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(54) **Title:** METHOD / DEVICE FOR GENERATING A CORRECTED VALUE OF AN ANALYTE CONCENTRATION IN A SAMPLE OF A BODY FLUID

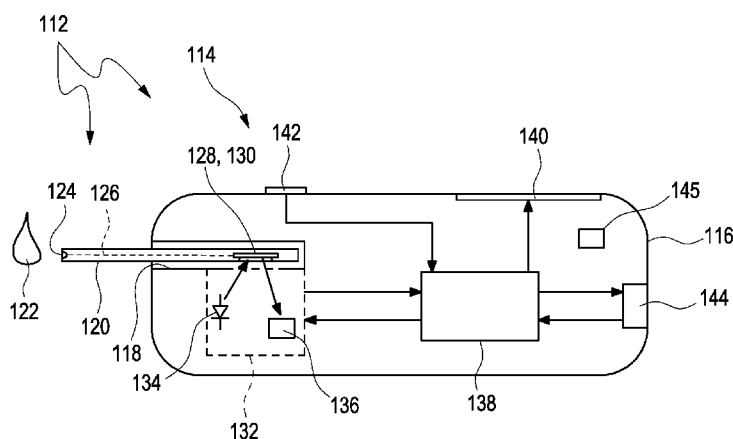


Fig. 1

(57) **Abstract:** A method for detecting an analyte in a body fluid is disclosed. The method has the following steps: a) applying a sample (122) of the body fluid to a test element (120), said test element (120) comprising at least (i) a test field (128) comprising at least one test material (130) adapted to change at least one measurable property in the presence of the analyte, (ii) a capillary element (126) adapted to guide the sample (122) across said test field (128) in a flow direction (146), (iii) a first and a second measurement location (158, 160) within said test field (128), wherein the second measurement location (160) is offset from the first measurement location (158) in the flow direction (146); b) measuring the measurable property in said at least one first measurement location (158), thereby generating at least one first measurement value; c) measuring the measurable property in said at least one second measurement location (160), thereby generating at least one second measurement value; d) detecting the analyte by using an evaluation algorithm having at least two input variables, wherein (i) at least one first input variable of the at least two input variables includes an information on a difference between the first measurement value and the second measurement value, and (ii) at least one second input variable of the at least two input variables includes a measurement information on an analyte-induced change of the measurable property of the test material (130) in at least part of the test field (128).



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5 **Method / Device for generating a corrected Value of an Analyte Concentration in a Sample
of a Body Fluid**

10 Field of the invention

The present invention relates to a method for detecting an analyte in a body fluid, the method having the following steps: a) applying a sample of the body fluid to a test element, said test element comprising at least (i) a test field having comprising at least one test material adapted to change at least one measurable property in the presence of the analyte, (ii) a capillary element adapted to guide the sample across said test field in a flow direction, (iii) a first and a second measurement location within said test field, wherein the second measurement location is offset from the first measurement location in the flow direction; (b) measuring the measurable property in said at least one first measurement location, thereby generating at least one first measurement value; (c) measuring the measurable property in said at least one second measurement location, thereby generating at least one second measurement value; (d) detecting the analyte by using an evaluation algorithm having at least two input variables, wherein (i) at least one first input variable of the at least two input variables includes an information on a difference between the first measurement value and the second measurement value, and (ii) at least one second input variable of the at least two input variables includes a measurement information on an analyte-induced change of the measurable property of the test material in at least part of the test field. The present invention further relates to a test device and to a test system adapted for performing the method of the present invention, and to the use of a difference of at least two measurement values measured in at least two different locations of a test field of a test element for generating a corrected value of an analyte concentration in a sample of a body fluid.

Related art

In the field of medical diagnostics, in many cases, one or more analytes have to be detected in samples of a body fluid, such as blood, interstitial fluid, urine, saliva or other types of body fluids. Examples of analytes to be detected are glucose, triglycerides, lactate, cholesterol or other types of analytes typically present in these body fluids. According to the concentration and/or the presence of the analyte, an appropriate treatment may be chosen, if necessary.

Generally, devices and methods known to the skilled person make use of test elements comprising one or more test chemistries, which, in presence of the analyte to be detected, are capable of performing one or more detectable detection reactions, such as optically detectable detection reactions. With regard to these test chemistries, reference may be made e.g. to J. Hoenes et al.: The Technology Behind Glucose Meters: Test Strips, Diabetes Technology & Therapeutics, Volume 10, Supplement 1, 2008, S-10 to S-26. Other types of test chemistry are possible and may be used for performing the present invention.

Typically, one or more optically detectable changes in the test chemistry are monitored, in order to derive the concentration of the at least one analyte to be detected from these changes. Examples of test fields, test chemistries and methods for monitoring one or more optically detectable changes in the test fields are disclosed in EP 0 821 234 A2. Thus, as an example, the relative remission of the test field may be optically detected as a function of time, up to a defined end point of the chemical detection reaction. From the change in relative remission, the concentration of the analyte may be derived. Similar measurements detecting the quantity of light reflected from the test field as a function of time, up to a defined end point of the detection reaction, are disclosed in EP 0 974 303 A1.

For detecting the at least one change of optical properties of the test field, various types of detectors are known in the art. Thus, various types of light sources for illuminating the test fields as well as various types of detectors are known. Besides single detectors such as photodiodes, various types of devices using detector arrays having a plurality of photosensitive devices are known. Thus, in US 2011/0201909 A1, an arrangement for measuring the concentration of an analyte contained in a sample of a body fluid is disclosed. The arrangement, inter alia, comprises a light source and a detector array. Similarly, EP 1 359 409 A2 discloses an apparatus for determining the concentration of an analyte in a physiological sample. The apparatus includes at least one light source and a detector array.

Further, when using detector arrays, methods are known in the art for detecting errors and artifacts in the images acquired by the detector arrays. Thus, US 2011/0201909 discloses a correc-

tion algorithm which, inter alia, is capable of correcting for imperfections present in the reaction spot observed by the detector array. Similarly, EP 1 359 409 A2 discloses means for determining whether a sufficient amount of sample is present on each of a plurality of different detector areas, wherein only light detected from those areas determined to have sufficient sample is used for determining the concentration of the analyte. In WO 2006/138226 A2, an arrangement and an algorithm for calculating the concentration of an analyte contained in a sample are disclosed. Therein, a color change rate of a test chemical is detected, and a hematocrit is derived from the color change rate. An appropriate correction factor indicative of the hematocrit is used for correcting a glucose concentration.

It has been known that measurement of a soluble analyte in a suspension additionally comprising at least one particulate compound is hampered by the fact that the measured value may deviate from the actual concentration depending on the concentration of said particulate compound. For the example of determining blood glucose levels, it has been proposed to use viscosity of the sample as a surrogate measure of the concentration of blood cells, i.e. the hematocrit (JP 2005/303 968). However, the viscosity of a blood sample depends on several other parameters, such as the concentration of fibrinogen and globulins, red blood cell and platelet aggregation, and the like, so the correction derived from direct or indirect viscosity measurement generally is affected by these parameters, thus rendering such a correction inaccurate to a certain extent. WO 2003/089658 discloses a biosensor using single-point measurement of the resistance between two electrodes to estimate the hematocrit level in the sample and to correct the measured value based on the estimated hematocrit level and on a set of pre-determined, empirical constants.

Problem to be solved

There is, thus, a need in the art to provide reliable means and methods to determine the concentration of a soluble analyte in a suspension further comprising a particulate compound and to provide for a correction of the measured concentration in dependence of the concentration of the particulate compound.

Summary of the invention

Thus, the present invention relates to a method for detecting an analyte in a body fluid, the method having the following steps:

- a) applying a sample of the body fluid to a test element, said test element comprising at least
 - (i) a test field comprising at least one test material adapted to change at least one measurable property in the presence of the analyte,

(ii) a capillary element adapted to guide the sample across said test field in a flow direction,

(iii) a first and a second measurement location within said test field, wherein the second measurement location is offset from the first measurement location in the flow direction;

b) measuring the measurable property in said at least one first measurement location, thereby generating at least one first measurement value;

c) measuring the measurable property in said at least one second measurement location, thereby generating at least one second measurement value;

d) detecting the analyte by using an evaluation algorithm having at least two input variables, wherein

(i) at least one first input variable of the at least two input variables includes an information on a difference between the first measurement value and the second measurement value, and

(ii) at least one second input variable of the at least two input variables includes a measurement information on an analyte-induced change of the measurable property of the test material in at least part of the test field.

As used herein, the expressions "have", "comprise" and "contain" as well as grammatical variations thereof are used in a non-exclusive way. Thus, the expression "A has B" as well as the expression "A comprises B" or "A contains B" may both refer to the fact that, besides B, A contains one or more further components and/or constituents, and to the case in which, besides B, no other components, constituents or elements are present in A.

The method of the present invention, preferably, is an in vitro method. Moreover, it may comprise steps in addition to those explicitly mentioned above. For example, further steps may relate, e.g., to obtaining a sample of a body fluid for step a), or displaying the result of the determination on an output element in step d). Moreover, one or more of said steps may be performed by automated equipment.

The term "analyte", as used herein, relates to a chemical compound present in a body fluid. Preferably, the analyte is a small molecule, i.e., preferably, the analyte is not a biological macromolecule, more preferably, the analyte is an organic molecule, most preferably an organic molecule capable of undergoing a redox reaction in the presence of the test chemistry according to the present invention. Preferably, the analyte is a molecule of the subject's metabolism. Also preferably, the analyte is a low molecular weight chemical compound, more preferably a chemical compound with a molecular mass of less than 1000 u (1000 Da; 1.66×10^{-24} kg). More preferably, the analyte is selected from the list consisting of glucose, lactate, cholesterol, and triglycer-

ides. Preferably, the analyte is blood glucose and the actual concentration to be determined is at least 10mg/dL, at least 50 mg/dL, at least 60 mg/dL, at least 70 mg/dL, at least 80 mg/dL, at least 90 mg/dL, at least 100 mg/dL, at least 110 mg/dL, at least 120 mg/dL, at least 130 mg/dL, at least 140 mg/dL, or at least 150 mg/dL.

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As used herein, the term "body fluid" relates to all bodily fluids of a subject known to comprise or suspected to comprise the analyte of the present invention, including blood, plasma, lacrimal fluid, urine, lymph, cerebrospinal fluid, bile, stool, sweat, and saliva. Preferably, the body fluid comprises at least one particulate component; preferably, the size difference between the particulate component and the analyte allows the separation of the particulate component from the analyte by a separation layer. More preferably, the size ratio (average size of the particulate component versus size of the analyte) is at least 10, at least 20, at least 50, at least 100, at least 200, at least 500, at least 1000, at least 2000, at least 5000, or at least 10000, at least 100000, or at least 1000000. Even more preferably, the particulate compound is cells; most preferably, the particulate compound is blood cells. Thus, preferably, the body fluid is blood, and the concentration of a particulate compound is the volume percentage of blood cells therein, i.e. the hematocrit. The term "sample" is understood by the skilled person and relates to any subportion of a bodily fluid, preferably removed from the subject prior to applying said sample to a test element. Samples can be obtained by well known techniques including, e.g., venous or arterial puncture, epidermal puncture, and the like.

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The term "detecting" relates to the quantification of the amount of analyte present in a sample of a body fluid, i.e. measuring the amount or concentration of said analyte, preferably semi-quantitatively or quantitatively. The detection of the amount of the analyte can be accomplished in a variety of ways known to the skilled person or detailed herein below. In accordance with the present invention, detecting the amount of the analyte can be achieved by all known means for detecting the amount of said analyte in a sample, provided that they are adapted to specifically detect the analyte of the present invention and are compatible with the requirements of the present invention. The term "amount" as used herein encompasses the absolute amount of the analyte referred to herein, the relative amount or concentration of the analyte referred to herein as well as any value or parameter which correlates thereto. Such values or parameters comprise intensity signal values from all specific physical or chemical properties obtained from the analyte referred to herein by measurements. It is to be understood that values correlating to the aforementioned amounts or parameters can also be obtained by all standard mathematical operations.

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The term "test element", as used herein, relates to a unit comprising the elements as described herein below i.e., the test element comprises at least one capillary element and at least one test field. Preferably, the test element is selected from an optical test element and an electrochemical

test element. The test element may further optionally comprise at least one puncture element, such as at least one lancing element, which, preferably, may be mounted movably with regard to the test field, in order to perform a puncture motion, a sampling motion or a lancing motion, thereby generating an incision in a skin surface. Preferably, the test field remains in a fixed position during the puncture, sampling or lancing motion, wherein a sample of a body fluid is transferred onto the test field, such as by a capillary action and/or by pressing the puncture element or a part thereof onto the test field after the puncture, sampling or lancing motion. Preferably, the test element is a test strip, a test tape, or a test disc.

As used herein, the term "capillary element" relates to any type of element adapted for taking up and/or transporting a liquid by capillary action. The capillary element may comprise a closed channel, such as a channel in a hollow needle, and/or an open channel, such as a capillary groove or a capillary slit. The closed channel may circumferentially be enclosed by a tubular capillary wall, whereas the open channel may provide an open surface along a longitudinal axis of the channel. In all embodiments, however, at least a part of the circumference of the capillary element is formed by or comprises at least part of the test field and the capillary element is adapted to guide a sample across the test field in a flow direction. Preferably, the capillary extends in longitudinal direction over at least 0.5 mm, 0.75 mm, 1 mm, 1.25 mm, 1.5 mm, 1.75 mm, 2 mm, 2.5 mm, 3 mm, 3.5 mm, 4 mm, 4.5 mm, 5 mm, or 10 mm. Preferably, the capillary element comprises at least one capillary slit extending across at least a part of the test field. More preferably, the capillary slit is formed by a surface of the test field and a guide surface disposed at a distance above the surface of the test field. Even more preferably, said guide surface is formed by a surface of a cover plate being disposed above the surface of the test field. Preferably, the capillary slit has a width of 30 μm to 300 μm , more preferably a width of 40 μm to 200 μm , even more preferably a width of 50 μm to 100 μm , still more preferably a width of 60 μm to 80 μm , and most preferably a width of 70 μm . Preferably, the test field is applied to a substrate on a surface of the substrate facing the capillary element. More preferably, said substrate contains at least one detection window wherein the measurable property is measured through the detection window. Most preferably, the detection window is an opening or a transparent detection window.

The term "test field" relates to a continuous or discontinuous amount of test chemistry, which, preferably, is held by at least one carrier, such as by at least one carrier film. Thus, the test chemistry may form or may be comprised in one or more films or layers of the test field, and/or the test field may comprise a layer setup having one or more layers, wherein at least one of the layers comprises the test chemistry. Thus, the test field may comprise a layer setup disposed on a carrier, wherein the sample of the body fluid may be applied to the layer setup from at least one application side, such as from an edge of the test field and/or from an application surface of the test field. Preferably, the test field has a multilayer setup, the multilayer setup comprising at least

one detection layer having the at least one test material and further comprising at least one separation layer adapted for separating off at least one particulate component contained in the body fluid, wherein the separation layer is located between the detection layer and the capillary element. It is understood by the skilled person that all layers present optionally between the body fluid and the test field are selected as to allow passage of at least the analyte. Preferably, the volume enclosed between the test layer and the separation layer is at most 1%, at most 2%, at most 3%, at most 4%, at most 5%, at most 6%, at most 7%, at most 8%, at most 9%, at most 10%, at most 15%, at most 20%, at most 25%, at most 30%, at most 35%, at most 40%, at most 45%, at most 50%, at most 75%, or at most 95% of the volume encompassed by the capillary element.

The terms "test chemistry" or "test material" refer to a substance or mixture of substances which is adapted to change at least one measurable property in the presence of the analyte. Preferably, the test material performs at least one optically or electrochemically detectable detection reaction in the presence of the analyte. More preferably, the detection reaction is a redox reaction. Most preferably, the detection reaction produces redox equivalents and/or electrons as intermediates and/or products. Preferably, the test reaction is at least in part mediated by at least one enzyme, thus, preferably, the test material comprises at least one enzyme adapted for performing at least one enzymatic reaction in the presence of the analyte. The detection reaction preferably may imply a color change of the test chemistry or of at least one part thereof. With regard to the test chemistry, various possibilities of designing the test chemistry are known in the art. In this regard, reference may be made to the above-mentioned prior art documents. Specifically, reference may be made to J. Hoenes et al.: The Technology Behind Glucose Meters: Test Strips, Diabetes Technology & Therapeutics, Volume 10, Supplement 1, 2008, S-10 to S-26. However, other types of test chemistry are possible. Preferably, the test chemistry comprises at least one enzyme, which preferably directly or indirectly reacts with the analyte, preferably with a high specificity, wherein, further, one or more optical indicator substances are present in the test chemistry, which perform at least one optically detectable property change when the at least one enzyme reacts with the analyte. Thus, the at least one indicator may comprise one or more dyes performing a color changing reaction indicative of the enzymatic reaction of the at least one enzyme and the analyte. Thus, the at least one enzyme may comprise glucose oxidase and/or glucose dehydrogenase. However, other types of enzymes and/or other types of test chemistry or active components of the test chemistry may be used.

