calculating a difference between the reference signal and the first noise signal.

28. The method of claim 27, further comprising applying a compensation voltage to a substrate located within the measurement environment, the compensation voltage being the voltage offset voltage with a reverse polarity.

29. The method of claim 27 or claim 28, wherein the obtaining of the noise cancelled data includes subtracting the voltage offset value from the response signal.

30. The method of any of claims 27 to 29, including providing the input signal at a plurality of input values.

31. The method of claim 30, including obtaining a plurality of voltage offset values each at a corresponding input value, and calculating a baseline from the plurality of voltage offset values.

32. The method of claim 31, including calibrating the response signal data to remove the baseline.

33. The method of 21 to 32, further including conditioning the response signal and/or the noise signal.

34. The method of claim 33, wherein the conditioning includes smoothing or filtering the response signal and/or the noise signal.

35. The method of any of claims 21 to 34, wherein the input signal is intermittently provided.

36. The method of claim 35, wherein obtaining the noise signal includes obtaining a signal from the at least one signal electrode or transducer, when the input signal is not provided.

37. The method of claim 36, wherein the input signal is an optical input.

38. The method of claim 37, wherein the optical input is provided by, at user defined times: switching a light source on and off; interrupting a light transmission from a light source; moving the at least one signal electrode or transducer to and from a light receiving position.

39. A computer programme, comprising instructions for controlling a computer to implement a method in accordance with any of claims 21 to 38.

40. An apparatus for obtaining a functional measurement for an object of interest, comprising a computer having a processor and memory supporting computer processes, the computer implementing a method as claimed in any of claims 21 to 38.

41. An electro-optical detection apparatus, comprising:
a first optrode, configured to receive a first light signal and generate a first optrode signal, the first optrode configure to be in contact with a sample of interest;
a second optrode, configured to receive a second light signal and generate a second optrode signal, the second optrode configured to be isolated from the sample of interest;
a receiver, configured to:

determine an output signal by applying an active noise cancellation algorithm to the first optrode signal and the second optrode signal.

42 The apparatus of claim 41, further comprising:
a light source, configured to generate a light signal; and
a light source splitter, configured to split the light signal into the first light signal and the second light signal.

43. The apparatus of any of claims 41 to 42, wherein generating a first optrode signal comprises:
receiving, and reflecting, by the first optrode, the first light signal into a photodiode;
generating, by the photodiode, an analogue electrical signal,
converting, by an analogue-to-digital converter, the analogue electrical signal to produce the first optrode signal.

44. The apparatus of any of claims 41 to 43, wherein applying an active noise cancellation algorithm comprises subtracting the second optrode signal from the first optrode signal.

45. The apparatus of any of claims 41 to 44, wherein applying an active noise cancellation algorithm comprises applying a Wiener filter to the first optrode signal and the second optrode signal.

46. The apparatus of any of claims 41 to 45, wherein applying an active noise cancellation algorithm comprises applying a one-tap adaptive filter to the first optrode signal.

47. The apparatus of any of claims 41 to 46, wherein applying an active noise cancellation algorithm comprises determining a cross-correlation of the first optrode signal and the second optrode signal.

48. The apparatus of claim 47, further comprising determining an auto-correlation of the second optrode signal.

49. The apparatus of claim 48, further comprising determining a filter coefficient based on the cross-correlation and the auto-correlation.

50. The apparatus of any of claims 41 to 49, wherein applying an active noise cancellation algorithm comprises applying a high-pass filter to the first optrode signal.

51. The apparatus of any of claims 41 to 50, wherein the first optrode comprises:
a polarisation-maintaining fibre;
a liquid crystal layer; and
a mirror.

52. A method of detecting a nerve signal, comprising:
generating, by a light source, a light signal;
splitting the light signal into a first light signal and a second light signal;
generating, based on the first light signal, by a first optrode, a first optrode signal, the first optrode configure to be in contact with a sample of interest;
generating, based on the second light signal, by a second optrode, a second optrode signal, the second optrode configure to be isolated from the sample of interest;
determining an output signal by applying an active noise cancellation algorithm to the first optrode signal and the second optrode signal.

53. The method of claim 53, wherein generating the first optrode signal comprises:

receiving, and reflecting, by the first optrode, the first light signal into a photodiode;
generating, by the photodiode, an analogue electrical signal,
converting, by an analogue-to-digital converter, the analogue electrical signal to produce the first optrode signal.

54. The method of any of claims 52 to 53, wherein applying an active noise cancellation algorithm comprises subtracting the second optrode signal from the first optrode signal.

55. The method of any of claims 52 to 54, wherein applying an active noise cancellation algorithm comprises applying a one-tap active filter to the first optrode signal and the second optrode signal.

56. The method of any of claims 52 to 55, wherein applying an active noise cancellation algorithm comprises applying a Wiener filter to the first optrode signal and the second optrode signal.

