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(54) SYSTEM AND METHODS FOR DETERMINATION OF ANALYTE CONCENTRATION USING TIME RESOLVED AMPEROMETRY

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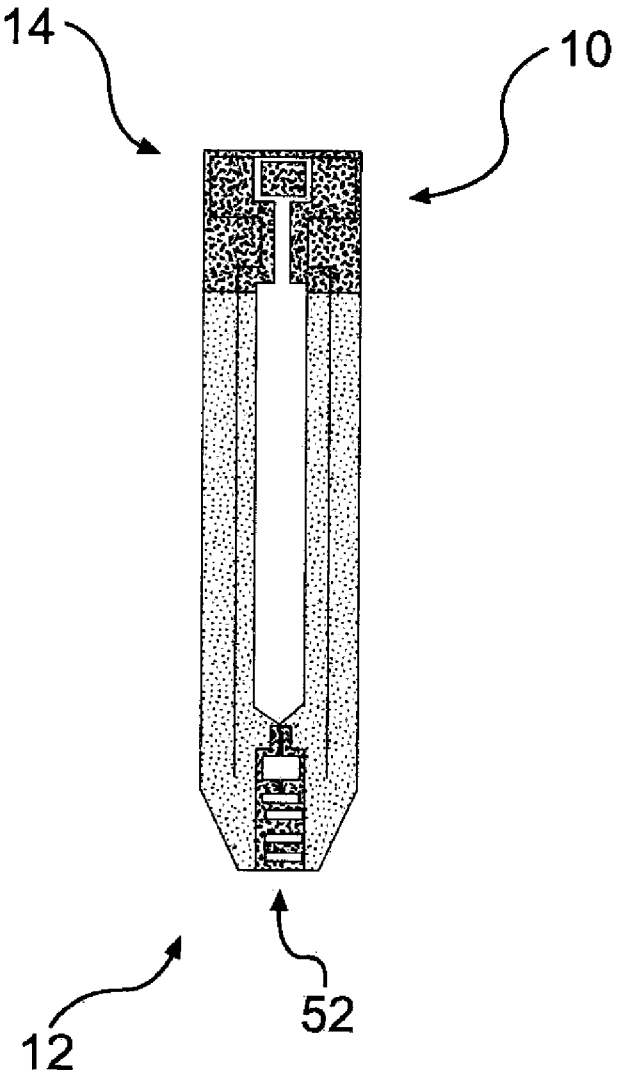
(52) **U.S. Cl.** **702/25**; 702/100

(57) **ABSTRACT**

This invention is a method for determining a concentration of an analyte. The steps include applying a potential excitation to a fluid sample containing an analyte, and measuring one or more currents associated with one or more time-segments. The method can also include calculating a final analyte concentration based on a first and second set of analyte concentrations, wherein each set of analyte concentration values is based on a first and second set of calibration data associated with first and second time-segments.