Thus, it is also envisaged by the present invention that the test chemistry includes a chemical reagent for reacting with the analyte to produce an electrochemical signal that represents the presence of the analyte in the sample fluid. The test chemistry is selected in respect to the analyte to be assessed. As is well known in the art, there are numerous chemistries available for use with each of various analytes. The selection of an appropriate chemistry is therefore well known with-

in the skill in the art, and further description herein is not required in order to enable one to make and use the present invention.

In the case of glucose as a preferred analyte, the active components of the test chemistry will typically include an enzyme utilizing, preferably specifically utilizing, glucose and a redox mediator. More preferably, said enzyme comprises at least one of glucose oxidase and glucose dehydrogenase. The enzyme oxidizes glucose in the sample, and the mediator in turn reacts with the reduced enzyme. The mediator thereafter shuttles the redox equivalent of analyte product to the electrode surface by diffusion. There the mediator is oxidized quantitatively at a defined anodic potential and the resulting current is related to the apparent glucose concentration. There are a number of reagent systems suitable for the detection of glucose, and examples comprise AC Excitation, Analyte Sensors, and Biosensor applications, U.S. Pat. Nos. 5,385,846 and 5,997,817, and U.S. (Reissue) patent application Ser. No. 10/008,788 ("Electrochemical Biosensor Test Strip"),"); the cNAD chemistry as described in WO 2007/012494, WO 2009/103540, WO 2011/012269, WO 2011/012270, and WO 2011/012271; and the SCV chemistry as described in EP 0 354 441, EP 0 431 456, which are hereby incorporated by reference. The glucose chemistry utilizes the redox mediator to mediate a current between the working electrode and the glucose analyte, which otherwise is not well suited for direct electrochemical reaction on an electrode. The mediator functions as an electron transfer agent that shuttles electrons between the analyte and the electrode. A great number of redox species are known and can be used as the redox mediator. In general, the preferred redox mediators are rapidly reducible and oxidizable molecules. Examples include ferricyanide, nitrosoaniline and derivatives thereof, and ferrocene and its derivatives.

It follows from the above, that the at least one measurable property may be any property of the test chemistry which changes in the presence of the analyte and which can be transferred into a physical signal of any kind. Preferably, the change of the measurable property and/or the signal generatable therefrom are proportional to the concentration of the analyte in the sample. Preferably, as described above, the measurable property is a change in color and/or in color intensity of the test chemistry, i.e., preferably, a change in the absorption and/or emission spectrum of the test chemistry. Thus, in the change of the measurable property the optical property preferably is selected from the group consisting of: a reflection property, preferably a reflectance and/or a remission; transmission property, preferably an absorption; a color; a luminescence, preferably a fluorescence. Also preferably, the measurable property is the concentration of a reduced or an oxidized redox mediator as described above, i.e., preferably, the measurable property is the redox state of said mediator comprised in the test chemistry.

Methods of converting the measurable property as defined above into a physical signal which can be read as a measurement value are well known in the art and are described e.g., in EP 0 821 234, EP 0 974 303, and US 2005/0023152.

5 The term "measurement location", as used herein, relates to an area within the test field. Preferably, the location extends over at most 1%, at most 5%, at most 10%, at most 20%, at most 30%, at most 35%, at most 50%, or at most 75% of the length of the test field, the term "length of a test field", as used in this specification, relating to the dimension of the test field in the flow direction of the capillary element. Thus, in a test field having a length of 2 - 2.5 mm, preferably,
10 the location extends over at most 0.05mm, at most 0.1 mm, at most 0.15 mm, at most 0.2 mm, at most 0.25, at most 0.3 mm, at most 0.5mm, at most 1 mm, at most 1.5 mm, at most 2 mm, or at most 5 mm in the flow direction. Also preferably, the location extends over at most 5%, at most 10%, at most 20%, at most 30%, at most 35%, at most 40%, at most 45%, at most 50%, at most 55%, at most 65%, at most 70%, at most 80%, at most 90%, or at most 100% of the width of the
15 test field. It is understood by the skilled person that the geometry, i.e. the shape, of the location may vary, depending on the detection system used.

The terms "first measurement location" or "first location", as used herein, relate to a first area within the test field. Preferably, the first location is centered within the first 75%, within the first
20 half, within the first third, within the first quarter, within the first fifth, within the first sixth, within the first seventh, within the first eighth, within the first ninth, within the first tenth, or within the first percent of the length of the test field, as determined starting from the application site of the sample. It is understood by the skilled person that a minimum distance from said application site may be necessary to obtain appropriate detection conditions.

25 Mutatis mutandis, the terms "second measurement location" or "second location" relate to a second area within the test field, wherein the second location is offset from the first location in the flow direction. Preferably, the second location is centered at an offset from the first location in the flow direction by at least 1%, at least 5%, at least 10%, at least 15%, at least 20%, at least
30 25%, at least 30%, at least 35%, at least 40%, at least 45%, at least 50%, at least 55%, at least 60%, at least 65%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, or at least 95% of the length of the test field.

It is understood by the skilled person that the parameters detailed above can be combined independently, e.g. in a test field of approx. 2 mm (longitudinal = flow direction) x 1.75 mm (width),
35 the first location may be centered at 0.2 mm (10%), extend in the flow direction over 0.3 mm (15%), and have a width of 0.35 mm (20%) and the second location may be centered at 1 mm (40% offset from the first location), extend in the flow direction over 0.2 mm (10%) and have a

width of 0.7 mm (40%). Preferably, however, the length and width of the first and the second location, and, more preferably, their geometry, are the same for a given test field.

The term "measurement value", as used herein, relates to a value of a physical signal generated by the test chemistry and determined as detailed above and correlating to the concentration of an analyte in a sample. Preferably, the measurement value is the value considered to most reliably correlate to the concentration of an analyte in a sample. It is understood that obtaining a measurement value may comprise several measurements of a measurable property over time and selecting the measurement value according to the data thus obtained, as detailed, e.g. in EP 0 974 303. Preferably, the second measurement value is obtained before the first measurement value or the second measurement value is measured within less than 5s, less than 1 s, less than 0.9 s, less than 0.8 s, less than 0.7 s, less than 0.6 s, less than 0.5 s, less than 0.4 s, less than 0.3 s, less than 0.2 s, less than 0.1 s, or less than 0.01s after the first measurement value. More preferably, the first and the second measurement value are measured essentially simultaneously. Most preferably, the first and the second measurement value are measured simultaneously, e.g., preferably, a predetermined time span after application of the sample of the body fluid to the test element. More preferably, the first and the second measurement value are measured at a point in time at which a measurement curve indicating the measurable property as a function of time fulfills at least one predetermined condition, preferably at least one threshold condition and more preferably wherein a slope of the measurement curve is below or above a predetermined threshold. Preferably, the first measurement value is measured at a point in time at which a measurement curve indicating the measurable property at the first measurement location as a function of time fulfills at least one predetermined condition, preferably at least one threshold condition and more preferably wherein a slope of the measurement curve is below or above a predetermined threshold, and the second measurement value is measured at a point in time at which a measurement curve indicating the measurable property at a second measurement location as a function of time fulfills at least one predetermined condition, preferably at least one threshold condition and more preferably wherein a slope of the measurement curve is below or above a predetermined threshold. More preferably, the first and the second measurement value are measured simultaneously at a point in time at which a measurement curve indicating the measurable property at the first measurement location or at the second measurement location as a function of time fulfills at least one predetermined condition, preferably at least one threshold condition and more preferably wherein a slope of the measurement curve is below or above a predetermined threshold. Preferably, the first measurement value and the second measurement value are selected from the group consisting of: an optical measurement value, preferably a remission; an electrical measurement value, preferably a current and/or a voltage. Preferably, generating at least one of the first and the second measurement value implies using at least one detector for generating the measurement value. Preferably, said detector includes at least one light source for illuminating at least one of

the first location and the second location and at least one optically sensitive element adapted to determine detection light from at least one of the first location and the second location. Preferably, the at least one first location and the at least one second location are illuminated by one of: light having the same wavelengths, light having different wavelengths. Thus, in a preferred embodiment, the detector comprises at least two separate light sources, e.g., preferably, light emitting diodes (LEDs), having the same wavelengths: a first light source illuminating a first location and a second light source illuminating a second location. In such case, preferably, illumination of said first location by said first light source is shifted in time as specified above relative to illumination of said second location by said second light source. More preferably, the detector comprises at least two separate light sources, e.g., preferably, light emitting diodes (LEDs), having different modulation frequencies: a first light source illuminating a first location with a first modulation frequency and a second light source illuminating a second location with a second modulation frequency. In such case, preferably, illumination of said first location by said first light source is shifted in time as specified above relative to illumination of said second location by said second light source; more preferably, illumination of said first location by said first light source is not shifted in time relative to illumination of said second location by said second light source. It is understood by the skilled artisan that the above applies mutatis mutandis in case more than two light sources and/or more than two measurement locations are used.

Preferably, the detection light is selected from the group consisting of: light reflected by the test field in at least one of the first location and the second location, light transmitted by the test field in at least one of the first location and the second location, light emitted by the test field in at least one of the first location and the second location.

Preferably, the optically sensitive element comprises at least one element adapted to detect light emitted by a light source and reflected and/or transmitted by a test field. Said optically sensitive element may, e.g., be a photo diode. It is understood by the skilled person that in case the illumination of a first location by a first light source is shifted in time relative to illumination of a second location by a second light source as specified above, the detection lights may be detected by one, i.e. by the same, optically sensitive element. The skilled person also understands that in case a first location is illuminated by a first light source having a different modulation frequency as compared to a second light source illuminating a second location, the detection lights may also be detected by one, i.e. by the same, optically sensitive element. More preferably, the optically sensitive element comprises at least one one-dimensional or two-dimensional matrix of optically sensitive elements, preferably at least one camera chip, and more preferably at least one CCD chip. It is understood by the skilled artisan that in case at least one one-dimensional or two-dimensional matrix of optically sensitive elements comprising at least two optically sensitive elements arranged in flow direction is used, it is possible to define a measurement location ac-

according to the present invention by selecting at least two different optically sensitive elements located at different positions along the flow direction and by detecting the signals generated by said at least two different optically sensitive elements. Thus, preferably, the sensor comprises at least one one-dimensional or two-dimensional matrix of optically sensitive elements comprising
5 at least two optically sensitive elements arranged in flow direction.

From the above, it is understood that the terms "first" and "second" are solely used in order to enable differentiation between two terms and, in the case of the term "measurement location", do only have a temporal implication in as far as the first location is wetted by the sample before the
10 second location, as detailed above. However, the measuring of the measurable property at the first and at the second location is performed at a point in time where both locations have been wetted by the sample.

As used herein, the term "first input variable" relates to an input variable comprising an infor-
15 mation on the difference between the first measurement value and the second measurement value. It is understood that the first variable may result from any mathematical operation providing or conserving said information. Preferably, the first variable is the difference of the first and the second measurement value, or the difference of the second and the first measurement value. It is, however, understood by the skilled person that said information is also comprised in the value
20 pair first and second measurement value itself. Preferably, the first input variable includes an information on a gradient of measurement values over at least part of the test field. More preferably, said gradient of measurement values over at least part of the test field is a gradient in the flow direction.

The term "second input variable" relates to an input variable including a measurement infor-
25 mation on an analyte-induced change of the test material in at least part of the test field. The value of the second variable is, preferably, obtained from any location within the test field. It is understood that said location may be different from both the first and the second location, i.e. be a third location. Preferably, the definitions above apply to the third location as well, as a whole or
30 in part. Thus, e.g., preferably, the third location is centered within the first 99%, the first 75%, within within the first half, within the first third, within the first quarter, within the first fifth, within the first sixth, within the first seventh, within the first eighth, within the first ninth, within the first tenth, or within the first percent of the length of the test field, as determined starting from the application site of the sample. It is understood by the skilled person that a minimum
35 distance from said application site may be necessary to obtain appropriate detection conditions. More preferably, the first measurement value is used as the measurement information, the second measurement value is used as the measurement information, an average value of the first measurement value and the second measurement value is used as the measurement information, or an

analyte-induced change of the measurable property is measured in at least one third measurement location of the test field, thereby generating at least one third measurement value, wherein the third measurement value is used as the measurement information.

5 The term "algorithm" is known in the art and relates to an arithmetical or computational procedure. The evaluation algorithm of the present invention determines the concentration of the analyte by applying a mathematical or graphical representation of the interdependency of analyte concentration in a sample, concentration of a particulate compound in said sample, and the difference between a first and second measurement value to the first and second input variable of
10 the present invention. It is understood by the skilled person that the evaluation algorithm may be any appropriate algorithm, preferably an algorithm using a multidimensional calibration surface or a multivariate statistical algorithm, e.g. a partial least squares regression (PLS regression) algorithm. Preferably, a plurality of evaluation algorithms is obtained for a plurality of values of at least one additional parameter known or expected to influence the first and/or the second input
15 variable. More preferably, said additional parameter is an ambient parameter; even more preferably, the additional parameter is temperature, most preferably ambient temperature. It is understood by the skilled person that the temperature at the test chemistry is the parameter most profoundly influencing the first and/or second parameter. It is, however, also understood by the skilled person that the mass of the test element and of the sample in conventional test elements
20 are small enough to have ambient temperature by the time of measurement. Thus, preferably, the method comprises a further step of measuring the ambient temperature. It is, however, also envisaged that the method comprises a step of measuring the temperature of the sample and/or of the test chemistry at the time of obtaining the measurement value, and/or that the method comprises a step of adjusting the temperature of the test element, and/or the test chemistry and/or the
25 sample.

Preferably, the evaluation algorithm is a one-step algorithm and the first input variable and the second input variable are simultaneously used for deriving the concentration of the analyte in the body fluid by using at least one predetermined calibration surface, the predetermined calibration
30 surface indicating the concentration of the analyte as a function of the two input variables. Thus, preferably, said representation of said interdependency is obtained by measuring the first and second measurement values for various analyte concentrations and at various concentrations of a particulate compound in the sample. This way, a three-dimensional graph representing a calibration surface is obtained. The skilled person knows how to approximate the calibration surface
35 thus obtained by an equation. Thus, having the first and the second input variable at hand, the skilled person can directly determine the corrected value of the analyte concentration, the term "corrected value of the analyte concentration" relating to a value of the analyte concentration

corrected for a deviation from the actual value of the analyte concentration caused by the presence of the particulate compound at the given concentration.

It is understood that the same result may be obtained by generating a series of calibration curves instead of a calibration surface. E.g. a series of graphs can be generated, wherein in each of the graphs the signal intensity is correlated to various concentrations of the analyte measured at a given concentration of a particulate compound equivalent to a certain intensity difference between the first and the second measurement location. The best estimation of the concentration of the analyte can then be determined by choosing the curve being closest to the measured intensity difference.

It is to be understood that the above algorithm may also be performed as a two-step-algorithm, wherein the algorithm comprises the two separate steps: in a first step of the algorithm, an estimate value of the concentration is derived from the second input variable by using at least one predetermined first calibration curve, the predetermined first calibration curve indicating an uncorrected concentration of the analyte as a function of the second input variable, and in a second step of the algorithm, the estimate value of the concentration is corrected by applying at least one correction algorithm to the estimate value, the correction algorithm providing a correction to the estimate value by using the first input variable. Preferably, the first calibration curve is a mathematical or graphical representation of the interdependency of analyte concentration in a sample and the second variable of the present invention at a fixed concentration of a particulate compound. Thus, preferably, said representation of said interdependency is obtained by obtaining a second variable for various analyte concentrations at a fixed concentration of a particulate compound, preferably at a fixed concentration of a particulate compound corresponding to the average concentration of a particulate compound present in a population of subjects. The estimate value thus obtained is then corrected by applying a correction algorithm using the first and the second variable.

Advantageously, it was found in the experiments underlying the present invention that the presence of a particulate component in a sample induces a deviation of measured values from the actual concentration of an analyte along a test element in the flow direction. Moreover, it was found that the deviation (bias) increases with increasing concentration of the particulate compound and with increasing distance from the application site. As a consequence, the gradient along the test element can be used to correct the measured values for the bias induced by the particulate compound; further, the best estimation of the actual concentration of the analyte without correction for said bias is obtained by measuring close to the application site. In particular, it was found in the experiments underlying the present invention that, depending on the hem-

atocrit of a blood sample, a concentration gradient along a test strip occurs, which allows to correct the measured values for the hematocrit.

5 The definitions made above apply mutatis mutandis to the following:

In a further embodiment, the present invention relates to a method for detecting an analyte in a body fluid, the method having the following steps:

- 10 a) applying a sample (122) of the body fluid to a test element (120), said test element (120) comprising at least
 - (i) a test field (128) having at least one test material (130) adapted to change at least one measurable property in the presence of the analyte,
 - (ii) a capillary element (126) adapted to guide the sample (122) across said test field (128) in a flow direction (146),
 - 15 (iii) at least one single measurement location (158) within said test field (128);
- b) measuring the measurable property in said single measurement location (158), thereby generating at least one measurement value;
- c) detecting the analyte by using an evaluation algorithm having the measurable property as an input variable,
- 20 wherein said single measurement location is located within the first third of the test field (128) as determined from the application site.