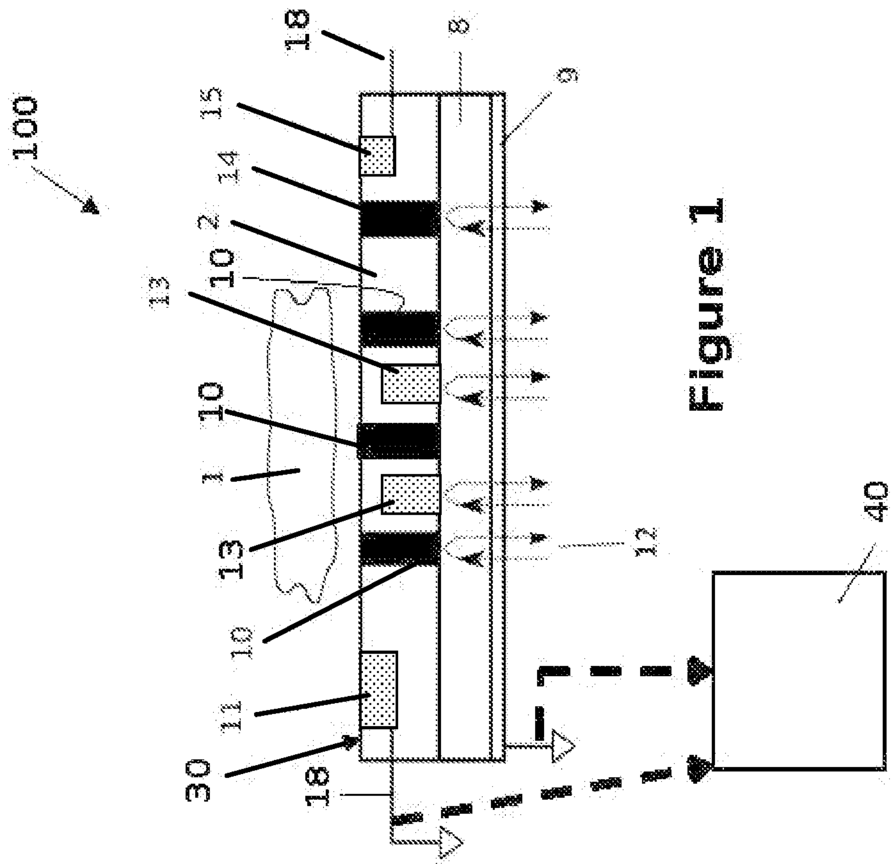


Figure 1

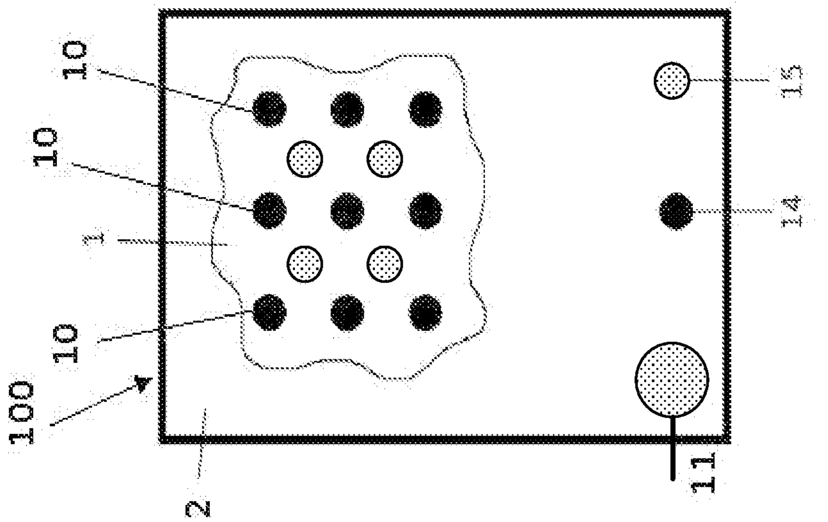


Figure 2

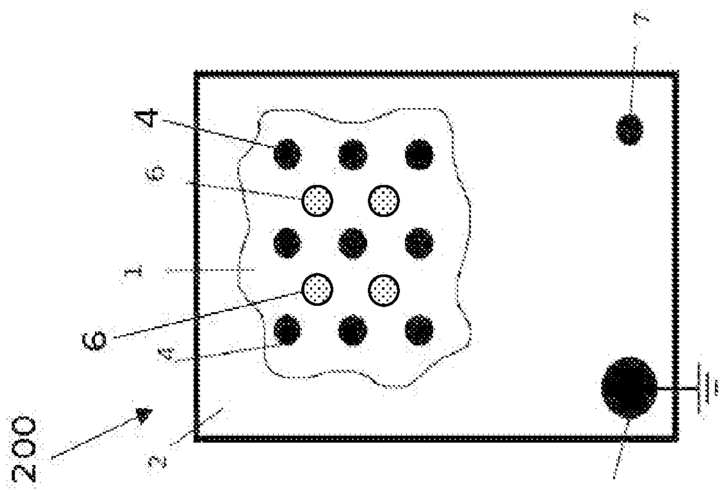


Figure 4

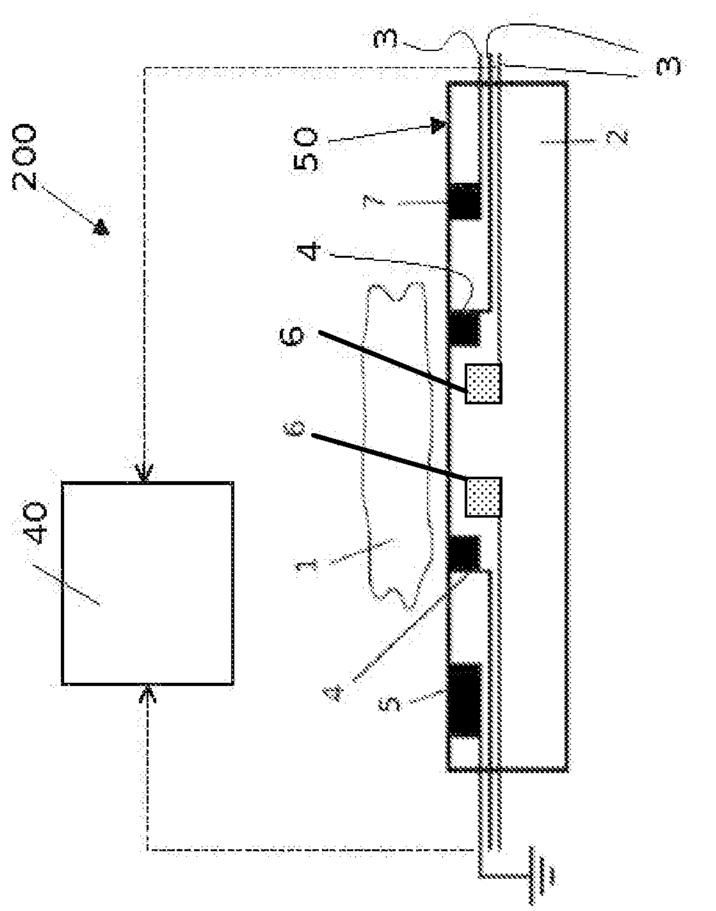


Figure 3

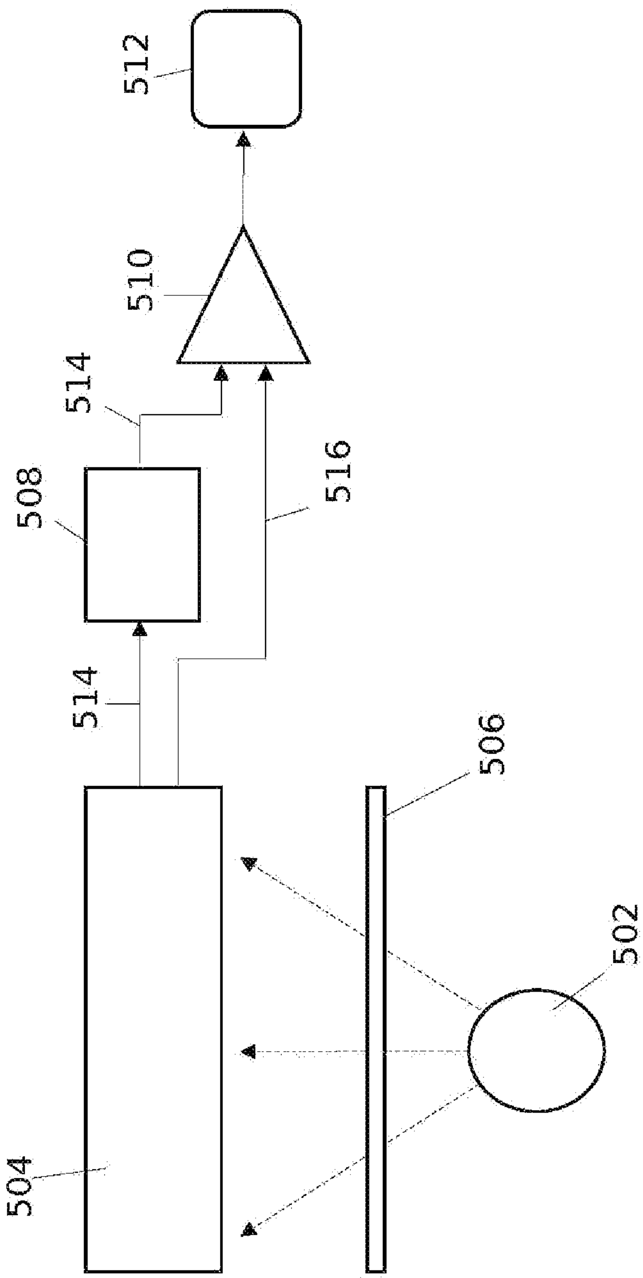


Figure 5

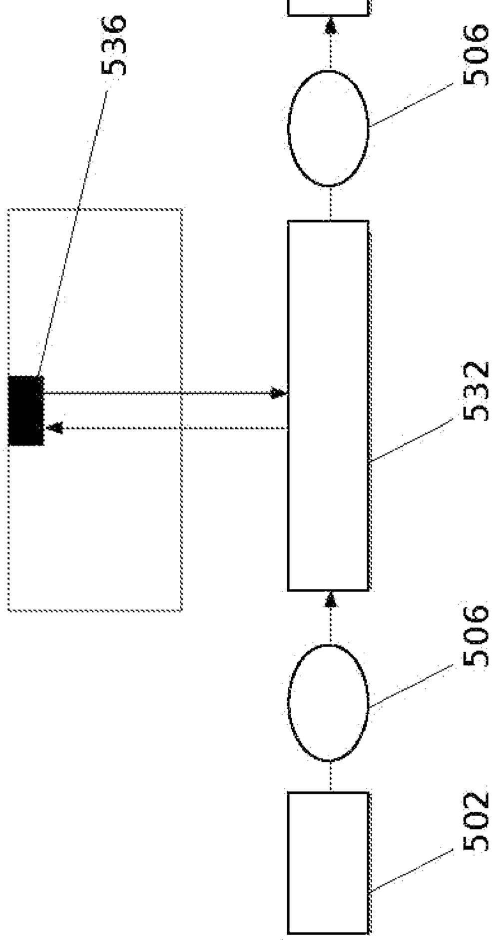


Figure 6-1

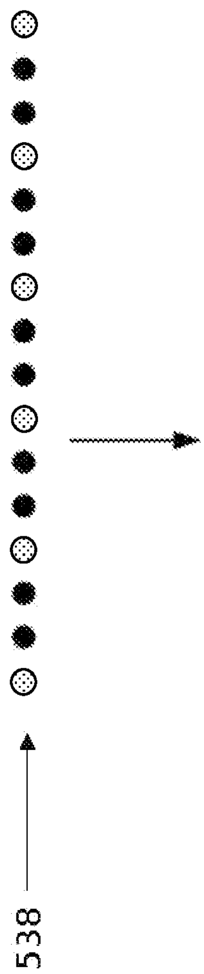


Figure 6-2

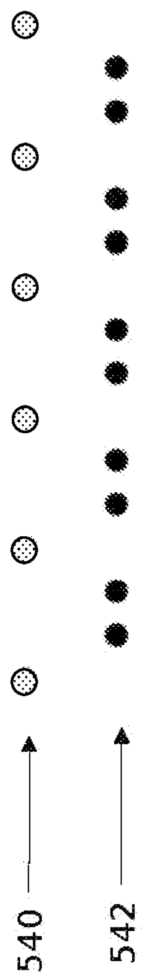
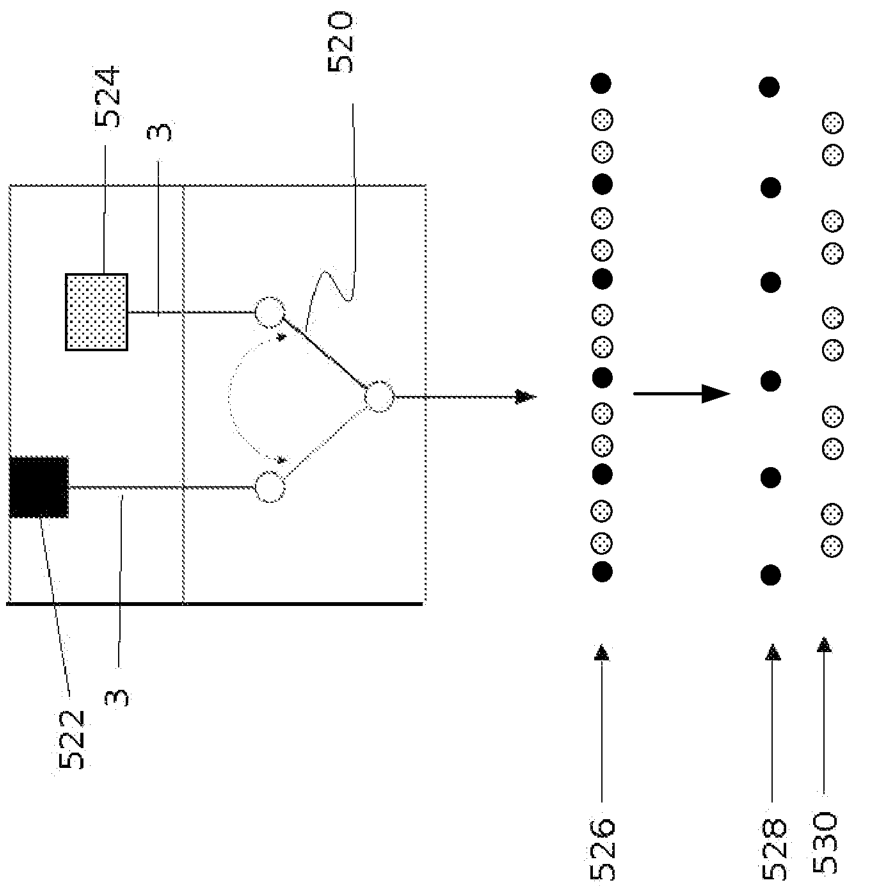


