(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
19 June 2014 (19.06.2014)

WIPO | PCT

(10) International Publication Number
WO 2014/092981 A1

(51) International Patent Classification:
G06F 7/00 (2006.01)

(21) International Application Number:
PCT/US2013/071509

(22) International Filing Date:
22 November 2013 (22.11.2013)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
61/736,454 12 December 2012 (12.12.2012) US

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— *with international search report (Art. 21(3))*

(54) Title: REMOVAL OF NOISE FROM STRUCTURED SIGNALS

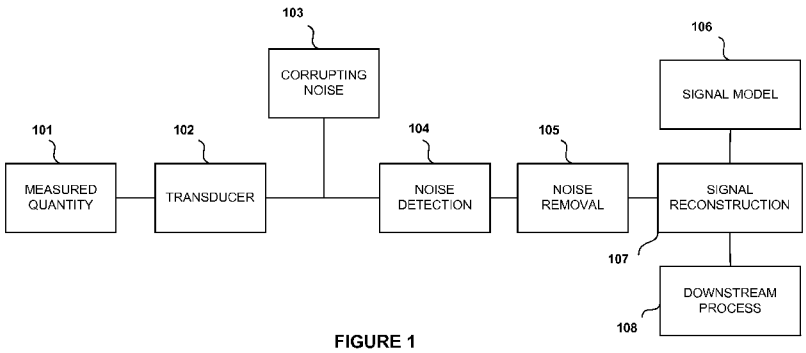

FIGURE 1

(57) Abstract: An exemplary method is directed to removing noise from a signal. The method comprises: receiving a signal time-history associated with a signal comprising corrupted data and uncorrupted data; identifying the uncorrupted data from the signal time-history; identifying the corrupted data from the signal time-history; removing the corrupted data from the signal time -history; determining replacement data for replacing the corrupted data in the signal time-history; and reconstructing the signal time-history based on the uncorrupted data and the replacement data. The signal comprises at least one of a first voltage signal substantially sensitive to a concentration of an analyte in a solution or a second voltage signal substantially sensitive to the solution and substantially insensitive to the concentration of the analyte in the solution. The reconstructing step enables determination of the concentration of the analyte in the solution.

WO 2014/092981 A1

REMOVAL OF NOISE FROM STRUCTURED SIGNALS

FIELD

[0001] The system described herein relates in general to the field of signal processing as such signals relate to the detection and monitoring of one or more analytes *in vivo*. More specifically, the system relates to noise rejection from signals where the corrupting signal is intermittent, large in amplitude and has frequency content similar to the frequency content of the signal of interest. Furthermore, the signal of interest has a predictable structure.

BACKGROUND

[0002] In many signal processing applications, the measured signal is corrupted by intermittent noise that varies slowly with time relative to the characteristic time-scale of the signal but is much larger in amplitude than the signal. Additionally, the signal of interest may present an inherent structure that is repetitive in time. Such signals occur, but are not limited to, biological transducers that measure a slowly changing biological property such as the concentration of an analyte *in-vivo* or *in-vitro*. Corrupting noise may arise from, among other sources, electro-magnetic interference or temporary misalignment or physical obstruction of the sensor from the analyte source. There is a need for a system that addresses noise corruption in a measured signal.

BRIEF SUMMARY

[0003] Embodiments described herein are directed to noise filtering. For example, a noise filtering system comprises a noise detection and data removal module for identifying and removing data from the signal time-history that is corrupted by noise, a signal modeling module for providing information about corrupted data-points based on non-corrupted data-points, and a signal reconstruction module that uses the signal model and the non-corrupted data-points to reconstruct the corrupted data-points.

[0004] The noise detection and removal module comprises a low-pass filter for removal of data artifacts outside of the spectral range of the corrupting noise, a differentiator for estimating the rate of change of the signal, and a rejection thresholding module whereby the

filtered and differentiated time-domain signal is processed so as to remove the corrupted data-points.

[0005] The signal model produced by the signal modeling module is based on an equation that includes one or more parameters that may be bounded in range and have typical values. The range and typical values are determined from analysis of uncorrupted signal data-points and may be performed real-time or prior to implementation of the system described herein. Alternatively or additionally, the signal model has a form derived from previous observations of the signal during uncorrupted data collection.

[0006] The signal reconstruction module may comprise a minimization module that chooses parameters for the signal model such that the normalized difference between the signal model and the uncorrupted data is small.

[0007] The data removal module described herein removes large and low frequency noise from slow-changing signals by first identifying noise-corrupted data-points and then reconstructing them.

[0008] The data reconstruction module described herein is applied to two or more transducer voltages representing response to solution and response to solution with analyte. The reconstructed signal obtained from this module is used to calculate the analyte concentration in solution.

[0009] The following is a more detailed summary of the apparatus, methods, and computer program products described herein.

[0010] An exemplary method for removing corrupted data from a signal comprises: receiving a signal time-history associated with a signal comprising corrupted data and uncorrupted data; identifying the uncorrupted data from the signal time-history; identifying the corrupted data from the signal time-history; removing the corrupted data from the signal time-history; determining replacement data for replacing the corrupted data in the signal time-history; and reconstructing the signal time-history based on the uncorrupted data and the replacement data. The replacement data is interpolated into the signal time-history to fill the gaps caused by the removed data.

[0011] In some embodiments, the signal comprises at least one of a first voltage signal substantially sensitive to a concentration of an analyte in a solution or a second voltage

signal substantially sensitive to the solution and substantially insensitive to the concentration of the analyte in the solution, and wherein the reconstructing step enables determination of the concentration of the analyte in the solution.

[0012] In some embodiments, the analyte comprises glucose and the solution is blood from the circulatory system of a subject.

[0013] In some embodiments, the corrupted data comprises a substantially corrupted time-segment from the signal time-history, and wherein the uncorrupted data comprises a substantially uncorrupted time-segment from the signal time-history.

[0014] In some embodiments, at least one of the determining step or the reconstructing step is based on at least one of a least squares fitting model, an adaptive model, a statistical model, or a heuristic model.

[0015] In some embodiments, at least one of the determining step or the reconstructing step is based on whether a system is being calibrated or whether the system is being used to measure a concentration of an analyte in a solution.

[0016] In some embodiments, the corrupted data comprises noise.

[0017] In some embodiments, the noise comprises at least one of high-frequency noise or low-frequency noise.

[0018] In some embodiments, the determining step comprises: accessing a model of the signal time-history; and determining the replacement data based on the uncorrupted data and the model.

[0019] In some embodiments, the model comprises substantially uncorrupted data.

[0020] In some embodiments, the model is based on a previous signal time-history associated with the signal.

[0021] In some embodiments, the model is generated in substantially real-time.

[0022] In some embodiments, the model is generated based on a minimization model such that a normalized difference between a parameter of the model and a parameter of the uncorrupted data is less than or equal to a predetermined threshold.

[0023] In some embodiments, the receiving step comprises: measuring a quantity; and converting, using a transducer, the measured quantity to the signal.

[0024] In some embodiments, the quantity is associated with the transducer, wherein the quantity comprises a voltage.

[0025] In some embodiments, the signal comprises at least one of a signal substantially sensitive to a solution, or a signal substantially sensitive to the solution and substantially insensitive to an analyte concentration associated with the solution.

[0026] In some embodiments, at least one of the identifying the corrupted data from the signal time-history step or removing the corrupted data from the signal time-history step comprises: low-pass filtering the signal time-history to remove artifacts that are outside a frequency range of the corrupted data; determining a rate of change of the filtered signal time-history; in response to determining the rate of change exceeds a first threshold, dropping the filtered signal time-history from a data set; and continuing to drop the signal time-history from the data set until the rate of the change of the filtered signal time-history falls below either the first threshold or a second threshold, wherein the second threshold is either above or below the first threshold.