As used herein, the term "single measurement location" or "single location" relates to a measurement location as defined above located within the first third of the test field (128) as determined from the application site. Preferably, the single measurement location is centered within
25 the first quarter, within the first fifth, within the first sixth, within the first seventh, within the first eighth, within the first ninth, within the first tenth, or within the first percent of the length of the test field, as determined starting from the application site of the sample. It is understood by the skilled person that a minimum distance from said application site may be necessary to obtain
30 appropriate detection.

In a further embodiment, the present invention relates to a test device for detecting an analyte in a body fluid, wherein the device contains

- 35 a) at least one test element receptacle for receiving at least one test element, the test element having
 - (i) at least one test field having at least one test material adapted to change at least one measurable property in the presence of the analyte and

- (ii) having a capillary element adapted to guide the sample across the test field in a flow direction,
- b) wherein the receptacle is adapted to locate the test element in at least one application position in which a sample of the body fluid is applicable to the test element,
- 5 c) wherein the device further contains at least one detector for measuring the measurable property, wherein the detector is adapted to measure the measurable property
 - (i) in at least one first location of the test field, thereby generating at least one first measurement value,
 - (ii) in at least one second location of the test field, thereby generating at least one sec-
10 ond measurement value, wherein the second location is offset from the first location in the flow direction,
- d) wherein the test device further comprises at least one evaluation unit adapted to determine the concentration of the analyte by using an evaluation algorithm having at least two input variables,
 - 15 (i) wherein at least one first input variable of the at least two input variables includes an information on a difference between the first measurement value and the second measurement value, and
 - (ii) wherein at least one second input variable of the at least two input variables in-
cludes a measurement information on an analyte-induced change of the test materi-
20 al in at least part of the test field.

The test device, preferably, is adapted to measure the analyte-induced change of the measurable property in at least two measurement locations as specified herein above. Preferably, the test device is further adapted to measure the analyte-induced change of the measurable property in at
25 least one third location of the test field, thereby generating at least a third measurement value. It is, however, more preferred that the measurable property is measured in two locations. Preferably, the test device further comprises at least one sensor for determining an ambient parameter. Preferably, the test device further comprises at least one temperature sensor for determining an ambient temperature. Also preferably, test device is a hand-held test device.

30 The term "test element receptacle" is known to the skilled person and relates to an element of the device shaped for receiving at least one test element according to the present invention, providing one or more connectors and/or detectors as appropriate for detecting an analyte in a body fluid, and adapted to locate the test element in at least one application position in which a sample
35 of the body fluid is applicable to the test element. The specific embodiment of the test element receptacle, preferably, will depend on the kind of test element and on the test chemistry used therein.

The term "detector" is also known to the skilled person. The skilled person, as described above, knows how to use different test chemistries and how to use an appropriate detector for the respective test chemistry. Thus, preferably, the detector is adapted to measure the measurable property of the test chemistry as described herein above. Preferably, the detector includes at least one light source for illuminating at least one of the first location and the second location and at least one optically sensitive element adapted to determine detection light from at least one of the first location and the second location.

As used herein, the term "evaluation unit" relates to a unit of a device applying at least one of the algorithms according to the present invention to the first and second input variable as defined herein above. Thus, the evaluation unit is adapted to determine the concentration of the analyte by using an evaluation algorithm having at least two input variables. Preferably, the evaluation unit further is adapted to select a measurement value as described herein above, to select an algorithm according to an ambient parameter, and/or to store reference values and or reference curves and/or reference areas. More preferably, the evaluation unit is adapted to perform all calculations and evaluations required to print out a value of a concentration of an analyte in a sample in a body fluid. Most preferably, the evaluation unit is adapted to receive one or more detector signals and to detect and print out a blood glucose level of a sample of blood in a test element inserted in a test element receptacle. Preferably, the evaluation unit comprises at least one data processing device, preferably at least one microcomputer.

In a further embodiment, the present invention relates to a test device (112) for detecting an analyte in a body fluid, wherein the test device (112) contains

- a) at least one receptacle (118) for receiving at least one test element (120), the test element (120) having
 - (i) at least one test field (128) having at least one test material (130) adapted to change at least one measurable property in the presence of the analyte and
 - (ii) at least one capillary element (126) adapted to guide the sample (122) across the test field (128) in a flow direction (146),
- b) wherein the receptacle (118) is adapted to locate the test element (120) in at least one application position in which a sample (122) of the body fluid is applicable to the test element (120),
- c) wherein the device further contains at least one detector (132) for measuring the measurable property, wherein the detector (132) is adapted to measure the measurable property in at least one single measurement location (158) of the test field (128), thereby generating at least one measurement value,

d) wherein the test device (112) further comprises at least one evaluation unit (138) adapted to determine the concentration of the analyte by using an evaluation algorithm having at least said measurement value as an input variable, wherein the detector is adapted to measure the measurable property within the first third of the test field.

In another embodiment, the present invention relates to a test system for detecting an analyte in a body fluid, the test system comprising at least one test device according to one of the preceding claims referring to a test device, and at least one test element, wherein the test element has at least one test field having at least one test material adapted to change at least one measurable property in the presence of the analyte and having a capillary element adapted to guide the sample across the test field in a flow direction.

In a further embodiment, the present invention relates to a use of a difference of at least two measurement values measured in at least two different locations of a test field of a test element for generating a corrected value of an analyte concentration in a sample of a body fluid, wherein the sample of the body fluid is guided across the test field by a capillary element in a flow direction, wherein the at least two different locations are offset in the flow direction.

The invention further discloses and proposes a computer program including computer-executable instructions for performing the method according to the present invention in one or more of the embodiments enclosed herein when the program is executed on a computer or computer network. Therein, one, more than one or all method steps of the method may be performed and/or supported by using a computer. Specifically, the computer program may be stored on a computer-readable data carrier.

The invention further discloses and proposes a computer program product having program code means, in order to perform the method according to the present invention in one or more of the embodiments disclosed herein when the program is executed on a computer or computer network. Specifically, the program code means may be stored on a computer-readable data carrier.

Further, the invention discloses and proposes a data carrier having a data structure stored thereon, which, after loading into a computer or computer network, such as into a working memory or main memory of the computer or computer network, may execute the method according to one or more of the embodiments disclosed herein.

The invention further proposes and discloses a computer program product with program code means are stored on a machine-readable carrier, in order to perform the method according to one

or more of the embodiments disclosed herein, when the program is executed on a computer or computer network. As used herein, a computer program product refers to the program as a tradable product. The product may generally exist in an arbitrary format, such as in a paper format, or on a computer-readable data carrier. Specifically, the computer program product may be distributed over a data network.

Finally, the invention proposes and discloses a modulated data signal containing instructions readable by a computer system or computer network, for performing the method according to one or more of the embodiments disclosed herein.

Preferably, referring to the computer-implemented aspects of the invention, one or more of the method steps or even all of the method steps of the method according to one or more of the embodiments disclosed herein may be performed by using a computer or computer network. Thus, generally, any of the method steps including provision and/or manipulation of data may be performed by using a computer or computer network. Generally, these method steps may include any of the method steps, typically except for method steps requiring manual work, such as providing the samples and/or certain aspects of performing the actual measurements.

Specifically, the present invention further discloses:

- A computer or computer network comprising at least one processor, wherein the processor is adapted to perform the method according to one of the embodiments described in this description,
- a computer loadable data structure that is adapted to perform the method according to one of the embodiments described in this description while the data structure is being executed on a computer,
- a computer program, wherein the computer program is adapted to perform the method according to one of the embodiments described in this description while the program is being executed on a computer,
- a computer program comprising program means for performing the method according to one of the embodiments described in this description while the computer program is being executed on a computer or on a computer network,
- a computer program comprising program means according to the preceding claim, wherein the program means are stored on a storage medium readable to a computer,
- a storage medium, wherein a data structure is stored on the storage medium and wherein the data structure is adapted to perform the method according to one of the embodiments described in this description after having been loaded into a main and/or working storage of a computer or of a computer network, and

- a computer program product having program code means, wherein the program code means can be stored or are stored on a storage medium, for performing the method according to one of the embodiments described in this description, if the program code means are executed on a computer or on a computer network.

5

Summarizing the findings of the present invention, the following embodiments are preferred:

Embodiment 1: A method for detecting an analyte in a body fluid, the method having the following steps:

- 10 a) applying a sample of the body fluid to a test element, said test element comprising at least
 - (i) a test field having at least one test material adapted to change at least one measurable property in the presence of the analyte,
 - (ii) a capillary element adapted to guide the sample across said test field in a flow direction,
 - (iii) a first and a second measurement location within said test field, wherein the second measurement location is offset from the first measurement location in the flow direction;
- 15 b) measuring the measurable property in said at least one first measurement location, thereby generating at least one first measurement value;
- c) measuring the measurable property in said at least one second measurement location, thereby generating at least one second measurement value;
- 20 d) detecting the analyte by using an evaluation algorithm having at least two input variables, wherein
 - (i) at least one first input variable of the at least two input variables includes an information on a difference between the first measurement value and the second measurement value, and
 - (ii) at least one second input variable of the at least two input variables includes a measurement
- 25 information on an analyte-induced change of the measurable property of the test material in at least part of the test field.

Embodiment 2: The method according to the preceding embodiment, wherein the measurement information on an analyte-induced change of the measurable property of the test material in at least part of the test field is generated by one or more of the following procedures:

- 30 - the first measurement value is used as the measurement information;
- the second measurement value is used as the measurement information;
- an average value of the first measurement value and the second measurement value is used as the measurement information;
- 35 - an analyte-induced change of the measurable property is measured in at least one third measurement location of the test field, thereby generating at least one third measurement value, wherein the third measurement value is used as the measurement information.

Embodiment 3: The method according to one of the preceding embodiments, wherein the measurement information used in step d) (ii) is a measurement value generated at a measurement location located within the first 75% of the test field in view of the flow direction, preferably the first half, more preferably within the first third of the test field, and most preferably within the first quarter of the test field.

Embodiment 4: The method according to one of the preceding embodiments, wherein method steps b) and c) are performed

- a predetermined time span after application of the sample of the body fluid to the test element;

- or

- at a point in time at which a measurement curve indicating the measurable property as a function of time fulfills at least one predetermined condition, preferably at least one threshold condition and more preferably wherein a slope of the measurement curve is below or above a predetermined threshold.

Embodiment 5: The method according to one of the preceding embodiments, wherein

- the evaluation algorithm comprises a one-step evaluation algorithm, and

- the first input variable and the second input variable are simultaneously used for deriving the concentration of the analyte in the body fluid by using at least one predetermined calibration curve, the predetermined calibration curve indicating the concentration of the analyte as a function of the two input variables.

Embodiment 6: The method according to one of the preceding embodiments, wherein

- the evaluation algorithm comprises at least two separate steps,

- in a first step of the algorithm an estimate value of the concentration is derived from the second input variable by using at least one predetermined first calibration curve, the predetermined first calibration curve indicating an uncorrected concentration of the analyte as a function of the second input variable, and

- in a second step of the algorithm the estimate value of the concentration is corrected by applying at least one correction algorithm to the estimate value, the correction algorithm providing a correction to the estimate value by using the first input variable.

Embodiment 7: The method according to the preceding embodiment, wherein

- the sample of the body fluid is blood,

- in the first step of the algorithm, an estimate value of a glucose concentration is generated, and
- in the second step of the algorithm, a correction of the estimate value for an actual hematocrit of the blood is provided, thereby generating an information on the glucose concentration in the blood without determining the actual hematocrit of the blood.

Embodiment 8: The method according to one of the preceding embodiments, wherein, in method step d), the at least one first input variable includes an information on a gradient of measurement values over at least part of the test field.

5 Embodiment 9: The method according to the preceding embodiment, wherein the gradient is a gradient in the flow direction.

10 Embodiment 10: The method according to one of the preceding embodiments, wherein, in method step d), the evaluation algorithm is chosen from a set of evaluation algorithms, wherein the choice is made in accordance with at least one ambient parameter.

15 Embodiment 11: The method according to the preceding embodiment, wherein the ambient parameter is an ambient temperature, wherein the set of evaluation algorithms contains a plurality of evaluation algorithms for different ambient temperatures.

Embodiment 12: The method according to the preceding embodiment, wherein the method further comprises at least one method step of measuring the ambient temperature.

20 Embodiment 13: The method according to one of the preceding embodiments, wherein the test material comprises at least one enzyme adapted for performing at least one enzymatic reaction in the presence of the analyte.

25 Embodiment 14: The method according to the preceding embodiment, wherein the enzyme comprises at least one of glucose oxidase and glucose dehydrogenase.

30 Embodiment 15: The method according to one of the preceding embodiments, wherein the first measurement value and the second measurement value are selected from the group consisting of: an optical measurement value, preferably a remission; an electrical measurement value, preferably a current and/or a voltage.

Embodiment 16: The method according to one of the preceding embodiments, wherein the test element is selected from an optical test element and an electrochemical test element.

35 Embodiment 17: The method according to one of the preceding embodiments, wherein the test material is adapted to change at least one optical property in the presence of the analyte.

Embodiment 18: The method according to the preceding embodiment, wherein the optical property is selected from the group consisting of: a reflection property, preferably a reflectance and/or a remission; transmission property, preferably an absorption; a color; a luminescence, preferably a fluorescence.

5 Embodiment 19: The method according to one of the two preceding embodiments, wherein at least one of method steps b) and c) implies using at least one detector for generating the measurement value.

10 Embodiment 20: The method according to the preceding embodiment, wherein the detector includes at least one light source for illuminating at least one of the first location and the second location and at least one optically sensitive element adapted to determine detection light from at least one of the first location and the second location.

15 Embodiment 21: The method according to the preceding embodiment, wherein the detection light is selected from the group consisting of: light reflected by the test field in at least one of the first location and the second location, light transmitted by the test field in at least one of the first location and the second location, light emitted by the test field in at least one of the first location and the second location.

20 Embodiment 22: The method according to one of the two preceding embodiments, wherein the optically sensitive element comprises at least one one-dimensional or two-dimensional matrix of optically sensitive elements, preferably at least one camera chip and more preferably at least one CCD chip.

25 Embodiment 23: The method according to one of the six preceding embodiments, wherein, in method steps b) and c), the at least one first location and the at least one second location are illuminated by one of: light having the same wavelengths, light having different wavelengths.

30 Embodiment 24: The method according to one of the seven preceding embodiments, wherein, in method steps b) and c), the at least one first location and the at least one second location are illuminated by modulated light having different modulation frequencies.

35 Embodiment 25: The method according to one of the preceding embodiments, wherein the body fluid is selected from the group consisting of: blood, plasma, urine and saliva.

Embodiment 26: The method according to one of the preceding embodiments, wherein the analyte preferably is a chemical compound with a molecular mass of less than 1000 u (1000 Da;

1.66×10⁻²⁴ kg) and more preferably is selected from the group consisting of: glucose, lactate, cholesterol, and triglycerides.

5 Embodiment 27: The method according to one of the preceding embodiments, wherein the test element is a test strip.

10 Embodiment 28: The method according to one of the preceding embodiments, wherein the test field has a multilayer setup, the multilayer setup comprising at least one detection layer having the at least one test material and further comprising at least one separation layer adapted for separating off at least one particulate component contained in the body fluid, wherein the separation layer is located between the detection layer and the capillary element.

15 Embodiment 29: The method according to one of the preceding embodiments, wherein the capillary element comprises at least one capillary slit extending across at least a part of the test field.

Embodiment 30: The method according to the preceding embodiment, wherein the capillary slit is formed by a surface of the test field and a guide surface disposed at a distance above the surface of the test field.

20 Embodiment 31: The method according to the preceding embodiment, wherein the guide surface is formed by a surface of a cover plate being disposed above the surface of the test field.

25 Embodiment 32: The method according to one of the three preceding embodiments, wherein the capillary slit has a width of 30 μm to 300 μm, preferably a width of 40 μm to 200 μm, more preferably a width of 50 μm to 100 μm, even more preferably a width of 60 μm to 80 μm, and most preferably a width of 70 μm.

30 Embodiment 33: The method according to one of the preceding embodiments, wherein the test field is applied to a substrate on a surface of the substrate facing the capillary element, wherein the substrate contains at least one detection window, wherein in method steps b) and c), the measurable property is measured through the detection window.

35 Embodiment 34: A test device for detecting an analyte in a body fluid, wherein the device contains
a) at least one test element receptacle for receiving at least one test element, the test element having
(i) at least one test field having at least one test material adapted to change at least one measurable property in the presence of the analyte and

(ii) having a capillary element adapted to guide the sample across the test field in a flow direction,

b) wherein the receptacle is adapted to locate the test element in at least one application position in which a sample of the body fluid is applicable to the test element,

5 c) wherein the device further contains at least one detector for measuring the measurable property, wherein the detector is adapted to measure the measurable property

(i) in at least one first location of the test field, thereby generating at least one first measurement value,

10 (ii) in at least one second location of the test field, thereby generating at least one second measurement value, wherein the second location is offset from the first location in the flow direction,

d) wherein the test device further comprises at least one evaluation unit adapted to determine the concentration of the analyte by using an evaluation algorithm having at least two input variables,

(i) wherein at least one first input variable of the at least two input variables includes an information on a difference between the first measurement value and the second measurement value,

15 and

(ii) wherein at least one second input variable of the at least two input variables includes a measurement information on an analyte-induced change of the test material in at least part of the test field.