Figure 6-3

Figure 7-1

Figure 7-2

Figure 7-3



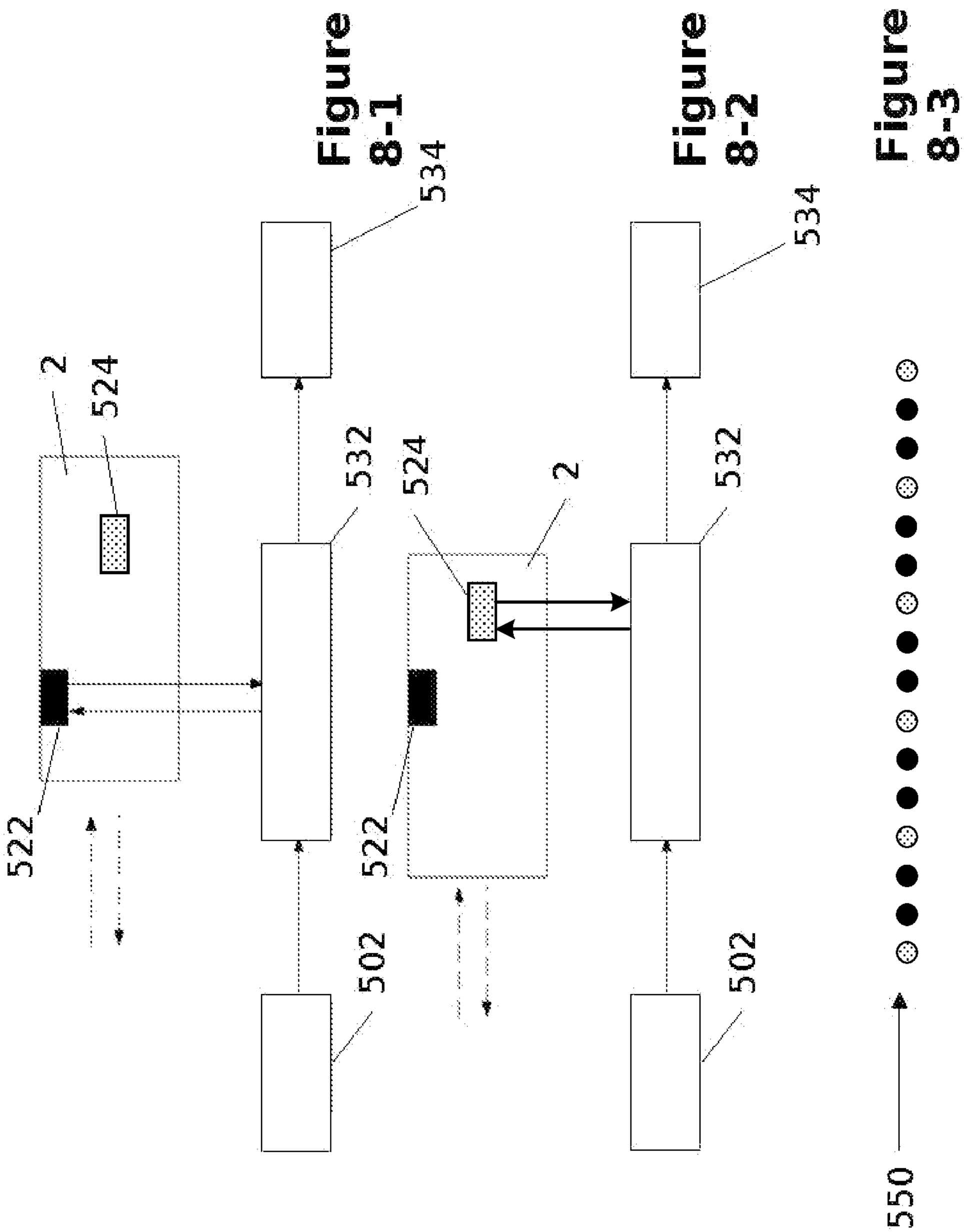


Figure 8-1

Figure 8-2

Figure 8-3

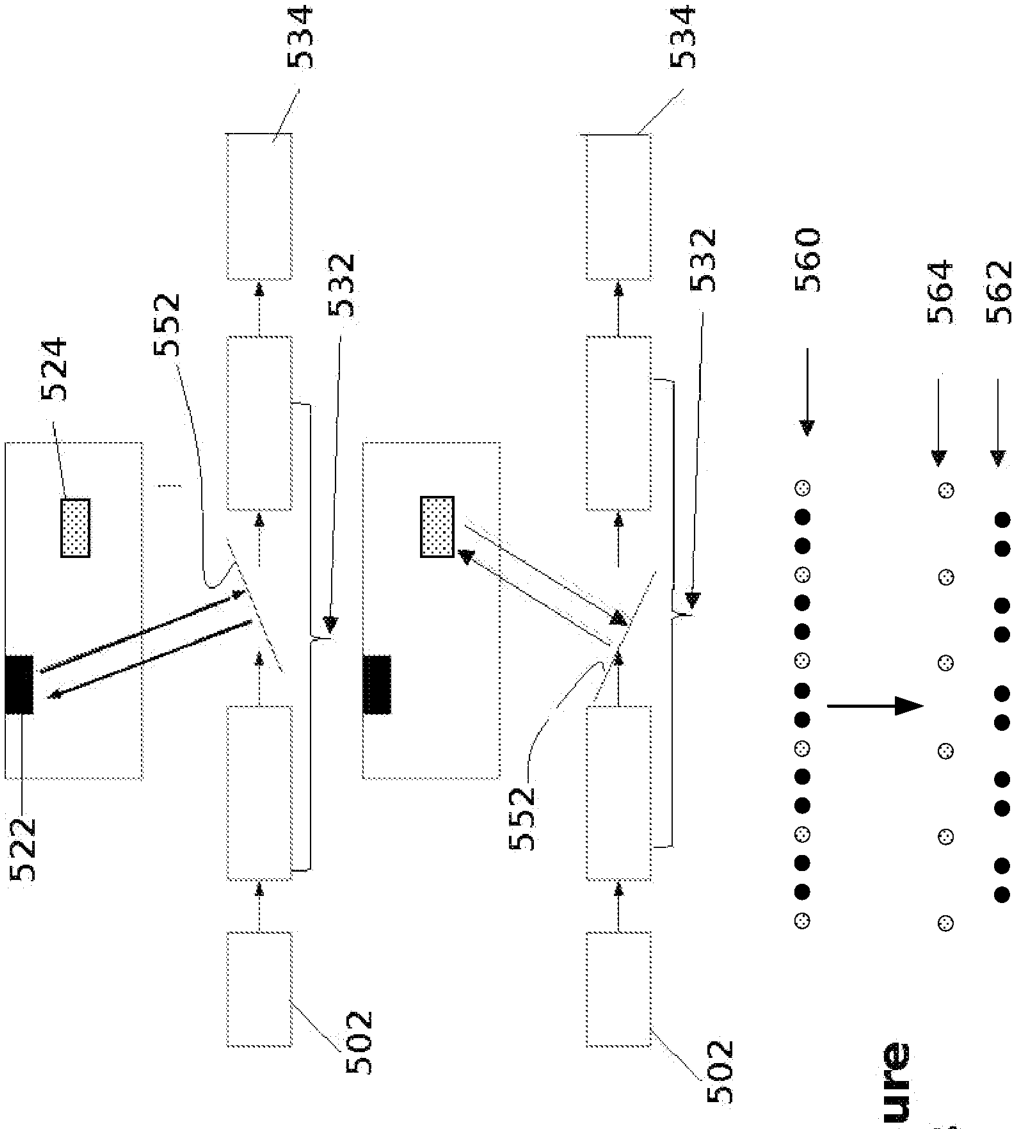


Figure 9-1

Figure 9-2

Figure 9-3

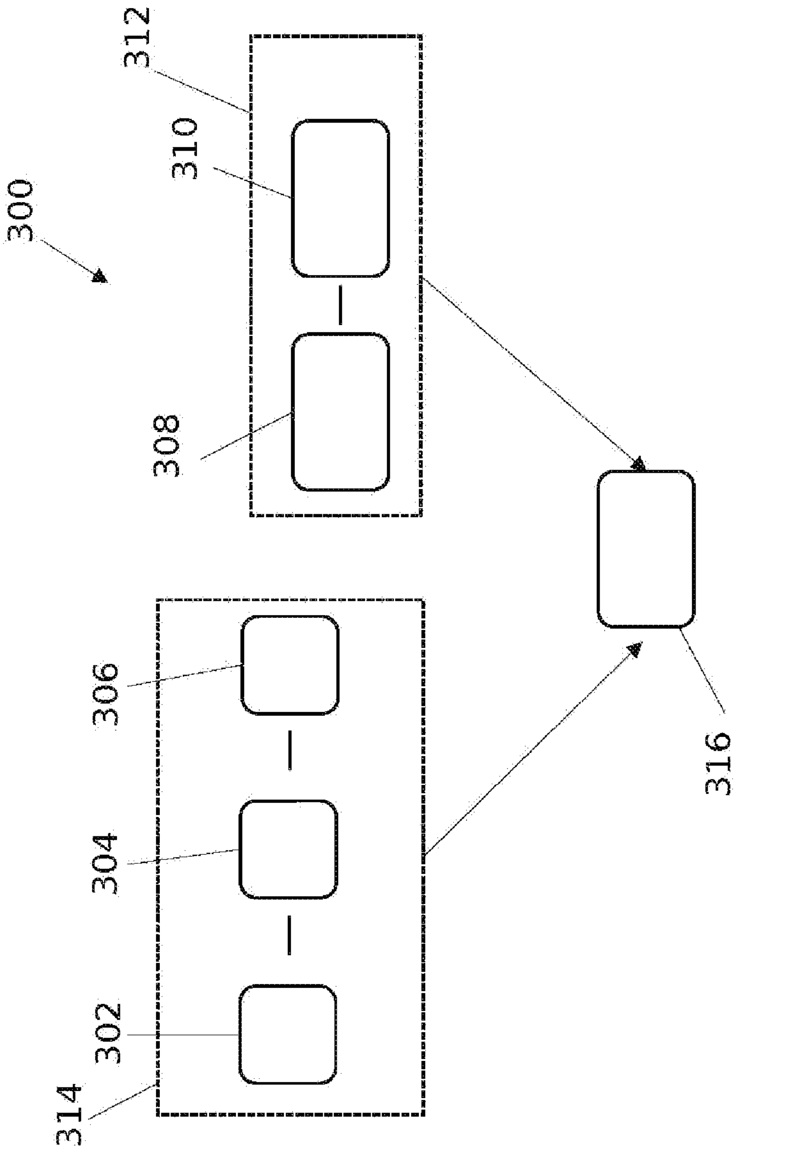


Figure 10

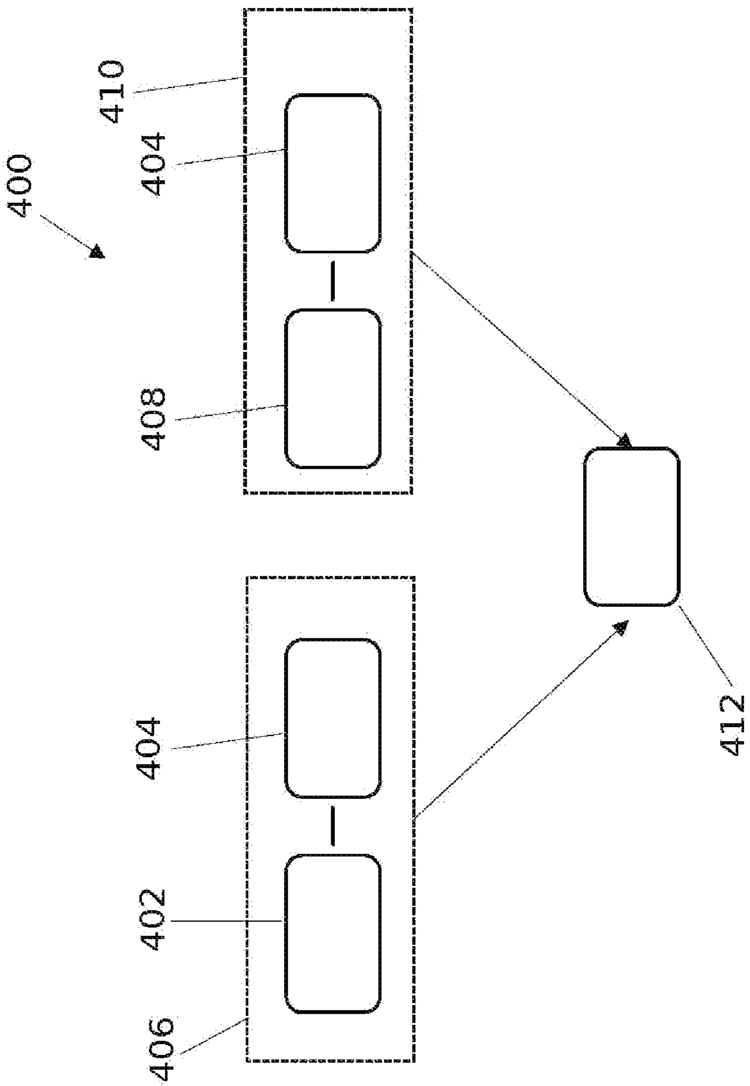


Figure 11

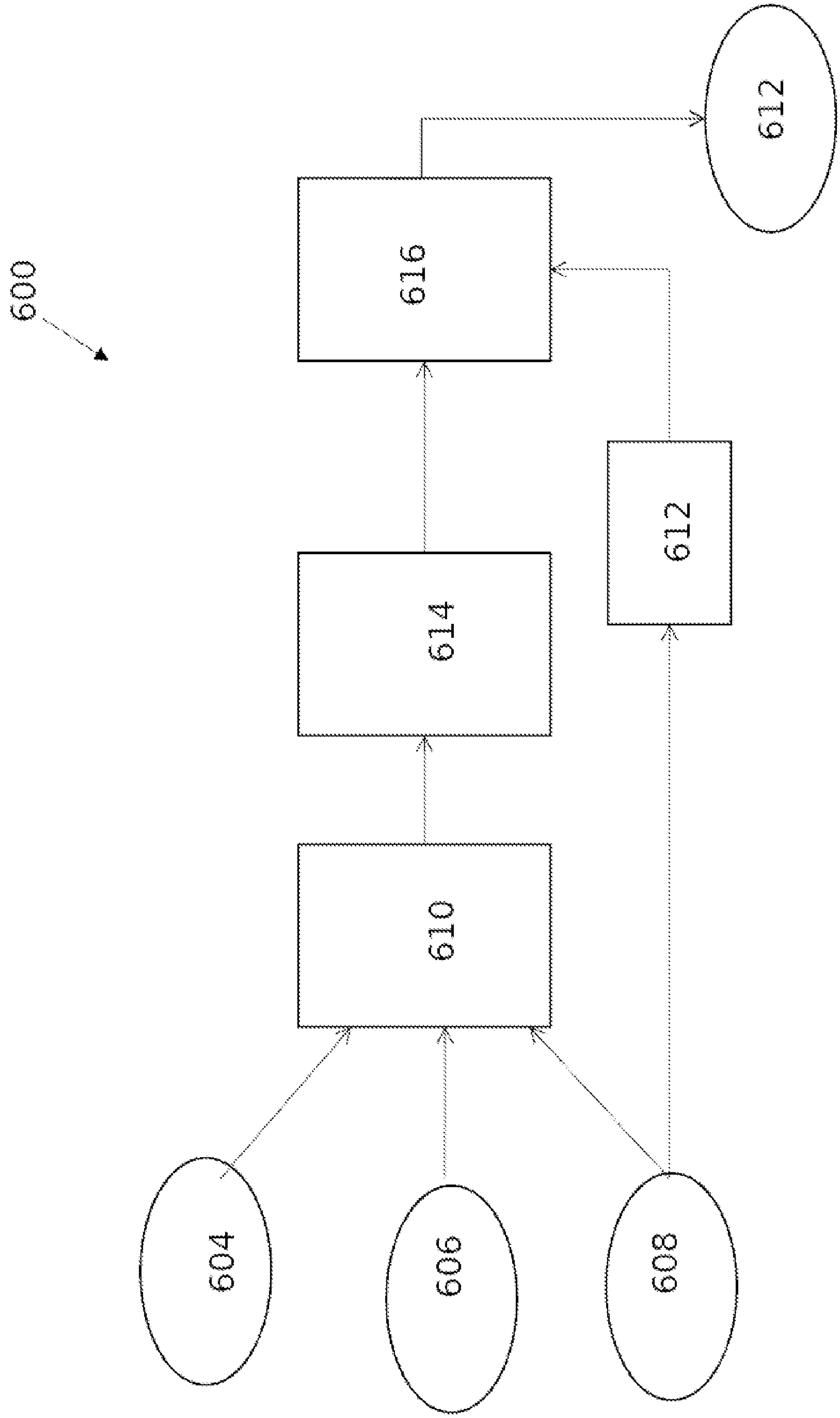


Fig. 12

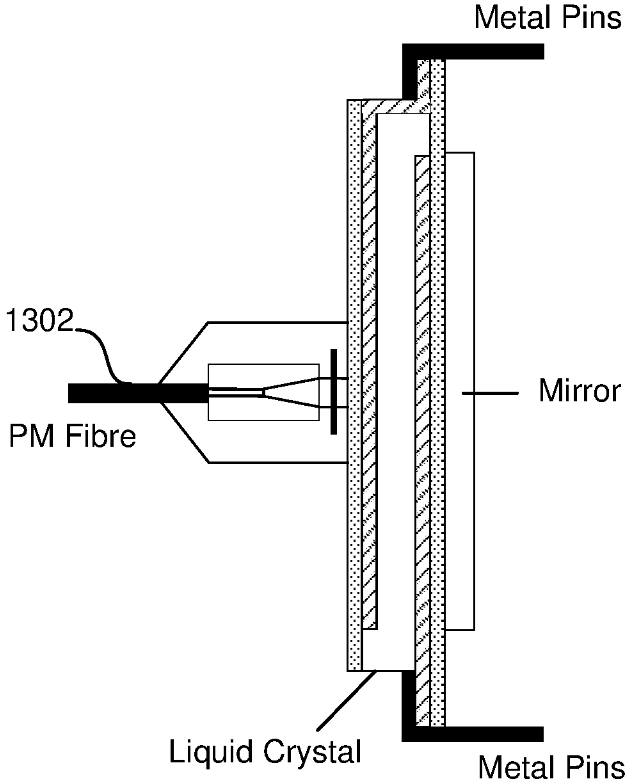


Figure 13

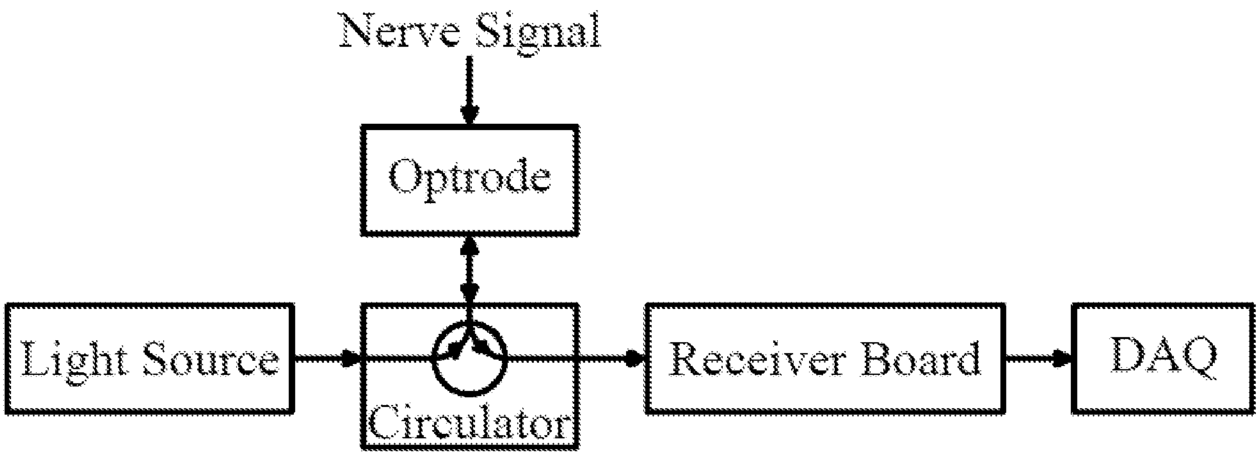


Figure 14

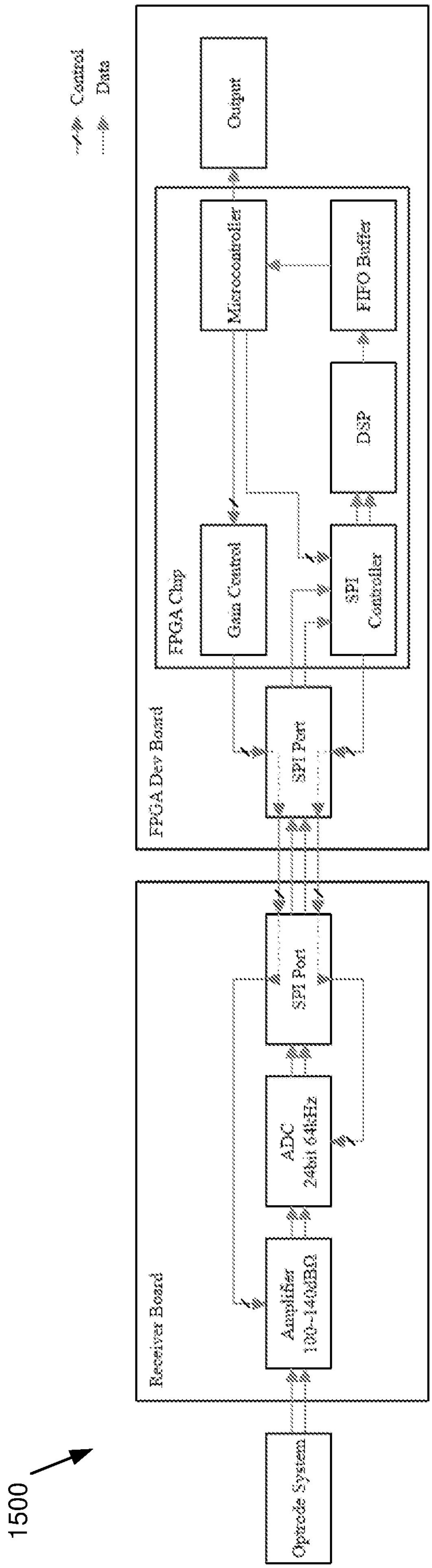

Control
Data
Output
Microcontroller
FIFO Buffer
DSP
Gain Control
SPI Controller
FPGA Chip
FPGA Dev Board
SPI Port
SPI Port
ADC 24bit 64kHz
Amplifier 100~140dBΩ
Receiver Board
Optrode System
1500

Figure 15

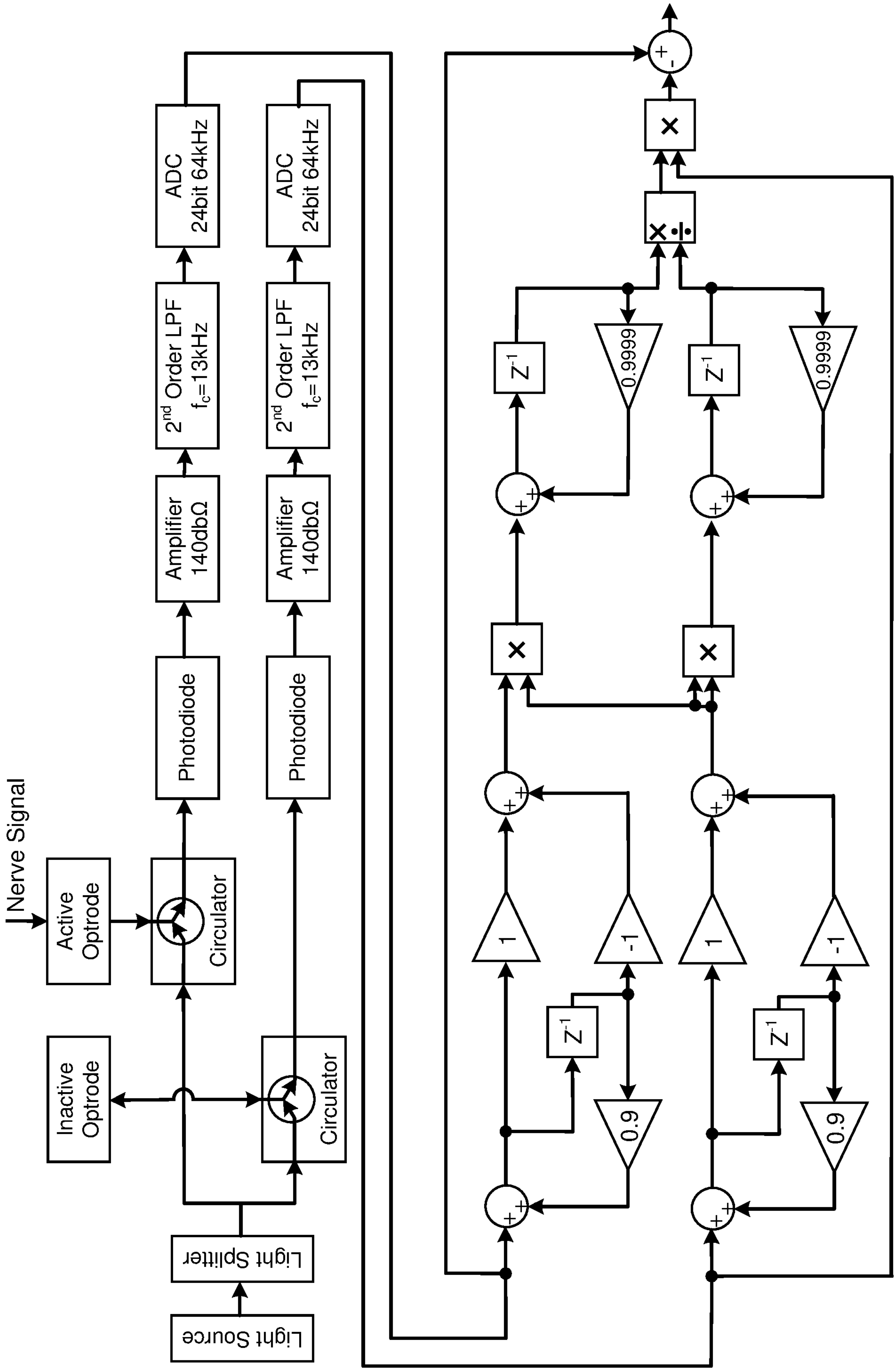

Nerve Signal
Active Optrode
Inactive Optrode
Circulator
Circulator
Photodiode
Photodiode