[0027] In some embodiments, the rate of change is based on a single derivative or a cascade of derivatives.

[0028] In some embodiments, the signal is generated by one or more electronic circuits.

[0029] In some embodiments, a polyelectrolyte coating is associated with a source of the signal.

[0030] In some embodiments, one or more electronic circuits and a polyelectrolyte coating are associated with a source of the signal.

[0031] In some embodiments, alone or in combination with any of the previous embodiments, an apparatus is provided for removing corrupted data from a signal. The apparatus comprises: a memory; a processor; at least one module, executable by the processor, and configured to: receive a signal time-history associated with a signal comprising corrupted data and uncorrupted data; identify the uncorrupted data from the signal time-history; identify the corrupted data from the signal time-history; remove the corrupted data from the signal time-history; determine replacement data for replacing the

corrupted data in the signal time-history; and reconstruct the signal time-history based on the uncorrupted data and the replacement data.

[0032] In some embodiments, a computer program product for removing corrupted data from a signal. The computer program product comprises a non-transitory computer-readable medium comprising a set of codes for causing a computer to: receive a signal time-history associated with a signal comprising corrupted data and uncorrupted data; identify the uncorrupted data from the signal time-history; identify the corrupted data from the signal time-history; remove the corrupted data from the signal time-history; determine replacement data for replacing the corrupted data in the signal time-history; and reconstruct the signal time-history based on the uncorrupted data and the replacement data.

BRIEF DESCRIPTION OF THE DRAWINGS

[0033] Having thus described embodiments of the system in general terms, reference will now be made to the accompanying drawings, where:

FIG. 1 is a flow chart showing one mode of implementation of the present system;

FIG. 2 is a flow chart showing in greater detail the noise detection block 104 of the present system, in accordance with some embodiments of the present system;

FIG. 3 shows a time-history example of a signal corrupted by noise where the noisy segments have been identified by the noise detection block 104;

FIG. 4 shows a time-history example of a signal corrupted by noise and reconstructed by the signal reconstruction block 107 in conjunction with the signal model 106;

FIG. 5 shows a time-history example of a downstream process 108 for *in-vivo* and *in-vitro* data;

FIG. 6 shows an exemplary glucose sensor, in accordance with embodiments of the present system.

DETAILED DESCRIPTION OF EMBODIMENTS

[0034] Embodiments of the present system now may be described more fully hereinafter with reference to the accompanying drawings, in which some, but not all, embodiments of the system are shown. Indeed, the system may be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are provided so that this disclosure may satisfy applicable legal requirements. Like numbers refer to like elements throughout.

[0035] An approach toward removing noise from signals is low-pass filtering which may be implemented in the hardware circuitry of a sensor or in software. A low pass filter significantly diminishes the amplitude components of the signal that are higher than the frequency of interest but "passes" low frequency content. However, when the corrupting noise is (i) large in amplitude and (ii) has frequency components that are close to the frequency components of the signal of interest, this approach is insufficient. In fact, a low pass filter spreads the large, intermittent corrupting noise over a longer temporal space and may obscure otherwise uncorrupted data.

[0036] Another approach that may be used is wavelet transform filtering. This approach leverages a-priori knowledge about the temporal shape or signature of the corrupting noise to decompose the corrupted signal such that the noise and original signal are separate. The noise channel can then be removed from the signal to produce the uncorrupted signal of interest. It may also occur, as is claimed here, that temporal signature of the noise is un-known a-priori as it may arise from various sources be they mechanical or electrical. For example, if the corrupting noise arises from concurrent operation of an electromechanical device, the noise amplitude and temporal signature may vary with the speed and duration of operation of the corrupting electromechanical device. Thus a wavelet transform or similar approach that assumes prior knowledge about the nature of shape of the noise may not be suitable.

[0037] Another approach toward rejecting intermittent corrupting noise is adaptive filtering. Unlike static filters that are designed and tuned once for all time, this approach assumes an a-priori structure of the noise but allows parameters that define the structure to change adaptively during operation. Thus, for example, if the frequency content of the

noise moves from frequency band A to frequency band B over time, the filter may detect this shift and adapt its filtering characteristics over time. Additionally, such filters may leverage a-priori knowledge about the ideal or uncorrupted system to identify the signal produced by the system embedded in the noisy signal. However, it may occur, as claimed here, that the frequency content of the noise — while it may change with time — will be similar to the frequency content of the signal of interest. Thus, adaptive filtering would not be able to remove the noise component of the filter without significantly corrupting the signal of interest.

[0038] Another approach toward filtering is to identify and ignore signals corrupted by noise. Corrupted signal may be detected by heuristic, statistical, or thresholding methods, among others. However, the corrupted signal may occur during a critical period. Ignoring data during this critical period may delay other operations or result in erroneous estimation of the analyte concentration as described herein.

[0039] Thus, a signal processing method is desired that identifies and rejects slow and intermittent noise without dropping or ignoring data during a potentially critical time. Furthermore, should noise occur during a critical period and corrupt the signal, the proposed method should reconstruct the signal during this critical period.

[0040] Embodiments described herein are directed to systems, methods, and computer program products for noise removal from a signal of interest. An exemplary method is disclosed for reconstructing time-histories corrupted by large and intermittent noise in signals that have a repetitive structure. The method first identifies data-segments corrupted by noise. The method then performs noise removal by dropping corrupted data-points from a time-series. The method then reconstructs the dropped data-points with a model-based interpolation technique. It is further claimed that the present approach can be applied to noise cancelation in signals measured by transducers used to measure analyte concentration *in-vivo* or *in-vitro* in the presence of intermittent and large magnitude noise. Finally, it is claimed that the present approach can be applied to *in-vivo* and *in-vitro* measurement of glucose concentration by such a transducer. As used herein, “data” and “data-points” may be used interchangeably.

[0041] The system described herein mitigates the effects of electrocautery, electrosurgical or electrocuting (collectively referred to as ESU) on a glucose measurement system. The signal (e.g., a voltage signal) described herein enables determination of an analyte concentration in a solution (e.g., the glucose concentration in a blood sample or any other fluid).

[0042] A first module of the system detects ESU noise and removes it from a dataset (e.g., a signal time-history) associated with a signal. This is accomplished by monitoring the first and second derivative of the signal time-history. ESU noise is characterized by spikes which in turn result in a high magnitude derivative (positive or negative). By properly choosing threshold values, the rising and falling edge of each spike can be detected and the entire spike (or at least a partial portion of the entire spike) removed.

[0043] The second module of the system processes the signal with missing data to recreate the original signal without ESU noise. This is accomplished by interpolating between the non-dropped data-points. Depending on the phase (measurement phase, calibration phase, etc.) or time-history selected from the signal, different interpolation techniques are used. The phases associated with the signal may comprise a calibration phase (when the system for measuring glucose concentration is being calibrated) and a measurement phase (when glucose concentration is being measured). For example, during the measurement phase, interpolation based on an exponential decay model is used.

[0044] FIG. 1 is a flow chart showing one mode of implementation of the present method. In FIG. 1, a measured quantity 101 is converted to a digital or analog signal by a transducer 102. The measured quantity may be a single value or multiple values and may be a measurement of a single process or multiple processes. The transduced signal 102 is corrupted by an external corrupting noise 103. The corrupting noise 103 may corrupt one or more channels of the transduced signal 102. Noise detection 104 is performed to distinguish time-segments in the corrupted transduced signal that are corrupted from those that are not corrupted. The noise detection block 104 may be implemented based on a number of methods or models including thresholding methods or models, statistical methods or models, or heuristic methods or models. Once detected, the noisy time-

segments are removed from the data time-history after passing through the noise removal block 105. As used herein, a method may also refer to a model.