20 Embodiment 35: The test device according to the preceding embodiment, wherein the test device is adapted to perform the method according to one of the preceding method embodiments.

Embodiment 36: The test device according to one of the preceding embodiments referring to a test device, wherein the at least one first input variable includes an information on a gradient of
25 measurement values over at least part of the test field.

Embodiment 37: The test device according to the preceding embodiment, wherein the gradient is a gradient in the flow direction.

30 Embodiment 38: The test device according to one of the preceding embodiments referring to a test device, wherein

- the test device is adapted to measure the analyte-induced change of the measurable property in at least one third location of the test field, thereby generating at least one third measurement value,

35 - the third measurement value is used as the measurement information,

- the test field extends in the flow direction, and wherein

- the third location is located within the first 75% or the first half of the test field in view of the flow direction, preferably within the first third of the test field and more preferably within the first quarter of the test field.

- 5 Embodiment 39: The test device according to one of the preceding embodiments referring to a test device, wherein the evaluation unit comprises at least one data processing device, preferably at least one microcomputer.

10 Embodiment 40: The test device according to one of the preceding embodiments referring to a test device, wherein the test device is a hand-held test device.

15 Embodiment 41: The test device according to one of the preceding embodiments referring to a test device, wherein the test device further comprises at least one temperature sensor for determining an ambient temperature.

20 Embodiment 42: The test device according to one of the preceding embodiments referring to a test device, wherein the first measurement value and the second measurement value are selected from the group consisting of: an optical measurement value, preferably a remission; an electrical measurement value, preferably a current and/or a voltage.

25 Embodiment 43: The test device according to one of the preceding embodiments referring to a test device, wherein the test element is selected from an optical test element and an electrochemical test element.

30 Embodiment 44: The test device according to one of the preceding embodiments referring to a test device, wherein the detector includes
- at least one light source for illuminating at least one of the first location and the second location, and
- at least one optically sensitive element adapted to measure detection light from at least one of the first location and the second location.

35 Embodiment 45: The test device according to the preceding embodiment, wherein the detection light is selected from the group consisting of: light reflected by the test field in at least one of the first location and the second location, light transmitted by the test field in at least one of the first location and the second location, light emitted by the test field in at least one of the first location and the second location.

Embodiment 46: The test device according to one of the two preceding embodiments, wherein the optically sensitive element comprises at least one one-dimensional or two-dimensional matrix of optically sensitive elements, preferably at least one camera chip and more preferably at least one CCD chip.

5 Embodiment 47: The test device according to one of the preceding embodiments referring to a test device, wherein the detector is adapted to illuminate the at least one first location and the at least one second location by one of: light having the same wavelengths, light having different wavelengths.

10 Embodiment 48: A test system for detecting an analyte in a body fluid, the test system comprising

- a) at least one test device according to one of the preceding embodiments referring to a test device, and
- 15 b) at least one test element, wherein the test element has at least one test field having at least one test material adapted to change at least one measurable property in the presence of the analyte and having a capillary element adapted to guide the sample across the test field in a flow direction.

20 Embodiment 49: The test system according to the preceding embodiment, wherein the test element is selected from the group consisting of: a test strip, a test tape, a test disc.

Embodiment 50: The test system according to one of the preceding embodiments referring to a test system, wherein the test material comprises at least one enzyme adapted for performing at
25 least one enzymatic reaction in the presence of the analyte.

Embodiment 51: The test system according to the preceding embodiment, wherein the enzyme comprises at least one of glucose oxidase and glucose dehydrogenase.

30 Embodiment 52: The test system according to one of the preceding embodiments referring to a test system, wherein the test material is adapted to change at least one optical property in the presence of the analyte.

Embodiment 53: The test system according to the preceding embodiment, wherein the optical
35 property is selected from the group consisting of: a reflection property, preferably a reflectance and/or a remission; transmission property, preferably an absorption; a color; a luminescence, preferably a fluorescence.

Embodiment 54: The test system according to one of the preceding embodiments referring to a test system, wherein the body fluid is selected from the group consisting of: blood, plasma, urine and saliva.

5 Embodiment 55: The test system according to one of the preceding embodiments referring to a test system, wherein the analyte is a chemical compound with a molecular mass of less than 1000 u (1000 Da; 1.66×10^{-24} kg), more preferably selected from the group consisting of: glucose, lactate, cholesterol, and triglycerides.

10 Embodiment 56: The test system according to one of the preceding embodiments referring to a test system, wherein the test element is a test strip.

Embodiment 57: The test system according to one of the preceding embodiments referring to a test system, wherein the test field has a multilayer setup, the multilayer setup comprising at least
15 one detection layer having the at least one test material and further comprising at least one separation layer adapted for separating off at least one particulate component contained in the body fluid, wherein the separation layer is located between the detection layer and the capillary element.

20 Embodiment 58: The test system according to one of the preceding embodiments referring to a test system, wherein the capillary element comprises at least one capillary slit extending across at least a part of the test field.

Embodiment 59: The test system according to one of the preceding embodiments referring to a
25 test system, wherein the capillary slit is formed by a surface of the test field and a guide surface disposed at a distance above the surface of the test field.

Embodiment 60: The test system according to the preceding embodiment, wherein the guide
surface is formed by a surface of a cover plate being disposed above the surface of the test field.

30 Embodiment 61: The test system according to one of the three preceding embodiments, wherein the capillary slit has a width of 30 μm to 300 μm , preferably a width of 40 μm to 200 μm , more preferably a width of 50 μm to 100 μm , even more preferably 60 μm to 80 μm , and most preferably 70 μm .

35 Embodiment 62: The test system according to one of the preceding embodiments referring to a test system, wherein the test field is applied to a substrate on a surface of the substrate facing the

capillary element, wherein the substrate contains at least one detection window, wherein the test device is adapted to measure the measurable property through the detection window.

Embodiment 63: The test system according to one of the preceding embodiments referring to a test system, wherein the capillary element comprises at least one application opening, wherein the capillary element is adapted to guide the body fluid from the application opening to the test field.

Embodiment 64: The test system according to the preceding embodiment, wherein the capillary element is adapted to guide the body fluid by capillary forces.

Embodiment 65: The test system according to one of the two preceding embodiments, wherein the application opening is located at a front face of the test element.

Embodiment 66: A use of a difference of at least two measurement values measured in at least two different locations of a test field of a test element for generating a corrected value of an analyte concentration in a sample of a body fluid, wherein the sample of the body fluid is guided across the test field by a capillary element in a flow direction, wherein the at least two different locations are offset in the flow direction.

Embodiment 67: The use according to the preceding embodiment, wherein the corrected value is dependent on the concentration of a particulate component in the body fluid, preferably a hematocrit.

All references cited in this specification are herewith incorporated by reference with respect to their entire disclosure content and the disclosure content specifically mentioned in this specification. The following Examples shall merely illustrate the invention. They shall not be construed, whatsoever, to limit the scope of the invention.

Short description of the Figures

Further optional features and embodiments of the invention will be disclosed in more detail in the subsequent description of preferred embodiments, preferably in conjunction with the dependent claims. Therein, the respective optional features may be realized in an isolated fashion as well as in any arbitrary feasible combination, as the skilled person will realize. The scope of the invention is not restricted by the preferred embodiments. The embodiments are schematically depicted in the Figures. Therein, identical reference numbers in these Figures refer to identical or functionally comparable elements.

In the Figures:

- 5 Figure 1 shows a cross-sectional view of an exemplary embodiment of a test system and a test device according to the present invention;
- Figure 2 shows a schematic cross-sectional view of a test element for use in the test system according to Figure 1;
- 10 Figures 3A-D show different embodiments of detector setups for measuring remission values in at least two different locations of a test field;
- 15 Figure 4 shows a schematic view of an image of a test field taken by a camera, wherein two different areas of the image are chosen for generating remission values in at least two different locations of the test field;
- 20 Figure 5 shows an exemplary embodiment of sub-dividing the test field into different locations along a flow path of a sample; left: embodiment of a test element; right: sub-division of the test element into 10 equally sized measurement locations; flow direction 146 along the test field is indicated.
- 25 Figure 6 shows the measured relative signal intensity (I_{rel}) along the test field for various hematocrit (HK) values at a glucose concentration of 200 mg/ml. % values in the labels of the abscissa relate to the percentage of the total length of the test field in flow direction spanned by a respective measurement location.
- 30 Figure 7 shows the dependence of the measurable intensity difference (ΔI) between sub-window 10 and subwindow 2 as shown in Fig. 5 on glucose concentration at two different hematocrit values.
- 35 Figure 8 shows dependence of the deviation of the glucose concentration as determined from a calibration curve from the actual glucose concentration (mean bias mb, vertical axis) on the position of the measurement location (f1 to f10, f4/5 being the mean value of f4 and f5) and on the hematocrit (HCT) of the sample. Subwindows closer to the beginning of the test field show less hematocrit dependence. The calibration curve was obtained at a hematocrit of 42%.

Figure 9 shows dependence of the actual glucose concentration (c) in a blood sample on the linearized remission (R) measured at measurement location subwindow 8 and the remission difference between the two measurement locations subwindow 10 and subwindow 8 (ΔR) using SCV chemistry. By determining said parameters at several glucose concentrations and at several hematocrit values, a code surface instead of a code curve is obtained. To obtain a linearized remission, remission was at first linearized using the standard curve at a hematocrit of 42%.

Figure 10 shows dependence of the actual glucose concentration (c) in a blood sample on the linearized remission measured at measurement location subwindow 8 (R) and the difference between the two measurement locations subwindow 10 and subwindow 8 (ΔR) using cNAD chemistry. By determining said parameters at several glucose concentrations and at several hematocrit values, a code surface instead of a code curve is obtained. Linearized remission was obtained as described for Fig. 9.

Figure 11 shows the mean deviation of the determined glucose concentration from the actual glucose concentration (mean bias, mb, vertical axis) in samples having various hematocrit (HCT) values (horizontal axis) as determined by a calibration curve (black bars) or as determined by a calibration area as shown in Fig. 10 (white bars). Remission difference was calculated from values measured in subwindows 8 and 10.

Figure 12 shows the mean deviation of the determined glucose concentration from the actual glucose concentration (mean bias, mb, vertical axis) in samples having various hematocrit values (HCT, horizontal axis) as determined by a calibration curve (black bars) or as determined by a calibration area as shown in Fig. 10 (white bars). Remission difference was calculated from values measured in subwindows 4 and 10.

Figure 13 shows mean deviation of the determined glucose concentration from the actual glucose concentration (mean bias, mb, vertical axis) in samples having various hematocrit values (HCT, horizontal axis) as determined by a calibration curve (black bars) or as determined by a calibration area as shown in Fig. 10 (white bars). Remission difference was calculated from values measured in subwindows 2 and 4.

Figure 14 shows the mean deviation of the determined glucose concentration from the actual glucose concentration (mean bias, mb, vertical axis) in samples having various hematocrit values (HCT, horizontal axis) as determined by a calibration curve (black bars) or as determined by a calibration area as shown in Fig. 9 (white bars).
Remission difference was calculated from values measured in subwindows 2 and 9.

Figure 15 shows dependence of the actual glucose concentration (c) in a blood sample on the remission measured at measurement location subwindow 2 (R) and the difference between the two measurement locations subwindow 9 and subwindow 2 (ΔR) using cNAD chemistry. By determining said parameters at several glucose concentrations and at several hematocrit values, a code surface instead of a code curve is obtained.

Detailed description of the embodiments

In Figure 1, a cross-sectional view of an embodiment of a test device 112 and a test system 114 according to the present invention is depicted. The test device 112, preferably, is embodied as a hand-held device. The test device 112 preferably comprises a casing 116, which may have a volume of less than 1000 cm³, preferably of less than 500 cm³, in order to be carried by a person. The test device 112 comprises a receptacle 118 for receiving a test element 120, which, besides the test device 112, forms a component of the test system 114. The receptacle is adapted to locate the test element 120 in at least one application position in which a sample 122 of the body fluid is applicable to the test element 120, such as to an application opening 124 of a capillary element 126, which will be explained in further detail below. The test element 120 comprises at least one test field 128 having at least one test material 130 adapted to change at least one measurable property in the presence of an analyte to be detected by the test system 114, such as glucose.

The test device 112 further comprises a detector 132 which, in this specific embodiment, comprises at least one light source 134 for illuminating the test field 128 and at least one optically sensitive element 136 adapted to measure detection light emitted and/or transmitted and/or reflected from the test field 128.

The test device 112 further comprises at least one evaluation unit 138 which is adapted to determine the concentration of the analyte by using the evaluation algorithm as disclosed above or as disclosed in further detail below. The evaluation unit 138 preferably may be or may comprise at least one data processing device, such as at least one computer and/or at least one application-

specific integrated circuit. As an example, the evaluation unit 138 may comprise a microcomputer. Further, the evaluation unit 138 may comprise one or more further elements, such as at least one data storage device and/or other components.

5 The evaluation unit 138 is unidirectionally or bidirectionally connected to the detector 132, such as for receiving measurement values from the detector 132. Further, the evaluation unit 138 may be adapted to control the overall functionality of the test device 112, such as for controlling the measurement process performed by the detector 132.

10 The test device 112 may further comprise one or more human-machine-interfaces, such as at least one display 140 and/or at least one control element 142, such as at least one push button. The elements 140, 142 may also be connected to the evaluation unit 138.

The test device 112 may further comprise one or more additional sensors for detecting one or
15 more ambient parameters, such as one or more temperature sensors 145 adapted for determining an ambient temperature. As outlined above, these one or more ambient parameters may be used by the evaluation unit 138 for choosing an appropriate algorithm.

The test device 112 may further comprise at least one electronic interface 144, for unidirectional
20 and/or bidirectional exchange of data and/or commands with one or more external devices, such as a wireless and/or a wire-based interface.

In Figure 2, a cross-sectional view of an exemplary embodiment of a test element 120 is depicted. In this exemplary embodiment, the test element 120 is designed as a test strip. However,
25 additionally or alternatively, other types of test elements 120 may be used, such as test tapes and/or test discs.

The test element 120, as outlined above, comprises at least one test field 128 and at least one capillary element 126. The capillary element 126 is adapted to guide the sample 122 of the body
30 fluid across the test field 128 in a flow direction 146. Thus, the capillary element 126 may suck the sample 122 over the test field 128 by capillary forces. For improving the capillary forces, the test element 120 may further comprise one or more venting openings 128.

The test field 128 comprises at least one detection layer 150 comprising the at least one test material 130. The test field 128 may further comprise one or more additional layers, such as at least
35 one separation layer 152 covering the detection layer 150 on the side facing the capillary element 126. The separation layer 152 may comprise one or more pigments, preferably inorganic pigments, such as an inorganic oxide, which may provide a wide optical background for optical

measurement. Further, the separation layer 152 may be adapted for separating off at least one particular component contained in the body fluid.

The test element 120 comprises at least one detection window in a substrate 156, through which a change of optical properties in the test field 128 may be detected by using the detector 132. It shall be noted that, in the embodiment depicted in Figure 2, an optical test element 120 is depicted, in which the test material 130 is adapted to change at least one optical property in the presence of the analyte to be detected. Additionally or alternatively, other types of test elements 120 may be used, such as electrochemical test elements 120, in which the at least one test material 130 is adapted to change at least one electrochemical property in the presence of the analyte to be detected. In the latter case, the test field 128 may comprise one or more electrodes adapted for providing appropriate voltage signals and/or current signals which may be used for generating appropriate measurement values.

In Figures 3A to 3D, four different potential setups of the detector 132 of the test device 112 according to Figure 1 are depicted. According to the present invention, the detector is adapted for measuring at least one optical property, such as at least one remission characteristics, of the test field 128 in at least two different locations of the test field 128. In Figures 3A to 3D, symbolically, a first location is denoted by reference number 158, and a second location symbolically is denoted by reference number 160. The locations 158, 160 are offset in the direction of the flow direction 146, which is also symbolically depicted in Figure 3C.

For measuring the optical property of the test field 128 in the first location 158 and the second location 160, various techniques are feasible. Thus, in Figure 3A, a setup is depicted in which the detector 132 comprises a first light source 162 and a second light source 164, wherein the first light source 162 illuminates the first location 158, and wherein the second light source 164 is adapted to illuminate the second location 160. The first and second light sources 162, 164 may, as an example, comprise one or more light-emitting devices such as one or more light-emitting diodes. Other types of light sources are feasible. The first and second light sources 162, 164 may be adapted to illuminate the first and second locations, respectively, with light having the same wavelengths and/or light having different wavelengths. Thus, the optical properties of light emitted by the first and second light sources 162, 164 may be identical or may differ. Further, optionally, the first and second light sources 162, 164 may emit light at the same time or may emit light at different points in time, such as by using an intermitting timing schedule.

