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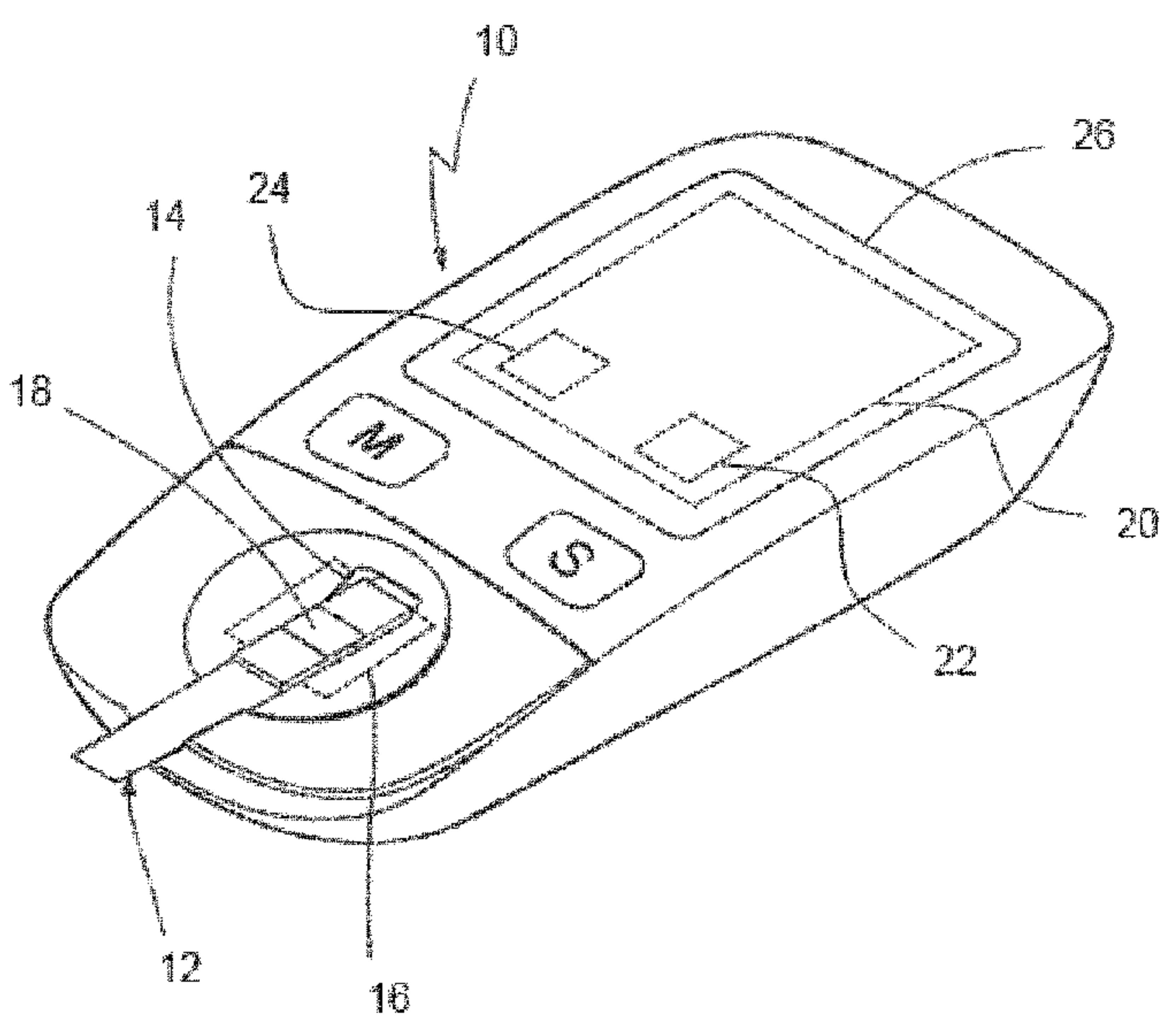

(57) Abrégé/Abstract:
The invention concerns a method and a device for determining sample application on an analytical test element in a photometric reflectance measuring device (10) specifically for glucose measurements, where the following measures are proposed: providing a disposable test element (12) for application of a body fluid sample, taking a sequence of reflectance readings from the test element (12), monitoring a change of the reflectance readings with respect to a sample application condition, adjusting the sample application condition in accordance with a drift correction. A value for drift correction of the reflectance readings caused by ambient measurement conditions, specifically, humidity, temperature, or UV radiation can be considered in a predefined signal decrease or in a predefined signal threshold for adjusting the sample application condition.