[0045] The time-history that enters the signal reconstruction block 107 consists of (i) data points assumed to be uncorrupted and (ii) data points that have been removed from the time-history. The signal reconstruction method 107 leverages the uncorrupted data-points with a prior signal model 106 of the measured quantity 101 and transducer 102 to replace the missing data points with interpolated data-points that best fit the uncorrupted data and the prior signal model 106. The signal reconstruction block 107 may be implemented based on a number of models including least squares fitting models, adaptive models, statistical models, or heuristic models. The signal model 106 may be constructed heuristically from previous observations of the signal. For example, if the signal is approximately oscillatory such that the amplitude and phase of each oscillation does not change significantly from the previous iteration, the signal model 106 used to reconstruct a current period of the signal could be derived from the previous uncorrupted period. To more clearly illustrate the present approach, the signal model block 106 is chosen to have the general form:

$$S = A\exp(-Bt) + C\,t + D \qquad \text{EQ. 1}$$

[0046] In the above equation, S is the signal current or voltage, t represents time, and the parameters A, B, C, and D are tunable parameters. EQ. 1 is chosen in this embodiment of the system model 106 since it can be generally applied to many physical processes that exhibit natural logarithmic or linear response to changes in measured quantity 101. In some embodiments, the signal current is measured, the signal current is converted to a signal voltage, and the signal voltage is subsequently digitized. In other embodiments, the signal voltage is measured directly, and subsequently digitized.

[0047] FIG. 2 is a flow chart showing one mode of implementation of the noise detection block 104. The noisy signal 201 is first low pass filtered 202 to remove artifacts that are outside of the frequency range of the corrupting noise 103. In an embodiment of the present system, the filtered signal 202 is differentiated to determine the rate of change of the signal. If the rate of change of the signal exceeds a rejection threshold 204, the signal is dropped from the data set 205. Furthermore, data is dropped for some time after

the initial threshold is exceeded or until the derivative of the signal falls below the initial threshold or some other threshold. Note that the derivative block 202 may be a single derivative or a cascade of derivatives, each corresponding to a threshold value which would induce data dropping. The present method detects the leading and falling edge of the noise signal for the purpose of removing it. Since the noise signal is large, regardless of its frequency content, the leading and falling edges will be distinct features in the signal and can be distinguished and removed.

[0048] FIG. 3 shows a sample time-history of two voltage signals 301-302 with dropped data points 303 indicated with thick black highlights. Corrupting noise 303 is apparent in the signal. Corrupted data 303 was successfully removed from the data set by the noise detection block (104, 201-205) and noise removal 105 blocks.

[0049] FIG. 4 shows a sample time-history of two voltage signals produced by a transducer 102. In this example, the measured quantity 101 is an analyte concentration. Additionally, the transducer produces a voltage signal sensitive to the concentration of analyte in solution 401 (commonly referred to as the working electrode) and a voltage signal sensitive only to the solution and insensitive to the concentration of analyte 402 (commonly referred to as the black electrode). In this example, the voltage signals 401-402 are corrupted by noise 103 to produce the curve 404. A close-up view of the time-history at time 405a is also shown 405b. Successful implementation of the method depicted in FIG. 1 and FIG. 2 result in the clean, reconstructed signals 406-407.

[0050] FIG. 5 shows an example time-history of an analyte concentration calculated from two voltage signals of the type depicted in FIG. 4. *In-vivo* and *in-vitro* results are shown. The corrupted unprocessed analyte concentration 501 exhibits larger perturbations from the trend seen in the uncorrupted data. The unprocessed analyte concentration exhibits a larger standard deviation due to noise. Furthermore, the unprocessed analyte concentration 501 is far from the true analyte concentration 503. On the contrary, the processed analyte concentration 502 follows the trend of uncorrupted points and is close to the true analyte concentration 503.

[0051] In FIG. 5, the data point represented by 501b is a corrupted data point. This data point is removed. The data point represented by 502b is an interpolated data point that is determined in order to replace the removed data point.

[0052] Any of the features described herein with respect to a particular process flow are also applicable to any other process flow. In accordance with embodiments described herein, the term "module" with respect to a system may refer to a hardware component of the system, a software component of the system, or a component of the system that includes both hardware and software. As used herein, a module may include one or more modules, where each module may reside in separate pieces of hardware or software.

[0053] In one embodiment, the system, methods, and computer software is combined with one or more electronic circuits and/or polyelectrolyte coatings. Any process block presented in FIG. 1 or FIG. 2 may comprise one or more electronic circuits. Additionally exemplary electronic circuits include those disclosed in co-assigned U.S. Published Application No. 2009/0120810 filed October 31, 2008, herein incorporated by reference. The circuits described in this application or described in any other application referred to herein may produce any signals described herein. Exemplary polyelectrolyte coatings include, by way of example, those disclosed in co-assigned U.S. Published Application No. 2010/0160756, filed December 11, 2009, herein incorporated by reference. Polyelectrolytes are high molecular weight materials having pendent ionizable groups. As electrolytes, polyelectrolytes exhibit the advantageous ionic properties required for stable sensor functioning, such as charge neutralization and charge transfer abilities. Due to their large size, polyelectrolytes substantially reduce or eliminate diffusion of the electrolytic species to the surrounding medium. Thus, a polyelectrolyte may substantially maintain electroneutrality about the sensor and/or reduce or eliminate output signal disruption when exposed to an external EMF or RF source. In one aspect, the polyelectrolyte may be comprised of polyacids, while other aspects may utilize polybases or polyampholytes as the polyelectrolyte. Further aspects may utilize a polyelectrolyte comprising a polyelectrolyte salt, or polysalt. In another aspect, the polyelectrolyte comprises pharmaceutically acceptable polysalts. A pharmaceutically acceptable salt is one which is safe and effective for use in humans. For example, pharmaceutically acceptable salts may

include polycations with counterions comprising sulfate, pyrosulfate, bisulfate, sulfite, bisulfite, phosphate, monohydrogenphosphate, dihydrogenphosphate, metaphosphate, pyrophosphate, (bi)carbonate, chloride, bromide, iodide, acetate, propionate, decanoate, caprylate, acrylate, formate, isobutyrate, caprate, heptanoate, propiolate, oxalate, malonate, succinate, suberate, sebacate, fumarate, maleate, butyne-1,4-dioate, hexyne-1,6-dioate, benzoate, chlorobenzoate, methylbenzoate, dinitrobenzoate, hydroxybenzoate, methoxybenzoate, phthalate, terephathalate, sulfonate, xylenesulfonate, phenylacetate, phenylpropionate, phenylbutyrate, citrate, lactate, beta-hydroxybutyrate, glycolate, maleate, tartrate, methanesulfonate, propanesulfonate, naphthalene-1-sulfonate, naphthalene-2-sulfonate, mandelate, or polyanions with positive counterions from elements such as aluminum, calcium, lithium, magnesium, potassium, sodium, and zinc, or from organic compounds such as benzalkonium, pyridinium, quaternary alkyl or arylammonium, or other organic cations, among others. Generally, polyelectrolytes have numerous ionizable groups, and thus may be highly charged. In one aspect, the polyelectrolyte may be comprised of polyelectrolytes with multiple ionizable groups. In a further aspect, the polyelectrolyte layer may be comprised of highly charged polyelectrolytes without terminal ionizable groups (e.g., Nafion). In one aspect, the polyelectrolyte may be comprised of a polyelectrolyte comprising sulfonate functionality. Incorporating a polyelectrolyte with sulfonate functionality may be advantageous for analyte sensors, as sulfonate groups are the salts of strong acids and therefore have little influence on the local pH. For example, a polystyrene sulfonate, such as poly(sodium-4-styrene sulfonate), or copolymers of polystyrene sulfonate and maleic acid, such as poly(4-styrene sulfonic acid-co-maleic acid) Na salt, or mixtures thereof may be utilized. In a further aspect, the polyelectrolyte may be comprised of heparin. Heparin, a naturally occurring polysaccharide polyelectrolyte with sulfonate functionality. In one aspect, benzalkonium heparin is used as the polyelectrolyte. Other salts of heparin may be used, preferably pharmaceutically acceptable salts of heparin. Benzalkonium heparin is frequently used as an anticoagulant on medical devices or used to inhibit blood coagulation in a patient. Thus, one advantage of heparin polyelectrolytes, such as benzalkonium heparin, is that any heparin polyelectrolyte released from the sensor would