The detector 132 further may comprise a first optically sensitive element, which is adapted to detect light emitted by the first light source 162 and reflected and/or transmitted by the test field 128 in the first location 158 and at least one second optically sensitive element 168, adapted to

detect light emitted by the second light source 164 and reflected and/or transmitted by the test field 128 in the second location 160. It shall be noted that, preferably, the optically sensitive elements 166, 168 are adapted to receive light scattered in the first and second locations 158, 160, respectively, such as by measuring a remission value in these locations 158, 160. Other measurement setups are possible in addition or alternatively. Thus, transmission light may be detected and/or the light sources 162, 164 may be adapted to stimulate an emission of light in the test field 128, such as fluorescence and/or phosphorescence.

In Figure 3B, a modification of the setup of Figure 3A is depicted, in which only one light source 134 is used for illuminating the at least one first location 158 and the at least one second location 160. Still, first and second optically sensitive elements 166, 168 are used for detecting light from the first location 158 and the second location 160, respectively. As in Figure 3A, the optically sensitive elements 166, 168 may be or may comprise an arbitrary type of optically sensitive element, such as a photodiode. Additionally or alternatively, a camera may be used, as will be explained in further detail below. Other embodiments are possible.

In Figure 3C, a further modification of the setup shown in Figure 3A is depicted. In this setup, only one light source 134 and only one optically sensitive element 136 is used for detecting light from the first and second locations 158, 160. Various measurement setups for fulfilling this purpose are feasible. Thus, an optical switch may be provided in order to subsequently illuminate the first and second locations 158, 160 at different points in time by using the same light source 134. Thereby, by using an intermitting timing scheme, light detected by the optically sensitive element 136 at a specific point in time may be allocated to one of the first and second positions 158, 160. Additionally or alternatively, the optically sensitive element 136 may be adapted to spatially resolve the detected light, in order to spatially distinguish between light from the first location 158 and light from the second location 160. Thus, as outlined above and as outlined in further detail below, the optically sensitive element 136 may be or may comprise a camera and/or a camera chip, such as a CCD chip.

In Figure 3D, a further modification of the setup shown in Figure 3A is depicted. In this setup, two light sources 134 and only one optically sensitive element 136 is used for detecting light from the first and second locations 158, 160. Various measurement setups for fulfilling this purpose are feasible. The light sources may be triggered subsequently to illuminate the first and second locations 158, 160 at different points in time. Thereby, by using an intermitting timing scheme, light detected by the optically sensitive element 136 at a specific point in time may be allocated to one of the first and second positions 158, 160. Additionally or alternatively, the optically sensitive element 136 may be adapted to spatially resolve the detected light, in order to spatially distinguish between light from the first location 158 and light from the second location

160. Thus, as outlined above and as outlined in further detail below, the optically sensitive element 136 may be or may comprise a camera and/or a camera chip, such as a CCD chip.

An embodiment of Fig. 3C or D is schematically depicted in Figure 4. In this embodiment, an image 170 of the test field 128 captured at a specific point in time is shown, wherein, again, reference number 146 schematically shows the flow direction of the body fluid 122 in the image 170. In the image 170, a first area 172 is marked, which corresponds to pixels of the image representing the first location 158, and a second area 174 is marked, which may contain pixels of the image 170 corresponding to the second location 160.

In Figure 5, a different way of sub-dividing the test field 128 is shown. Therein, an image 170 of the test field 128 is sub-divided into ten different areas, numbered by 1 to 10 in Figure 5. An arbitrary one of the areas 1 to 10 in Figure 5 may be chosen as the first location 158 and/or as the first area 172. Further, a combination of areas may be used for the first location 158 and/or the first area 172. Similarly, an arbitrary area of the areas 1 to 10 or a combination of areas of the areas 1 to 10 of Figure 5 may be chosen as the second location 160 and/or the second area 174, as long as the second area is offset from the first area in the flow direction 146.

In the following, several measurements will be shown for demonstrating that optical measurement values taken in the first location 158 and the second location 160 and differences between these measurement values may be used for correcting the analyte concentration for a hematocrit of the body fluid. Therein, different types of test materials 130 were used. Generally, with regard to test materials 130 usable for the present invention, reference may be made to the prior art documents listed above. Further, reference may be made to J. Hoenes et al.: The Technology Behind Glucose Meters: Test Strips, Diabetes Technology & Therapeutics, vol. 10, Supplement 1, 2008, S-10 to S-26. Additionally or alternatively, other types of test materials 130 may be used. Thus, in the following, reference will be made to the following types of test material:

Firstly, a test material was used which also is referred to as "SCV chemistry". This SCV test chemistry is disclosed e.g. in EP 0 354 441 A2 and may contain a PQQ-dependent dehydrogenase and a direct electron acceptor which may be an aromatic nitroso compound or an oxim. Further, one or more indicators may be present, such as one or more dyes. Thus, as an example, heteropoly blue indicator may be used, as disclosed in EP 0 431 456 A1.

As a second type of test material 130, also referred to as "cNAD chemistry", the test material as disclosed in WO 2007/012494 A1, WO 2009/103540 A1, WO 2011/012269 A2, WO 2011/012270 A1 and WO 2011/012271 A2 is disclosed. Thus, in WO 2007/012494 A1, cNAD derivatives are disclosed. In WO 2009/103540 A1, stabilized enzyme/coenzyme complexes are

disclosed. In WO 2011/012269 A2, WO 2011/012270 A1 and WO 2011/012271 A2, the synthesis of cNAD and cNAD/derivatives as well as intermediates/precursors is disclosed.

5 Measurements were performed at 10 glucose concentrations: 0mg/dl, 25mg/dl, 50mg/dl, 75mg/dl, 100mg/dl, 150mg/dl, 250mg/dl, 350mg/dl, 450mg/dl, 550mg/dl, and at 5 hematocrit values for every glucose concentration: 20%, 30%, 42%, 50%, 60%; Measurements were repeated 10 times, using a test field of 2.07 mm length in flow direction, and a width of 1.76 mm.

10 Measurements represented in Figs. 6-9, 11-13, and 15 were performed using the cNAD-chemistry; measurements represented in Fig. 10 and 14 were performed using the SCV chemistry.

List of reference numbers

112	test device
114	test system
116	casing
118	receptacle
120	test element
122	sample
124	application opening
126	capillary element
128	test field
130	test material
132	detector
134	light source
136	optically sensitive element
138	evaluation unit
140	display
142	control element
144	interface
145	temperature sensor
146	flow direction
148	venting opening
150	detection layer
152	separation layer
154	detection window
156	substrate
158	first location
160	second location
162	first light source
164	second light source
166	first optically sensitive element
168	second optically sensitive element
170	image
172	first area
174	second area

Claims

1. A method for detecting an analyte in a body fluid, the method having the following steps:
 - a) applying a sample (122) of the body fluid to a test element (120), said test element (120) comprising at least
 - (i) a test field (128) comprising at least one test material (130) adapted to change at least one measurable property in the presence of the analyte,
 - (ii) a capillary element (126) adapted to guide the sample (122) across said test field (128) in a flow direction (146),
 - (iii) a first and a second measurement location (158, 160) within said test field (128), wherein the second measurement location (160) is offset from the first measurement location (158) in the flow direction (146);
 - b) measuring the measurable property in said at least one first measurement location (158), thereby generating at least one first measurement value;
 - c) measuring the measurable property in said at least one second measurement location (160), thereby generating at least one second measurement value;
 - d) detecting the analyte by using an evaluation algorithm having at least two input variables, wherein
 - (i) at least one first input variable of the at least two input variables includes an information on a difference between the first measurement value and the second measurement value, and
 - (ii) at least one second input variable of the at least two input variables includes a measurement information on an analyte-induced change of the measurable property of the test material (130) in at least part of the test field (128).
2. The method according to the preceding claim, wherein the measurement information on an analyte-induced change of the measurable property of the test material (130) in at least part of the test field (128) is generated by one or more of the following procedures:
 - the first measurement value is used as the measurement information;
 - the second measurement value is used as the measurement information;
 - an average value of the first measurement value and the second measurement value is used as the measurement information;

- an analyte-induced change of the measurable property is measured in at least one third measurement location of the test field (128), thereby generating at least one third measurement value, wherein the third measurement value is used as the measurement information.

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3. The method according to one of the preceding claims, wherein the measurement information used in step d) (ii) is a measurement value generated at a measurement location located within the first half of the test field (128) in view of the flow direction (146).

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4. The method according to one of the preceding claims, wherein method steps b) and c) are performed at one of:

- a predetermined time span after application of the sample (122) of the body fluid to the test element (120); and

15

- at a point in time at which a measurement curve indicating the measurable property as a function of time fulfills at least one predetermined condition, preferably at least one threshold condition and more preferably wherein a slope of the measurement curve is below or above a predetermined threshold.

20

5. The method according to one of the preceding claims, wherein

- the evaluation algorithm comprises a one-step evaluation algorithm, and
- the first input variable and the second input variable are simultaneously used for deriving the concentration of the analyte in the body fluid by using at least one predetermined calibration curve, the predetermined calibration curve indicating the concentration of the analyte as a function of the two input variables.

25

6. The method according to one of the preceding claims, wherein

- the evaluation algorithm comprises at least two separate steps,
- in a first step of the algorithm, an estimate value of the concentration is derived from the second input variable by using at least one predetermined first calibration curve, the predetermined first calibration curve indicating an uncorrected concentration of the analyte as a function of the second input variable, and
- in a second step of the algorithm, the estimate value of the concentration is corrected by applying at least one correction algorithm to the estimate value, the correction algorithm providing a correction to the estimate value by using the first input variable.

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35

7. The method according to the preceding claim, wherein

- the sample (122) of the body fluid is blood,
- in the first step of the algorithm, an estimate value of a glucose concentration is generated, and
- 5 - in the second step of the algorithm, a correction of the estimate value for an actual hematocrit of the blood is provided, thereby generating an information on the glucose concentration in the blood without determining the actual hematocrit of the blood.

10 8. A method for detecting an analyte in a body fluid, the method having the following steps:

a) applying a sample (122) of the body fluid to a test element (120), said test element (120) comprising at least

15 (i) a test field (128) having at least one test material (130) adapted to change at least one measurable property in the presence of the analyte,

(ii) a capillary element (126) adapted to guide the sample (122) across said test field (128) in a flow direction (146),

(iii) at least one single measurement location (158) within said test field (128);

20 b) measuring the measurable property in said single measurement location (158), thereby generating at least one measurement value;

c) detecting the analyte by using an evaluation algorithm having the measurable property as an input variable,

wherein said single measurement location is located within the first third of the test field (128) as determined from the application site.

25

9. A test device (112) for detecting an analyte in a body fluid, wherein the test device (112) contains

a) at least one receptacle (118) for receiving at least one test element (120), the test element (120) having

30 (i) at least one test field (128) having at least one test material (130) adapted to change at least one measurable property in the presence of the analyte and

(ii) at least one capillary element (126) adapted to guide the sample (122) across the test field (128) in a flow direction (146),

35 b) wherein the receptacle (118) is adapted to locate the test element (120) in at least one application position in which a sample (122) of the body fluid is applicable to the test element (120),

- c) wherein the device further contains at least one detector (132) for measuring the measurable property, wherein the detector (132) is adapted to measure the measurable property
- (i) in at least one first location (158) of the test field (128), thereby generating at least one first measurement value,
- (ii) in at least one second location (160) of the test field (128), thereby generating at least one second measurement value, wherein the second location (160) is offset from the first location (158) in the flow direction (146),
- d) wherein the test device (112) further comprises at least one evaluation unit (138) adapted to determine the concentration of the analyte by using an evaluation algorithm having at least two input variables,
- (i) wherein at least one first input variable of the at least two input variables includes an information on a difference between the first measurement value and the second measurement value, and
- (ii) wherein at least one second input variable of the at least two input variables includes a measurement information on an analyte-induced change of the test material (130) in at least part of the test field (128).
10. The test device (112) according to the preceding claim, wherein the test device (112) is adapted to perform the method according to one of the preceding method claims.
11. The test device (112) according to one of the preceding claims referring to a test device (112), wherein the at least one first input variable includes an information on a gradient of measurement values over at least part of the test field (128).
12. The test device (112) according to one of the preceding claims referring to a test device (112), wherein
- the test device (112) is adapted to measure the analyte-induced change of the measurable property in at least one third location of the test field (128), thereby generating at least one third measurement value,
 - the third measurement value is used as the measurement information,
 - the test field (128) extends in the flow direction (146), and wherein
 - the third location is located within the first 99% of the test field (128) in view of the flow direction (146), preferably within the first third of the test field (128) and more preferably within the first quarter of the test field (128).

13. The test device (112) according to one of the preceding claims referring to a test device (112), wherein the test device (112) further comprises at least one temperature sensor (145) for determining an ambient temperature.

5 14. A test device (112) for detecting an analyte in a body fluid, wherein the test device (112) contains

e) at least one receptacle (118) for receiving at least one test element (120), the test element (120) having

(iii) at least one test field (128) having at least one test material (130) adapted to change at least one measurable property in the presence of the analyte and

10 (iv) at least one capillary element (126) adapted to guide the sample (122) across the test field (128) in a flow direction (146),

f) wherein the receptacle (118) is adapted to locate the test element (120) in at least one application position in which a sample (122) of the body fluid is applicable to the test element (120),

15 g) wherein the device further contains at least one detector (132) for measuring the measurable property, wherein the detector (132) is adapted to measure the measurable property in at least one single measurement location (158) of the test field (128), thereby generating at least one measurement value,

20 h) wherein the test device (112) further comprises at least one evaluation unit (138) adapted to determine the concentration of the analyte by using an evaluation algorithm having at least said measurement value as an input variable,

wherein the detector is adapted to measure the measurable property within the first third of the test field.

25 15. A test system (114) for detecting an analyte in a body fluid, the test system comprising

a) at least one test device (112) according to one of the preceding claims referring to a test device (112), and

30 b) at least one test element (120), wherein the test element (120) has at least one test field (128) having at least one test material (130) adapted to change at least one measurable property in the presence of the analyte and having a capillary element (126) adapted to guide the sample (122) across the test field (128) in a flow direction (146).

35 16. A use of a difference of at least two measurement values measured in at least two different locations (158, 160) of a test field (128) of a test element (120) for generat-

ing a corrected value of an analyte concentration in a sample (122) of a body fluid, wherein the sample (122) of the body fluid is guided across the test field (128) by a capillary element (126) in a flow direction (146), wherein the at least two different locations (158, 160) are offset in the flow direction (146).