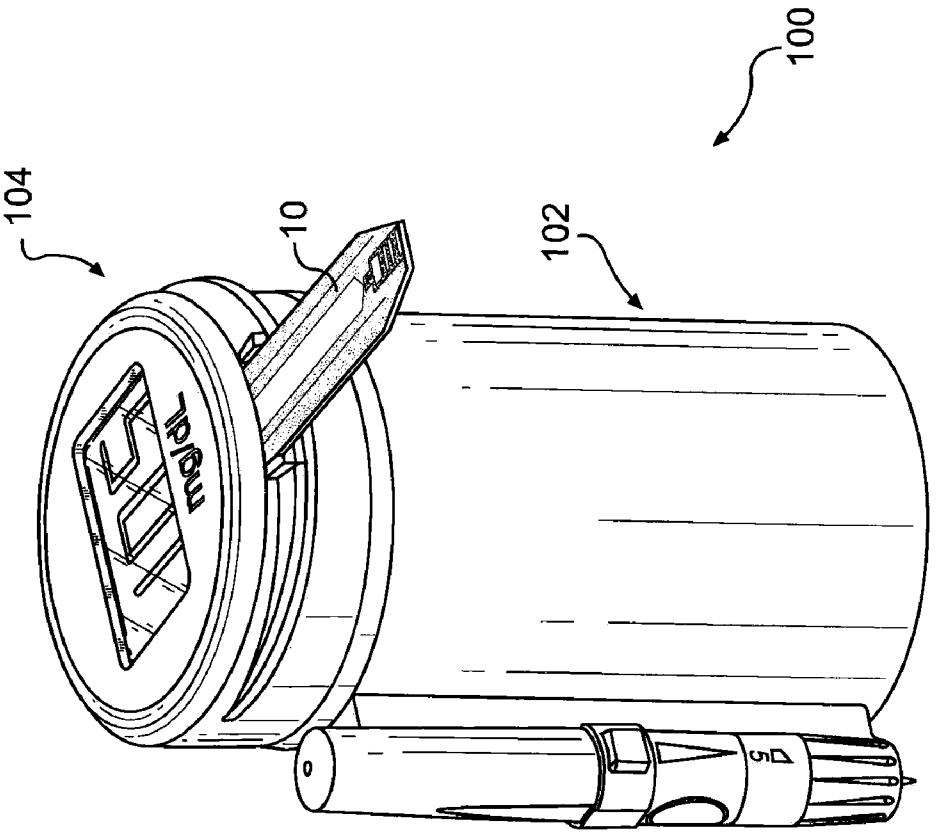


FIG. 1B

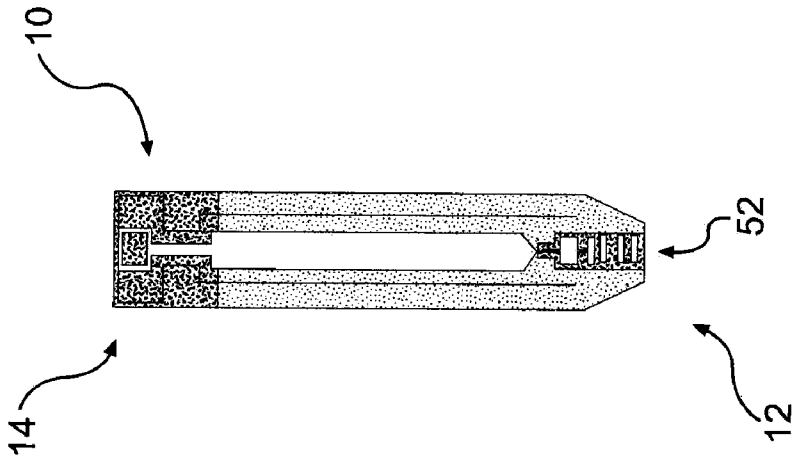


FIG. 1A

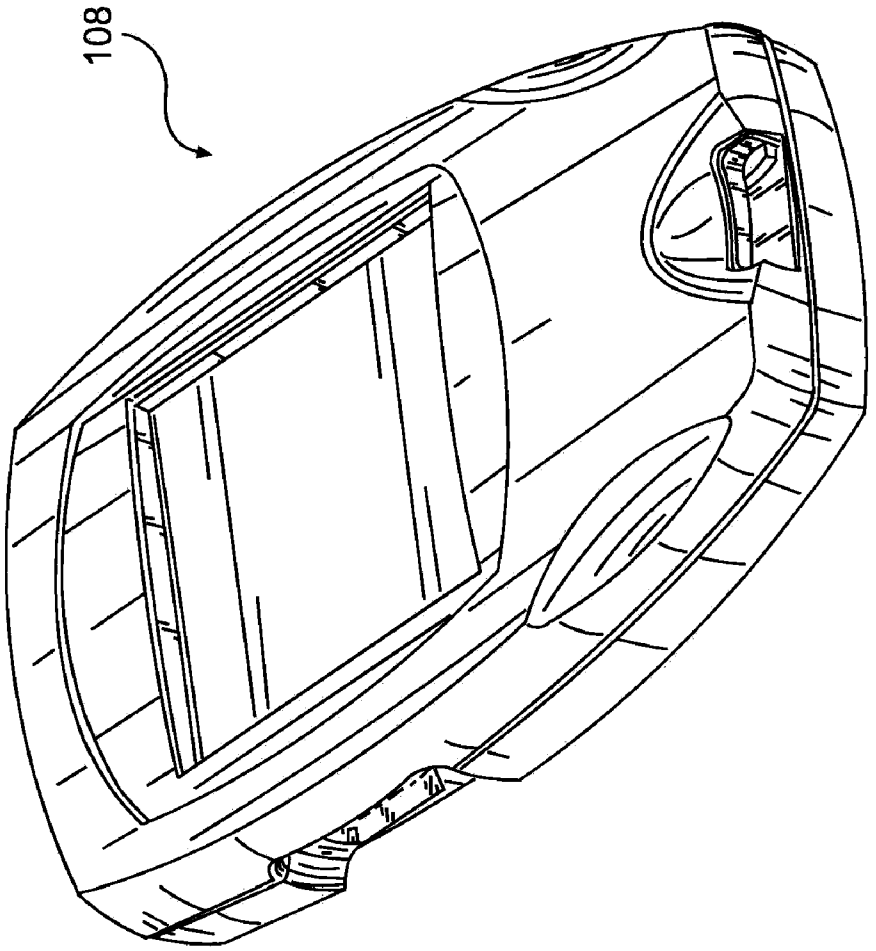


FIG. 1C

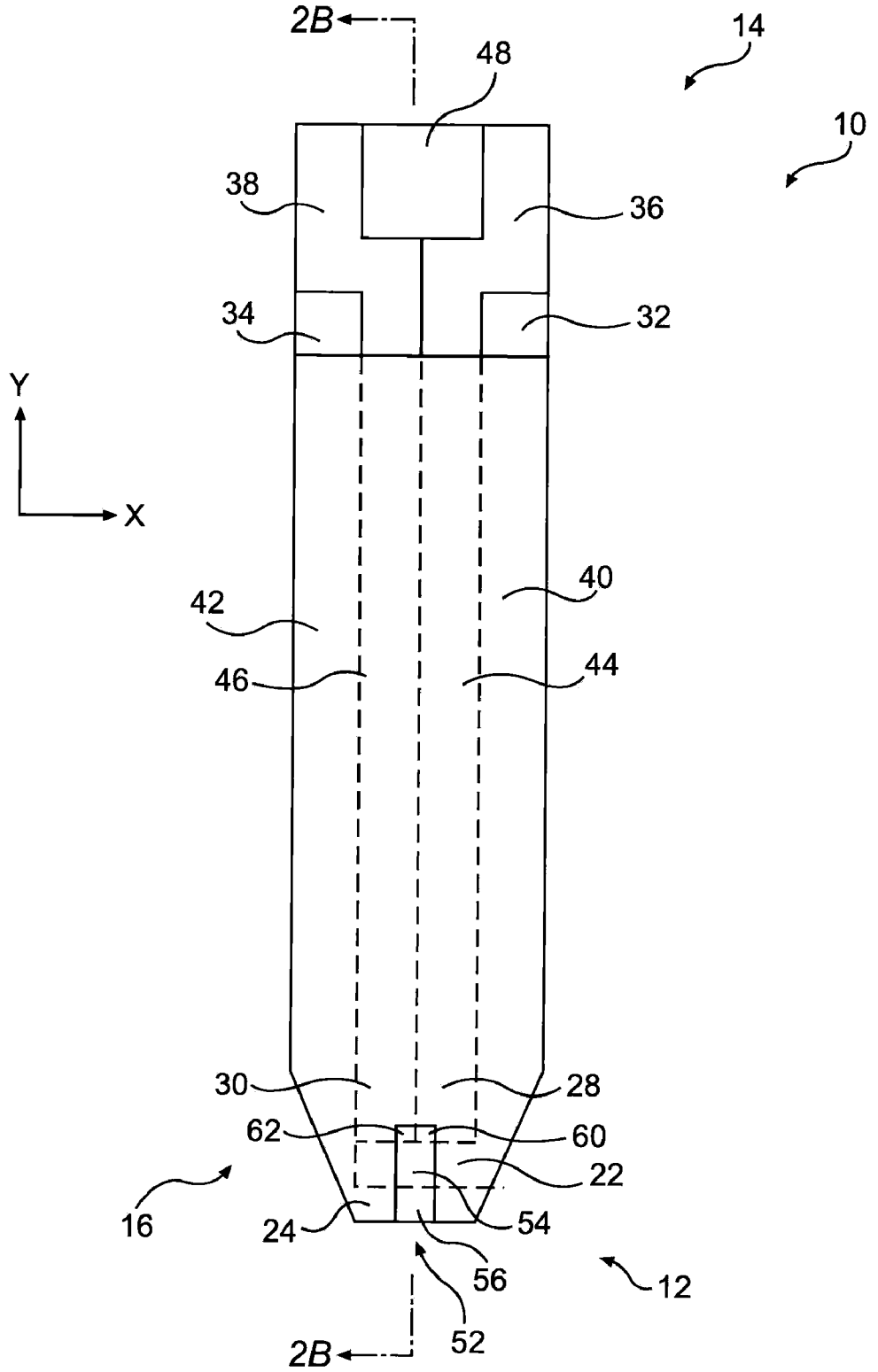

2B
48
14
10
38
36
34
32
Y
X
42
40
46
44
30
28
62
60
22
16
24
54
56
12
52
2B

FIG. 2A

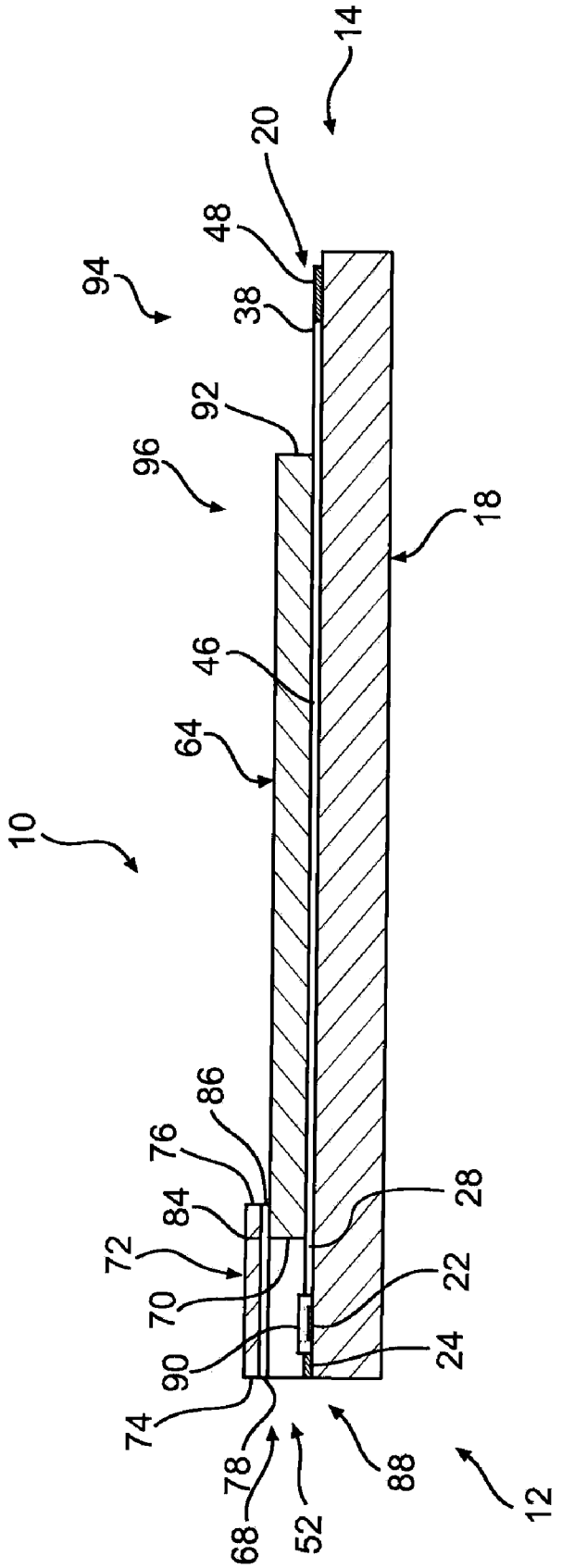

14
20
48
94
38
92
96
18
46
64
10
86
76
84
28
72
22
70
90
24
74
78
88
12
68
52

FIG. 2B

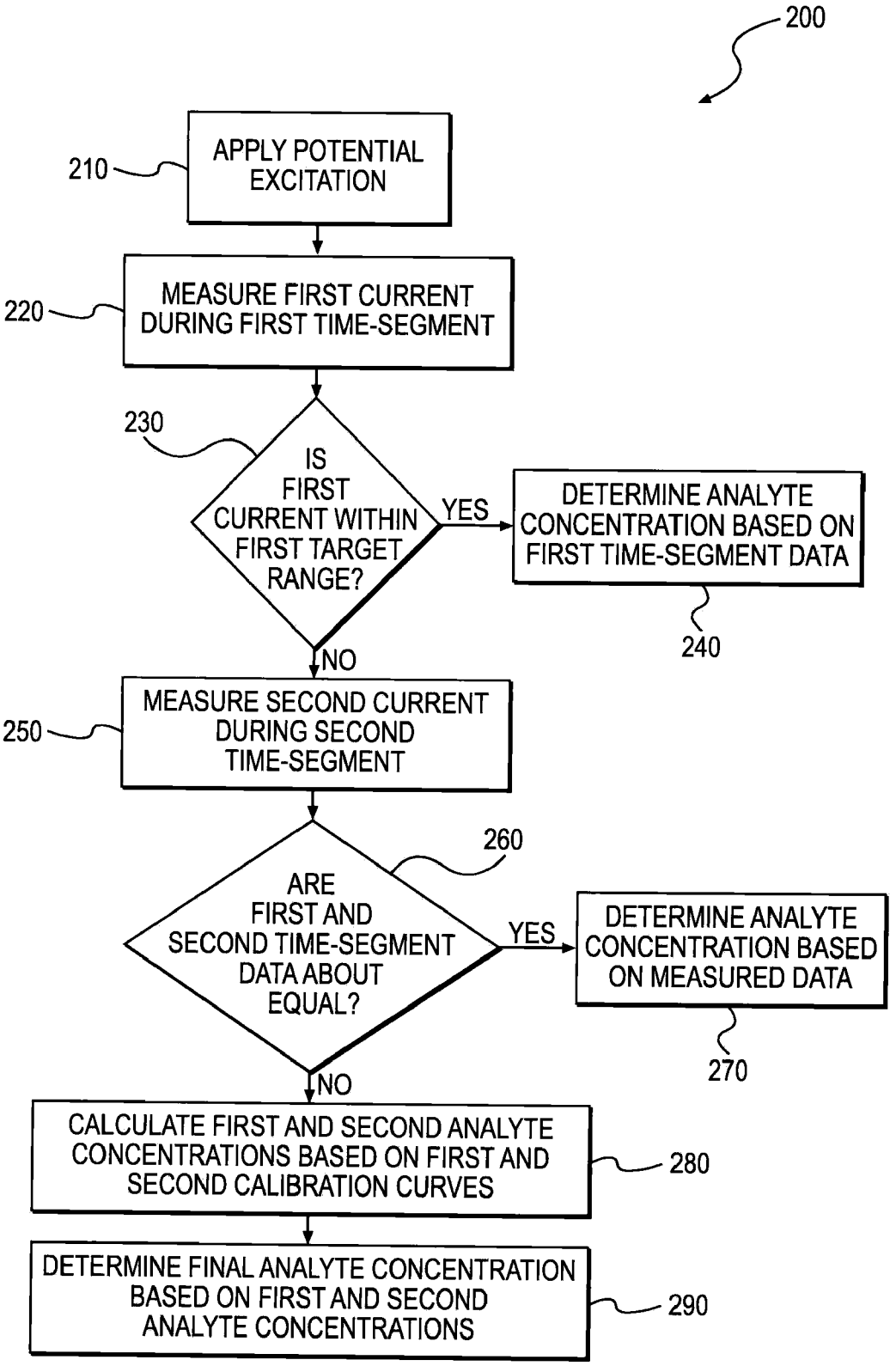

200
210
APPLY POTENTIAL EXCITATION
220
MEASURE FIRST CURRENT DURING FIRST TIME-SEGMENT
230
IS FIRST CURRENT WITHIN FIRST TARGET RANGE?
YES
DETERMINE ANALYTE CONCENTRATION BASED ON FIRST TIME-SEGMENT DATA
240
NO
250
MEASURE SECOND CURRENT DURING SECOND TIME-SEGMENT
260
ARE FIRST AND SECOND TIME-SEGMENT DATA ABOUT EQUAL?
YES
DETERMINE ANALYTE CONCENTRATION BASED ON MEASURED DATA
270
NO
CALCULATE FIRST AND SECOND ANALYTE CONCENTRATIONS BASED ON FIRST AND SECOND CALIBRATION CURVES
280
DETERMINE FINAL ANALYTE CONCENTRATION BASED ON FIRST AND SECOND ANALYTE CONCENTRATIONS
290

FIG. 3

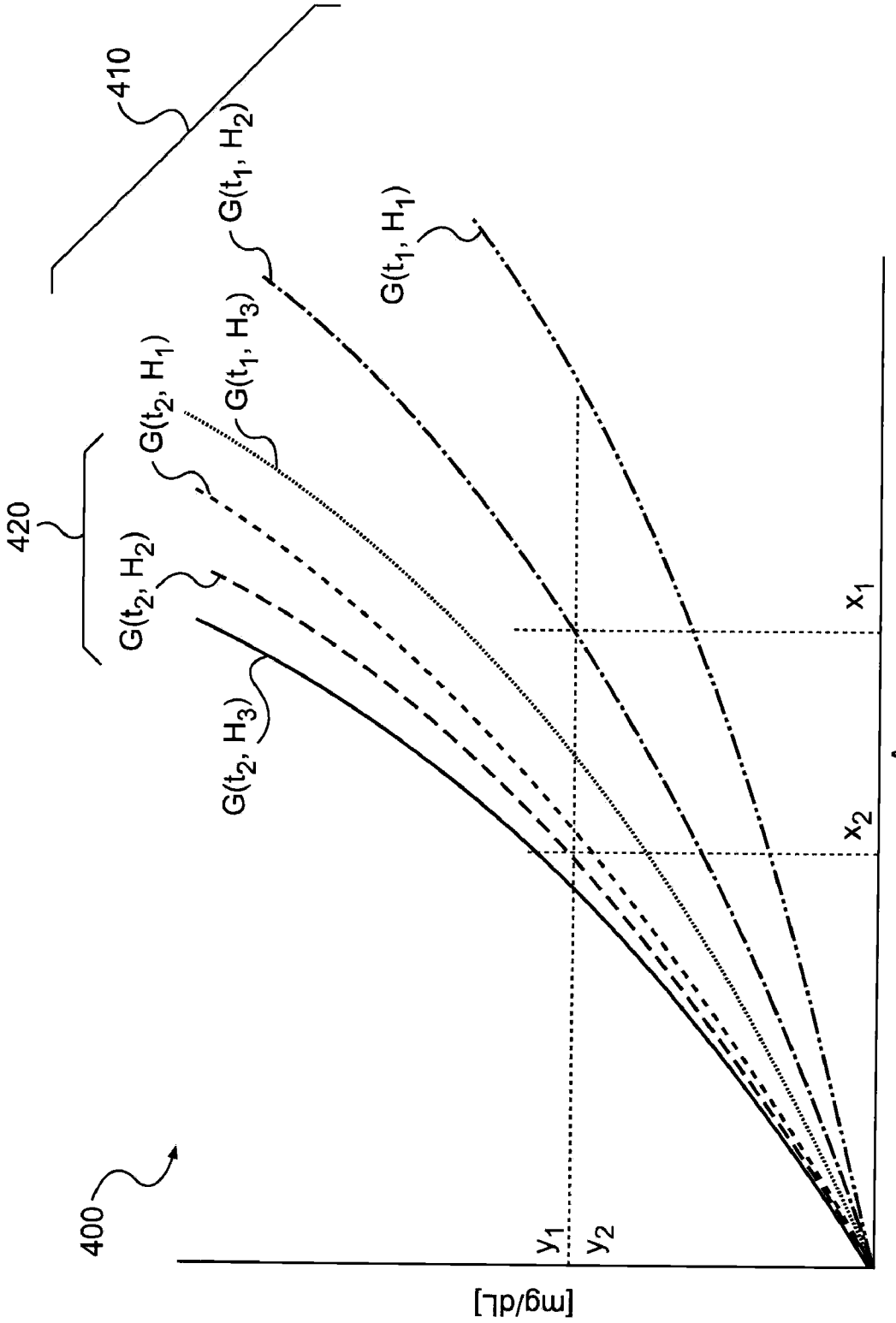

400
410
420
G(t1, H1)
G(t1, H2)
G(t1, H3)
G(t2, H1)
G(t2, H2)
G(t2, H3)
x1
x2
y1
y2
nA
[mg/dL]