likely not cause a toxic response in the subject. In another aspect, the polyelectrolyte may comprise carboxylic acid functionality. Examples of suitable polyelectrolytes with carboxylic acid functionality include polyacrylic acid and polyalkylacrylic acid, where the alkyl is C_1-C_4. In one aspect, the polyelectrolytes with carboxylic acid functionality include polyacrylic acid, polymethacrylic and copolymers or blends thereof. Any non-toxic polyelectrolyte salt could be utilized as the hydrophilic polymer membrane. One skilled in the art of polymer science can appreciate the very wide diversity of possible combinations of polyions (polymers containing repeat linkages with positive or negative charges) and the associated counterions, and will recognize that the list above is not by any means exhaustive, and other possible combinations are considered to be inclusive, including the possible combination of one or more polyanion and one or more polycation to form a relatively insoluble polyelectrolyte. The polyelectrolyte can be coated on one or more portions of the source of the signal, such as the exterior of an analyte sensor configured for insertion in the circulatory system of a subject.

[0054] FIG. 6 illustrates a schematic block diagram of a system 20 for operating an electro-chemical biosensor such as an amperometric or potentiometric sensor, such as a glucose sensor. The sensor may be used for measuring the concentration of an analyte in solution as described herein. Each block or element presented in FIG. 6 includes one or more electronic circuits. The signal (e.g., voltage signal, current signal, impedance signal, concentration signal, or the like) described herein may be generated by any of the blocks or elements presented in FIG. 6. In particular, FIG. 6 discloses a system comprising an amperometric biosensor. As more fully disclosed in U.S. patent application Ser. No. 11/696,675, filed Apr. 4, 2007, and titled ISOLATED INTRAVENOUS ANALYTE MONITORING SYSTEM, a typical system for operating an amperometric sensor includes a potentiostat 22 in communication with the sensor 10. In normal operation, the potentiostat both biases the electrodes of the sensor and provides outputs regarding operation of the sensor. As illustrated in FIG. 6, the potentiostat 22 receives signals WEI, WE2, and REF respectively from the first working electrode 12, second working electrode 14, and the reference electrode 16. The potentiostat further provides a bias voltage CE input to the counter electrode 18. The potentiostat 22, in turn, outputs the signals WEI,

WE2 from the working electrodes 12 and 14 and a signal representing the voltage potential VBIAS between the counter electrode 18 and the reference electrode 16.

[0001] A potentiostat is a controller and measuring device that, in an electrolytic cell, keeps the potential of the working electrode 12 at a constant level with respect to the reference electrode 16. It consists of an electric circuit which controls the potential across the cell by sensing changes in its electrical resistance and varying accordingly the electric current supplied to the system: a higher resistance will result in a decreased current, while a lower resistance will result in an increased current, in order to keep the voltage constant.

[0002] Another function of the potentiostat is receiving electrical current signals from the working electrodes 12 and 14 for output to a controller. As the potentiostat 22 works to maintain a constant voltage for the working electrodes 12 and 14, current flow through the working electrodes 12 and 14 may change. The current signals indicate the presence of an analyte of interest in blood. In addition, the potentiostat 22 holds the counter electrode 18 at a voltage level with respect to the reference electrode 16 to provide a return path for the electrical current to the bloodstream, such that the returning current balances the sum of currents drawn in the working electrodes 12 and 14.

[0003] While a potentiostat is disclosed herein as the first or primary power source for the electrolytic cell and data acquisition device, it must be understood that other devices for performing the same functions may be employed in the system and a potentiostat is only one example. For example, an amperostat, sometimes referred to as a galvanostat, could be used.

[0004] As illustrated in FIG. 6, the output of the potentiostat 22 is typically provided to a filter 28, which removes at least some of the spurious signal noise caused by either the electronics of the sensor or control circuit and/or external environmental noise. The filter 28 is typically a low pass filter, but can be any type of filter to achieve desired noise reduction.

[0005] In addition to electrical signal noise, the system may also correct analyte readings from the sensor based on operating temperature of the sensor. With reference to FIG. 6, a temperature sensor 40 may be collocated with the biosensor 10. Since chemical reaction rates (including the rate of glucose oxidation) are typically affected by

temperature, the temperature sensor 40 may be used to monitor the temperature in the same environment where the working electrodes 12 and 14 of the biosensor are located. In the illustrated embodiment, the temperature sensor may be a thermistor, resistance temperature detector (RTD), or similar device that changes resistance based on temperature. An R/V converter 38 may be provided to convert the change in resistance to a voltage signal Vt that can be read by a processor 34. The voltage signal Vt represents the approximate temperature of the biosensor 10. The voltage signal Vt may then be output to the filter 28 and used for temperature compensation.

[0006] As illustrated in FIG. 6, a multiplexer may be employed to transfer the signals from the potentiostat 22, namely 1) the signals WEI, WE2 from the working electrodes 12 and 14; 2) the bias signal VBIAS representing the voltage potential between the counter electrode 18 and the reference electrode 16; and 3) the temperature signal Vt from the temperature sensor 40 to the processor 34. The signals are also provided to an analog to digital converter (ADC) 32 to digitize the signals prior to input to the processor.

[0007] The processor uses algorithms in the form of either computer program code where the processor is a microprocessor or transistor circuit networks where the processor is an ASIC or other specialized processing device to determine the amount of analyte in a substance, such as the amount of glucose in blood. The results determined by the processor may be provided to a monitor or other display device 36. As illustrated in FIG. 6 and more fully described in U.S. patent application Ser. No. 11/696,675, filed Apr. 4, 2007, and titled ISOLATED INTRAVENOUS ANALYTE MONITORING SYSTEM, the system may employ various devices to isolate the biosensor 10 and associated electronics from environmental noise. For example, the system may include an isolation device 42, such as an optical transmitter for transmitting signals from the processor to the monitor to avoid backfeed of electrical noise from the monitor to the biosensor and its associated circuitry. Additionally, an isolated main power supply 44 may be provided for supplying power to the circuit, such as an isolation DC/DC converter.

[0008] Although many embodiments of the present system have just been described above, the present system may be embodied in many different forms and should not be construed as limited to the embodiments set forth herein; rather, these embodiments are

provided so that this disclosure will satisfy applicable legal requirements. Also, it will be understood that, where possible, any of the advantages, features, functions, devices, and/or operational aspects of any of the embodiments of the present system described and/or contemplated herein may be included in any of the other embodiments of the present system described and/or contemplated herein, and/or vice versa. In addition, where possible, any terms expressed in the singular form herein are meant to also include the plural form and/or vice versa, unless explicitly stated otherwise. Accordingly, the terms "a" and/or "an" shall mean "one or more," even though the phrase "one or more" is also used herein. Like numbers refer to like elements throughout.