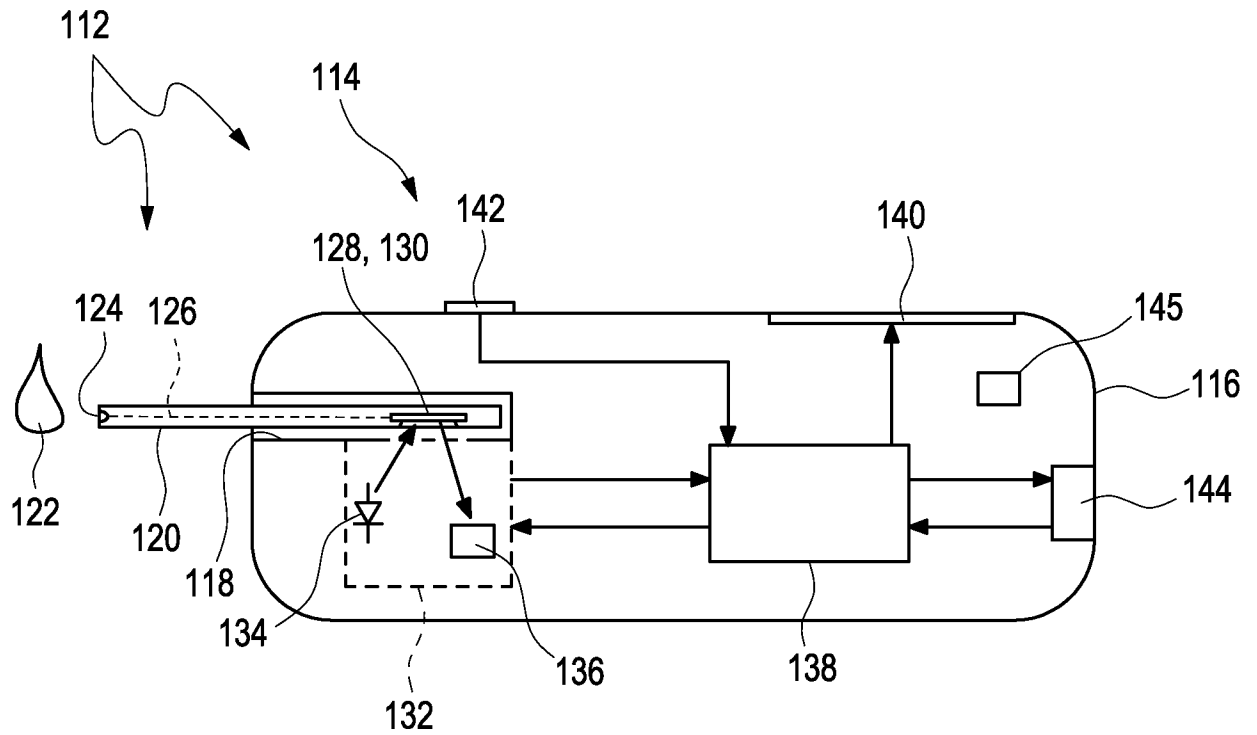


Fig. 1

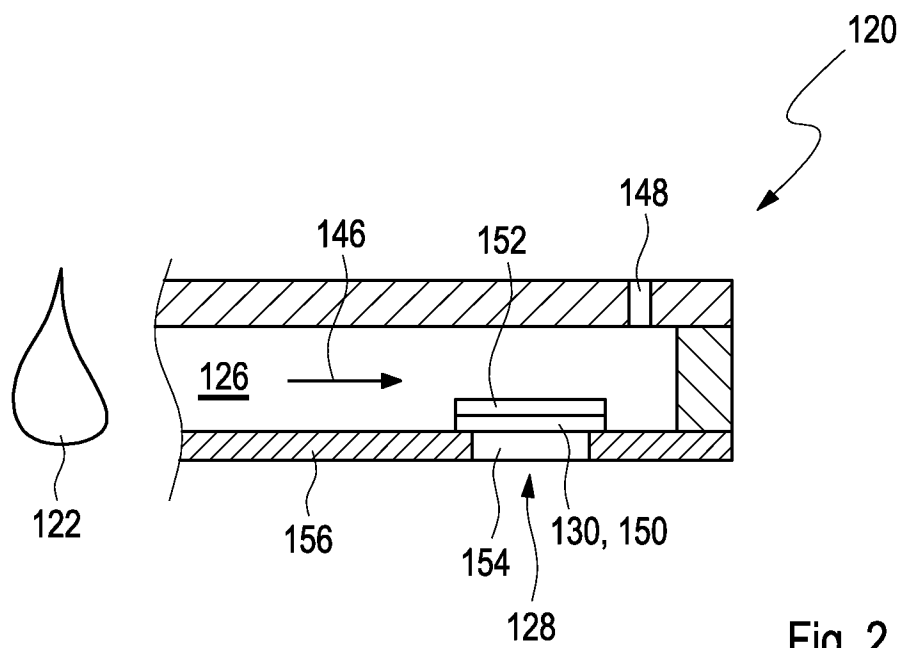


Fig. 2

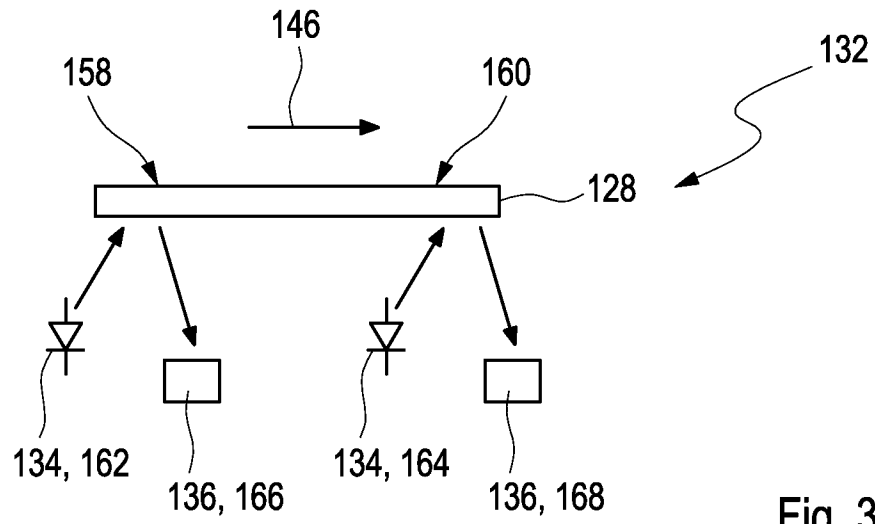


Fig. 3 A

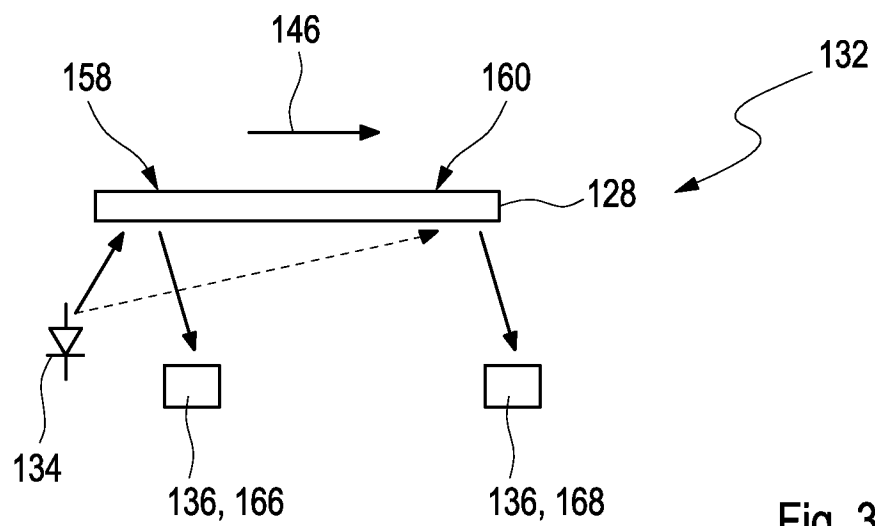


Fig. 3 B

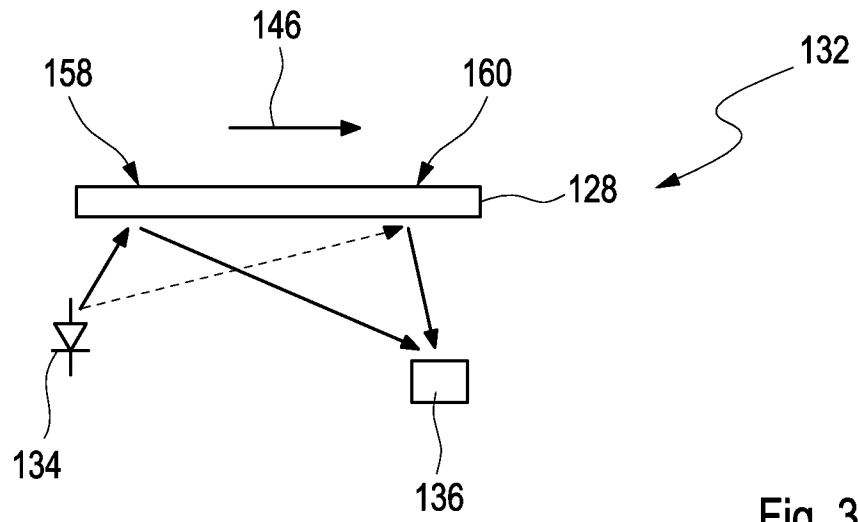


Fig. 3 C

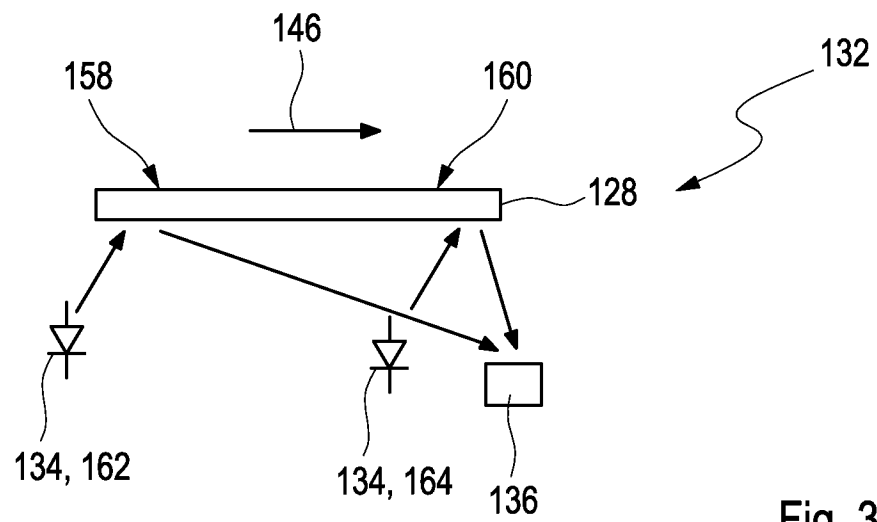


Fig. 3 D

4/14

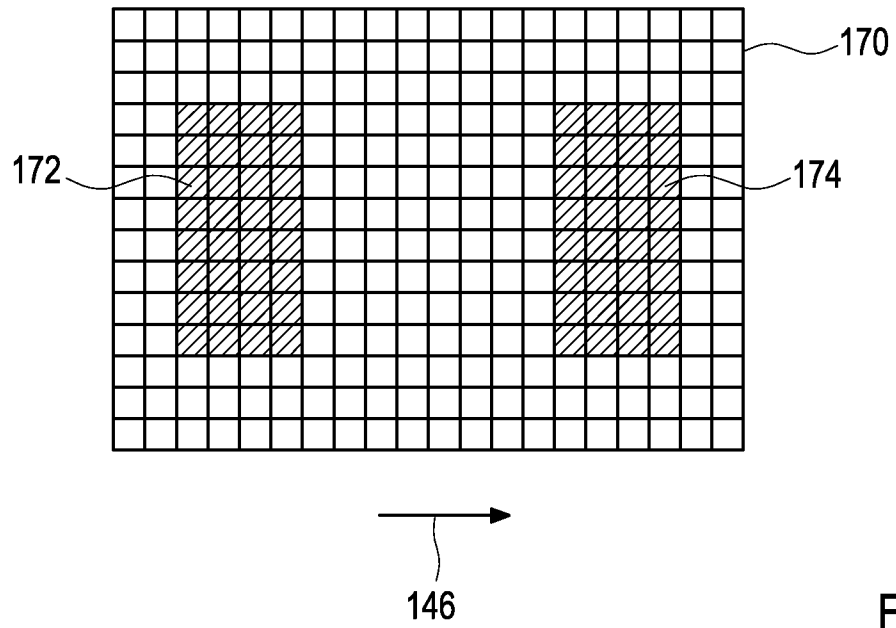


Fig. 4

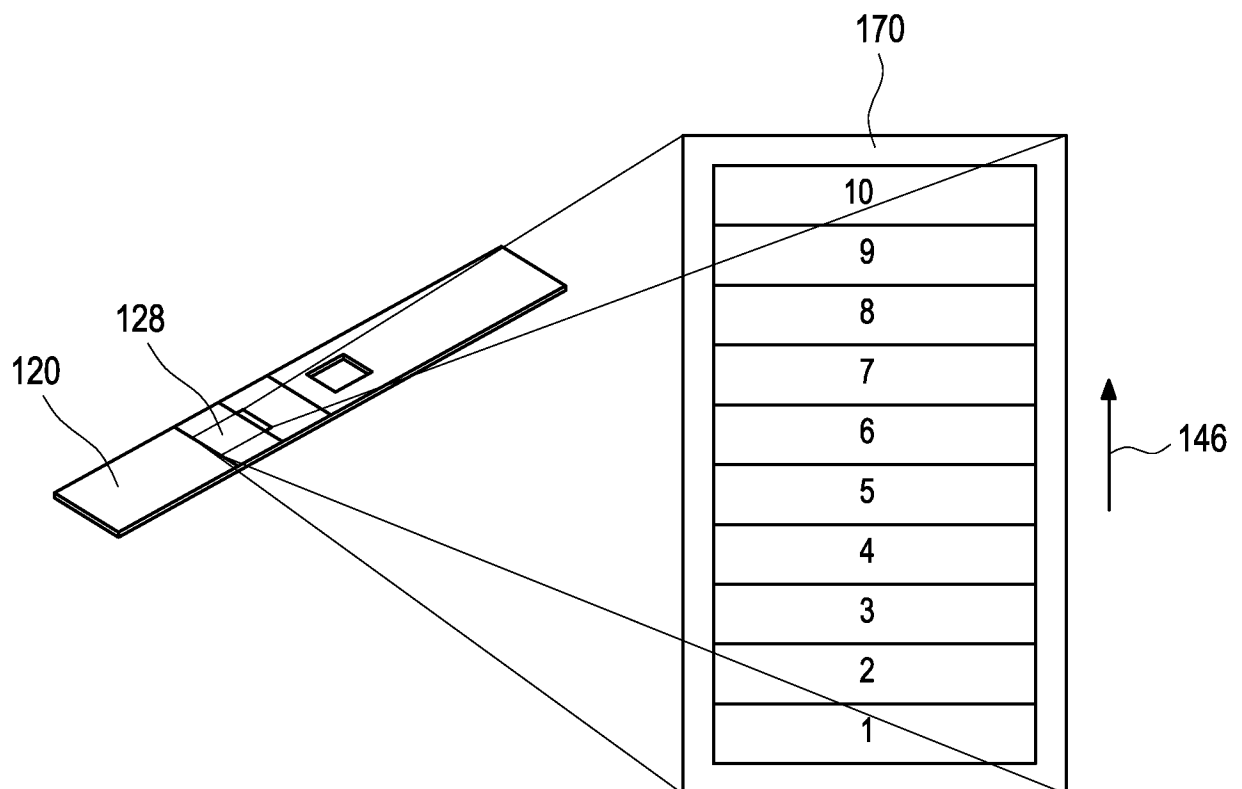


Fig. 5

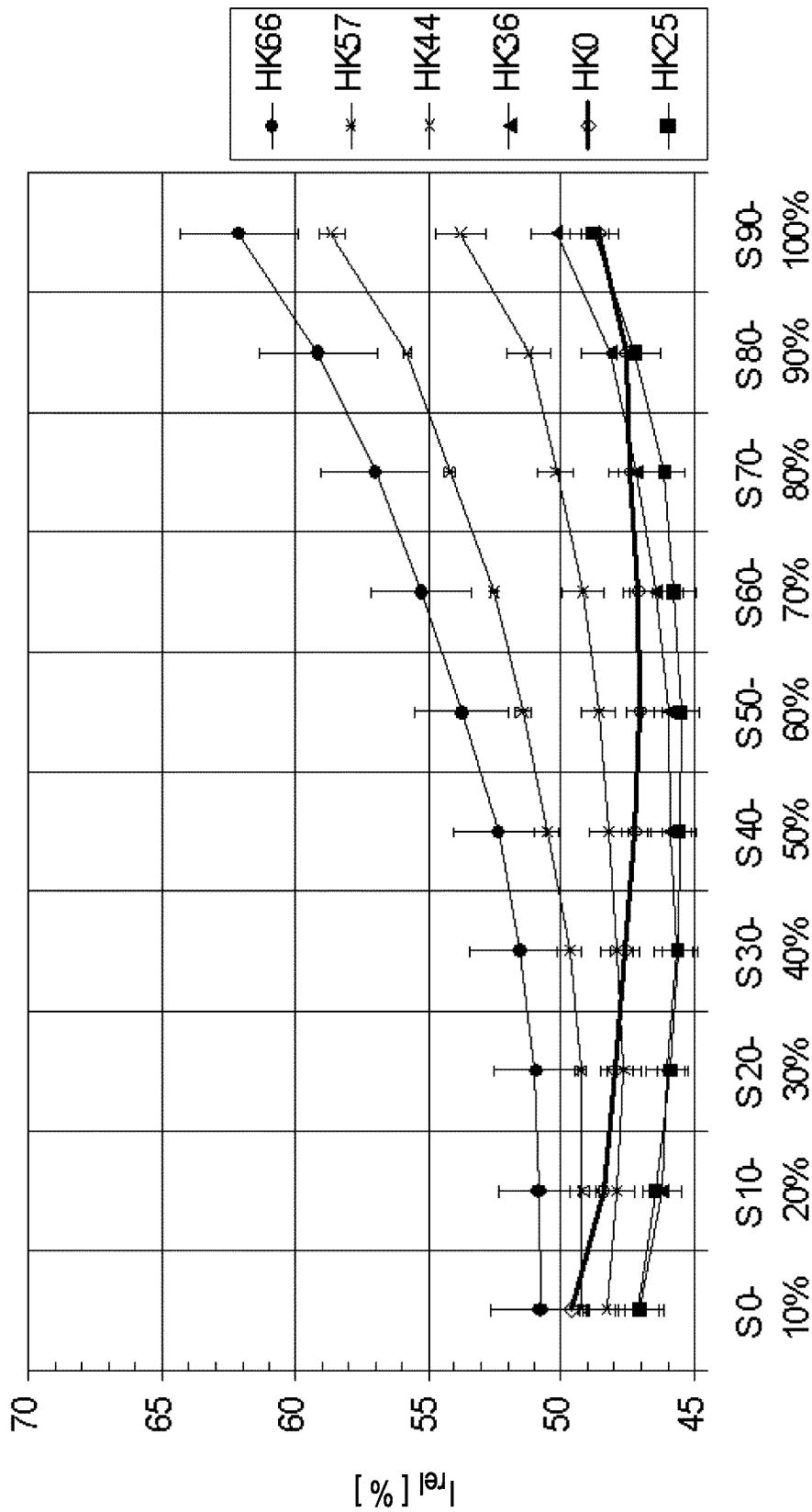


Fig. 6

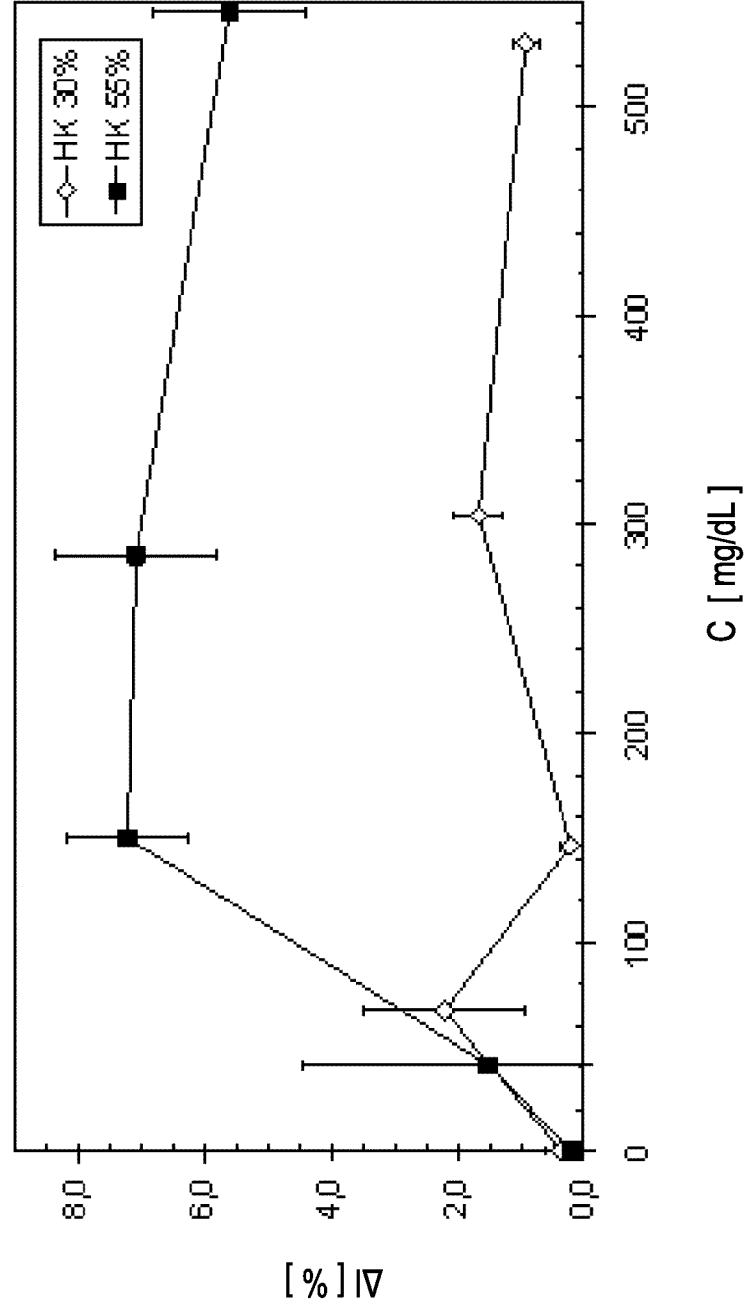


Fig. 7

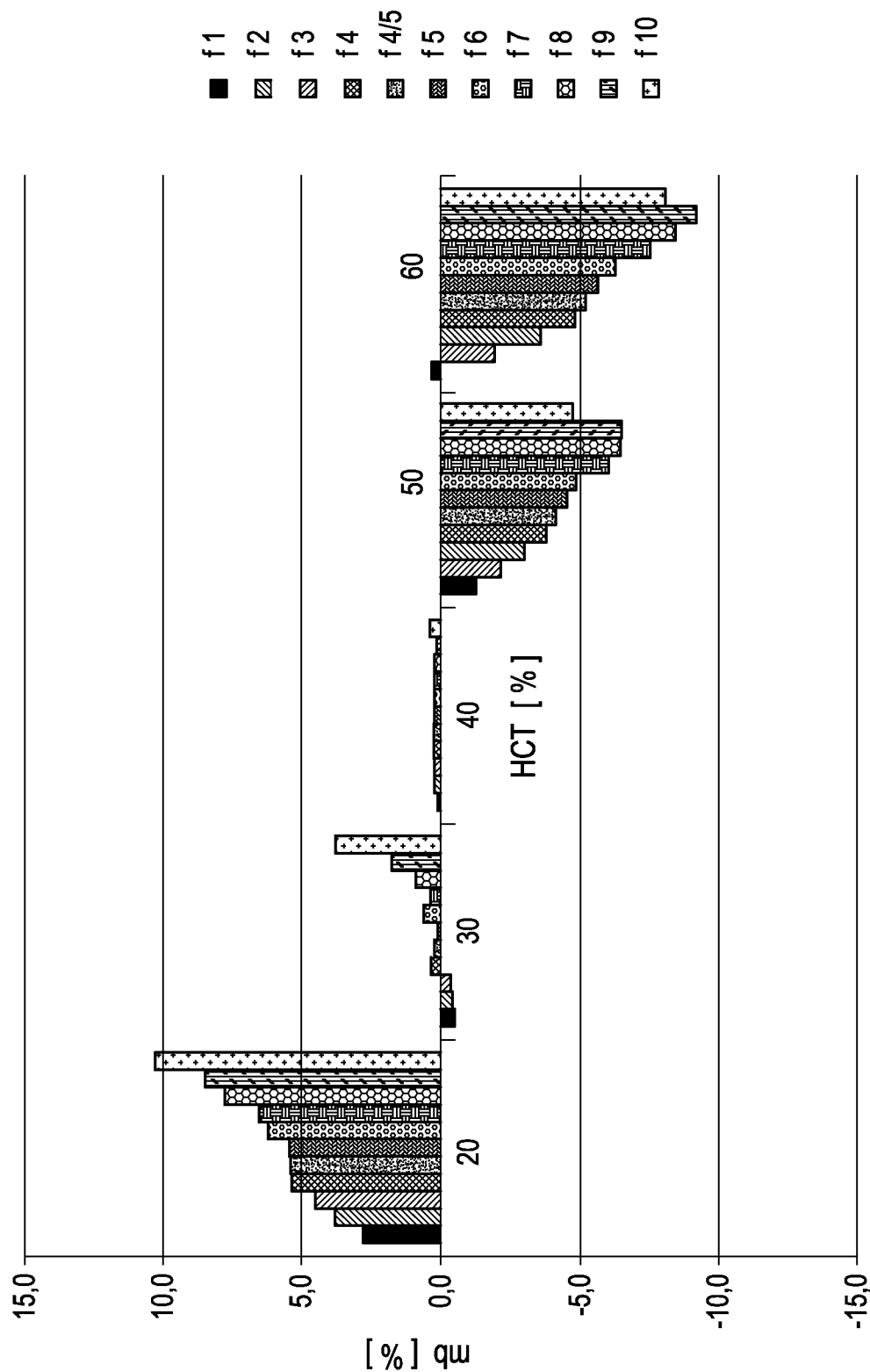


Fig. 8

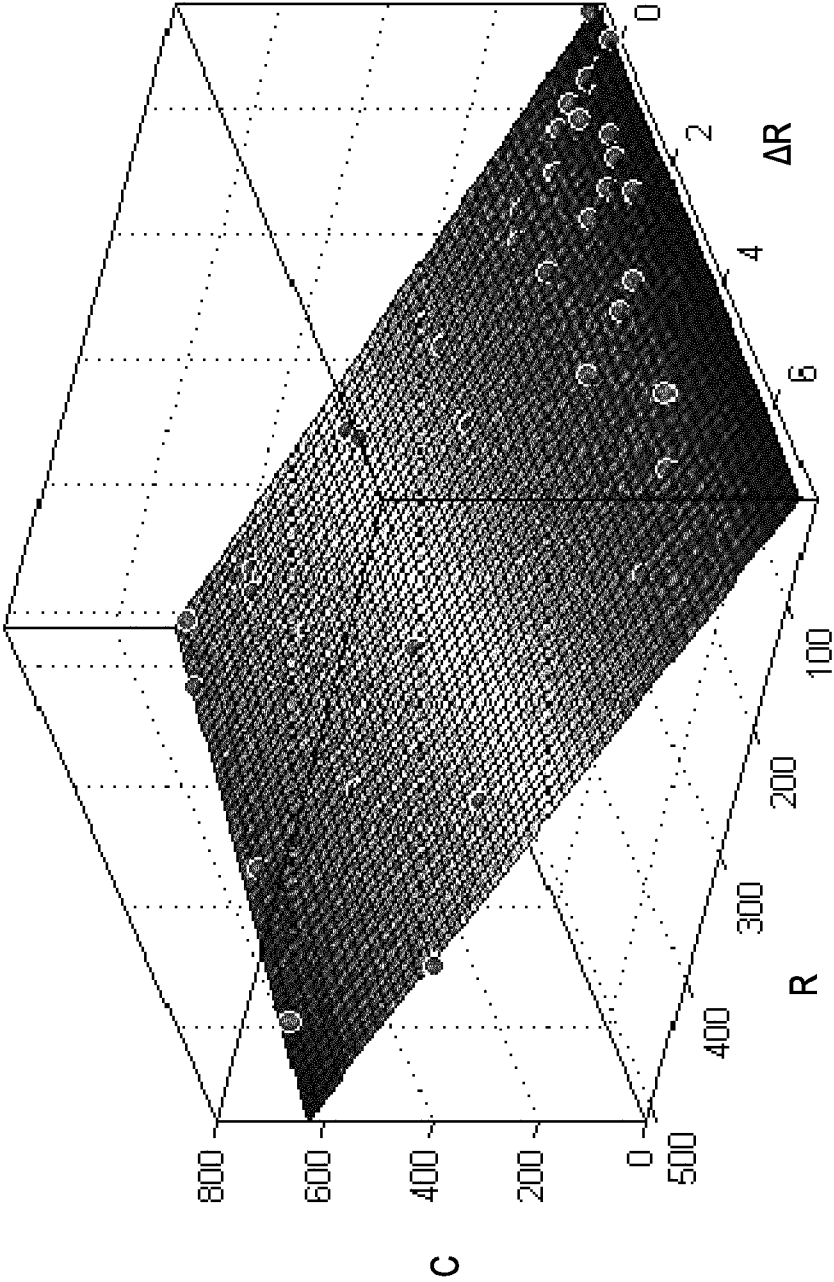


Fig. 9

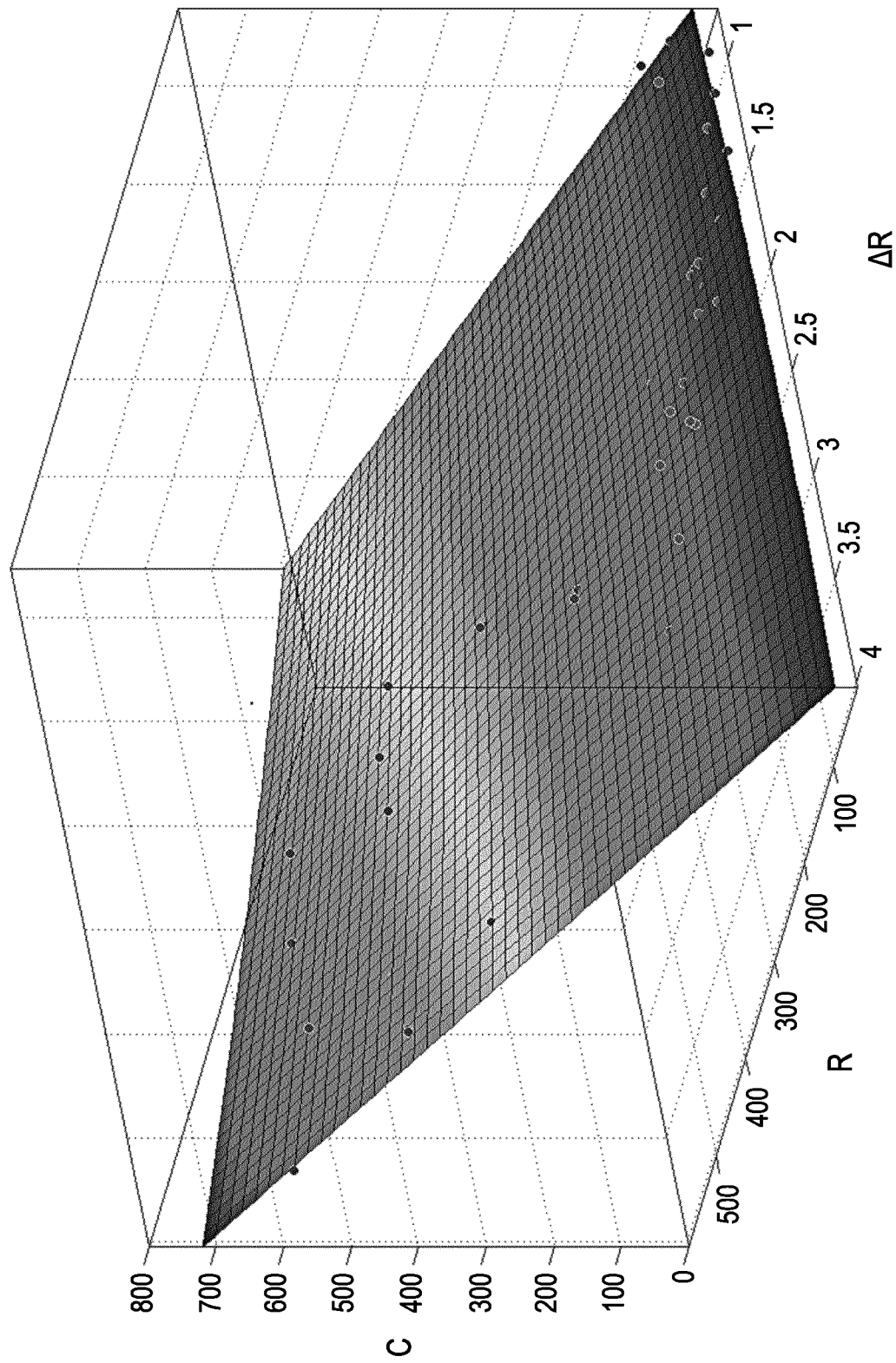


Fig. 10

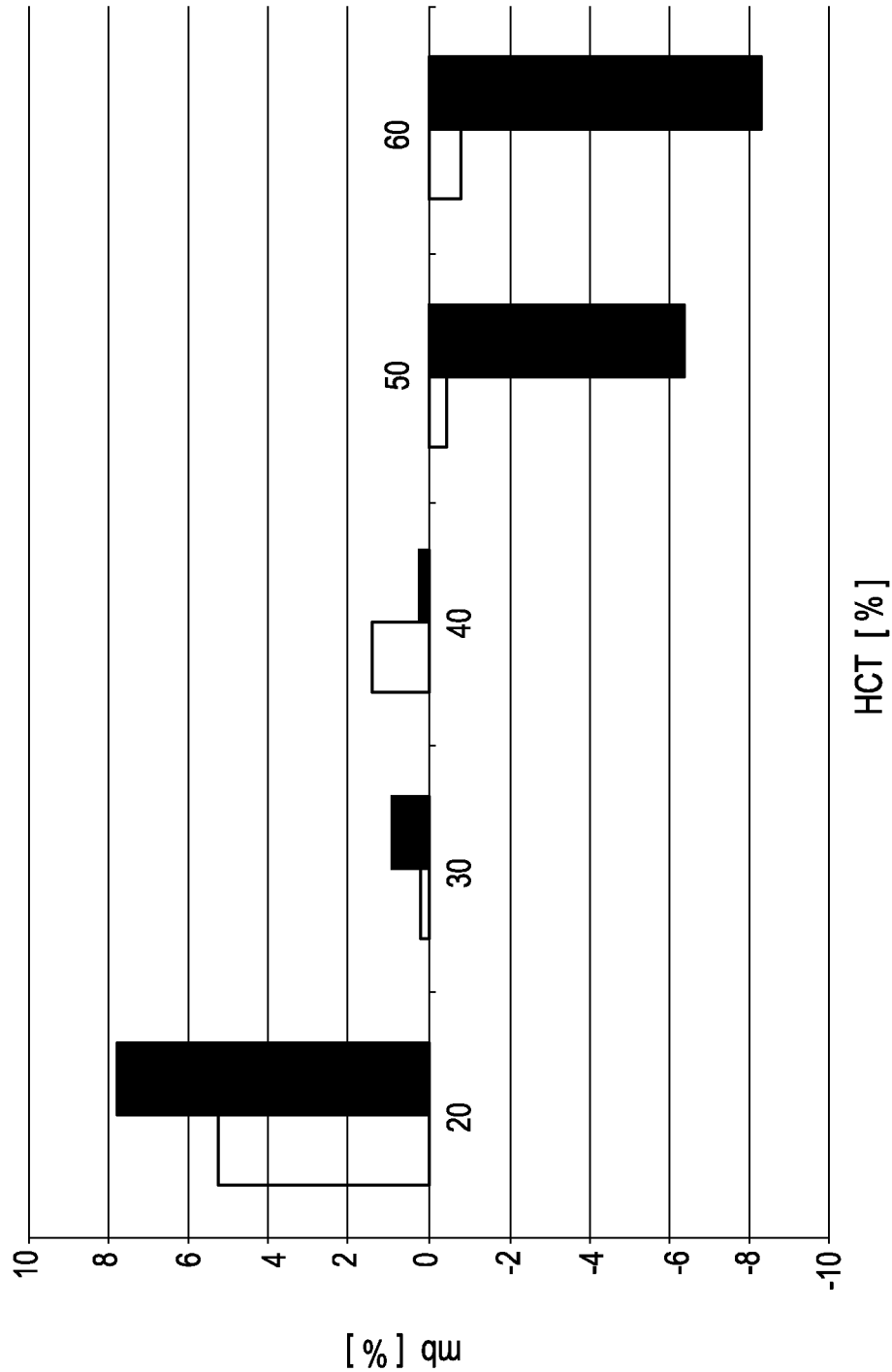


Fig. 11

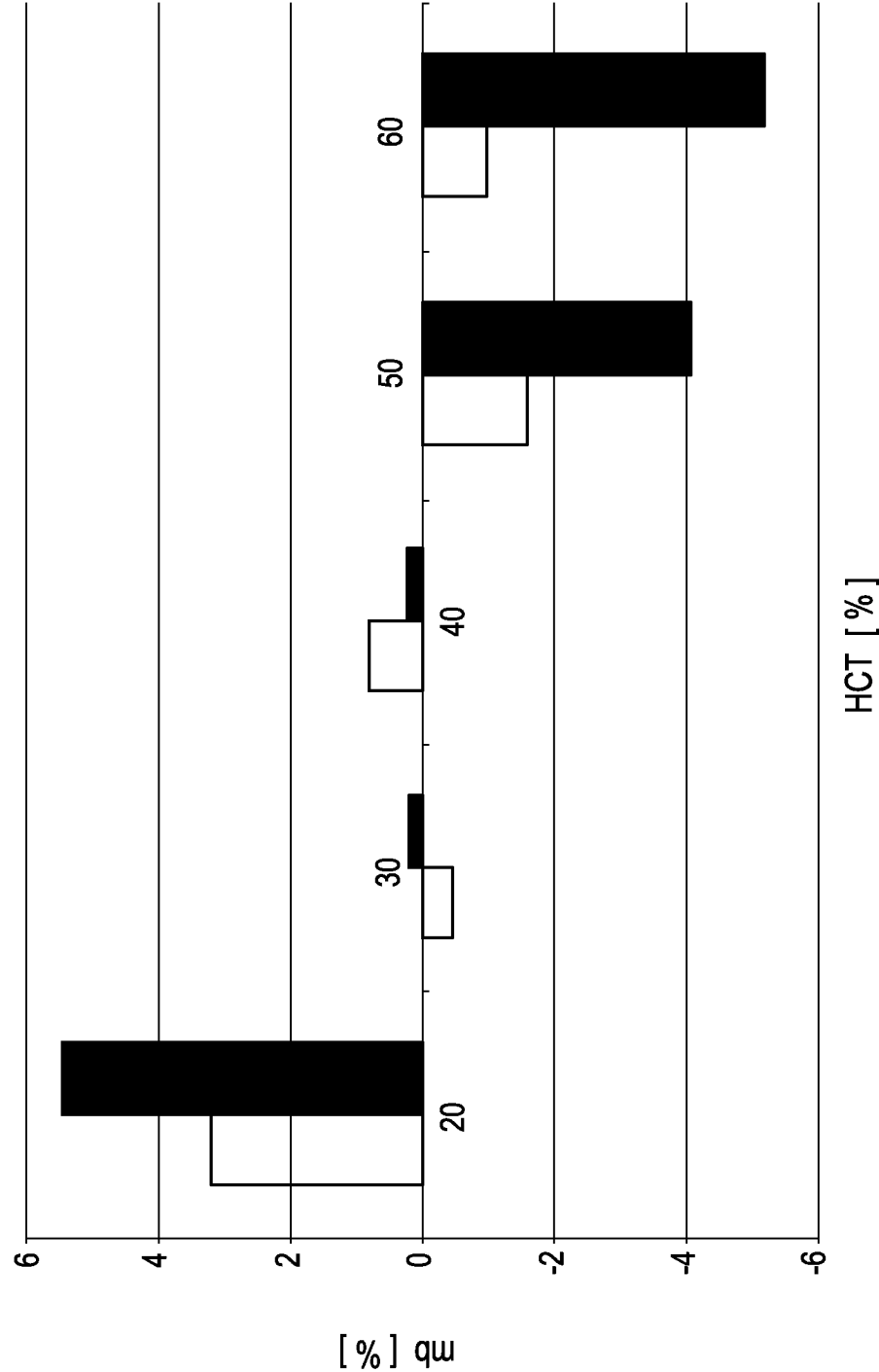


Fig. 12

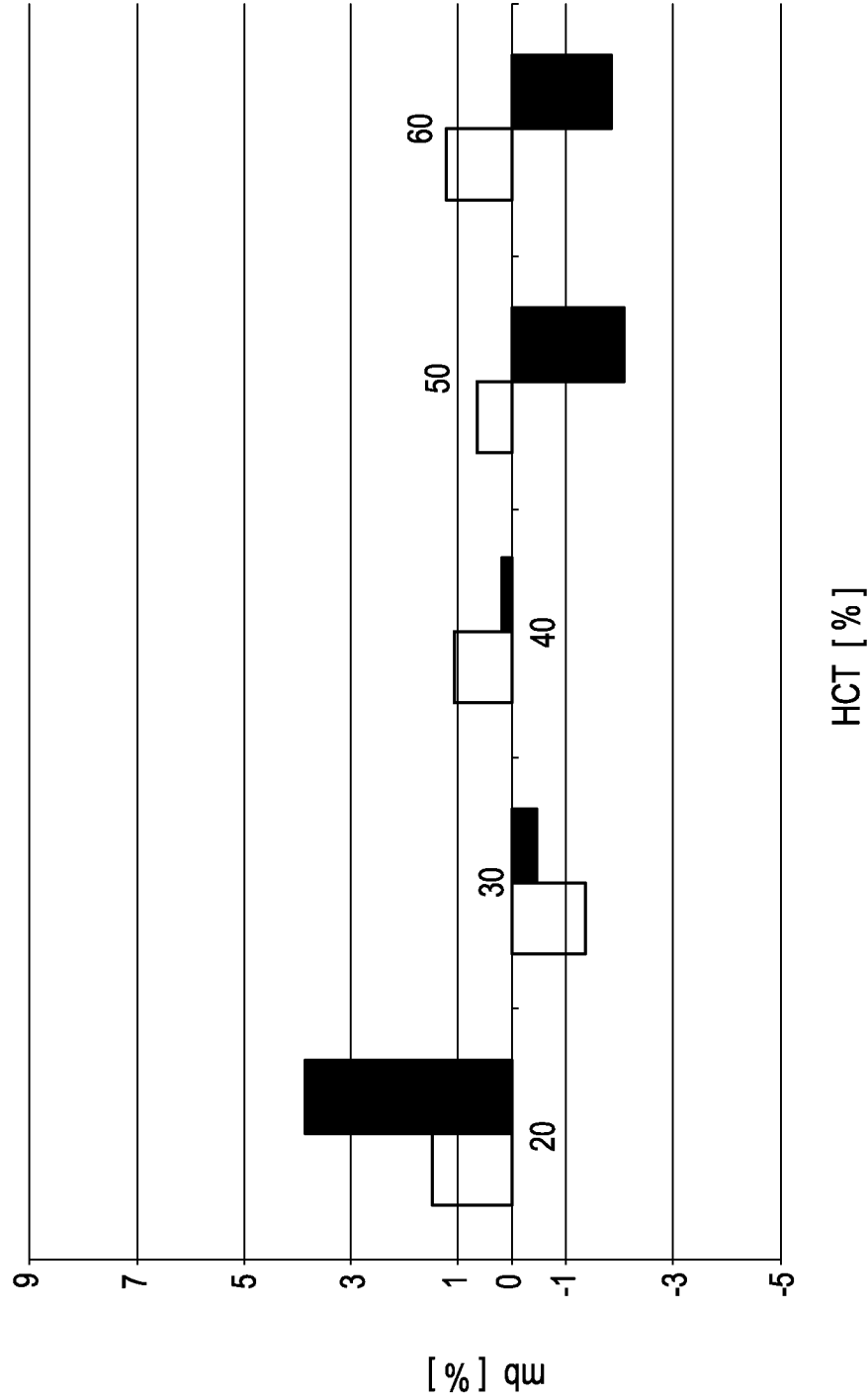


Fig. 13

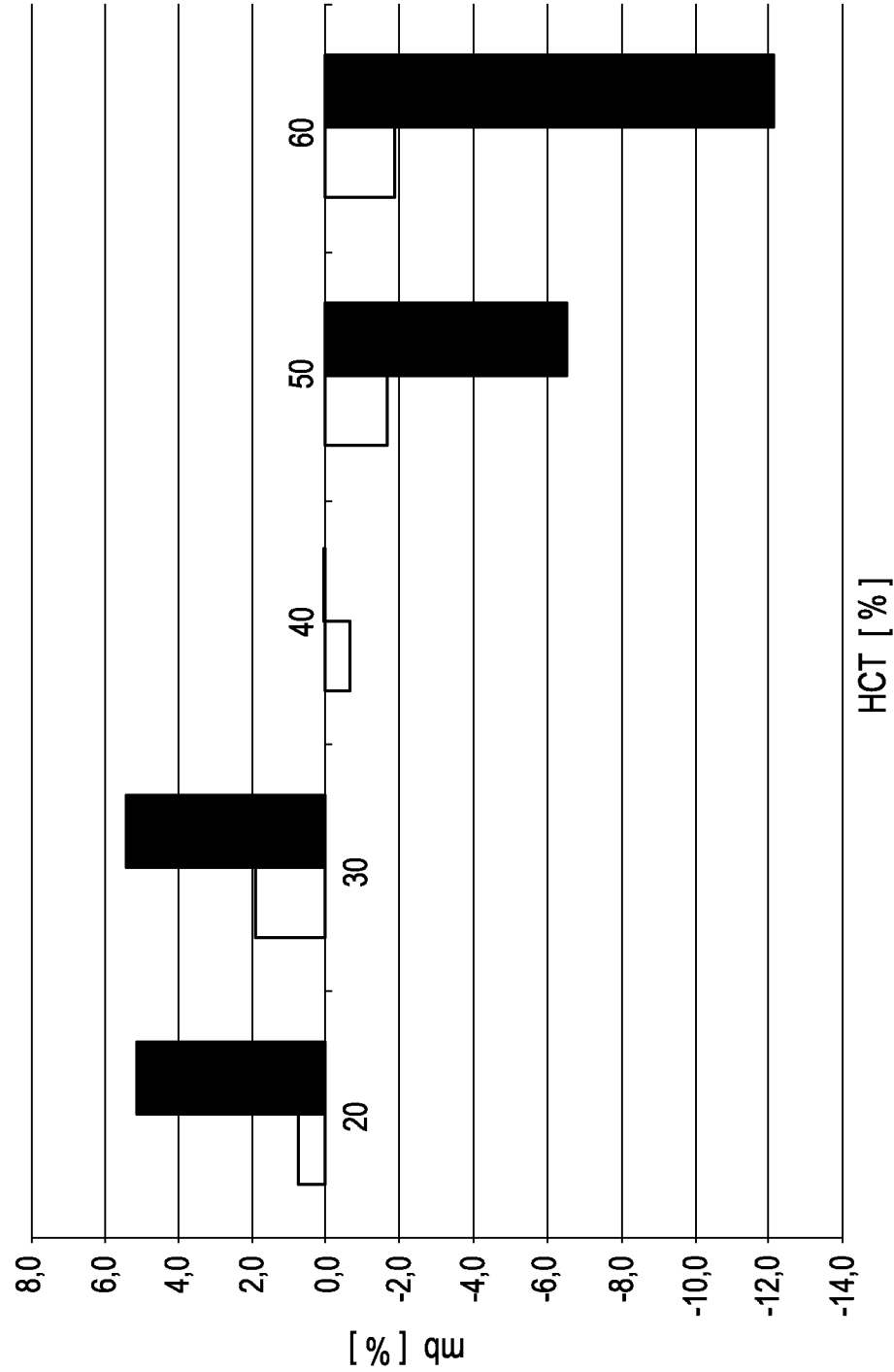