FIG. 4A

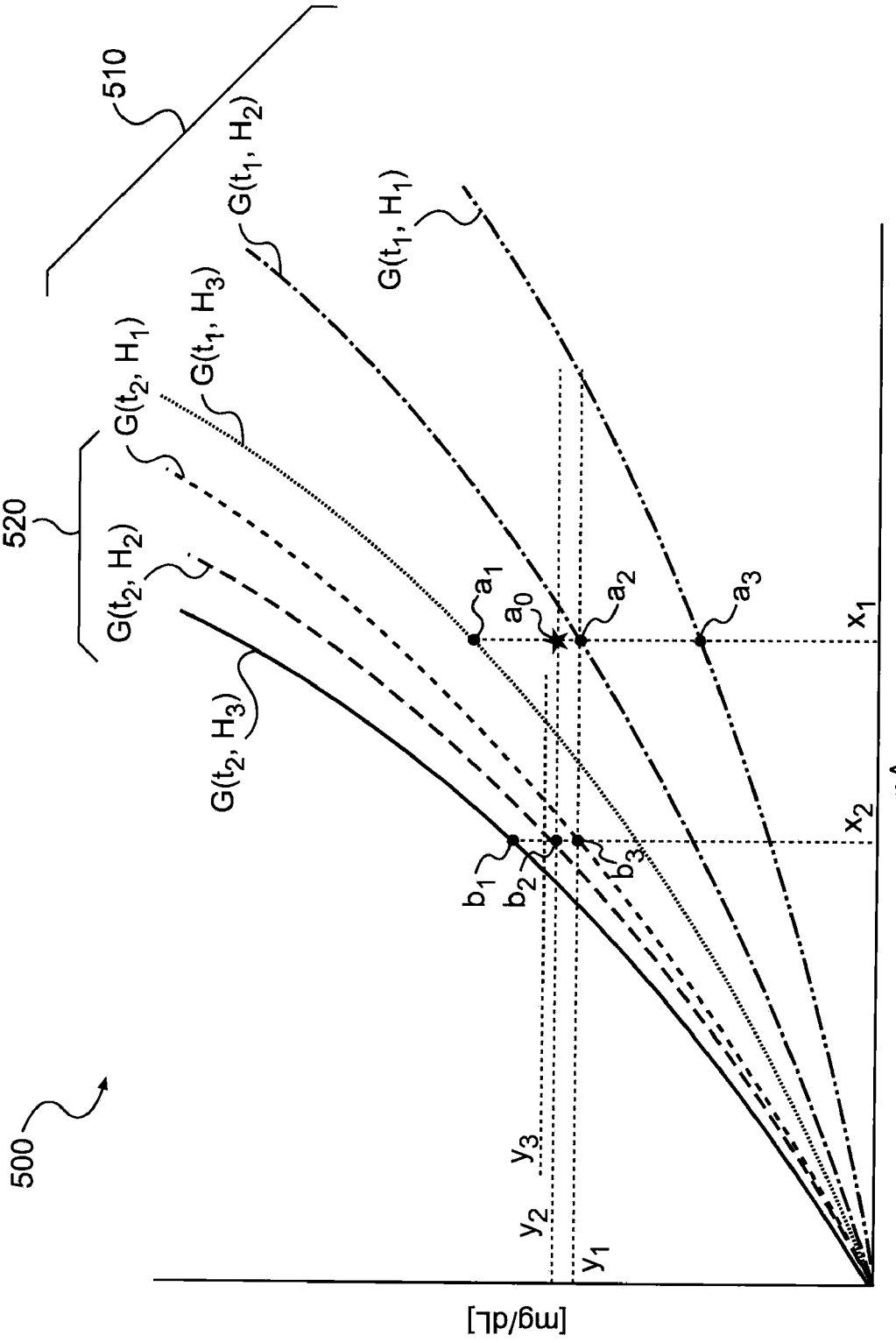

500
510
520
G(t1, H2)
G(t1, H1)
G(t1, H3)
G(t2, H1)
G(t2, H2)
G(t2, H3)
a0
a1
a2
a3
b1
b2
b3
x1
x2
y1
y2
y3
nA
[mg/dL]

FIG. 4B

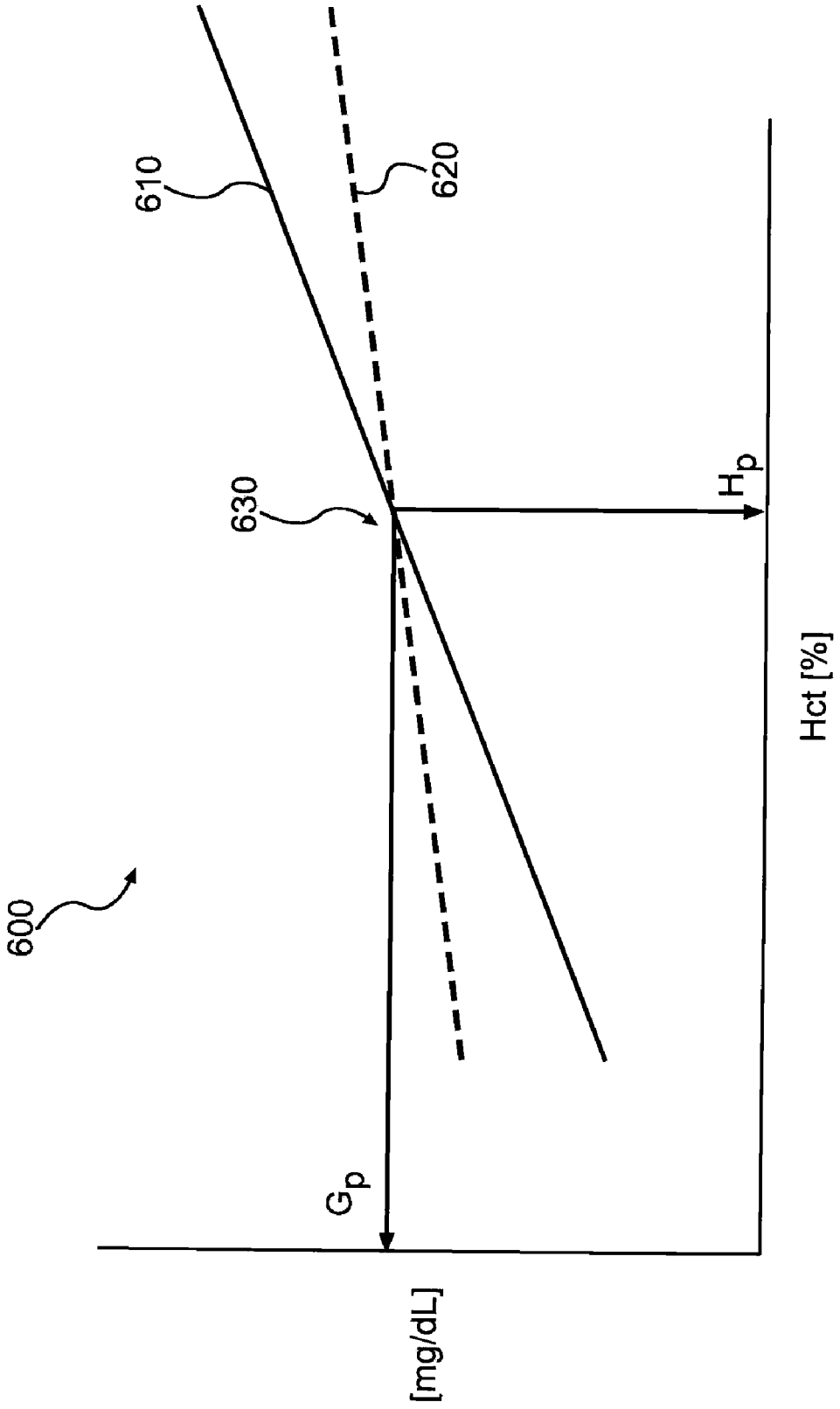


FIG. 4C

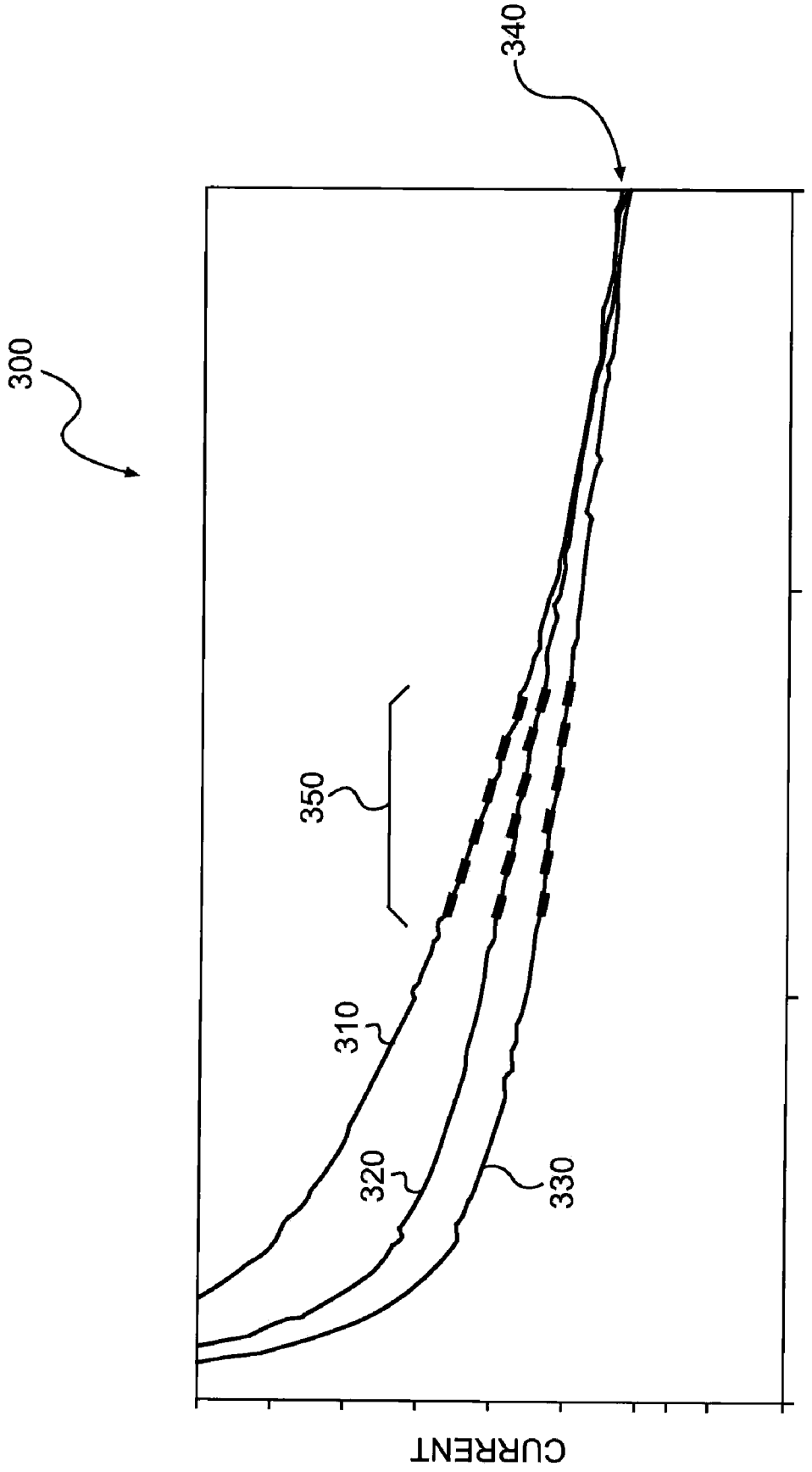


FIG. 5

SYSTEM AND METHODS FOR DETERMINATION OF ANALYTE CONCENTRATION USING TIME RESOLVED AMPEROMETRY

[0001] This application claims priority to U.S. Provisional Patent Application No. 60/952,076, filed Jul. 26, 2007, which is incorporated herein by reference in its entirety.