Amplifier 140dbΩ
Amplifier 140dbΩ
2nd Order LPF fc=13kHz
2nd Order LPF fc=13kHz
ADC 24bit 64kHz
ADC 24bit 64kHz
Light Splitter
Light Source
Z-1
0.9999
0.9
1
-1

Figure 16

(a) $$x_1(i) = s(i) + n(i), x_2(i) = m(i) + kn(i)$$

(b) $$x_{cc}(i) = \sum_{i=1}^{N} x_1(i)x_2(i), x_{ac}(i) = \sum_{i=1}^{N} x_2(i)x_2(i)$$

(c) $$\frac{x_{cc}(i)}{x_{ac}(i)} = \frac{\sum_{i=1}^{N} \left(s(i)m(i) + ks(i)n(i) + n(i)m(i) + n^2(i)k\right)}{\sum_{i=1}^{N} \left(m^2(i) + k^2n^2(i) + 2km(i)n(i)\right)}$$

(d) $$\sum_{i=1}^{N} s(i)m(i) = 0$$

(e) $$\sum_{i=1}^{N} k^2n^2(i) \gg \sum_{i=1}^{N} m^2(i)$$

(f) $$\frac{x_{cc}(i)}{x_{ac}(i)} = \frac{\sum_{i=1}^{N} kn^2(i)}{\sum_{i=1}^{N} m^2(i) + \sum_{i=1}^{N} k^2n^2(i)} \approx \frac{1}{k}$$

(g) $$\begin{aligned} y(i) &= x_1(i) - \frac{1}{k}x_2(i) \\ &= s(i) + n(i) - \frac{1}{k}m(i) + n(i) = s(i) - \frac{1}{k}m(i) \end{aligned}$$