Fig. 14

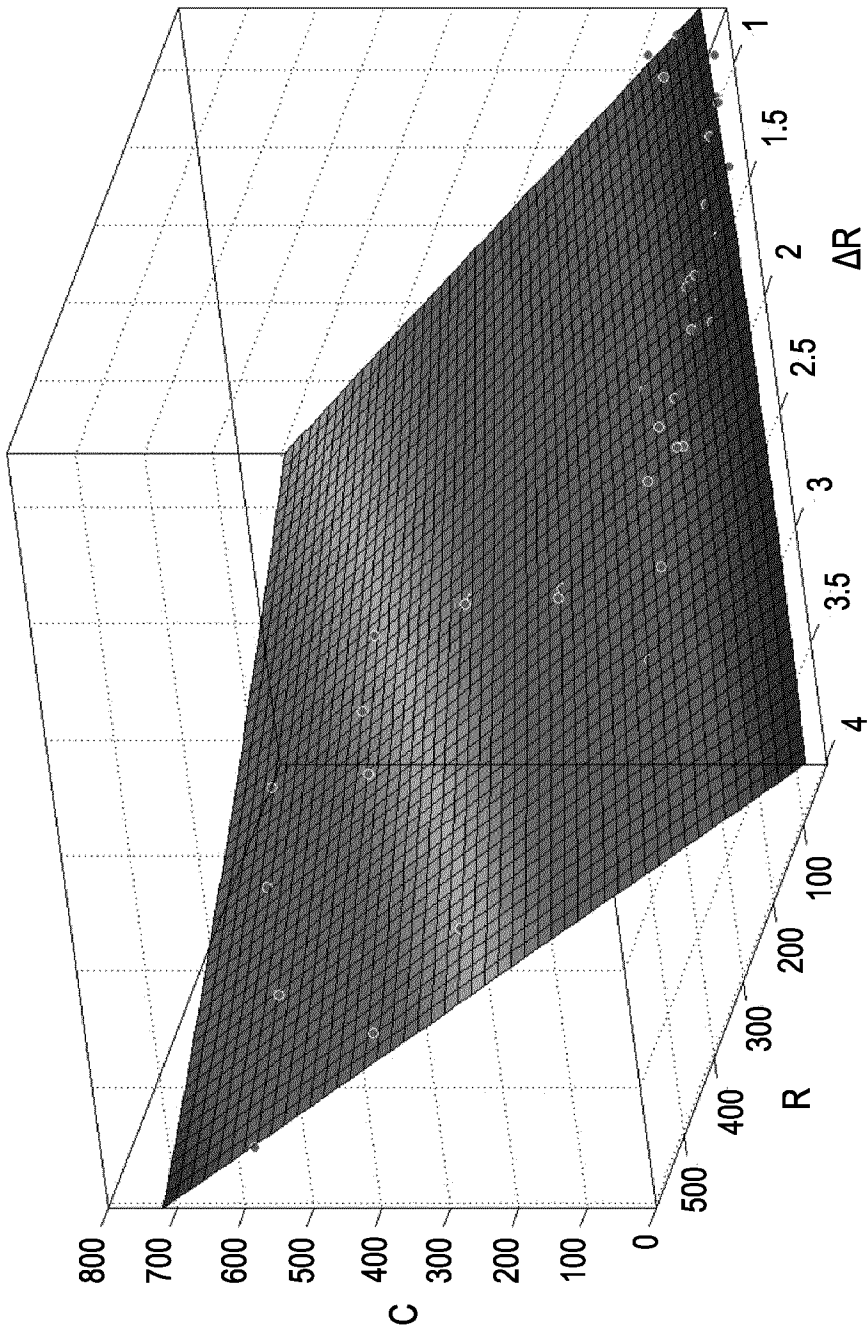


Fig. 15

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/055418

A. CLASSIFICATION OF SUBJECT MATTER
INV. G01N33/543
ADD.

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

B. FIELDS SEARCHED

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

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

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

EPO-Internal, BIOSIS, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/089658 A1 (NOVA BIOMEDICAL CORP [US]) 30 October 2003 (2003-10-30) abstract page 7, paragraph 3 page 8 page 9, last paragraph	1-16
A	----- WO 2008/150436 A1 (ABBOTT DIABETES CARE INC [US]; FELDMAN BENJAMIN J [US]; WANG YI [US];) 11 December 2008 (2008-12-11) abstract	1-16
A	----- WO 2012/091728 A1 (LIFESCAN INC [US]; CHATELIER RONALD C [AU]; HODGES ALASTAIR M [AU]) 5 July 2012 (2012-07-05) abstract	1-16
	----- -/-	



Further documents are listed in the continuation of Box C.



See patent family annex.

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

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

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

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

"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

1 April 2014

Date of mailing of the international search report

14/04/2014

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INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2014/055418

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 00/73785 A2 (NOVA BIOMEDICAL CORP [US]) 7 December 2000 (2000-12-07) abstract figures 1-6 -----	1-16

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2014/055418

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