DESCRIPTION OF THE INVENTION

[0002] 1. Field of the Invention

[0003] The present invention relates to the field of diagnostic testing systems for determining the concentration of an analyte in a solution and, more particularly, to systems and methods for measuring an analyte concentration using interpolate time resolved amperometry.

[0004] 2. Background of the Invention

[0005] The present disclosure relates to a biosensor system for measuring an analyte in a bodily fluid, such as blood. The system includes a process and system for improved determination of analyte concentration over a wide range of analyte concentrations.

[0006] Electrochemical sensors have long been used to detect or measure the presence of substances in fluid samples. Electrochemical sensors include a reagent mixture containing at least an electron transfer agent (also referred to as an "electron mediator") and an analyte specific bio-catalytic protein (e.g. a particular enzyme), and one or more electrodes. Such sensors rely on electron transfer between the electron mediator and the electrode surfaces and function by measuring electrochemical redox reactions. When used in an electrochemical biosensor system or device, the electron transfer reactions are monitored via an electrical signal that correlates to the concentration of the analyte being measured in the fluid sample.

[0007] The use of such electrochemical sensors to detect analytes in bodily fluids, such as blood or blood-derived products, tears, urine, and saliva, has become important, and in some cases, vital to maintain the health of certain individuals. In the health care field, people such as diabetics, for example, must monitor a particular constituent within their bodily fluids. A number of systems are capable of testing a body fluid, such as, blood, urine, or saliva, to conveniently monitor the level of a particular fluid constituent, such as, cholesterol, proteins, and glucose. Patients suffering from diabetes, a disorder of the pancreas where insufficient insulin production prevents the proper digestion of sugar, have a need to carefully monitor their blood glucose levels on a daily basis. Routine testing and controlling blood glucose for people with diabetes can reduce their risk of serious damage to the eyes, nerves, and kidneys.

[0008] A number of systems permit people to conveniently monitor their blood glucose levels. Such systems typically include a test strip where the user applies a blood sample and a meter that "reads" the test strip to determine the glucose level in the blood sample. An exemplary electrochemical biosensor is described in U.S. Pat. No. 6,743,635 ('635 patent) which describes an electrochemical biosensor used to measure glucose level in a blood sample. The electrochemical biosensor system is comprised of a test strip and a meter. The test strip includes a sample chamber, a working electrode, a counter electrode, and fill-detect electrodes. A reagent layer is disposed in the sample chamber. The reagent layer contains an enzyme specific for glucose, such as, glucose oxidase, glucose dehydrogenase, and a mediator, such as, potassium ferricyanide or ruthenium hexamine. When a user applies a blood sample to the sample chamber on the test strip, the reagents react with the glucose in the blood sample and the meter applies a voltage to the electrodes to cause redox reactions. The meter measures the resulting current that flows between the working and counter electrodes and calculates the glucose level based on the current measurements.

[0009] In some instances, electrochemical biosensors may be adversely affected by the presence of certain blood components that may undesirably affect the measurement and lead to inaccuracies in the detected signal. This inaccuracy may result in an inaccurate glucose reading, leaving the patient unaware of a potentially dangerous blood sugar level, for example. As one example, the particular blood hematocrit level (i.e. the percentage of the amount of blood that is occupied by red blood cells) can erroneously affect a resulting analyte concentration measurement. Another example can include various constituents affecting blood viscosity, cell lysis, concentration of charged species, pH, or other factors that may affect determination of an analyte concentration. For example, under certain conditions temperature could affect analyte readings and calculations.

[0010] Variations in a volume of red blood cells within blood can cause variations in glucose readings measured with disposable electrochemical test strips. Typically, a negative bias (i.e., lower calculated analyte concentration) is observed at high hematocrits, while a positive bias (i.e., higher calculated analyte concentration) is observed at low hematocrits. At high hematocrits, for example, the red blood cells may impede the reaction of enzymes and electrochemical mediators, reduce the rate of chemistry dissolution since there less plasma volume to solvate the chemical reactants, and slow diffusion of the mediator. These factors can result in a lower-than-expected glucose reading as less current is produced during the electrochemical process. Conversely, at low hematocrits, less red blood cells may affect the electrochemical reaction than expected, and a higher measured current can result. In addition, the blood sample resistance is also hematocrit dependent, which can affect voltage and/or current measurements.

[0011] Several strategies have been used to reduce or avoid hematocrit based variations on blood glucose. For example, test strips have been designed to incorporate meshes to remove red blood cells from the samples, or have included various compounds or formulations designed to increase the viscosity of red blood cell and attenuate the affect of low hematocrit on concentration determinations. Other test strips have included lysis agents and systems configured to determine hemoglobin concentration in an attempt to correct hematocrit. Further, biosensors have been configured to measure hematocrit by measuring optical variations after irradiating the blood sample with light, or measuring hematocrit based on a function of sample chamber fill time. These methods have the disadvantages of increasing the cost and complexity of test strips and may undesirably increase the time required to determine an accurate glucose measurement.

[0012] In addition, alternating current (AC) impedance methods have also been developed to measure electrochemical signals at frequencies independent of a hematocrit effect. Such methods suffer from the increased cost and complexity of advanced meters required for signal filtering and analysis.

[0013] Accordingly, systems and methods for determining analyte concentration are desired that overcome the drawbacks of current biosensors and improve upon existing electrochemical biosensor technologies.

SUMMARY OF THE INVENTION

[0014] Some embodiments of this invention are directed to methods and systems for determining a concentration of an analyte using one or more sets of calibration data. Embodiments of this invention can use two or more sets of calibration data associated with two or more time-segments. Fluid samples containing similar analyte concentrations but different sample matrix (e.g. different hematocrit values) can produce different calibration data. However, these calibration data were found to converge over time under certain conditions. Generally, fluid samples containing low analyte concentrations can converge faster than fluid samples containing high analyte concentrations. Based on this convergence behavior, an analyte concentration can be more accurately determined by dynamically selecting an appropriate time-segment and a calibration data associated with the selected time-segment.

[0015] One embodiment consistent with the principles of this invention is a method for analyzing an analyte described as follows. The steps include applying a potential excitation to a fluid sample containing an analyte, and measuring a first current during a first time-segment following application of the potential excitation. The method also includes measuring a second current during a second time-segment following application of the potential excitation, and calculating a plurality of first analyte concentrations based on the first measured current and a first set of calibration data associated with the first time-segment. Lastly, the method includes calculating a plurality of second analyte concentrations based on the second measured current and a second set of calibration data associated with the second time-segment.

[0016] Another embodiment of this invention is directed to a system for analyzing an analyte in a fluid sample. The system includes a set of electrodes configured to apply a potential excitation to a fluid sample containing an analyte. The system also includes a processor configured to measure a first current during a first time-segment following application of the potential excitation, and measure a second current during a second time-segment following application of the potential excitation. The processor is further configured to calculate a plurality of first analyte concentrations based on the first measured current and a plurality of first calibration curves associated with the first time-segment and calculate a plurality of second analyte concentrations based on the second measured current and a plurality of second calibration curves associated with the second time-segment.

[0017] Another embodiment of this invention is directed to a computer readable media, wherein the media comprises a plurality of instructions configured to direct a processor to measure a first current during a first time-segment following application of a potential excitation, wherein the potential excitation is applied to a fluid sample containing an analyte, and measure a second current during a second time-segment following application of the potential excitation. The instructions also direct the processor to calculate a plurality of first analyte concentrations based on the first measured current and a first set of calibration data associated with the first time-segment, and calculate a plurality of second analyte concentrations based on the second measured current and a second set of calibration data associated with the second time-segment.

[0018] Additional embodiments consistent with principles of the invention are set forth in the detailed description which follows or may be learned by practice of methods or use of systems or articles of manufacture disclosed herein. It is understood that both the foregoing general description and the following detailed description are exemplary and explanatory only, and are not restrictive of the invention as claimed. Additionally, it is to be understood that other embodiments may be utilized and that electrical, logical, and structural changes may be made without departing form the spirit and scope of the present invention.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate several embodiments of the invention and together with the description, serve to explain the principles of the invention. In the drawings:

[0020] FIG. **1**A illustrates test media associated with an exemplary meter system, according to an exemplary embodiment of the present disclosure.

[0021] FIG. **1**B illustrates a test meter that can be used with test media, according to an exemplary embodiment of the present disclosure.

[0022] FIG. **1**C illustrates another test meter that can be used with test media, according to an exemplary embodiment of the present disclosure.

[0023] FIG. **2**A is a top plan view of a test strip, according to an exemplary embodiment of the present disclosure.

[0024] FIG. **2**B is a cross-sectional view of the test strip of FIG. **2**A, taken along line **2**B-**2**B.

[0025] FIG. **3** depicts flow chart of a method of determining an analyte concentration, according to an exemplary embodiment of the present disclosure.

[0026] FIG. **4**A depicts a plurality of calibration curves on a graph of current versus glucose concentration, according to an exemplary embodiment of the present disclosure.

[0027] FIG. **4**B depicts a plurality of calibration curves on a graph of current versus glucose concentration, according to an exemplary embodiment of the present disclosure.

[0028] FIG. **4**C depicts two line-plots, according to an exemplary embodiment of the present disclosure.

[0029] FIG. **5** depicts a plurality of current decay curves on a graph of current versus time, according to an exemplary embodiment of the present disclosure.

DESCRIPTION OF THE EMBODIMENTS

[0030] Reference will now be made in detail to the present embodiments of the invention, examples of which are illustrated in the accompanying drawings. Wherever possible, the same reference numbers will be used throughout the drawings to refer to the same or like parts.

[0031] In accordance with an exemplary embodiment, a method of determining an analyte concentration is described. Many industries have a commercial need to monitor the concentration of particular analytes in various fluids. The oil refining industry, wineries, and the dairy industry are examples of industries where fluid testing is routine. In the health care field, people such as diabetics, for example, need to routinely monitor analyte levels of their bodily fluids using

biosensors. A number of systems are available that allow people to test a physiological fluid (e.g. blood, urine, or saliva), to conveniently monitor the level of a particular analyte present in the fluid, such as, for example, glucose, cholesterol, ketone bodies, or specific proteins. Such systems can include a meter configured to determine the analyte concentration and/or display representative information to a user. In addition, such metering systems can incorporate disposable test strips configured for single-use testing of a fluid sample.

[0032] While such metering systems have been widely adopted, some are susceptible to inaccurate readings resulting from analyzing fluids of differing properties. For example, blood glucose monitoring using electrochemical techniques can be highly dependent upon hematocrit and/or temperature fluctuations. The present method reduces unwanted influences by measuring one or more current values associated with one or more time-segments. Various mathematical techniques are then used to solve for one or more variables, such as, for example, glucose concentration and hematocrit. The present disclosure provides methods and systems for improved determination of analyte concentration.

[0033] FIG. **1**A illustrates a diagnostic test strip **10**, according to an exemplary embodiment of the present disclosure. Test strip **10** of the present disclosure may be used with a suitable test meter **100**, **108**, as shown in FIGS. **1**B and **1**C, configured to detect, and/or measure the concentration of one or more analytes present in a sample solution applied to test strip **10**. As shown in FIG. **1**A, test strip **10** can be generally planar and elongated in design. However, test strip **10** may be provided in any suitable form including, for example, ribbons, tubes, tabs, discs, or any other suitable form. Furthermore, test strip **10** can be configured for use with a variety of suitable testing modalities, including electrochemical tests, photochemical tests, electro-chemiluminescent tests, and/or any other suitable testing modality.

[0034] Test strip **10** can be in the form of a generally flat strip that extends from a proximal end **12** to a distal end **14**. For purposes of this disclosure, "distal" refers to the portion of test strip **10** further from the fluid source (i.e. closer to the meter) during normal use, and "proximal" refers to the portion closer to the fluid source (e.g. a finger tip with a drop of blood for a glucose test strip) during normal use. In some embodiments, proximal end **12** of test strip **10** may include a sample chamber **52** configured to receive a fluid sample, such as, for example, a blood sample. Sample chamber **52** and test strip **10** of the present specification can be formed using materials and methods described in commonly owned U.S. Pat. No. 6,743,635, which is hereby incorporated by reference in its entirety.

[0035] Test strip **10** can be any convenient size. For example, test strip **10** can measure approximately 35 mm long (i.e., from proximal end **12** to distal end **14**) and approximately 9 mm wide. Proximal end **12** can be narrower than distal end **14** in order to assist the user in locating the opening where the blood sample is to be applied. Further, test meter **100**, **108** can be configured to operate with, and dimensioned to receive, test strip **10**.