[0009] As will be appreciated by one of ordinary skill in the art in view of this disclosure, the present system may include and/or be embodied as an apparatus (including, for example, a system, machine, device, computer program product, and/or the like), as a method (including, for example, a method, computer-implemented process, and/or the like), or as any combination of the foregoing. Accordingly, embodiments of the present system may take the form of an entirely method embodiment, an entirely software embodiment (including firmware, resident software, micro-code, stored procedures in a database, etc.), an entirely hardware embodiment, or an embodiment combining method, software, and hardware aspects that may generally be referred to herein as a "system." Furthermore, embodiments of the present system may take the form of a computer program product that includes a computer-readable storage medium having one or more computer-executable program code portions stored therein. As used herein, a processor, which may include one or more processors, may be "configured to" perform a certain function in a variety of ways, including, for example, by having one or more general-purpose circuits perform the function by executing one or more computer-executable program code portions embodied in a computer-readable medium, and/or by having one or more application-specific circuits perform the function.

[0010] It will be understood that any suitable computer-readable medium may be utilized. The computer-readable medium may include, but is not limited to, a non-transitory computer-readable medium, such as a tangible electronic, magnetic, optical, electromagnetic, infrared, and/or semiconductor system, device, and/or other apparatus.

For example, in some embodiments, the non-transitory computer-readable medium includes a tangible medium such as a portable computer diskette, a hard disk, a random access memory (RAM), a read-only memory (ROM), an erasable programmable read-only memory (EPROM or Flash memory), a compact disc read-only memory (CD-ROM), and/or some other tangible optical and/or magnetic storage device. In other embodiments of the present system, however, the computer-readable medium may be transitory, such as, for example, a propagation signal including computer-executable program code portions embodied therein.

[0011] One or more computer-executable program code portions for carrying out operations of the present system may include object-oriented, scripted, and/or unscripted programming languages, such as, for example, Java, Perl, Smalltalk, C++, SAS, SQL, Python, Objective C, JavaScript, and/or the like. In some embodiments, the one or more computer-executable program code portions for carrying out operations of embodiments of the present system are written in conventional procedural programming languages, such as the "C" programming languages and/or similar programming languages. The computer program code may alternatively or additionally be written in one or more multi-paradigm programming languages.

[0012] Some embodiments of the present system are described herein with reference to flowchart illustrations and/or block diagrams of apparatus and/or methods. It will be understood that each block included in the flowchart illustrations and/or block diagrams, and/or combinations of blocks included in the flowchart illustrations and/or block diagrams, may be implemented by one or more computer-executable program code portions. These one or more computer-executable program code portions may be provided to a processor of a general purpose computer, special purpose computer, and/or some other programmable data processing apparatus in order to produce a particular machine, such that the one or more computer-executable program code portions, which execute via the processor of the computer and/or other programmable data processing apparatus, create mechanisms for implementing the steps and/or functions represented by the flowchart(s) and/or block diagram block(s).

[0013] The one or more computer-executable program code portions may be stored in a transitory and/or non-transitory computer-readable medium (e.g., a memory, etc.) that can direct, instruct, and/or cause a computer and/or other programmable data processing apparatus to function in a particular manner, such that the computer-executable program code portions stored in the computer-readable medium produce an article of manufacture including instruction mechanisms which implement the steps and/or functions specified in the flowchart(s) and/or block diagram block(s).

[0014] The one or more computer-executable program code portions may also be loaded onto a computer and/or other programmable data processing apparatus to cause a series of operational steps to be performed on the computer and/or other programmable apparatus. In some embodiments, this produces a computer-implemented process such that the one or more computer-executable program code portions which execute on the computer and/or other programmable apparatus provide operational steps to implement the steps specified in the flowchart(s) and/or the functions specified in the block diagram block(s). Alternatively, computer-implemented steps may be combined with, and/or replaced with, operator- and/or human-implemented steps in order to carry out an embodiment of the present system.

[0015] While certain exemplary embodiments have been described and shown in the accompanying drawings, it is to be understood that such embodiments are merely illustrative of and not restrictive on the broad system, and that this system not be limited to the specific constructions and arrangements shown and described, since various other changes, combinations, omissions, modifications and substitutions, in addition to those set forth in the above paragraphs, are possible. Those skilled in the art will appreciate that various adaptations, modifications, and combinations of the just described embodiments can be configured without departing from the scope and spirit of the system. Therefore, it is to be understood that, within the scope of the appended claims, the system may be practiced other than as specifically described herein.

WHAT IS CLAIMED IS:

1. A method for removing corrupted data from a signal, the method comprising:

receiving a signal time-history associated with a signal comprising corrupted data and uncorrupted data;

identifying the uncorrupted data from the signal time-history;

identifying the corrupted data from the signal time-history;

removing the corrupted data from the signal time-history;

determining replacement data for replacing the corrupted data in the signal time-history; and

reconstructing the signal time-history based on the uncorrupted data and the replacement data.

2. The method of claim 1, wherein the signal comprises at least one of a first voltage signal substantially sensitive to a concentration of an analyte in a solution or a second voltage signal substantially sensitive to the solution and substantially insensitive to the concentration of the analyte in the solution, and wherein the reconstructing step enables determination of the concentration of the analyte in the solution.

3. The method of claim 2, wherein the analyte comprises glucose.

4. The method of claim 1, wherein the corrupted data comprises a substantially corrupted time-segment from the signal time-history, and wherein the uncorrupted data comprises a substantially uncorrupted time-segment from the signal time-history.

5. The method of claim 1, wherein at least one of the determining step or the reconstructing step is based on at least one of a least squares fitting model, an adaptive model, a statistical model, or a heuristic model.

6. The method of claim 1, wherein at least one of the determining step or the reconstructing step is based on whether a system is being calibrated or whether the system is being used to measure a concentration of an analyte in a solution.

7. The method of claim 1, wherein the corrupted data comprises noise.

8. The method of claim 7, wherein the noise comprises at least one of high-frequency noise or low-frequency noise.

9. The method of claim 1, wherein the determining step comprises:
accessing a model of the signal time-history;
determining the replacement data based on the uncorrupted data and the model.

10. The method of claim 9, wherein the model comprises substantially uncorrupted data.

11. The method of claim 9, wherein the model is based on a previous signal time-history associated with the signal.

12. The method of claim 9, wherein the model is generated in substantially real-time.

13. The method of claim 9, wherein the model is generated based on a minimization model such that a normalized difference between a parameter of the model and a parameter of the uncorrupted data is less than or equal to a predetermined threshold.

14. The method of claim 1, wherein the receiving step comprises:
measuring a quantity;
converting, using a transducer, the measured quantity to the signal.

15. The method of claim 14, wherein the quantity is associated with the transducer, wherein the quantity comprises a voltage.

16. The method of claim 14, wherein the signal comprises at least one of a signal substantially sensitive to a solution, or a signal substantially sensitive to the solution and substantially insensitive to an analyte concentration associated with the solution.

17. The method of claim 1, wherein at least one of the identifying the corrupted data from the signal time-history step or removing the corrupted data from the signal time-

history step comprises:

low-pass filtering the signal time-history to remove artifacts that are outside a frequency range of the corrupted data;

determining a rate of change of the filtered signal time-history;

in response to determining the rate of change exceeds a first threshold, dropping the filtered signal time-history from a data set;

continuing to drop the signal time-history from the data set until the rate of the change of the filtered signal time-history falls below either the first threshold or a second threshold, wherein the second threshold is either above or below the first threshold.