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(54) **Title**: METHOD AND DEVICE FOR DETERMINING SAMPLE APPLICATION

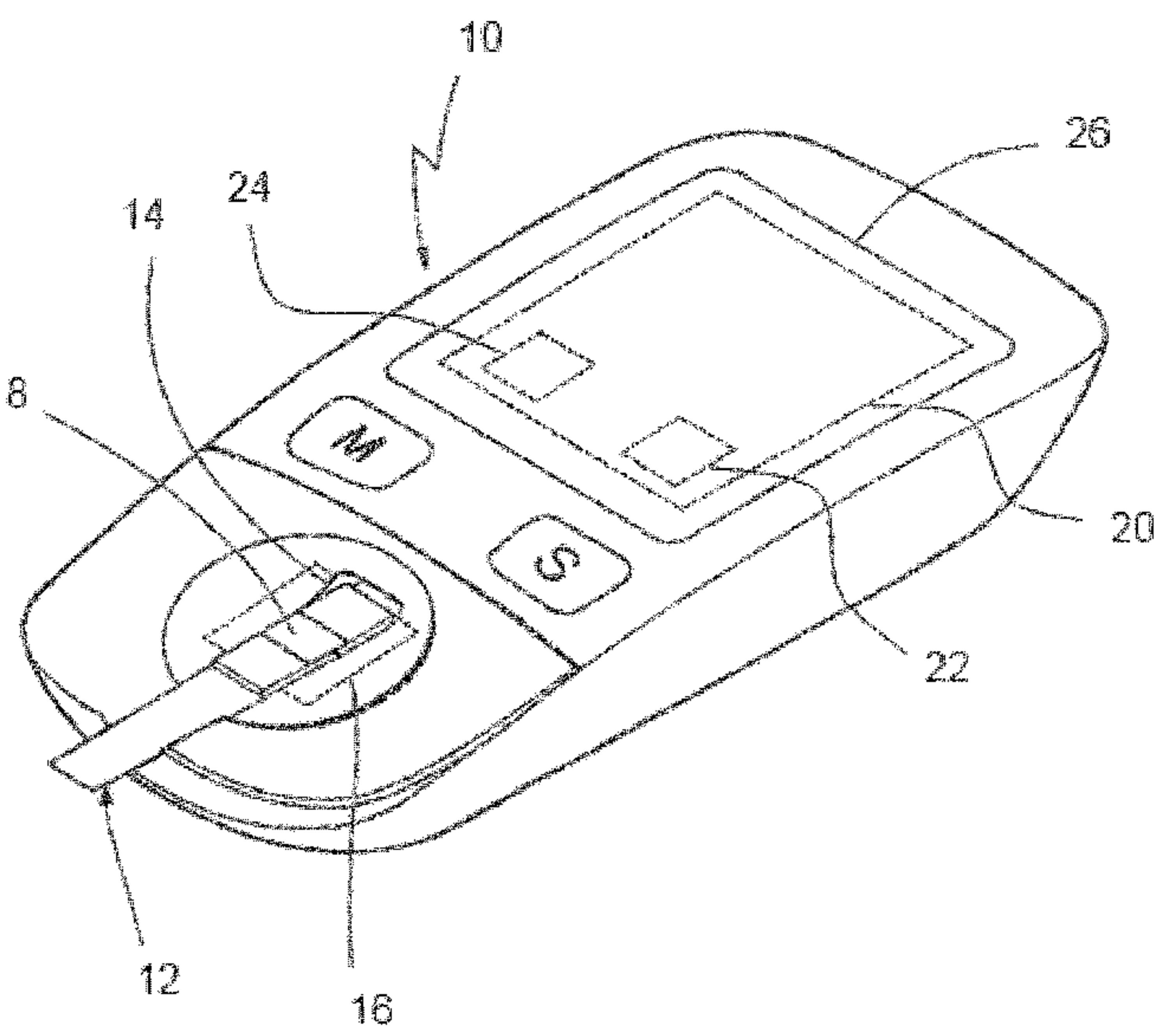

Fig. 1

(57) **Abstract**: The invention concerns a method and a device for determining sample application on an analytical test element in a photometric reflectance measuring device (10) specifically for glucose measurements, where the following measures are proposed: providing a disposable test element (12) for application of a body fluid sample, taking a sequence of reflectance readings from the test element (12), monitoring a change of the reflectance readings with respect to a sample application condition, adjusting the sample application condition in accordance with a drift correction. A value for drift correction of the reflectance readings caused by ambient measurement conditions, specifically, humidity, temperature, or UV radiation can be considered in a predefined signal decrease or in a predefined signal threshold for adjusting the sample application condition.