[0036] Test meter **100**, **108** may be selected from a variety of suitable test meter types. For example, as shown in FIG. **1**B, test meter **100** includes a vial **102** configured to store one or more test strips **10**. The operative components of test meter **100** may be contained in a meter cap **104**. Meter cap **104** may contain electrical meter components, can be packaged with test meter **100**, and can be configured to close and/or seal vial **102**. Alternatively, test meter **108** can include a monitor unit separated from storage vial, as shown in FIG. **1**C. In some embodiments, meter **100** can include one or more circuits, processors, or other electrical components configured to perform one or more steps of the disclosed method of determining an analyte concentration. Any suitable test meter may be selected to provide a diagnostic test using test strip **10** produced according to the disclosed methods.

Test Strip Configuration

[0037] FIGS. **2**A and **2**B show a test strip **10**, in accordance with an exemplary embodiment of the present disclosure. As shown in FIG. **2**B, test strip **10** can include a generally layered construction. Working upwardly from the bottom layer, test strip **10** can include a base layer **18** extending along the entire length of test strip **10**. Base layer **18** can be formed from an electrically insulating material that has a thickness sufficient to provide structural support to test strip **10**. For example, base layer **18** can be a polyester material about 0.35 mm thick.

[0038] According to the illustrative embodiment, a conductive layer **20** can be disposed on base layer **18**. Conductive layer **20** includes a plurality of electrodes disposed on base layer **18** near proximal end **12**, a plurality of electrical contacts disposed on base layer **18** near distal end **14**, and a plurality of conductive regions electrically connecting the electrodes to the electrical contacts. In the illustrative embodiment depicted in FIG. **2**A, the plurality of electrodes includes a working electrode **22**, a counter electrode **24**, and a pair of fill-detect electrodes **28**, **30**. As described in detail below, the term "working electrode" refers to an electrode at which an electrochemical oxidation and/or reduction reaction occurs, e.g., where an analyte, typically the electron mediator, is oxidized or reduced. "Counter electrode" refers to an electrode paired with working electrode **22**.

[0039] The electrical contacts at distal end **14** can correspondingly include a working electrode contact **32**, a proximal electrode contact **34**, and fill-detect electrode contacts **36**, **38**. The conductive regions can include a working electrode conductive region **40**, electrically connecting working electrode **22** to working electrode contact **32**, a counter electrode conductive region **42**, electrically connecting counter electrode **24** to counter electrode contact **36**, and fill-detect electrode conductive regions **44**, **46** electrically connecting fill-detect electrodes **28**, **30** to fill-detect contacts **36**, **38**. Further, the illustrative embodiment is depicted with conductive layer **20** including an auto-on conductor **48** disposed on base layer **18** near distal end **14**.

[0040] In addition to auto-on conductor **48**, the present disclosure provides test strip **10** that includes electrical contacts near distal end **14** that are resistant to scratching or abrasion. Such test strips can include conductive electrical contacts formed of two or more layers of conductive and/or semi-conductive material. Further, information relating to electrical contacts that are resistant to scratching or abrasion are described in co-owned U.S. patent application Ser. No. 11/458,298 which is incorporated by reference herein in its entirety.

[0041] The next layer of test strip **10** can be a dielectric spacer layer **64** disposed on conductive layer **20**. Dielectric spacer layer **64** can be composed of an electrically insulating material, such as polyester. Dielectric spacer layer **64** can be about 0.100 mm thick and covers portions of working electrode **22**, counter electrode **24**, fill-detect electrodes **28**, **30**, and conductive regions **40**-**46**, but in the illustrative embodi-

ment does not cover electrical contacts **32-38** or auto-on conductor **48**. For example, dielectric spacer layer **64** can cover substantially all of conductive layer **20** thereon, from a line just proximal of contacts **32** and **34** all the way to proximal end **12**, except for sample chamber **52** extending from proximal end **12**. In this way, sample chamber **52** can define an exposed portion **54** of working electrode **22**, an exposed portion **56** of counter electrode **24**, and exposed portions **60**, **62** of fill-detect electrodes **28**, **30**.

[0042] In some embodiments, sample chamber **52** can include a first opening **68** at proximal end **12** of test strip **10**, and a second opening **86** for venting sample chamber **52**. Further, sample chamber **52** may be dimensioned and/or configured to permit, by capillary action, a blood sample to enter through first opening **68** and remain within sample chamber **52**. For example, sample chamber **52** can be dimensioned to receive about 1 micro-liter or less. For example, first sample chamber **52** can have a length (i.e., from proximal end **12** to distal end **70**) of about 0.140 inches, a width of about 0.060 inches, and a height (which can be substantially defined by the thickness of dielectric spacer layer **64**) of about 0.005 inches. Other dimensions could be used, however.

[0043] A cover **72**, having a proximal end **74** and a distal end **76**, can be attached to dielectric spacer layer **64** via an adhesive layer **78**. Cover **72** can be composed of an electrically insulating material, such as polyester, and can have a thickness of about 0.1 mm. Additionally, the cover **72** can be transparent. Adhesive layer **78** can include a polyacrylic or other adhesive and have a thickness of about 0.013 mm. A break **84** in adhesive layer **78** can extend from distal end **70** of first sample chamber **52** to an opening **86**, wherein opening **86** can be configured to vent sample chamber **52** to permit a fluid sample to flow into sample chamber **52**. Alternatively, cover **72** can include a hole (not shown) configured to vent sample chamber **52**. It is also contemplated that various materials, surface coatings (e.g. hydrophilic and/or hydrophobic), or other structure protrusions and/or indentations at proximal end **12** may be used to form a suitable sample reservoir.

[0044] As shown in FIG. **2**B, a reagent layer **90** can be disposed in sample chamber **52**. In some embodiments, reagent layer **90** can include one or more chemical constituents to enable the level of glucose in the blood sample to be determined electrochemically. Reagent layer **90** may include an enzyme specific for glucose, such as glucose oxidase or glucose dehydrogenase, and a mediator, such as potassium ferricyanide or ruthenium hexamine. In other embodiments, other reagents and/or other mediators can be used to facilitate detection of glucose and other analytes contained in blood or other physiological fluids. In addition, reagent layer **90** may include other components, buffering materials (e.g., potassium phosphate), polymeric binders (e.g., hydroxypropylmethyl-cellulose, sodium alginate, microcrystalline cellulose, polyethylene oxide, hydroxyethylcellulose, and/or polyvinyl alcohol), and surfactants (e.g., Triton X-100 or Surfynol 485). For example, an exemplary formulation contains 50-250 mM potassium phosphate at pH 6.75-7.50, 150-190 mM ruthenium hexamine, 3500-5000 U/mL PQQ-dependent glucose dehydrogenase, 0.5-2.0% polyethylene oxide, 0.025-0.20% NATROSOL 250M (hydroxyethylcellulose), 0.675-2.5% Avicel (microcrystalline cellulose), 0.05-0.25% TRITON-X (surfactant) and 2.5-5.0% trehalose.

[0045] In some embodiments, various constituents may be added to reagent layer **90** to at least partially reduce unwanted bias of an analyte measurement. For example, various polymers, molecules, and/or compounds may be added to reagent layer **90** to reduce cell migration and hence may increase the accuracy of a measurement based on an electrochemical reaction. Also, one or more conductive components may be coated with a surface layer (not shown) to at least partially restrict cell migration onto the one or more conductive components. These and other techniques known in the art may be used to reduce unwanted signal bias.

[0046] Although FIGS. **2**A and **2**B illustrate an illustrative embodiment of test strip **10**, other configurations, chemical compositions and electrode arrangements could be used. For example, fill-detect electrode **30** can function with working electrode **22** to perform a fill-detect feature, as previously described. Other configurations of electrodes on test strip **10** are possible, such as, for example, a single fill-detect electrode, multiple fill-detect electrodes aligned in the y-axis (as opposed to the x-axis as shown in FIG. **2**A), and/or multiple working electrodes.

[0047] In some embodiments, working electrode **22** and counter electrode **24** can be spaced further apart. For example, this electrode pair may be spaced at a distance of 500 μm to 1000 μm such that a two-pulse measurement obtained from the electrode pair can be optimized for correction of the influence of hematocrit, temperature, or other factors.

Test Strip and Meter Operation

[0048] As previously described, test strip **10** can be configured for placement within meter **100**, or similar device, configured to determine the concentration of an analyte contained in a solution in contact with test strip **10**. Meter **100** can include electrical components, circuitry, and/or processors configured to perform various operations to determine analyte concentration based on electrochemical techniques. For example, the metering system, such as meter **100** and associated test strip **10**, may be configured to determine the glucose concentration of a blood sample. In some embodiments, systems and methods of the present disclosure permit determination of blood glucose levels generally unaffected by blood constituents, hematocrit levels, and temperature.

[0049] In operation, the battery-powered meter **100** may stay in a low-power sleep mode when not in use. When test strip **10** is inserted into meter **100**, one or more electrical contacts at distal end **14** of test strip **10** could form electrical connections with one or more corresponding electrical contacts in meter **100**. These electrical contacts may bridge electrical contacts in meter **100**, causing a current to flow through a portion of the electrical contacts. Such a current flow can cause meter **100** to "wake-up" and enter an active mode.

[0050] Meter **100** can read encoded information provided by the electrical contacts at distal end **14**. Specifically, the electrical contacts can be configured to store information, as described in U.S. patent application Ser. No. 11/458,298. In particular, an individual test strip **10** can include an embedded code containing data associated with a lot of test strips, or data particular to that individual strip. The embedded information can represent data readable by meter **100**. For example, a microprocessor associated with meter **100** could access and utilize a specific set of stored calibration data specific to an individual test strip **10** and/or a manufactured lot test strips **10**. Individual test strips **10** may be calibrated using standard solutions, and associated calibration data could be applied to test strips **10** of the same or similar lots of manufactured test strips **10**.

[0051] In some embodiments, "lot specific" calibration information can be encoded on a code chip accompanying a vial of strips, or coded directly onto one or more test strips **10** manufactured in a common lot of test strips. Lot calibration can include any suitable process for calibrating test strip **10** and/or meter **100**. For example, calibration can include applying at the factory a standard solution to one or more test strips **10** from a manufacturing lot, wherein the standard solution can be a solution of known glucose concentration, hematocrit, temperature, or any other appropriate parameter associated with the solution. Following application of the standard solution, one or more pulses can be applied to test strip **10**, as described below. Calibration data may then be determined by correlating various measurements to be determined by the meter **100** during use by the patient with one or more parameters associated with the standard solution. For example, a measured current may be correlated with a glucose concentration, or a voltage correlated with hematocrit. Such calibration data, that can vary from lot to lot with the performance of the test strips, may then be stored on test strip **10** and/or meter **100**, and used to determine analyte concentration of an analyte sample, as described below.

[0052] Test strip **10** can be tested at any suitable stage during a manufacturing process. Also, a test card (not shown) could be tested during any suitable stage of a manufacturing process, as described in co-owned U.S. patent application Ser. No. 11/504,710 which is incorporated by reference herein in its entirety. Such testing of test strip **10** and/or the test card can permit determination and/or encoding of calibration data at any suitable stage during a manufacturing process. For example, calibration data associated with methods of the present disclosure can be encoded during the manufacturing process.

[0053] In operation meter **100** can be configured to identify a particular test to be performed or provide a confirmation of proper operating status. Also, calibration data pertaining to the strip lot, for either the analyte test or other suitable test, could be otherwise encoded or represented, as described above. For example, meter **100** can identify the inserted strip as either test strip **10** or a check strip (not shown) based on the particular code information.

[0054] If meter **100** detects test strip **10**, it may perform a test strip sequence. The test strip sequence may confirm proper functioning of one or more components of test strip **10**. For example, meter **100** could validate the function of working electrode **22**, counter electrode **24**, and, if included, the fill-detect electrodes, by confirming that there are no low-impedance paths between any of these electrodes. If the electrodes are valid, meter **100** could provide an indication to the user that a sample may be applied to test strip **10**.

[0055] If meter **100** detects a check strip, it may perform a check strip sequence. The system may also include a check strip configured to confirm that the instrument is electrically calibrated and functioning properly. The user may insert the check strip into meter **100**. Meter **100** may then receive a signal from the check strip to determine if meter **100** is operating within an acceptable range.