18. The method of claim 17, wherein the rate of change is based on a single derivative or a cascade of derivatives.

19. The method of claim 1, wherein the signal is generated by one or more electronic circuits.

20. The method of claim 1, wherein a polyelectrolyte coating is associated with a source of the signal.

21. The method of claim 1, wherein one or more electronic circuits and a polyelectrolyte coating are associated with a source of the signal.

22. An apparatus for removing corrupted data from a signal, the apparatus comprising:

a memory;

a processor;

at least one module, executable by the processor, and configured to:

receive a signal time-history associated with a signal comprising corrupted data and uncorrupted data;

identify the uncorrupted data from the signal time-history;

identify the corrupted data from the signal time-history;

remove the corrupted data from the signal time-history;

determine replacement data for replacing the corrupted data in the signal time-

reconstruct the signal time-history based on the uncorrupted data and the replacement data.

23. A computer program product for removing corrupted data from a signal, the computer program product comprising:

a non-transitory computer-readable medium comprising a set of codes for causing a computer to:

receive a signal time-history associated with a signal comprising corrupted data and uncorrupted data;

identify the uncorrupted data from the signal time-history;

identify the corrupted data from the signal time-history;

remove the corrupted data from the signal time-history;

determine replacement data for replacing the corrupted data in the signal time-history; and

reconstruct the signal time-history based on the uncorrupted data and the replacement data.

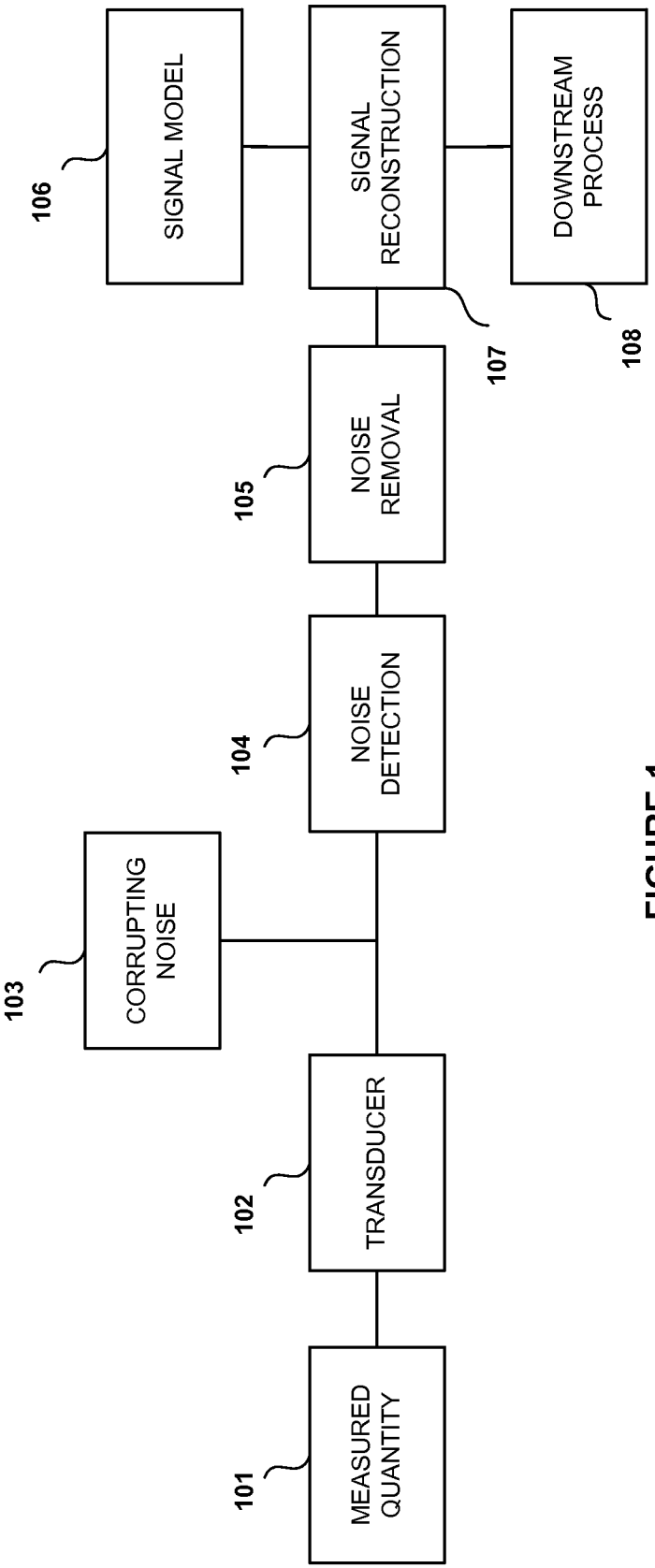
MEASURED QUANTITY
101
TRANSDUCER
102
CORRUPTING NOISE
103
NOISE DETECTION
104
NOISE REMOVAL
105
SIGNAL MODEL
106
SIGNAL RECONSTRUCTION
107
DOWNSTREAM PROCESS
108

FIGURE 1

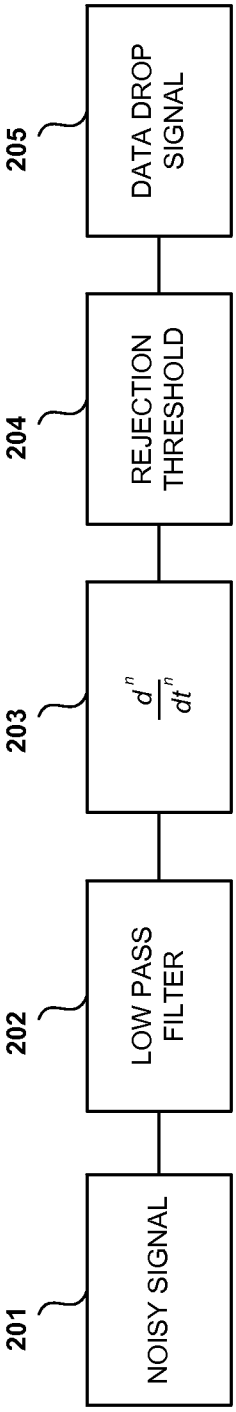
201
NOISY SIGNAL
202
LOW PASS FILTER
203
$\frac{d^n}{dt^n}$
204
REJECTION THRESHOLD
205
DATA DROP SIGNAL