Figure 17

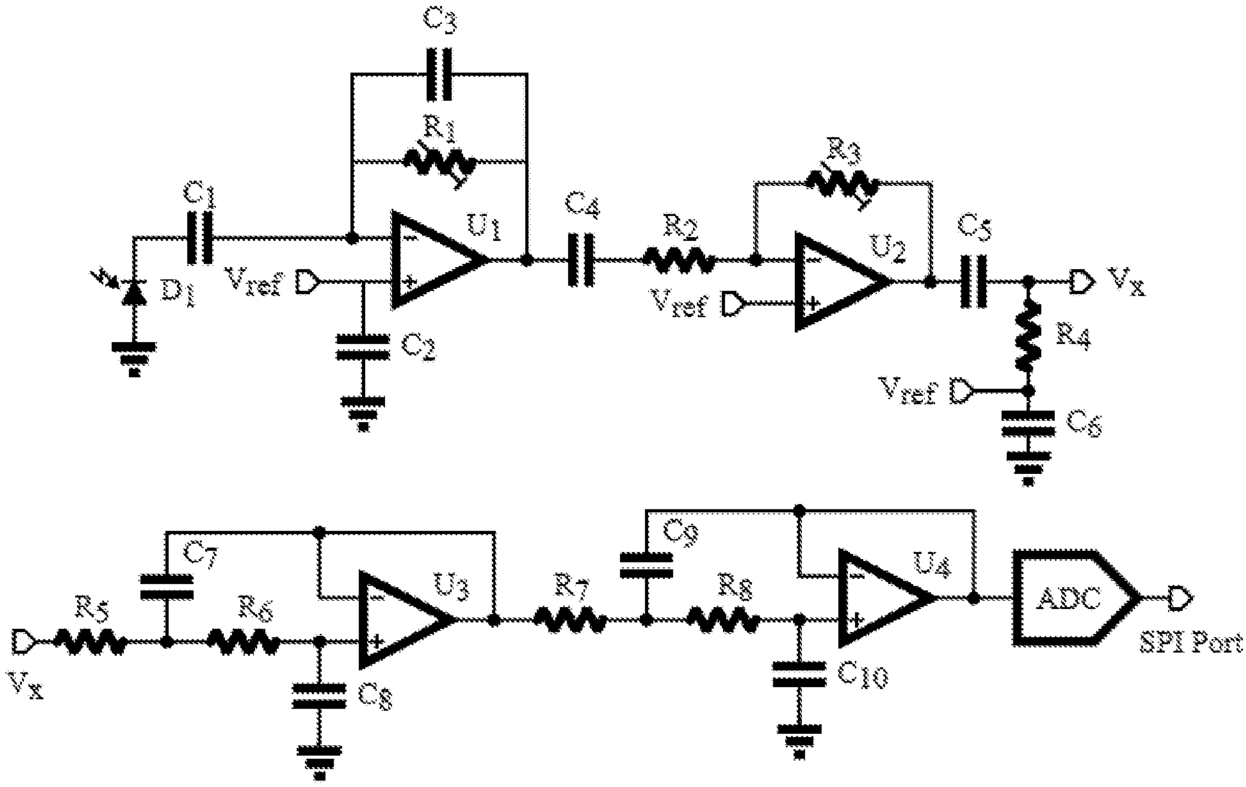


Figure 18

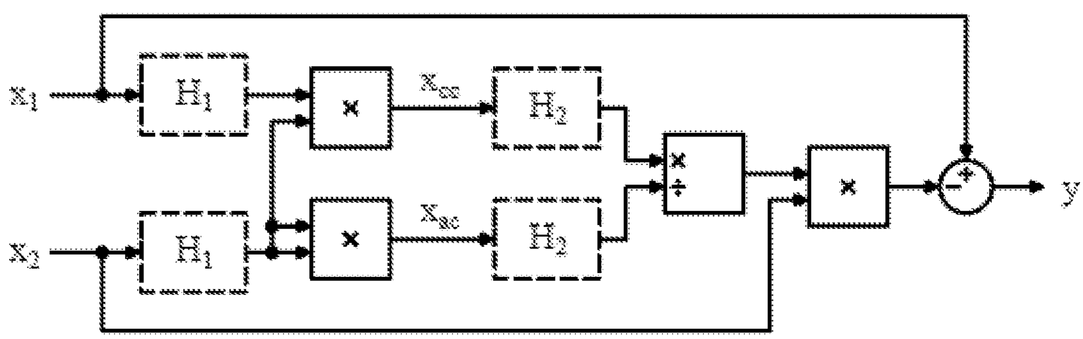


Figure 19

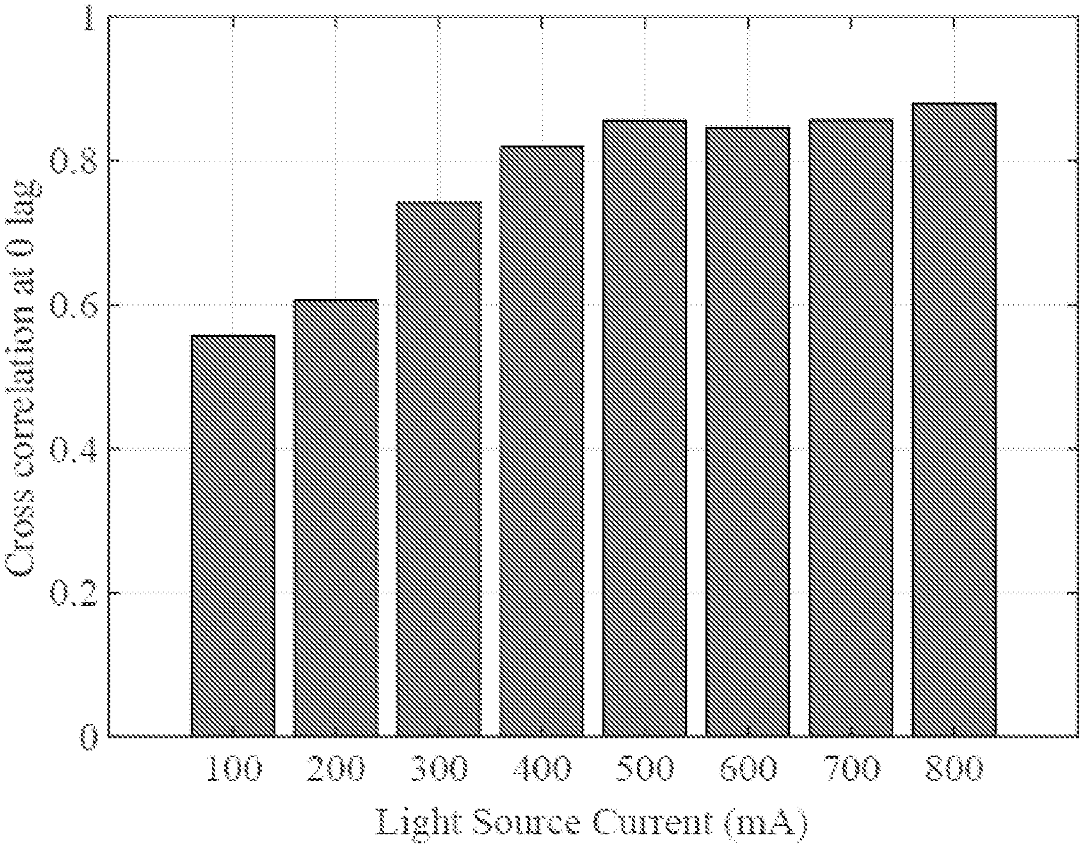

1
0.8
0.6
0.4
0.2
0
Cross correlation at 0 lag
100 200 300 400 500 600 700 800
Light Source Current (mA)

Figure 20

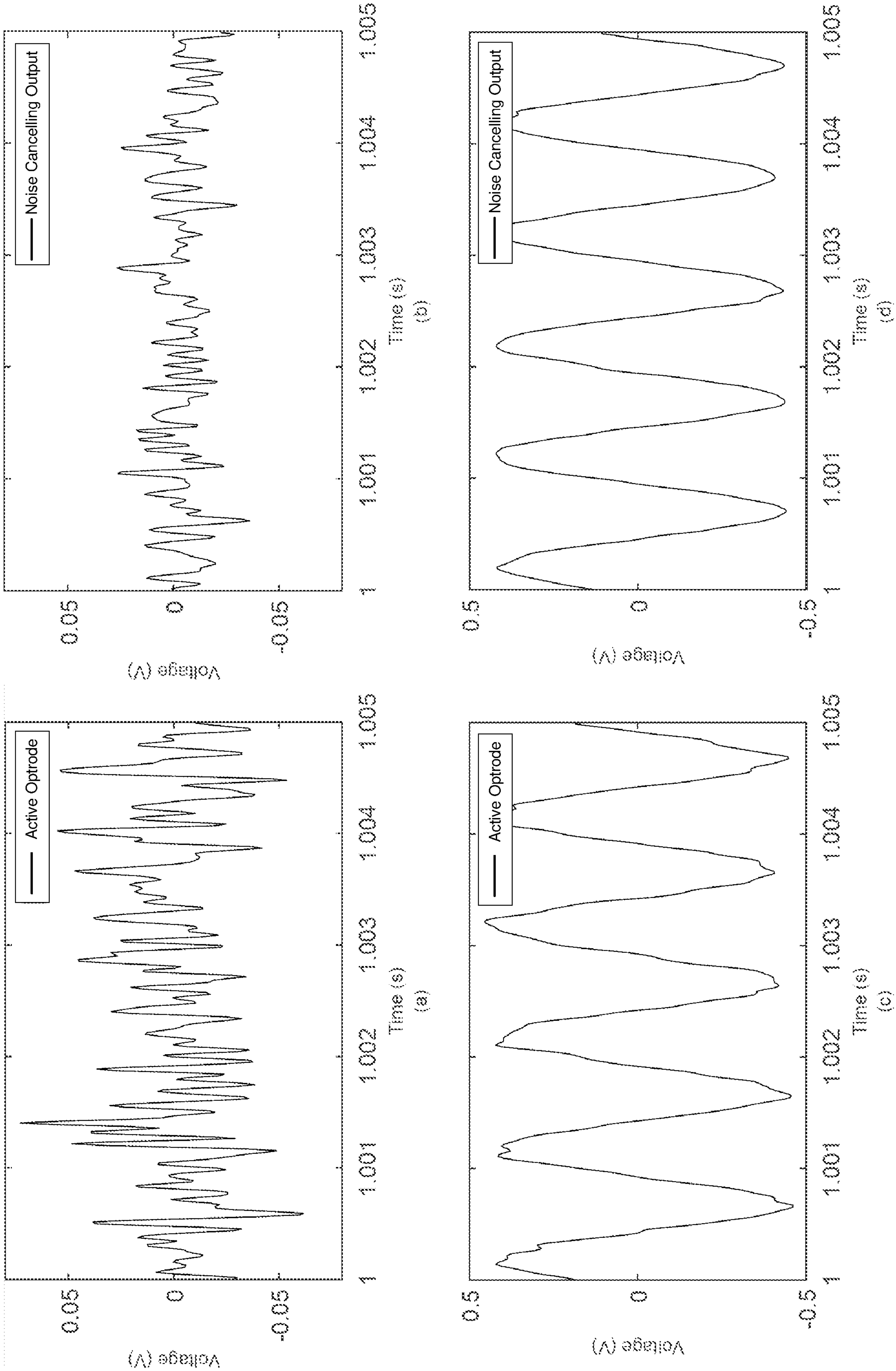

Active Optrode
Noise Cancelling Output
Active Optrode
Noise Cancelling Output
Voltage (V)
Time (s)
(a)
(b)
(c)
(d)
0.05
0
-0.05
0.5
-0.5
1
1.001
1.002
1.003
1.004
1.005