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Method and device for determining sample application

Description

The invention concerns a method for determining sample application on an analytical test element in a photometric reflectance measuring device specifically for glucose measurements, comprising the steps of providing a disposable test element for application of a body fluid sample, taking a sequence of reflectance readings from the test element starting with a blank reading and monitoring a change of the reflectance readings with respect to a sample application condition to determine if sample has been applied. The invention further concerns a photometric measuring device adapted for determining sample application on an analytical test element.

EP 2 221 608 A1 discloses a test method and test device for analysing a body fluid by means of analytical test fields stored on a test tape. In order to ensure an increased security against operating and measuring errors a control value is determined from a time-dependent and/or wavelength-dependent change of the measurement signals and the measurement signals are processed as valid or discarded as erroneous depending on a preset threshold value of the control value. This document further mentions that high air humidity as well as exposure to UV radiation could lead to a signal change similar to sample application and thus result in a start of the measurement. In this context, it is proposed that an application of liquid is detected when a signal change is above a predetermined threshold value (of for example about 5 %) and a fault is detected when it is below this value if necessary after a specified waiting time. In the latter case, the test field is discarded and the measurement must be repeated.

On this basis the object of the invention is to further improve the known method and device to achieve reliable results and to avoid a loss of test elements even under unfavorable circumstances.

The combination of features stated in the independent claims is proposed to achieve this object. Advantageous embodiments and further developments of the invention are derived from the dependent claims.

The invention is based on the idea of providing a correction for slow signal drift without aborting sample recognition. Accordingly it is proposed according to the invention that the sample application condition is adjusted in accordance with a drift correction calculated from a drift of the reflectance readings prior to sample application. The sample application condition is defined by a limit for a reflectance decrease or a reflectance threshold. The change of the reflectance readings is monitored in a sample recognition cycle, wherein a value for drift correction is provided for adjusting the sample application condition without aborting the sample recognition cycle. Thereby, it is possible to avoid the loss of a test element as a consequence of an error detection. The test element remains usable and the measuring procedure can be finished without additional delay.

According to an advantageous embodiment, the sample application condition is automatically regarded as fulfilled when a difference between the blank reading and an actual reflectance reading in the sequence of reflectance readings is higher than a given reflectance decrease. In this case, it is automatically determined that sample has been applied. Such a given reflectance decrease can be advantageously obtained by adding a value for drift correction to a predefined signal decrease.

According to an alternative advantageous embodiment, the sample application condition is automatically regarded as fulfilled when an actual reflectance reading in the sequence of reflectance readings is less than a given reflectance threshold. Then, it is automatically determined that sample has been applied. Such a given reflectance threshold can be advantageously determined by subtracting a value for drift correction from a predefined signal threshold.

Another improvement provides that a value for drift correction is calculated from the blank reading and one or more last or most recent reflectance readings taken before the sample application condition is fulfilled.

In order to average small short-time deviations, a mean actual reflectance can be calculated as a mean value from a given number of last reflectance readings and can be subtracted from the blank reading to obtain a value for drift correction.

For further improvement of the measurement certainty, it is advantageous when the application of the sample is confirmed by a further reflectance reading after fulfillment of the sample application condition.

It is also advantageous for a further automatic processing when the concentration of an analyte in the sample is determined using at least one reflectance reading after fulfillment of the sample application condition.

In order to avoid extreme conditions, it is advantageous when defining a limit for the drift correction and terminating the measurement if the limit is exceeded.

The proposed drift correction is particularly effective when a drift of the reflectance readings is caused by ambient measurement conditions, specifically humidity or temperature or UV radiation.

For a reliable discrimination it is favorable when upon sample application a drop in reflectance of the test element occurs significantly faster than a drift of the reflectance readings.

With regard to a photometric measuring device adapted for determining sample application on an analytical test element specifically for glucose measurements measurement system, in order to solve the aforementioned object, it is proposed that an arithmetic unit is adapted to calculate a drift correction from the reflectance readings prior to sample application and to adjust the sample application condition in accordance with the drift correction.

Another improvement provides that the test element comprises a reagent that reacts with an analyte in the sample and alters the reflectance of a test field of the test element.

Also with regard to simplifying the handling it is of particular advantage when the test element is a disposable test strip and the receiving unit is formed as a strip grip to accurately position the test strip with respect to the detector.