[0056] In other embodiments, test strip **10** and/or meter **100** may be configured to perform a calibration process based on a standard solution, also termed a control solution. The control solution may be used to periodically test one or more functions of meter **100**. For example, a control solution may include a solution of known electrical properties, and an electrical measurement of the solution may be performed by meter **100**. Upon detecting the presence of a control solution, meter **100** can perform an operational check of test strip **10** functionality to verify measurement integrity. For example, the read-out of meter **100** may be compared to a known glucose value of the solution to confirm that meter **100** is functioning to an appropriate accuracy. In addition, any data associated with a measurement of a control solution may be processed, stored or displayed using meter **100** differently to any data associated with a glucose measurement. Such different treatment of data associated with the control solution may permit meter **100**, or user, to distinguish a glucose measurement, or may permit exclusion of any control measurements when conducting any mathematical analysis of glucose measurements.

Analyte Concentration Determination

[0057] Meter **100** can be configured to apply a signal to test strip **10** to determine a concentration of an analyte contained in a solution contacting test strip **10**. In some cases, the signal can be applied following a determination that sample chamber **52** of test strip **10** contains a sufficient quantity of fluid sample. To determine the presence of sufficient fluid, meter **100** can apply a detect voltage between any suitably configured electrodes, such as, for example, fill-detect electrodes. The detect voltage can detect the presence of sufficient quantity of fluid (e.g. blood) within sample chamber **52** by detecting a current flow between the fill-detect electrodes. In addition, to determine that the fluid sample has traversed reagent layer **90** and mixed with the chemical constituents in reagent layer **90**, meter **100** may apply a fill-detect voltage to the one or more fill-detect electrodes and measure any resulting current. If the resulting current reaches a sufficient level within a predetermined period of time, meter **100** can indicate to a user that adequate sample is present. Meter **100** can also be programmed to wait for a predetermined period of time after initially detecting the blood sample to allow the blood sample to react with reagent layer **90**. Alternatively, meter **100** can be configured to immediately begin taking readings in sequence.

[0058] Meter **100** can be configured to apply various signals to test strip **10**. For example, an exemplary fluid measurement sequence could include amperometry, wherein an assay voltage is applied between working and counter electrodes **22**, **24** of test strip **10**. The magnitude of the assay voltage can include any suitable voltage, and could be approximately equal to the redox potential of constituents of reagent layer **90**. Following application of an assay voltage, also termed potential excitation, meter **100** could be configured to measure one or more current values between working and counter electrodes **22**, **24**. Such a measured current can be mathematically related to the concentration of analyte in the fluid sample, such as, for example, glucose concentration in a blood sample.

[0059] For example, one or more constituents of reagent layer **90** may react with glucose present in a blood sample such that glucose concentration may be determined using electrochemical techniques. Suitable enzymes of reagent layer **90** (e.g. glucose oxidase or glucose dehydrogenase) could react with blood glucose. Glucose could be oxidized to form gluconic acid, which may in turn reduce a suitable mediator, such as, for example, potassium ferricyanide or ruthenium hexamine. Voltage applied to working electrode **22** may oxidize the ferrocyanide to form ferricyanide, and generating a current proportional to the glucose concentration of the blood sample.

[0060] As previously discussed, measurements of analyte concentration using a biosensor may be inaccurate due to unwanted effects of various blood components. For example, the hematocrit level (i.e. the percentage of blood occupied by red blood cells) of blood can erroneously affect a measurement of analyte concentration. In order to reduce inaccuracies associated with a determination of analyte concentration, it may be advantageous to use multiple sets of calibration data. Such calibration data can reduce errors due to hematocrit or other factors that may adversely affect analyte concentration determination.

[0061] Exemplary embodiments disclosed herein use multiple sets of calibration data to permit more precise determinations of analyte concentration over a wider range of analyte concentrations than can be achieved using traditional techniques. The influence of hematocrit, temperature, blood constituents, and other factors that may adversely affect determination of blood glucose concentration can be reduced using techniques that employ multiple calibration data. The precision and/or accuracy of monitoring blood glucose levels using biosensors may be improved using the method or systems of the present disclosure. Different sets of calibration data can be associated with different ranges of analyte concentrations, currents, voltages, or sampling times. In particular, a set of calibration data can include one or more of a calibration curve, a lookup table, a data array, or a mathematical equation.

[0062] One exemplary embodiment is directed to a method that includes calculating an analyte concentration based on two measured currents and two sets of calibration curves. Each set of calibration curves can include a plurality of calibration curves that may be associated with a time-segment, as explained in detail below. For example, at a time during the first time-segment, a first analyte concentration can be calculated using two or more calibration curves associated with the first time-segment. If the calculated first analyte concentration is within a pre-determined concentration range associated with the first time-segment, current measurement can stop, analyte concentration can be determined and the result displayed. If the calculated analyte concentration is outside the pre-determined range, the current measurement can continue to a time during a second time-segment. At that time, a second analyte concentration can be calculated using parameters associated with a second time-segment. If the second analyte concentration is about equal to the first analyte concentration, current measurement can stop, a final analyte concentration can be determined and the result displayed. Otherwise, the method can continue to determine a final analyte concentration based on a plurality of first analyte concentrations and a plurality of second analyte concentrations. As explained in detail below, various mathematical algorithms can be used to determine a final analyte concentration. For example, a first plurality of analyte concentrations may provide an initial glucose concentration and a second plurality of analyte concentrations may provide a different glucose concentration based on a presumed hematocrit level. The difference in calculated glucose concentration could be used, along with two or more calibration curves, to refine the calculation using interpolative and/or extrapolative techniques. In some embodiments, the calculation may be refined using iterative techniques to converge to a final analyte concentration. Such methods permit use of multiple sets of calibration data associated with time, current, voltage, analyte concentrations, or other parameters, to improve the precious or accuracy of electrochemical techniques used to determine an analyte concentration.

[0063] In some embodiments, analyte concentration may be determined by first applying a potential excitation to a fluid sample in contact with test strip **10**. An applied potential can include any suitable voltage signal, such as, for example, signals with constant, variable, or pulse-train voltages. Meter **100** may then measure a current value associated with the potential excitation, as previously described.

[0064] In some embodiments, a current may be measured at one or more time-points. A time-point can include a discrete time following application of a potential excitation. For example, a first current can be measured at a first time-point of 0.1 seconds, and a second current can be measured at a second time-point 0.2 seconds. The first time-point can occur 0.1 seconds following the application of the potential, and the second time-point can occur 0.2 seconds following the application of the potential. In some cases, a plurality of current values can be measured at any number of time-points following the application of a potential excitation.

[0065] Time-points can include irregular or regular time periods, and can include any suitable sampling rate. For example, the sampling rate could be 10 Hz, and in other embodiments the sampling rate could be 0.1, 1, 100, or 1000 Hz. In other embodiments, time-points could be sampled at non-constant sampling rates. For example, time-points could be sampled at increasing, decreasing, or non-uniform sampling rates.

[0066] In some embodiments, current values can be measured over a plurality of time-segments, wherein a time-segment can include a series of time-points or span a specific time period. For example, a first time-segment could include any number of time-points up to about six seconds, and a second time-segment could include any number of time-points following about six seconds. In other embodiments, a first time-segment could include a time period less than about six seconds, and a second time-segment could include a time period greater than about six seconds. In yet other embodiments, a first time-segment could be less than about twenty seconds, and a second time-segment could be any time period following the first time-period.

[0067] The time period of any time-segment could vary depending upon various factors, including configuration of test strip **10**, meter **100**, bodily sample analyzed, or reagents of test strip **10**. For example, a first time-segment could span a time from about zero to about two to ten seconds following application of a potential excitation. Further, in some embodiments the end of a time-segment may coincide with the beginning of the next time-segment, while in other embodiments, a prior and later time segment may not coincide. For example, a first time-segment may span the time period from about zero to ten seconds and a second time-segment may span the time period from about two to fourteen seconds.

[0068] Current values measured in the first time-segment could include one or more currents measured at 0.1, 0.2, 1.6, 2.0, 3.4, or 5.99 seconds, or at any other suitable times. Current values measured in the second time-segment could include one or more currents measured at 6.2, 6.63, 7.0, or 9.97 seconds, or at any other suitable times. These one or more current values measured within different time-segments can then be used to determine analyte concentration based on calibration information associated with the different time-segments. For example, a low analyte concentration can be

determined during an early time-segment, such as a first time-segment, based on calibration data associated with the low analyte concentration. Conversely, a high analyte concentration can be determined during a later time-segment, such as a second time-segment, based on calibration data associated with the higher analyte concentration.

[0069] In some embodiments, calibration data can be described by a plurality of calibration curves, wherein each time-segment can be associated with a plurality of calibration curves. For example, a first time-segment can be associated with a plurality of first calibration curves. Each first calibration curve can be associated with a first time-segment and various other variables, such as, for example, hematocrit. Other calibration curves may be associated with temperature, sample, test strip **10**, or meter **100**.

[0070] As explained in detail below, a first set of calibration data can include a plurality of calibration curves representing data associated with blood samples of different levels of hematocrit. Specifically, one curve may be associated with a low level of hematocrit, another curve with a medium level of hematocrit, and a third curve with a high level of hematocrit. In some instances only two calibration curves may be used. These plurality of calibration curves may be associated with a first time-segment, while another set of calibration data may be associated with a second time-segment.

[0071] In some embodiments, the plurality of calibration curves associated with a first time-segment can be used to determine a plurality of first analyte concentrations. For example, a plurality of calibration curves representing different levels of hematocrit may be used to determine a plurality of analyte concentrations associated with these different levels of hematocrit. Further, a plurality of calibration curves associated with a second time-segment can be used to determine a plurality of second analyte concentrations. In some embodiments, two, three, four, or more, calibration curves can be used to determine analyte concentration, wherein each calibration curve can be associated with a corresponding time-segment. Two, three, four, or more, time-segments may be used by the following method.

[0072] FIG. **3** depicts a method **200** for determining analyte concentration, according to an exemplary embodiment of the present disclosure. Initially, a potential excitation can be applied to a fluid sample containing an analyte (Step **210**). For example, the fluid sample may be contained within test strip **10**. As described above, meter **100** can be configured to supply the potential excitation across electrodes **22**, **24** within test strip **10**. Meter **100** could also be configured to measure a current during one or more time-segments following application of the potential excitation. Meter **100** may then determine an analyte concentration, such as, for example, a blood glucose level, based on multiple sets of calibration data associated with the time-segments. Other test strips, meters, or analyte monitoring systems could also be configured to incorporate method **200**.

[0073] Following application of a potential excitation, a first current may be measured, wherein the first current can be measured during a first time-segment (Step **220**). As described above, a first time-segment can include a time period of less than about two to ten seconds.

[0074] Next, the first current may be compared with a first target-range (Step **230**). Specifically, the first measured current can be compared with a first target-range of current values associated with a first range of analyte concentrations. If the measured current is within the first target-range, then the analyte concentration of the fluid sample should also be within the corresponding first range of analyte concentrations. For example, a first range of glucose concentrations may be less than about 50, 100, or 150 mg/dL. Each different range may also be associated with a corresponding target-range of current values. If the measured current value falls within any of these target-ranges, then a glucose concentration within a first range of 50, 100, or 150 mg/dL can be presumed. Specifically, a final analyte concentration may be determined based on the data associated with the first time-segment (Step **240**). This data may include the first measured current value obtained by Step **220**, and various other data associated with the first time-segment. Various methods for determining analyte concentration are known in the art. In some embodiments, these calculations can use data associated with the first calibration data.

[0075] To illustrate by way of an example, the first target-range may include a maximum glucose concentration of 50 mg/dL. Generally, lower analyte concentrations are associated with earlier time-segments, and higher analyte concentrations are associated with later time-segments. If the first measured current is about equal to or less than 50 mg/dL, method **200** may determine an analyte concentration based on the data associated with the first time-segment. Such a determination may include the use of one or more sets of calibration data associated with the first time-segment, as explained below. Various target-ranges, calibration data, time-segments, and other parameters can be determined empirically and can vary depending on test strip and meter design, manufacturing conditions, fluid type, operating conditions, etc.

[0076] In some embodiments, a suitable range of analyte concentrations may be encompassed by two or more target-ranges. For example, a first target-range could be associated with a glucose concentration of about 10 to about 50 mg/dL, and a second target-range could be associated with a glucose concentration above about 50 mg/dL. The limits of various target-ranges may overlap, and a third, fourth, or any other number of target-ranges could also be used.