FIGURE 2

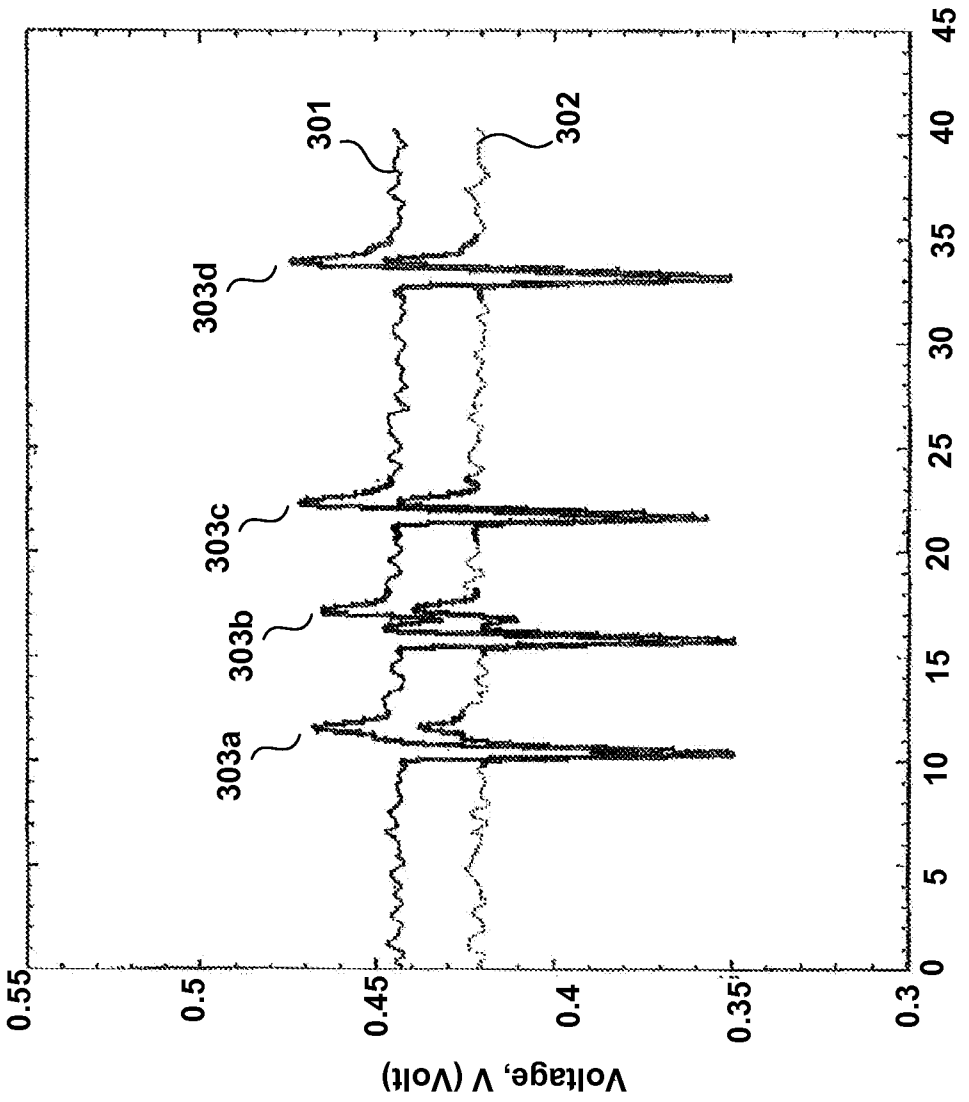
0.55
0.5
0.45
0.4
0.35
0.3
0
5
10
15
20
25
30
35
40
45
Voltage, V (Volt)
Time, t (s)
301
302
303a
303b
303c
303d

FIGURE 3

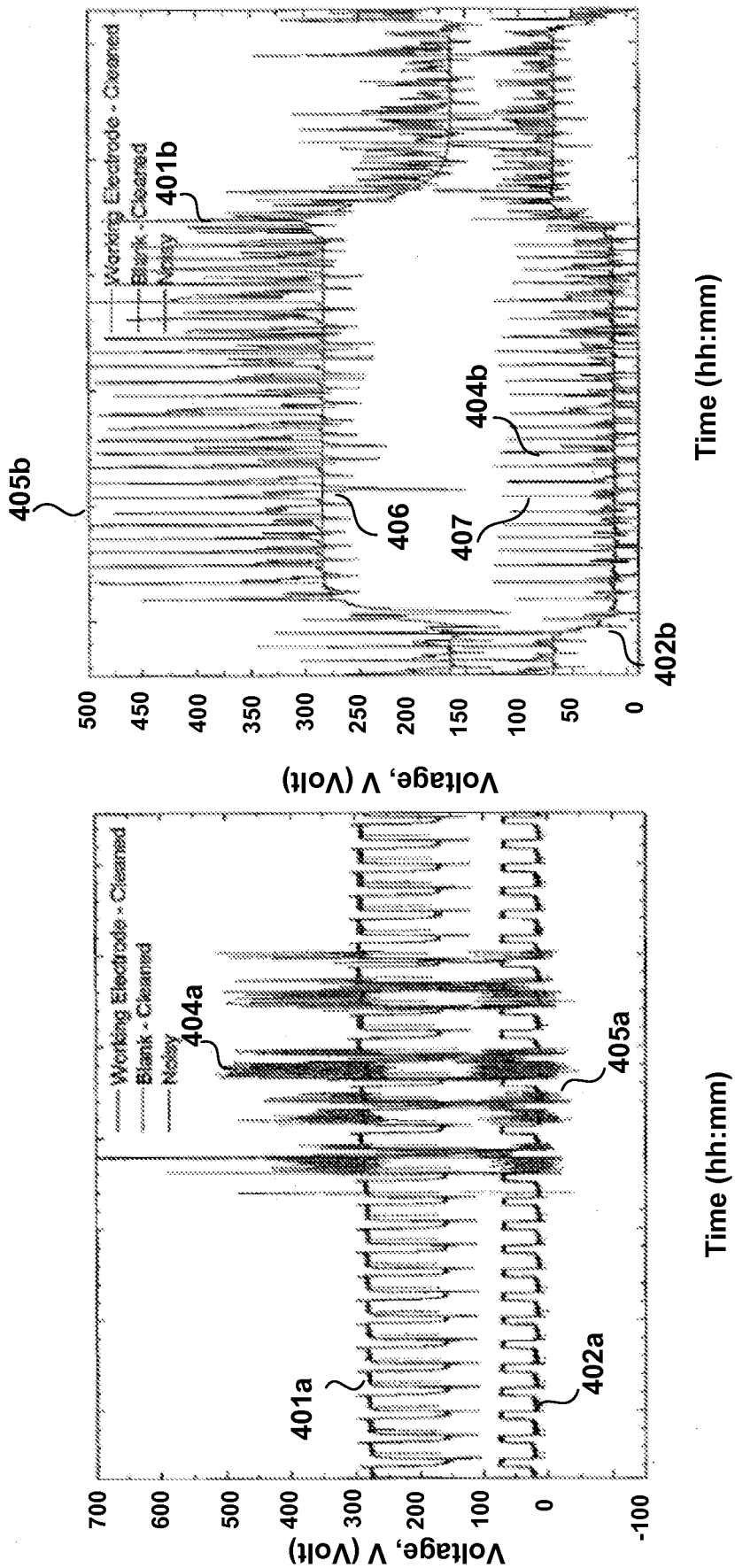
Working Electrode - Cleaned
Blank - Cleaned
Noisy
401b
404b
405b
406
407
402b
Voltage, V (Volt)
Time (hh:mm)
401a
404a
405a
402a
Voltage, V (Volt)
Time (hh:mm)