The invention is further elucidated in the following on the basis of embodiment examples shown schematically in the drawings, where

Fig. 1 is a partially schematic perspective view of a glucose meter with a test strip inserted for application of a blood sample;

Fig. 2 is a time diagram of a sequence of reflectance readings taken from the test strip before and after application of a blood sample;

Fig. 3 is a time diagram of reflectance readings illustrating a signal drift due to air humidity;

Fig. 4 is a schematic diagram illustrating a method for operating a blood glucose meter;

Fig. 5 and 6 are flowcharts showing different examples of a method for determining sample application on the test strip in the meter of Fig. 1.

FIG. 1 schematically illustrates a photometric reflectance measuring device designed as handheld blood glucose meter 10 for insertion of a disposable test strip 12. The meter 10 comprises a holder or strip grip 14 to position the test strip 12 in the optical path of a reflection photometer 16 as a detector to read the reflectance of an analytical test pad 18 of the strip 12 at a plurality of time points. A small volume of sample can be applied to the upper surface of the test pad 18, wherein a reagent reacts with an analyte, specifically glucose leading to a change in reflectance. This can be detected from the bottom of the test pad 18 with the photometer 16 comprising a light source and a light sensor arranged in a reflection path for diffuse reflection or remission of light (not shown). The change in reflectance (remission) over a predetermined time period as a result of formation of reaction product is then related to the amount of analyte in the sample. Such measurements are known to the skilled person e.g. from DE 199 32 846 A1 and need not to be elucidated in further details.

In order to process the measurement signals or reflectance readings, a device electronics 20 comprises a signal processor 22 in combination with an arithmetic unit 24 to provide a measurement result on a display 26 directly to the user. The signal processor 22 allows amplification and A/D conversion of the reflectance readings, and the arithmetic unit 24 enables further data handling specifically with respect to a drift correction, as explained below.

Fig. 2 illustrates a characteristic time course of reflectance readings using the meter of Fig. 1 where a time period in which the sample is applied is highlighted by an ellipse. The diagram shows remission values taken at constant intervals over the time and normalized to 100%. In a first phase, before sample is applied, the reflectance of the yet unused test pad 14 remains essentially constant under normal conditions. Upon sample application, a sudden decrease in the remission behaviour occurs due to the dry-wet transition of the test pad 18. This significant decrease can be used to automatically recognize the sample application and to set the time zero point for the reaction kinetics of the reagent with the analyte. Subsequently, the remission gradually begins lowering until the monitoring of the kinetics is terminated. Then, the glucose concentration can be determined from the kinetics e.g. by calculating a quotient from an end and starting remission value.

Turning now to Fig. 3, the time course of the reflectance or remission of an unused test strip 12 is illustrated for different ambient conditions. The diamonds indicate measurements at relatively low air humidity with no significant change, whereas the circles indicate measurements at high humidity resulting in a slow signal drift as compared to the fast dry-wet transition mentioned above. Nevertheless, if the deviation of such a slow drift is falsely interpreted as a sample application by the meter, a measurement cycle could be started leading to a gross wrong result. A signal drift before sample application can also be caused by other unfavourable boundary conditions, specifically by exposure to strong UV radiation.

Fig. 4 shows a simplified function scheme useful in understanding the concept of the invention. After providing the test strip 12 and before application of the sample, a first reflectance reading on the dry test pad 18 is recorded as blankreading. Thereafter a sample recognition cycle is started in which a change of the intermittently recorded reflectance readings is monitored with respect to a sample application condition, which can either be defined by a given reflectance decrease or reflectance threshold. Included in this recognition cycle is a drift correction routine to compensate for eventual deviation due to a slow signal drift. If the sample application condition is fulfilled, the actual sample application is again confirmed, and thereafter the reaction kinetics is recorded in order to obtain a valid measurement result.

Fig. 5 provides a more detailed flowchart of a first example for determining sample application. Initially, a blankreading value B is determined as a first reflectance reading on the dry test strip 12. At this time of initialization, a value D for drift correction and a number n of measurements used therefor is set to zero.

As a next step, the sample recognition cycle is started. A new drift value D is calculated if a sufficient number n ≥ 1 of further reflectance readings designated as sample application measurements M_x is available after the blankreading. For example, the three latest measurements (n = 3) may be taken to determine a mean reflectance value which is continuously recalculated in the sequence of further reflectance readings. The drift value D may then be determined according to the following equation (1):

$$D = B - \left(\sum_{x}^{x-n+1} M_x \right) / n \qquad (1)$$

Accordingly, the drift value D is the difference between the initial blankreading and the mean reflectance value of a number of most recent reflectance readings.