Figure 21

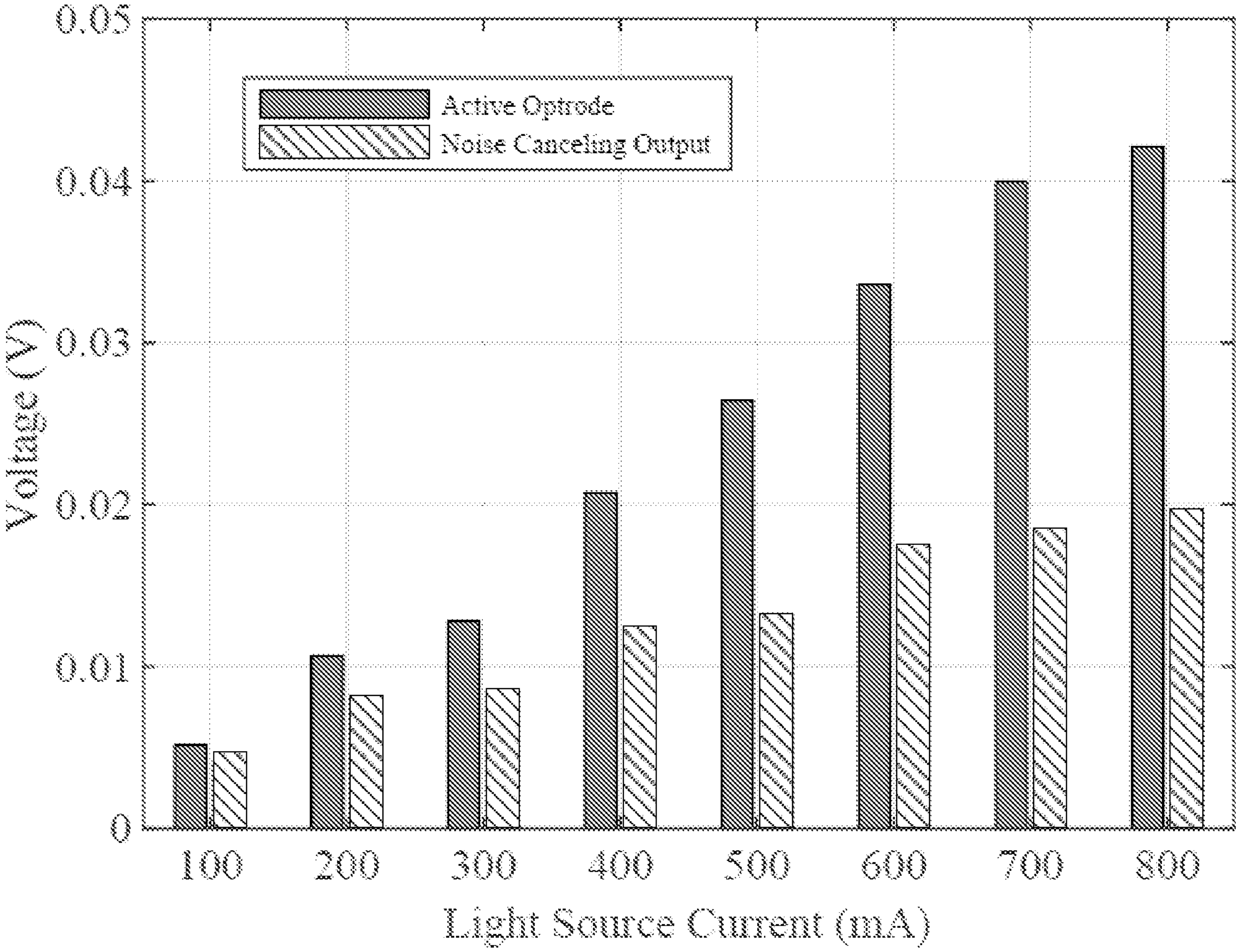

0.05
0.04
0.03
0.02
0.01
0
Voltage (V)
Active Optrode
Noise Canceling Output
100
200
300
400
500
600
700
800
Light Source Current (mA)

Figure 22

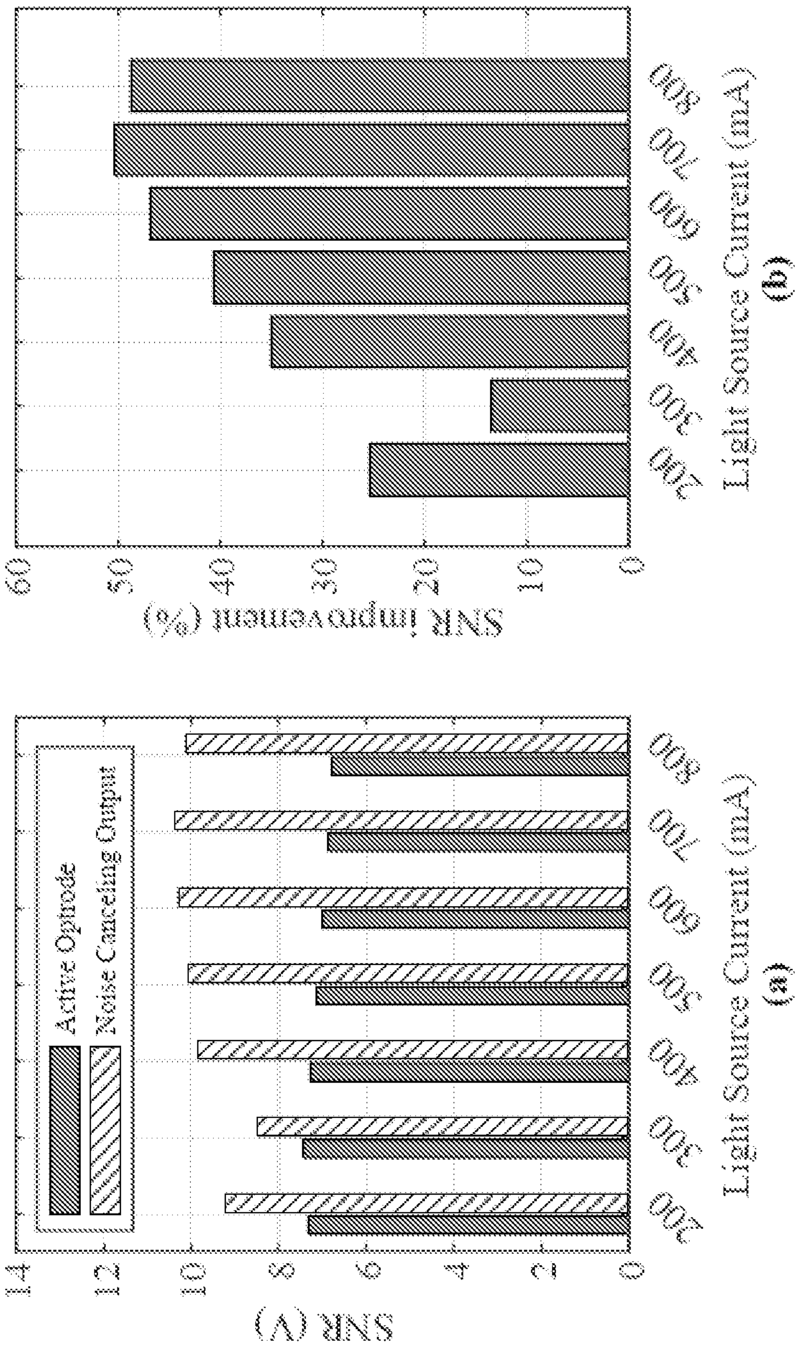

SNR improvement (%)
Light Source Current (mA)
(b)
SNR (V)
Active Optrode
Noise Canceling Output
Light Source Current (mA)
(a)

Figure 23

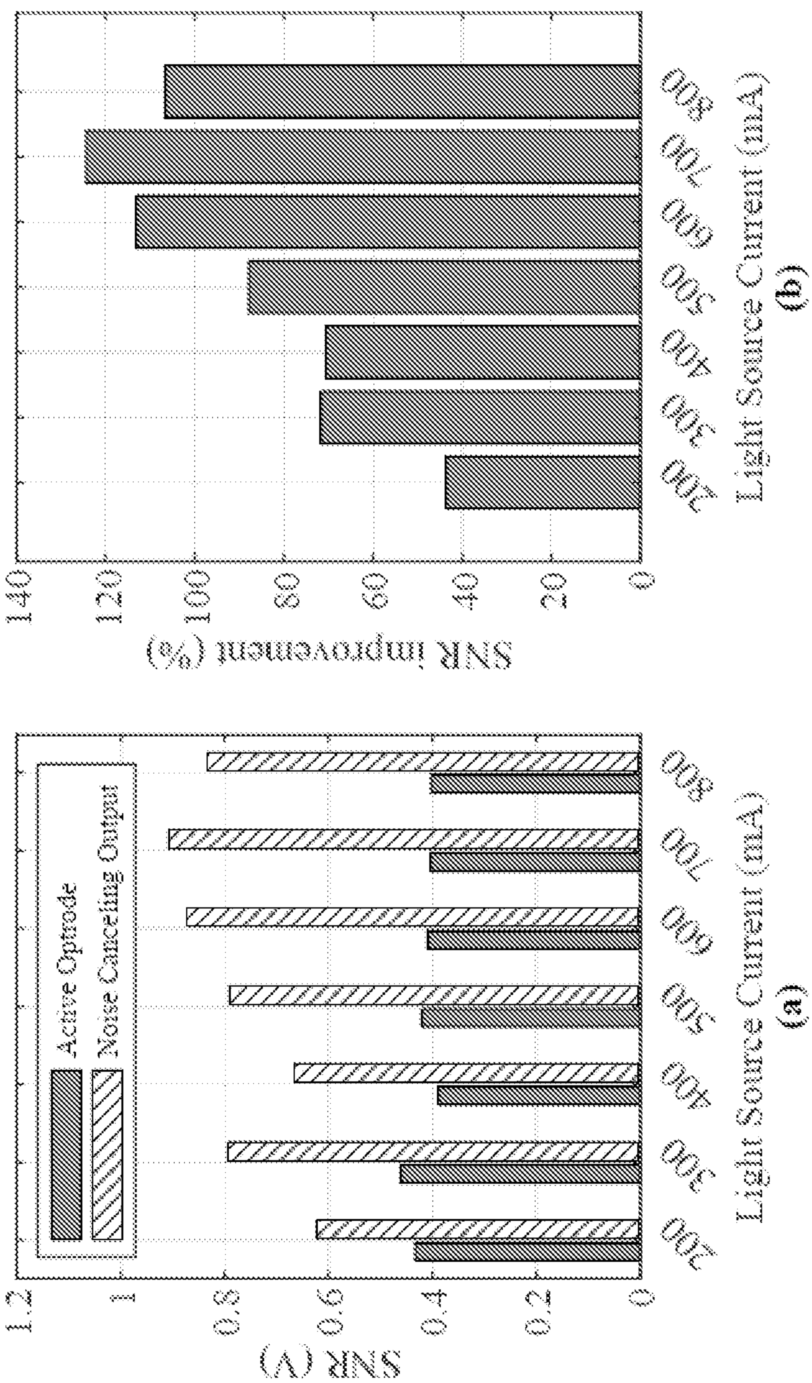

SNR (V)
1.2
1
0.8
0.6
0.4
0.2
0
Active Optrode
Noise Canceling Output
200
300
400
500
600
700
800
Light Source Current (mA)
(a)
SNR improvement (%)
140
120
100
80
60
40
20
0
200
300
400
500
600
700
800
Light Source Current (mA)
(b)