FIGURE 4

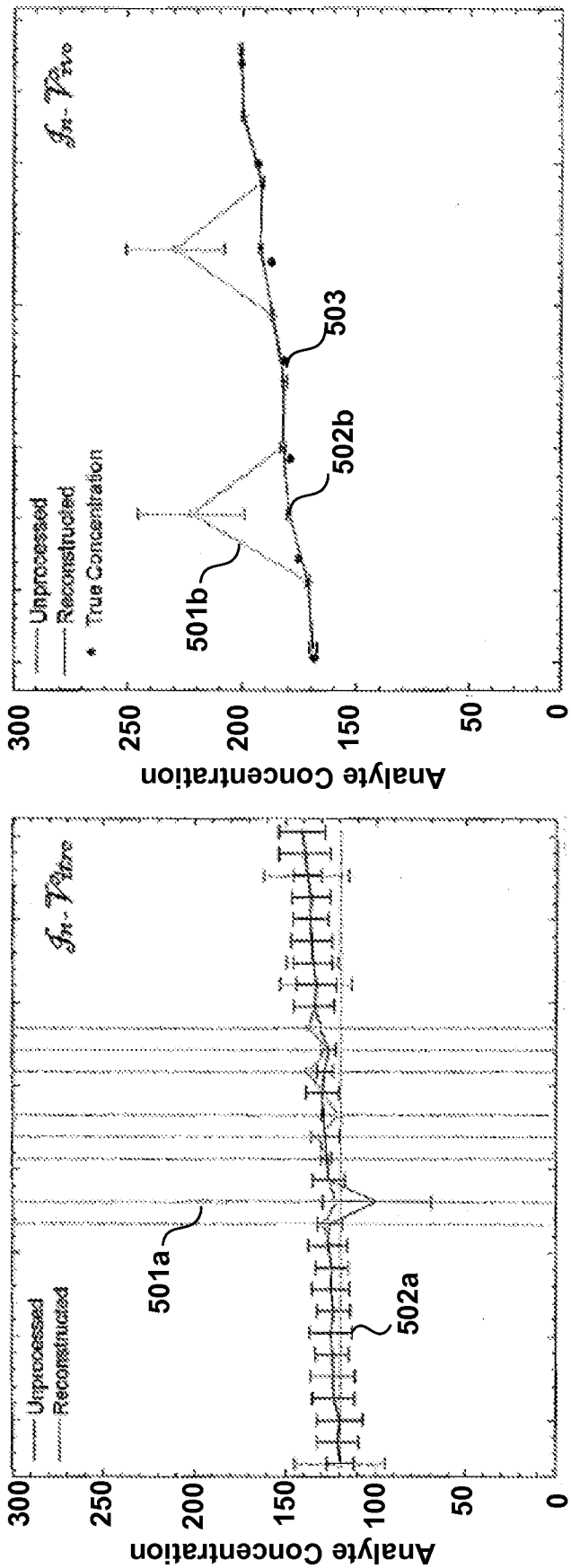
In-Vitro
Unprocessed
Reconstructed
501a
502a
Analyte Concentration
Time
In-Vivo
Unprocessed
Reconstructed
True Concentration
501b
502b
503
Analyte Concentration
Time

FIGURE 5

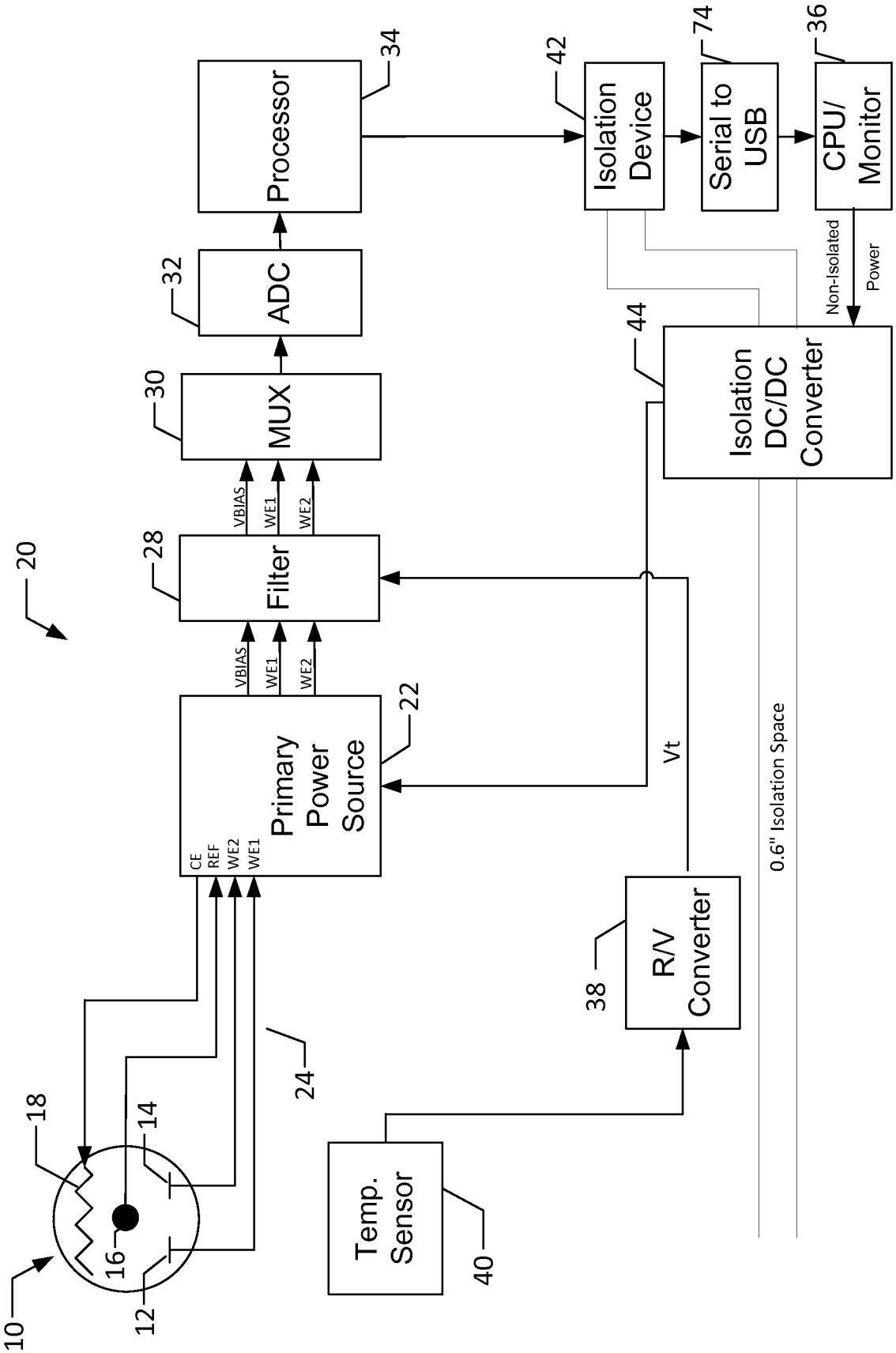
10
12
14
16
18
20
22
24
Primary Power Source
CE
REF
WE2
WE1
VBIAS
WE1
WE2
28
Filter
VBIAS
WE1
WE2
30
MUX
32
ADC
34
Processor
38
R/V Converter
40
Temp. Sensor
42
Isolation Device
74
Serial to USB
36
CPU/ Monitor
Non-Isolated
Power
44
Isolation DC/DC Converter
Vt
0.6" Isolation Space

FIGURE 6

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2013/071509

A. CLASSIFICATION OF SUBJECT MATTER

G06F 7/00(2006.01)i

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)
G06F 7/00; G08B 1/08; G01N 33/48; A61B 5/02; G10L 15/14; A61B 5/00

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: corrupted data, time-history, replacement, reconstruction, concentration, analyte, and similar terms.

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2011-0130998 A1 (GOODE, PAUL V. JR. et al.) 2 June 2011 See paragraphs [0200], [0229], [0243], [0247], [0253]-[0255], [0274], [0281], [0299], [0303], [0310]-[0311], [0331]-[0333], [0339]-[0340], [0343], [0358], [0360], and [0365]-[0367]; and figures 1-2, 5, 7A-8, 10A, and 11.	1-12,14-16,19-23
A		13,17-18
Y	US 6,173,197 B1 (BOGGETT, DAVID et al.) 19 January 2001 See column 7, lines 17-24; claims 1 and 5; figures 1-2.	1-12,14-16,19-23
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☐ Further documents are listed in the continuation of Box C. ☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"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
07 March 2014 (07.03.2014)	**10 March 2014 (10.03.2014)**

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