Going further in the flowchart of Fig. 5, an actual sample application measurement M_x is monitored with respect to a sample application condition, which is in turn adjusted to take account of an eventual drift. In this example, the sample application condition is regarded as fulfilled when a difference between the blankreading B and the actual reading M_x is higher than a given reflectance decrease, i.e. higher than the sum of a predefined signal decrease SD and the drift D. The predefined signal decrease may be set according to the signal drop observed for the dry-wet transition as marked in Fig. 2, e.g. to 5%.

If the sample application condition is found to be fulfilled, a confirmation step is executed, in which after a defined waiting time the sample application measurement is repeated and the sample application condition is again controlled. In case of positive confirmation of the sample application, the recording of the reaction kinetics can be started.

The alternative example of Fig. 6 only differs in the definition of the sample application condition. Here, a given reflectance threshold is controlled instead of monitoring a signal decrease. The given reflectance threshold is determined as the difference of an initial signal threshold ST (for example 95% of remission) and the drift D. The sample application condition is regarded as fulfilled when the actual reflectance reading M_x is less than said difference

ST-D.

WHAT IS CLAIMED IS:

1. A method for determining sample application on an analytical test element in a photometric reflectance measuring device for glucose measurements, comprising the steps of
   a. providing a disposable test element for application of a body fluid sample,
   b. taking a sequence of reflectance readings from the test element starting with a blank reading,
   c. monitoring a change of the reflectance readings in a sample recognition cycle with respect to a sample application condition to determine if sample has been applied,

   wherein
   d. adjusting the sample application condition in accordance with a drift correction calculated from the reflectance readings prior to sample application, wherein the sample application condition is defined by a limit for a reflectance decrease or a reflectance threshold, wherein a value for drift correction is provided for adjusting the sample application condition without aborting the sample recognition cycle; and
   e. confirming application of the sample by a further reflectance reading after fulfillment of the sample application condition.

2. The method of claim 1 wherein the sample application condition is regarded as fulfilled when a difference between the blank reading and an actual reflectance reading in the sequence of reflectance readings is higher than a given reflectance decrease.

3. The method of claim 2, wherein the value for the drift correction is added to a predefined signal decrease to obtain said given reflectance decrease.

4. The method of claim 1 wherein the sample application condition is regarded as fulfilled when an actual reflectance reading in the sequence of reflectance readings is less than a given reflectance threshold.

5. The method of claim 4, wherein the value for the drift correction is subtracted from a predefined signal threshold to obtain said given reflectance threshold.

6. The method according to any of claims 1 to 5 further comprising calculating the value for the drift correction from the blank reading and one or more reflectance readings taken before the sample application condition is fulfilled.

7. The method according to any of claims 1 to 6 wherein a mean actual reflectance is calculated as a mean value from a given number of last reflectance readings in said sequence and is subtracted from the blank reading to obtain the value for the drift correction.

8. The method according to any of claims 1 to 7 further comprising determining a concentration of an analyte in the sample using at least one reflectance reading after fulfillment of the sample application condition.

9. The method according to any of claims 1 to 8 further comprising defining a limit for the drift correction and terminating the measurement if the limit is exceeded.

10. The method according to any of claims 1 to 9 wherein a drift of the reflectance readings is caused by ambient measurement conditions.

11. The method of claim 10, wherein the ambient measurement conditions are humidity or temperature or UV radiation.

12. The method according to any of claims 1 to 9 wherein upon sample application a drop in reflectance of the test element occurs significantly faster than a drift of the reflectance readings.

13. The method according to any of claims 10 to 11 wherein upon sample application a drop in reflectance of the test element occurs significantly faster than the drift of the reflectance readings.

14. A photometric measuring device adapted for determining sample application on an analytical test element for glucose measurements, comprising
    a. a receiving unit configured to receive a disposable test element on which a body fluid sample can be applied,
    b. a detector adapted to take a sequence of reflectance readings from the test element starting with a blank reading,
    c. a signal processor adapted to monitor a change of the reflectance readings in a sample recognition cycle with respect to a sample application condition to determine if sample has been applied,

    wherein

    d. an arithmetic unit adapted to calculate a drift correction from the reflectance readings prior to sample application and to adjust the sample application condition in accordance with the drift correction, wherein the sample application condition is defined by a limit for a reflectance decrease or a reflectance threshold, wherein a value for drift correction is provided for adjusting the sample application condition without aborting the sample recognition cycle, and further to confirm application of the sample by a further reflectance reading after fulfillment of the sample application condition.