Figure 24

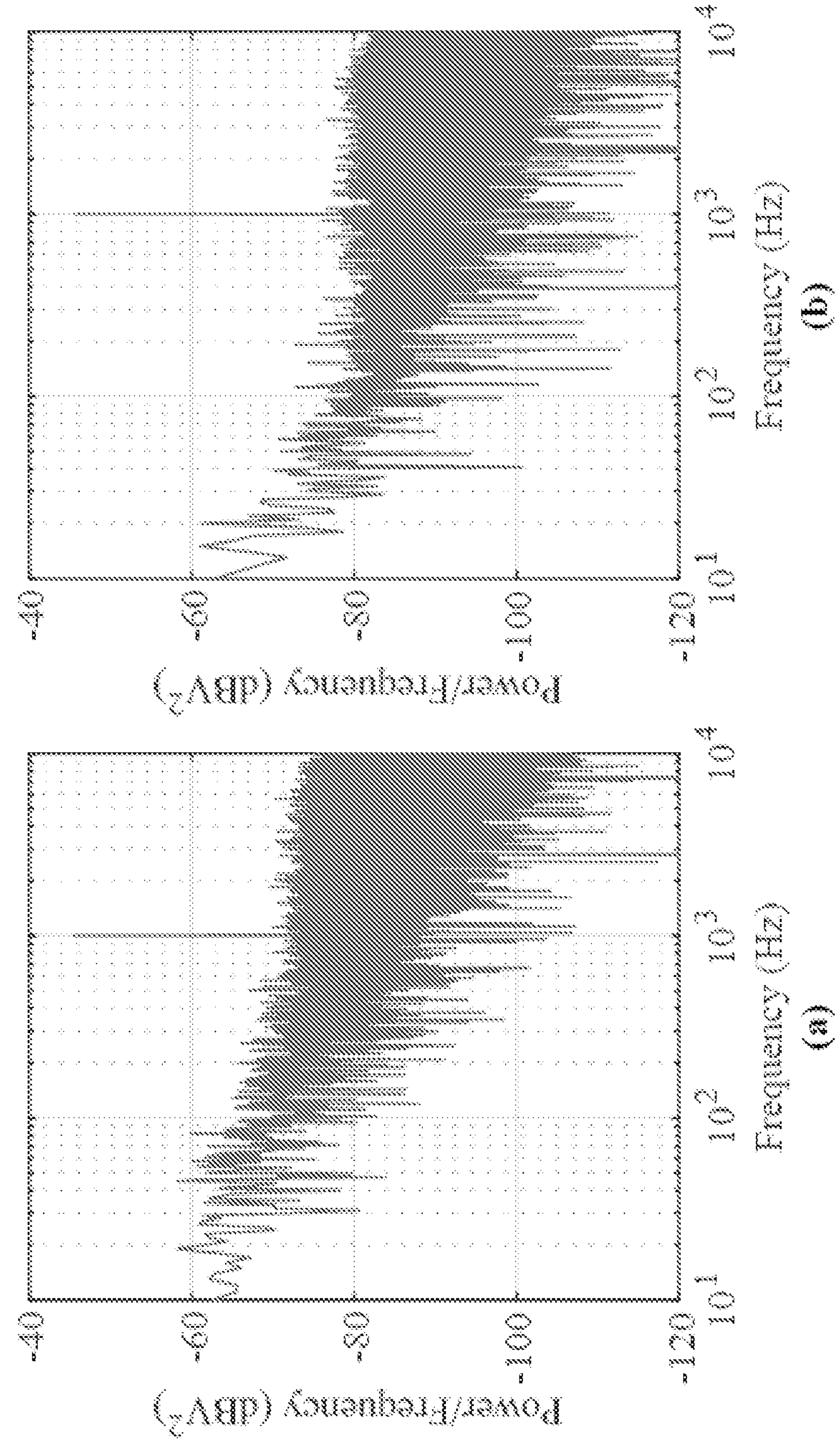

Power/Frequency (dBV^2)
-40
-60
-80
-100
-120
10^1
10^2
10^3
10^4
Frequency (Hz)
(a)
(b)

Figure 25

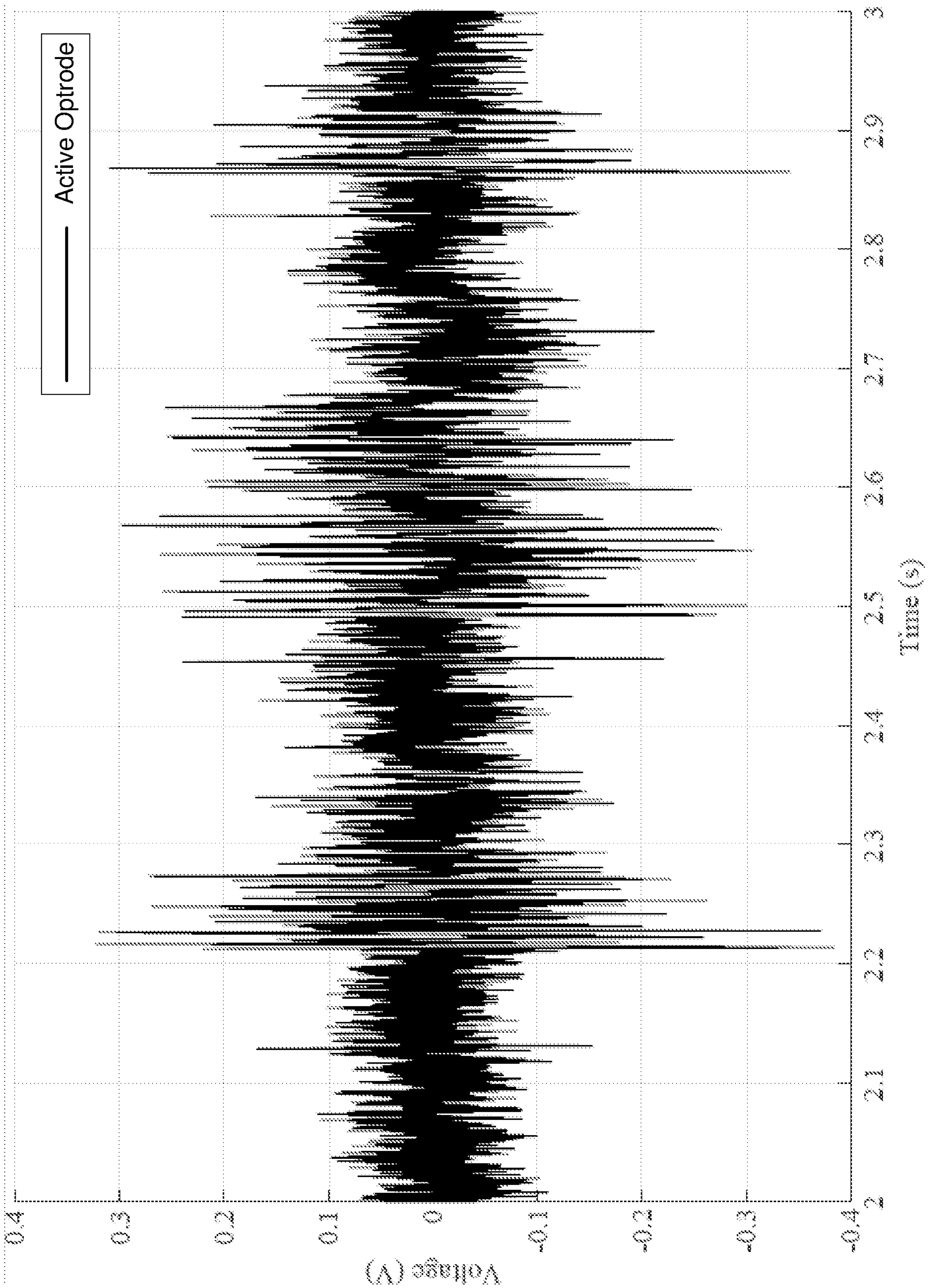

Active Optrode
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
Voltage (V)
2
2.1
2.2
2.3
2.4
2.5
2.6
2.7
2.8
2.9
3
Time (s)

Figure 26

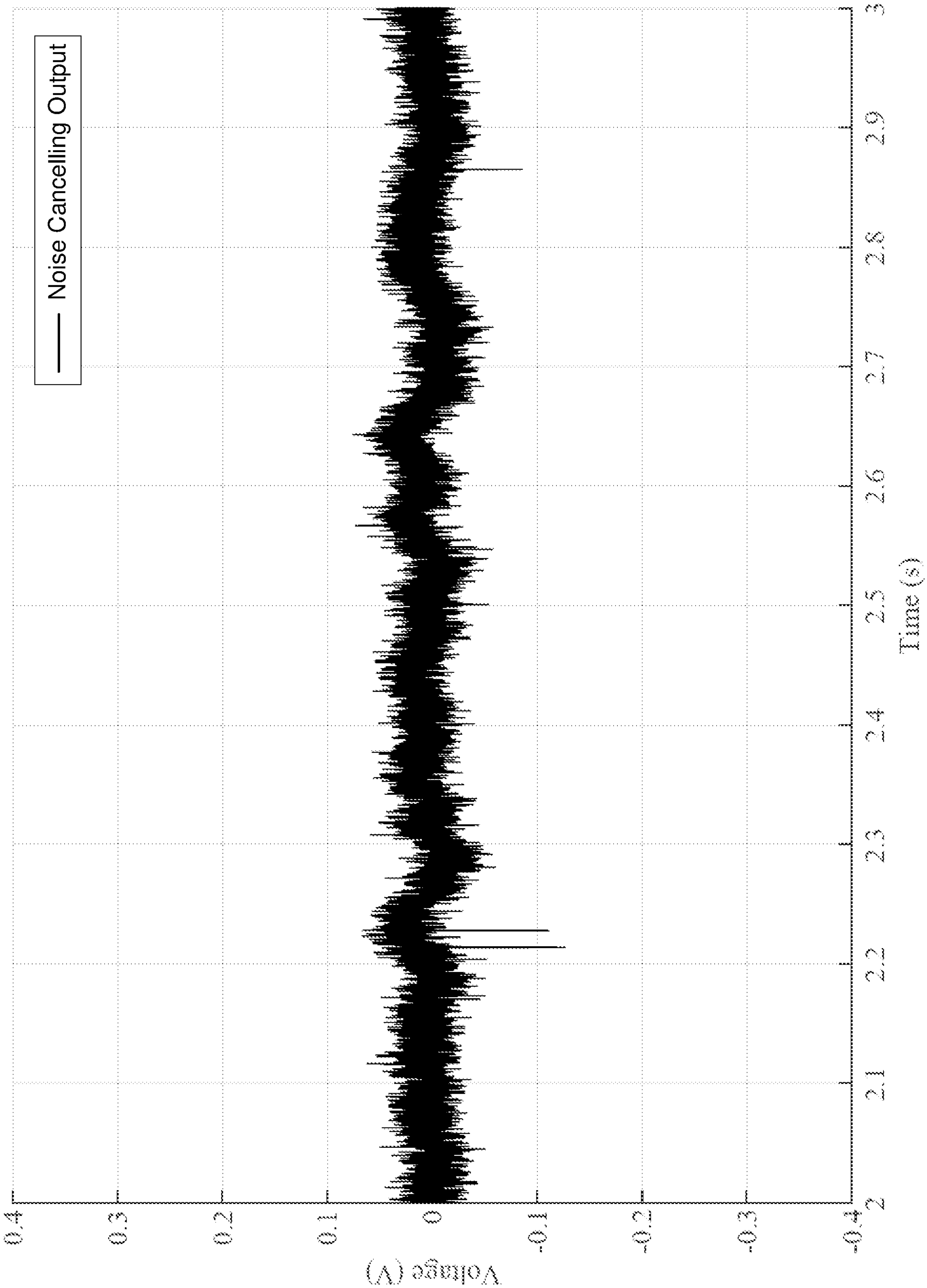

Noise Cancelling Output
Voltage (V)
Time (s)
0.4
0.3
0.2
0.1
0
-0.1
-0.2
-0.3
-0.4
2
2.1
2.2
2.3
2.4
2.5
2.6
2.7
2.8
2.9
3

Figure 27

INTERNATIONAL SEARCH REPORT

International application No.
PCT/AU2024/050874

A. CLASSIFICATION OF SUBJECT MATTER

A61B 5/00 (2006.01) A61B 5/291 (2021.01) A61B 5/31 (2021.01) A61B 5/384 (2021.01) G01N 21/17 (2006.01) G10K 11/178 (2006.01) H04R 1/10 (2006.01)

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)

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)

Databases: Google Patents, Google, Google Scholar, PATENW (WPIAP, EPODOC, TXTE and TXTMT), INSPEC, NPL; IPC/CPC: A61B5/7214, G01N2021/6434, G01N21/00, A61B5/721, A61B5/1455, G01N21/00, A61B5/0295, A61B5/0261, A61B5/00; Keywords: optrode, noise cancellation, neural interfacing, neuro plasmonic, photo plethysmo graphic, reference, artifact, background noise, active noise, wiener, correlation, and like terms.