[0077] Various calibration data may be associated with a time-segment, whereby calibration data could include any suitable information associated with a time-segment. For example, a calibration curve may represent calibration data corresponding to an analyte concentration between a lower and an upper analyte concentration. Such an association can permit use of concentration-dependent calibration information. For example, one set of calibration information may exist for low analyte concentrations while another set of calibration information may exist for high analyte concentrations. In some embodiments, two, three, four or more different sets of calibration data could be used to determine analyte concentration, whereby the different sets of calibration data each correspond to different ranges of analyte concentrations.

[0078] Each set of calibration data could include empirical data associated with a range of analyte concentrations, termed "calibration-range." In some embodiments, the calibration-range may be different to the corresponding target-range. For example, a first target-range may be associated with a glucose concentration of about 10 to 50 mg/dL, while a first calibration-range may be associated with a glucose concentration of about 0 to 75 mg/dL. A calibration-range larger than the corresponding target-range can permit greater accuracy in determining the corresponding calibration data as a greater range of empirical data could be used to determine the calibration data. Also, as explained in detail below, adjacent

calibration-ranges can overlap and provide additional data for determining a set of calibration data.

[0079] In some embodiments, two calibration-ranges can be used to determine two sets of calibration data. For example, a first calibration-range can be associated with a glucose concentration of about 0 to about 75 mg/dL, and a second calibration-range can be associated with a glucose concentration of above about 50 mg/dL. In some embodiments, the second calibration-range can be associated with a glucose concentration of about 30 mg/dL to about 240 mg/dL, and a third calibration-range can be associated with a glucose concentration of about 75 to about 600 mg/dL. In yet other embodiments, a fourth calibration-range could be used. For example, a third time-segment could be triggered at about nine seconds, a fourth time-segment at about fourteen seconds, a third target-range could be associated with a glucose concentration of about 350 mg/dL, and a fourth target-range with a glucose concentration of about 600 mg/dL. Also, each particular set of calibration data can be associated with a corresponding calibration-range such that a first set of calibration data is associated with a first calibration-range, a second set of calibration data is associated with a second calibration-range, and so forth.

[0080] For example, FIG. **4**A depicts a chart **400** representing two sets of calibration data used for determining a glucose concentration. A plurality of first calibration curves **410** can be associated with a first time-segment (t_1). As illustrated, three calibration curves are shown for t_1, although two, four, five, or more curves could be determined or used. First set of calibration curves **410** can be associated with t_1, a first measured current x_1, or any other variable associated with a first time-segment. In some embodiments, the first set of calibration curves can be determined using a first calibration-range of glucose concentrations, such as, for example, 0 to 75 mg/dL.

[0081] A plurality of second calibration curves **420** can be associated with a second time-segment. As previously described for first set of calibration curves **410**, second set of calibration curves **420** can include two, four, five, or more curves. As shown, second set of calibration curves **420** is associated with second time-segment t_2, and second measured current x_2, although other variables could be used. In some embodiments, second set of calibration curves **420** can be determined using a second calibration-range of glucose concentrations, such as, for example, above about 50 mg/dL. Although not shown in FIG. **4**A, a third, fourth, or other sets of calibration curves could also be determined and/or used in conjunction with method **200**.

[0082] FIG. **4**A shows individual calibration curves with generally curved and different slopes. In other embodiments, such curves may be generally linear, and may or may not have different slopes. Also, these various calibration curves could also be represented in any suitable data format. Such calibration data could include any suitable representation of calibration information, such as, for example, slopes, relationships, charts, tables, equations, algorithms, or data formats. Various equations could include quadratic, polynomial, data-fitted, or other mathematical descriptions. Calibration data could include strip, lot, or meter specific information, and may account for hematocrit, temperature, pH, or other variations in testing conditions, analyte type, or physiological sample. Such calibration data may be encoded on strip **10** or within meter **100**.

[0083] An event triggering Step **230** could include any suitable event. For example, a set period of time could elapse after applying the excitation potential in Step **210**. Or, once the end of a first time-segment is reached, such as four seconds, Step **230** could be triggered. In other embodiments, a current reading could trigger the event. For example, Step **230** could be triggered if a measured current drops below a predefined level, such as, 3 mA. Certain values, or value ranges, of voltage, impedance, or other parameters associated with various electrochemical techniques could also be used as a triggering event.

[0084] As shown in method **200**, if the first measured current is not within the first target-range, method **200** may then continue to measure a second current during a second time-segment (Step **250**). Specifically, one or more current measurements can occur at a time following that of the first current measurement. For example, one or more additional current measurements could occur in a second time-segment, such as, about two seconds to ten seconds following excitation application in Step **210**. Step **250** could occur as described above for Step **220**, measurement of the first current during a first time-segment.

[0085] Following Step **250**, data associated with the first and second time-segments can be compared. Such data can include analyte concentration, current, voltage, or any other suitable information. The comparison of first and second time-segment data can include determining if such data are about equal (Step **260**). Method **200** may require such data be equal, or about equal, whereby the difference can be within an acceptable range, such as, for example, 10%, 5%, or 2% variation.

[0086] If the first and second time-segment data are about equal, the final analyte concentration can be determined based on the measured data (Step **270**). This data could include the first or second time-segment data, or some combination. Such a determination could be similar to the determination described above for Step **240**. By way of example, FIG. **4**A shows an exemplary embodiment whereby the first and second-segment data are about equal.

[0087] FIG. **4**A shows two sets of calibration data on chart **400**, plotted as a series of curves on the axes of analyte concentration (mg/dL) axis and current (nA). First plurality of calibration curves **410** as shown includes three curves $G(t_1, H_1)$, $G(t_1, H_2)$, and $G(t_1, H_3)$. In other embodiments, calibration curves **410** could include two, four, or more curves. Alternatively, these or other calibration data could be represented by a table, graph, or equation, and may include empirical and/or modeled data.

[0088] As shown, each calibration curve **410** represents calibration data associated with a first time t_1, whereby t_1 is a time point within the first time-segment. For example, t_1 could be 2, 4, or 6 seconds following application of a potential. Calibration curves **410** can also represent calibration data associated with one or more variables, such as, for example, hematocrit or temperature. As shown, each calibration curve **410** represents calibration data associated with three different levels of hematocrit, H_1, H_2, H_3. For example, H_1 could represent a low hematocrit level, H_2 could represent a physiological hematocrit level, and H_3 could represent a high hematocrit level. Each calibration curve could also include data associated with additional or other variables as required. Further, different calibration curves may be required for different test strips **10**, or meters **100**.

[0089] Chart **400** also shows second plurality of calibration curves **420** as including three curves $G(t_2, H_1)$, $G(t_2, H_2)$, and $G(t_2, H_3)$. As noted above, in other embodiments calibration curves **420** could include two, four, or more curves. As shown, each calibration curve **420** represents calibration data associated with a second time t_2, whereby t_2 is a time point within the second time-segment. For example, t_2 could be 6, 8, 10 or 12 seconds following application of a potential. As described previously, each calibration curve **420** represents calibration data associated with three different levels of hematocrit, H_1, H_2, H_3, although data associated with other variables are also contemplated.

[0090] As outlined above, a first current x_1 can be measured during a first time-segment, as described in Step **220**. Initially, method **200** may assume the fluid sample has a physiological hematocrit level, i.e., H_2. Referring to FIG. **4**A, a first current x_1, measured at time t_1, and assuming H_2 hematocrit level, results in an analyte concentration of y_1. If required, a second current x_2 can be measured during a second time-segment, as described in Step **250**.

[0091] Referring to FIG. **4**A, a second current x_2, measured at time t_2, and assuming H_2 hematocrit level, results in an analyte concentration of y_2. As shown in FIG. **4**A, both y_1 and y_2 are about equal. Such a result may then indicate that a final analyte concentration may be determined based on the measured data, as in Step **270**. A different calculation may be required if the first and second time-segment data are not sufficiently equal or the difference between the data is not within an acceptable range.

[0092] Returning to FIG. **3**, following comparison of first and second time-segment data in Step **260**, and determination that the data are not about equal, method **200** can then calculate first and second analyte concentrations (Step **280**). Various methods for determining analyte concentration are known in the art. In some embodiments, these calculations can use data associated with the first and second sets of calibration data. If the first and second analyte concentrations are about equal, a determination of a final analyte concentration can be made as described above for Step **270** and as illustrated by FIG. **4**A. If such analyte concentrations are not equal, or within a suitable range, then both sets of calibration data may be required to accurately determine a final analyte concentration, as shown in FIG. **4**B.

[0093] FIG. **4**B illustrates an exemplary embodiment similar to FIG. **4**A, showing a chart **500** that includes a first plurality of calibration curves **510** and a second plurality of calibration curves **520**. First current x_1 may include a plurality of analyte concentrations associated with first plurality of calibration curves **510**. Specifically, first current x_1 may include analyte concentrations a_1, a_2, and a_3, associated with calibration curves $G(t_1, H_3)$, $G(t_1, H_2)$, and $G(t_1, H_1)$ respectively. That is, at first current x_1, using calibration curve $G(t_1, H_3)$ results in analyte concentration value a_1, while using calibration curve $G(t_1, H_1)$ results in analyte concentration value a_3. Similarly, second current x_2 may include analyte concentrations b_1, b_2, and b_3, associated with calibration curves $G(t_2, H_3)$, $G(t_2, H_2)$, and $G(t_2, H_1)$ respectively. As shown in FIG. **4**B, three calibration curves are used, although two, four, five, or more calibration curves could also be used.

[0094] Method **200** may be used with any calibration data displaying a general convergence property. For example, here data associated with a first time-segment (data associated with x_1) displays convergence at a second time-segment (data associated with x_2). Specifically, (b_1-b_3) the difference between the upper and lower bounds of calibration data associated with x_2, is less than (a_1-a_3), the upper and lower bounds of calibration data associated with x_1. An iterative method, based on the various analyte concentration values associated with different calibration data, can be used to determine a final analyte concentration based on this convergence property, i.e., $(b_1-b_3)<(a_1-a_3)$.

[0095] One method of using the property of convergence will be described by way of example, although other convergence-based methods are also contemplated. Initially, an average of a set of calibrated data (e.g., a median calibration curve), could be assumed. For example, as shown in FIG. **4**B, an average hematocrit value (H_2) could be initially assumed and used to calculate an initial analyte concentration. At a first current x_1, such an initial analyte concentration is represented by a_2. As explained above, if the second current x_2 results in an analyte concentration of b_2, whereby a_2 is about equal to b_2, then a final analyte concentration can be determined based on either x_1 or x_2 data. However, a_2 and b_2 may not be sufficiently converged whereby the difference between a_2 and b_2 is beyond a desired degree of accuracy, such as, for example, 5%.

[0096] If the difference between the initial calibration data associated with first and second time-segments is too large, then various algorithmic techniques can be used to optimize the determination of a final analyte concentration (Step **290**). For example, assume a first estimate of analyte concentration is b_2, and (a_2-b_2) is outside an acceptable value. As shown in FIG. **4**B, a revised hematocrit value may be calculated based on a_0, the analyte concentration corresponding to b_2 but associated with first current x_1. The analyte concentration associated with first current x_1 may be modified by interpolating between a_1, a_2, or a_3. As shown in FIG. **4**B, a_0 is between a_1 and a_2. A revised hematocrit value (HCT) could be determined based on the following equation:

$$\frac{(HCT - H_2)}{(H_1 - H_2)} = \frac{(a_0 - a_2)}{(a_1 - a_2)}$$

The equation could be solved for HCT as the other variables are all known.

[0097] Following determination of the revised hematocrit value based on the calibration data associated with first current x_1, the analyte concentration y_2 could then be revised. For example, the revised value y_3 could be determined based on the following equation:

$$\frac{(y_3 - y_2)}{(b_1 - b_2)} = \frac{(a_0 - a_2)}{(a_1 - a_2)}$$

The equation could be solved for y_3 as the other variables are all known. Further, in some embodiments this process could be repeated as necessary to revise one or both of the values of analyte concentration and hematocrit, or any other calibration variable.

[0098] Various algorithms could be used to solve for one or more variables associated with calibration data. For example, the techniques described above could be used in combination with iterative methods to refine a calculation to within a desired accuracy range. Other optimization techniques are also known in the art, such as, for example, extrapolation or

interpolation using linear or non-linear methods. Extrapolation methods could be used to determine appropriate calibration data beyond a given data range. Interpolative methods may cap calibration data within upper or lower values, or naturally extend (extrapolate) data depending upon variance or bias statistics associated with actual data. For example, as explained above, the analyte concentration may be modified by extrapolating beyond a_1, a_2, or a_3.

[0099] The method described above can use two or more sets of calibration data, whereby each set of calibration data can be associated with a different time-segment, to solve for two or more unknown variables. A set of calibration data can include a lookup table, array, mathematical equation, or any other suitable data structure configured to represent calibration data, and various multiple types of calibration data could be used with method **200**. In particular, method **200** can use at least two sets of calibration curves, wherein each plurality of calibration curves can be associated with a different time-segment. For example, method **200** could use three sets of calibration data associated with any three suitably defined time-segments, such as, about four, seven, and ten seconds. Each time-segment may include specifically derived calibration data associated with that particular time-segment.

[0100] Method **200** can be used to solve for two unknown variables, such as, for example, hematocrit and analyte concentration as outline above. In other embodiments, three or more different variables could also be solved. For example, a third variable, such as, temperature, may also be included in a set of calibration data. In some embodiments, at low hematocrit levels an analyte concentration may be relatively less temperature dependent than high hematocrit levels which may be relatively more temperature dependent. Additional calibration data and/or time-segments may be used to solve for a temperature variable using the methods described herein.

[0101] Another mathematical method that may be employed with method **200** uses two or more line-plots generated from data associated with two or more time-segments. As described previously, multiple calibration curves may be generated for multiple time-segments, as shown in FIG. **4**A. Then, data associated with each time-segment may be determined based on one or more measured current values. As shown in FIG. **4**B, current value x_1 may include the associated data a_1, a_2, and a_3, while current value x_2 may include the associated data b_1, b_2, and b_3. These two sets of associated data may then be plotted to form two line-plots, as shown in FIG. **4**C.

[0102] FIG. **4**C illustrates an exemplary embodiment showing a chart **600**, that includes a first line-plot **610** and a second line-plot **620**. First line-plot **610** may include a_1, a_2, a_3, or other data associated with x_1, while second line-plot **620** may include b_1, b_2, b_3, or other data associated with x_2. The resulting line-plots may be plotted with respect to two unknown variables, such as, for example, glucose concentration (mg/dL) and hematocrit (%), as shown in FIG. **4**C. These resulting line-plots may be generally linear, curved, or irregular in form, and generally intersect about a point **630**. Point **630** may be generally defined if the two line-plots are irregular, or if the line-plots show general intersection about a limited range of values. Consequently, point **630** may encompass a limited range of values of one or more unknown variables. Based on point **630**, a predicted glucose concentration (G_P) and a predicted hematocrit (H_P) can be readily determined. As point **630** may encompass a range of values, so to may G_P or H_P encompass a limited range of values.

[0103] Another embodiment consistent with the principles of this invention extrapolates a current decay measured during a first time-segment to determine a current value at much longer time. This can be achieved by formulating an extrapolation algorithm using experimental data at longer test times. The extrapolated current, or "predicted current," can be correlated to analyte concentration with improved accuracy and precision. If the calculated analyte concentration is outside a pre-determined range, the measurement continues to the second time-segment, similar to the method previously described. The extrapolation algorithm and analyte concentration determination can be determined using any number of sets of calibration data, as previously described. Further, this method can be repeated until the entire measurement range is covered.

[0104] FIG. **5** depicts a chart **300** of three different fluid samples showing current decay curves over time after the application of a potential excitation. While the three samples depicted contain similar glucose concentrations, all three samples contain different amounts of red blood cells, i.e. different hematocrit values. The sample with the lowest hematocrit value is depicted by a line **310**, and has the steepest slope over an indicated dashed range **350**. In contrast, the sample with the highest hematocrit value is depicted by a line **330**, and has the flattest slope over indicated range **350**. A line **320** represents a sample with an intermediate hematocrit value. As shown, all three lines **310**, **320**, **330** approximately converge toward a generally common current value at a future time-point, as depicted by a region **340**.

[0105] In some embodiments, glucose concentration can affect the shape of a current decay curve. For example, different hematocrit values can affect the convergence of current decay curves. In particular, samples containing lower glucose concentrations may reach a generally common current value faster than samples containing higher glucose concentrations. As such, current decay curves representing samples containing lower glucose concentrations may converge in a shorter time period than samples containing higher glucose concentrations. Determining a wide range of glucose concentrations could require two or more time-segments, and calibration data associated with different time segments may be different.

[0106] In another embodiment, extrapolation techniques could be applied to one or more time-segments of one or more current decay curves to determine a generally common current value that could be reached at a longer time. For example, data associated with slope information of a single decay curve could be used to determine a future current value or associated time value. Data contained within dashed range **350** could be extrapolated, using linear or other curve fitting techniques, to determine a current associated with region **340**. Such a technique offers another method of determining glucose concentration within a shorter test time. Also, such slope or other relational data could be used in association with any one or more time-segments.

[0107] To determine slope information associated with a current decay curve, current data from two or more current measurements associated with two time-points may be obtained as previously described. These current data may then be fit with appropriate mathematical equations configured to provide a predicted current value at some future time-point. For example, an illustrative method could include measuring a first current value associated with the potential

excitation at a first time-point and measuring a second current value associated with the potential excitation at a second time-point. The method could then determine a predicted current at a future time-point, wherein the predicted current could be determined using an extrapolated current decay curve based on the first and second current values. Analyte concentration could then be calculated based on the predicted current and dynamically-selected calibration data, as described above.

[0108] In some embodiments, the extrapolated current decay curve could be selected from a plurality of extrapolated current decay curves. These extrapolated current decay curves could be based on empirical data, or obtained using any suitable method known in the art. Such current decay curves may also be associated with one or more time-segments, analyte concentrations, or other parameters previously discussed.

[0109] Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. It is intended that the specification and examples be considered as exemplary only, with a true scope and spirit of the invention being indicated by the following claims.

What is claimed is:

1. A method for analyzing an analyte, the steps comprising:
- applying a potential excitation to a fluid sample containing an analyte;
- measuring a first current during a first time-segment following application of the potential excitation;
- measuring a second current during a second time-segment following application of the potential excitation;
- calculating a plurality of first analyte concentrations based on the first measured current and a first set of calibration data associated with the first time-segment; and
- calculating a plurality of second analyte concentrations based on the second measured current and a second set of calibration data associated with the second time-segment.

2. The method of claim **1**, further comprising:
- determining a final analyte concentration based on at least one of the first analyte concentrations and at least one of the second analyte concentrations.

3. The method of claim **2**, wherein determining the final analyte concentration includes at least one of an iterative algorithm, an interpolative algorithm, a line-plot, and an extrapolative algorithm.

4. The method of claim **1**, wherein a set of calibration data includes at least one of a plurality of calibration curves, a lookup table, a data array, and a mathematical equation.

5. The method of claim **1**, wherein the first time-segment is less than about two to ten seconds, and the second time-segment is more than about two to ten seconds.

6. The method of claim **5**, wherein the first time-segment is less than about eight seconds, and the second time-segment is more than about eight seconds.

7. The method of claim **1**, wherein at least part of the calibration data is determined using at least one of empirical data, and predicted data.

8. The method of claim **1**, wherein the first and second sets of calibration data are associated with different levels of hematocrit.

9. The method of claim **8**, wherein the different levels of hematocrit include at least one of a high level greater than about 42%, a physiological level of about 42%, and a low level less than about 42%.

10. The method of claim **1**, further comprising:
- measuring a third current during a third time-segment following application of the potential excitation;
- calculating a plurality of third analyte concentrations based on the third measured current and a third set of calibration data associated with the third time-segment; and
- determining a final analyte concentration based on at least one of the first and second analyte concentrations and at least one of the third analyte concentrations.

11. The method of claim **1**, wherein the analyte is glucose and the fluid sample includes blood.

12. The method of claim **1**, wherein the fluid sample includes an enzyme of at least one of glucose oxidase and glucose dehydrogenase and a mediator of at least one of potassium ferricyanide and ruthenium hexamine.

13. A system for analyzing an analyte in a fluid sample, comprising:
- a set of electrodes configured to apply a potential excitation to a fluid sample containing an analyte;
- a processor configured to:
  - measure a first current during a first time-segment following application of the potential excitation;
  - measure a second current during a second time-segment following application of the potential excitation;
  - calculate a plurality of first analyte concentrations based on the first measured current and a plurality of first calibration curves associated with the first time-segment; and
  - calculate a plurality of second analyte concentrations based on the second measured current and a plurality of second calibration curves associated with the second time-segment.

14. The system of claim **13**, further comprising a processor configured to:
- determine a final analyte concentration based on at least one of the first analyte concentrations and at least one of the second analyte concentrations.

15. The system of claim **14**, wherein the final analyte concentration is determined using at least one of an iterative algorithm, an interpolative algorithm, a line-plot, and an extrapolative algorithm.

16. The system of claim **14**, wherein the system is further configured to a display a value representative of the final analyte concentration.

17. The system of claim **13**, wherein the first time-segment is less than about two to ten seconds, and the second time-segment is more than about two to ten seconds.

18. The system of claim **13**, wherein the first time-segment is less than about eight seconds, and the second time-segment is more than about eight seconds.

19. The system of claim **13**, wherein at least one of the calibration curves is determined using at least one of empirical data, and predicted data.

20. The system of claim **13**, wherein the plurality of first and second calibration curves are associated with different levels of hematocrit.

21. The system of claim **20**, wherein the different levels of hematocrit include at least one of a high level greater than about 42%, a physiological level of about 42%, and a low level less than about 42%.

22. The system of claim **13**, further comprising a processor configured to:
- measure a third current during a third time-segment following application of the potential excitation;
- calculate a plurality of third analyte concentrations based on the third measured current and a plurality of third calibration curves associated with the third time-segment; and

determine a final analyte concentration based on at least one of the first and second analyte concentrations and at least one of the third analyte concentrations.

23. The system of claim **13**, wherein the analyte is glucose and the fluid sample includes blood.

24. The system of claim **13**, wherein the fluid sample includes an enzyme of at least one of glucose oxidase and glucose dehydrogenase and a mediator of at least one of potassium ferricyanide and ruthenium hexamine.

25. The system of claim **13**, wherein the set of electrodes are contained within in a test strip.

26. The system of claim **13**, wherein the processor is contained within a meter.

27. A computer readable media, wherein the media comprises a plurality of instructions configured to direct a processor to:

measure a first current during a first time-segment following application of a potential excitation, wherein the potential excitation is applied to a fluid sample containing an analyte;

measure a second current during a second time-segment following application of the potential excitation;

calculate a plurality of first analyte concentrations based on the first measured current and a first set of calibration data associated with the first time-segment; and

calculate a plurality of second analyte concentrations based on the second measured current and a second set of calibration data associated with the second time-segment.

28. The computer readable media of claim **27**, wherein the instructions further direct the processor to:

determine a final analyte concentration based on at least one of the first analyte concentrations and at least one of the second analyte concentrations.

29. The computer readable media of claim **28**, wherein the final analyte concentration is determined using at least one of an iterative algorithm, an interpolative algorithm, a line-plot, and an extrapolative algorithm.

30. The computer readable media of claim **27**, wherein the calibration data includes at least one of a plurality of calibration curves, a lookup table, a data array, and a mathematical equation.

31. The computer readable media of claim **27**, wherein the first time-segment is less than about two to ten seconds, and the second time-segment is more than about two to ten seconds.

32. The computer readable media of claim **31**, wherein the first time-segment is less than about eight seconds, and the second time-segment is more than about eight seconds.

33. The computer readable media of claim **27**, wherein at least part of the calibration data is determined using at least one of empirical data, and predicted data.

34. The computer readable media of claim **27**, wherein the first and second sets of calibration data are associated with different levels of hematocrit.

35. The computer readable media of claim **34**, wherein the different levels of hematocrit include at least one of a high level greater than about 42%, a physiological level of about 42%, and a low level less than about 42%.

36. The computer readable media of claim **27**, wherein the instructions further direct the processor to:

measure a third current during a third time-segment following application of the potential excitation;

calculate a plurality of third analyte concentrations based on the third measured current and a third set of calibration data associated with the third time-segment; and

determine a final analyte concentration based on at least one of the first and second analyte concentrations and at least one of the third analyte concentrations.

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