Applicant(s)/Inventor(s) name searched in external databases DOCDB and DWPI and internal databases provided by IP Australia.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Documents are listed in the continuation of Box C	

[X] Further documents are listed in the continuation of Box C [X] 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
"D" document cited by the applicant in the international application
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 November 2024	14 November 2024

Name and mailing address of the ISA/AU	**Authorised officer**
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA Email address: pct@ipaustralia.gov.au	Eugene Koh AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No. +61 2 6283 2580

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	Kim S.A., et al., "In vivo optical neural recording using fiber-based surface plasmon resonance", Optical Letters, 37(4):pp 614-616, 15 February 2012	
X	whole document, in particular Abstract; Figures 1, 2(b); pages 614-615	41-43, 46, 50, 52-53 and 55
Y	whole document, in particular Abstract; Figures 1, 2(b); pages 614-615	51
	Gan, K. B., et al., "Application of Adaptive Noise Cancellation in Transabdominal Fetal Heart Rate Detection Using Photoplethysmography", Adaptive Filtering Applications, pp 141-156, 5 July 2011	
X	whole document, in particular Figures 1, 2, 6, 9; pages 142-144, 146, 151-152	41, 43-44, 46-50 and 52-55
Y	whole document, in particular Figures 1, 2, 6, 9; pages 142-144, 146, 151-152	51
	US 2002/0077536 A1 (DIAB et al.) 20 June 2002	
X	whole document, in particular Figs. 4a, 4b, 5a, 11-13; paras. [0003], [0087]-[0089], [0093], [0146], [0159], [0240], [0247], [0252], [0435]	41, 44-47, 50, 52 and 54-56
Y	whole document, in particular Figs. 4a, 4b, 5a, 11-13; paras. [0003], [0087]-[0089], [0093], [0146], [0159], [0240], [0247], [0252], [0435]	51
	Al Abed, A., et al., "Liquid crystal electro-optical transducers for electrophysiology sensing applications", Journal of Neural Engineering, 19(5), 10 October 2022	
Y	Figure 2(A)	51

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

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

1. ☐ Claims Nos.:

   because they relate to subject matter not required to be searched by this Authority, namely:

   the subject matter listed in Rule 39 on which, under Article 17(2)(a)(i), an international search is not required to be carried out, including

2. ☐ Claims Nos.:

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

3. ☐ Claims Nos:

   because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a)

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

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

See Supplemental Box for Details

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

   41-51 and 52-56

Remark on Protest

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

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

☐ No protest accompanied the payment of additional search fees.

Supplemental Box

Continuation of: **Box III**
This International Application does not comply with the requirements of unity of invention because it does not relate to one invention or to a group of inventions so linked as to form a single general inventive concept.

This Authority has found that there are different inventions based on the following features that separate the claims into distinct groups.

Group I – claims 1-14, claim 15, and claim 20 (when dependent on any of the claims 1-15)

Claims 1-14 are directed to a recording apparatus. Claim 15 is directed to a multi-channel recording apparatus. Claim 20 is optionally dependent on any one of the claims 1-15.

This group of claims seemingly relate to the acquisition of signals in a recording apparatus.

Specific to this group of claims is the feature of a plurality of "conductive devices" (in the case of claims 1-14) or a plurality of "optical-electrical transducers" (in the case of claim 15).

The claimed plurality of "conductive devices" (as claimed by claims 1-14) include at least one signal conduction device adapted to conduct a signal from an object of interest, and at least one noise conduction device adapted to conduct a noise signal.

The claimed plurality of "optical-electrical transducers" (as claimed by claim 15) include at least one signal recording transducer adapted to transduce an optical input into an electrical input to an object of interest, and at least one noise recording transducer adapted to receive a response signal from the object of interest and transduce it into an output optical signal.

Group II – claims 16-19, and claim 20 (when dependent on any of the claims 16-19)

Claims 16-19 are directed to an electrical measurement apparatus. Claim 20 is optionally dependent on any one of the claims 16-19.

This group of claims seemingly relate to the "simulation" of an object of interest for the purpose of recording a signal from the object.

Specific to this group of claims is the feature of an input device adapted to "simulate" an object of interest at user defined times.

Group III – claims 21-40

Claims 21-40 are directed to a signal recording method.

This group of claims seemingly relate to the conditioning of a response signal and/or a noise signal for noise cancellation.

Specific to this group of claims are the steps of

obtaining a response signal from the object of interest;

obtaining a noise data from a location within the measurement environment; and

obtaining a noise cancelled data, the obtaining of the noise cancelled data including subtracting the noise signal from the response signal.

Group IV – claims 41-51 and claims 52-56

Claims 41-51 are directed to an electro-optical detection apparatus. Claims 52-56 are directed to a method of detecting a nerve signal.

This group of claims seemingly relate to the application of an active noise cancellation algorithm to a signal from a sample of interest.

Specific to this group of claims are the features of

Supplemental Box

a first optrode, configured to receive a first light signal and generate a first optrode signal, the first optrode configure to be in contact with a sample of interest;

an second optrode, configured to receive a second light signal and generate a second optrode signal, the second optrode configured to be isolated from the sample of interest; and

a receiver, configured to determine an output signal by applying an active noise cancellation algorithm to the first optrode signal and the second optrode signal.

Lack of Unity

PCT Rule 13.2, first sentence, states that unity of invention is only fulfilled when there is a technical relationship among the claimed inventions involving one or more of the same or corresponding special technical features. PCT Rule 13.2, second sentence, defines a special technical feature as a feature which makes a contribution over the prior art.

When there is no special technical feature common to all the claimed inventions there is no unity of invention.

In the above groups of claims, the identified features may have the potential to make a contribution over the prior art but are not common to all the claimed inventions and therefore cannot provide the required technical relationship.

Common to all of the claims of Groups I to IV are devices to acquire a signal of interest and a noise signal, e.g., variously having signal conduction devices, or optical-electrical transducers, or electrodes, or transducers, or optrodes to obtain a signal of interest, and further to obtain a noise signal.

Also, common to the claims of Groups III and IV is a noise cancellation step.

These common features however are generic in this particular art. As examples, see the respective Abstracts of each of these documents:

US 2003/0033144 A1 (SILVERMAN et al.) 13 February 2003

US 2003/0040908 A1 (YANG et. al.) 27 February 2003

US 2013/0208923 A1 (SUVANTO) 15 August 2013

Therefore the common features cannot be a special technical feature. Hence there is no special technical feature common to all the claimed embodiments and the requirements for unity of invention are consequently not satisfied *a posteriori*.

The claims of Group IV i.e. claims 41-51 and claims 52-56 were searched and reported upon because the applicant elected for this group of claims in response to an invitation to pay additional search fees.

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document/s Cited in Search Report		**Patent Family Member/s**	
Publication Number	**Publication Date**	**Publication Number**	**Publication Date**
US 2002/0077536 A1	20 June 2002	US 2002077536 A1	20 Jun 2002
		US 6745060 B2	01 Jun 2004
		AU 1536992 A	06 Oct 1992
		AU 658177 B2	06 Apr 1995
		AU 3962395 A	15 May 1996
		AU 699762 B2	17 Dec 1998
		CA 2105682 A1	08 Sep 1992
		CA 2199016 A1	02 May 1996
		CA 2357059 A1	02 May 1996
		CN 101426426 A	06 May 2009
		CN 101426426 B	31 Aug 2011
		CN 1168624 A	24 Dec 1997
		EP 0574509 A1	22 Dec 1993
		EP 0574509 B1	15 Sep 1999
		EP 0784448 A2	23 Jul 1997
		EP 0930045 A2	21 Jul 1999
		EP 1357481 A2	29 Oct 2003
		EP 1755422 A2	28 Feb 2007
		EP 1905352 A1	02 Apr 2008
		EP 1905352 B1	16 Jul 2014
		EP 1942810 A2	16 Jul 2008
		EP 1942810 B1	08 Aug 2012
		EP 2341446 A1	06 Jul 2011
		JP 2005185834 A	14 Jul 2005
		JP 4223001 B2	12 Feb 2009
		JP 2008504847 A	21 Feb 2008
		JP 2009039548 A	26 Feb 2009
		JP H06507485 A	25 Aug 1994
		JP 3363150 B2	08 Jan 2003
		JP H10507118 A	14 Jul 1998
		JP 3705814 B2	12 Oct 2005
		MX 9702434 A	31 May 1998
		US 2001029326 A1	11 Oct 2001

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/AU2024/050874**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document/s Cited in Search Report		**Patent Family Member/s**	
Publication Number	**Publication Date**	**Publication Number**	**Publication Date**
		US 6501975 B2	31 Dec 2002
		US 2002128544 A1	12 Sep 2002
		US 2003036689 A1	20 Feb 2003
		US 6650917 B2	18 Nov 2003
		US 2003097049 A1	22 May 2003
		US 6826419 B2	30 Nov 2004
		US 2004064020 A1	01 Apr 2004
		US 7254433 B2	07 Aug 2007
		US 2004068164 A1	08 Apr 2004
		US 7496393 B2	24 Feb 2009
		US 2004204636 A1	14 Oct 2004
		US 7215984 B2	08 May 2007
		US 2004204638 A1	14 Oct 2004
		US 2004210146 A1	21 Oct 2004
		US 7530955 B2	12 May 2009
		US 2004236196 A1	25 Nov 2004
		US 7469157 B2	23 Dec 2008
		US 2005209517 A1	22 Sep 2005
		US 8948834 B2	03 Feb 2015
		US 2005256385 A1	17 Nov 2005
		US 7215986 B2	08 May 2007
		US 2006016006 A1	26 Jan 2006
		US 7395563 B2	08 Jul 2008
		US 2006089549 A1	27 Apr 2006
		US 7383070 B2	03 Jun 2008
		US 2006217609 A1	28 Sep 2006
		US 7454240 B2	18 Nov 2008
		US 2007005090 A1	04 Jan 2007
		US 2007185376 A1	09 Aug 2007
		US 2007225581 A1	27 Sep 2007
		US 8942777 B2	27 Jan 2015
		US 2007249918 A1	25 Oct 2007
		US 8046042 B2	25 Oct 2011
		US 2007291832 A1	20 Dec 2007
		US 8036728 B2	11 Oct 2011
		US 2008004514 A1	03 Jan 2008

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/AU2024/050874**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document/s Cited in Search Report		**Patent Family Member/s**	
Publication Number	**Publication Date**	**Publication Number**	**Publication Date**
		US 8046041 B2	25 Oct 2011
		US 2008033266 A1	07 Feb 2008
		US 8019400 B2	13 Sep 2011
		US 2008045823 A1	21 Feb 2008
		US 7509154 B2	24 Mar 2009
		US 2009076400 A1	19 Mar 2009
		US 8128572 B2	06 Mar 2012
		US 2009099430 A1	16 Apr 2009
		US 7937130 B2	03 May 2011
		US 2009182211 A1	16 Jul 2009
		US 8126528 B2	28 Feb 2012
		US 2009247819 A1	01 Oct 2009
		US 8216125 B2	10 Jul 2012
		US 2011022034 A1	27 Jan 2011
		US 8425404 B2	23 Apr 2013
		US 2011245654 A1	06 Oct 2011
		US 2012149997 A1	14 Jun 2012
		US 8364226 B2	29 Jan 2013
		US 2012165624 A1	28 Jun 2012
		US 8359080 B2	22 Jan 2013
		US 2012165631 A1	28 Jun 2012
		US 8755856 B2	17 Jun 2014
		US 2012220843 A1	30 Aug 2012
		US 8463349 B2	11 Jun 2013
		US 2013345523 A1	26 Dec 2013
		US 5482036 A	09 Jan 1996
		US 5490505 A	13 Feb 1996
		US 5632272 A	27 May 1997
		US 5685299 A	11 Nov 1997
		US 5769785 A	23 Jun 1998
		US 6036642 A	14 Mar 2000
		US 6081735 A	27 Jun 2000
		US 6157850 A	05 Dec 2000
		US 6206830 B1	27 Mar 2001
		US 6236872 B1	22 May 2001
		US 6263222 B1	17 Jul 2001

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.

INTERNATIONAL SEARCH REPORT Information on patent family members	International application No. **PCT/AU2024/050874**

This Annex lists known patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document/s Cited in Search Report		**Patent Family Member/s**	
Publication Number	**Publication Date**	**Publication Number**	**Publication Date**
		US 7328053 B1	05 Feb 2008
		US 7376453 B1	20 May 2008
		US 7962190 B1	14 Jun 2011
		US 8560034 B1	15 Oct 2013
		WO 2005096764 A2	20 Oct 2005
		WO 2007022159 A2	22 Feb 2007
		WO 9215955 A1	17 Sep 1992
		WO 9612435 A2	02 May 1996

End of Annex

Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.