15. A photometric measuring device according to claim 14 wherein the test element comprises a reagent that reacts with an analyte in the sample and alters the reflectance of a test field of the test element.

16. A photometric measuring device according to claim 14 or 15 wherein the test element is a disposable test strip and the receiving unit is formed as a strip grip to position the test strip with respect to the detector.

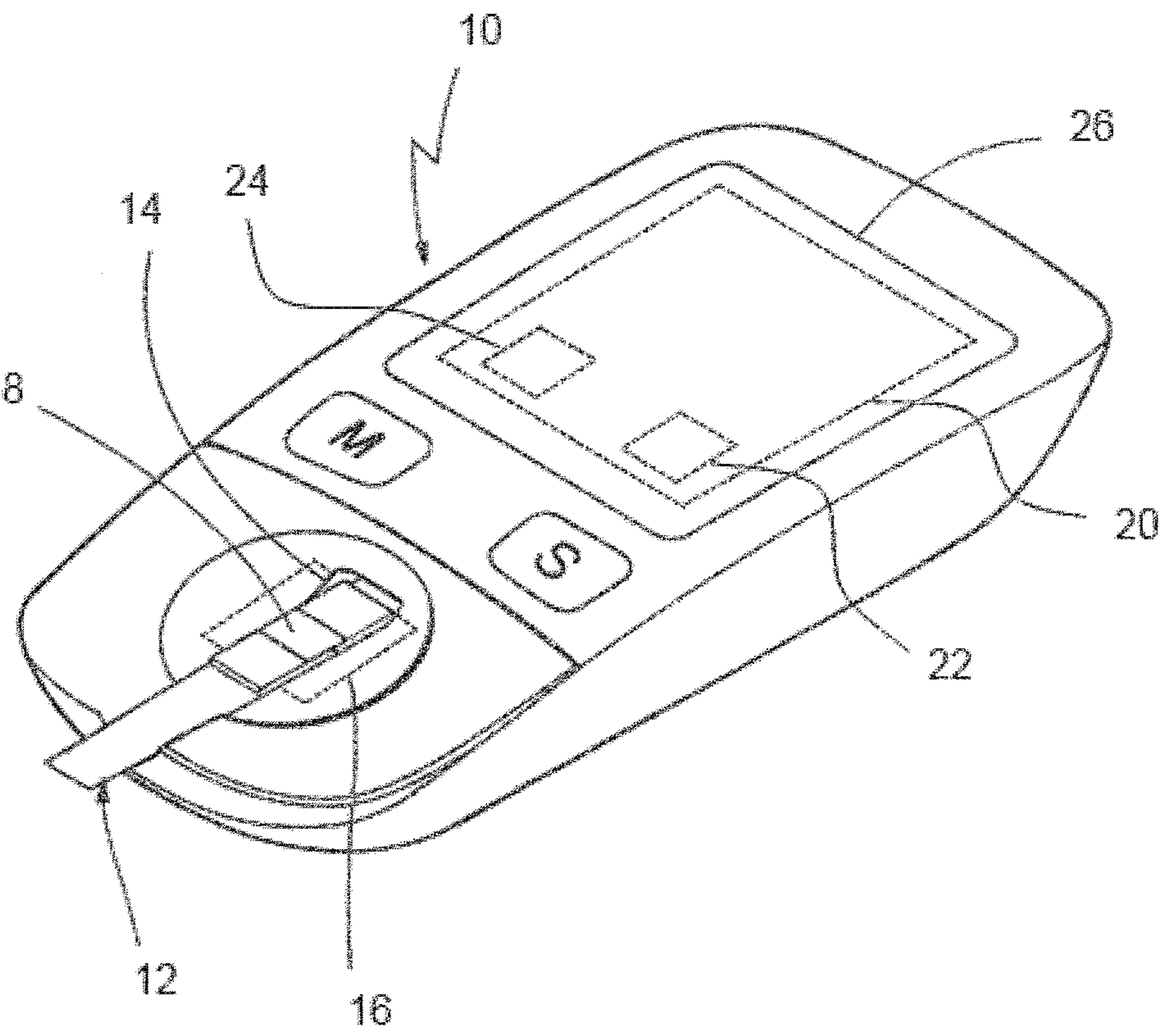
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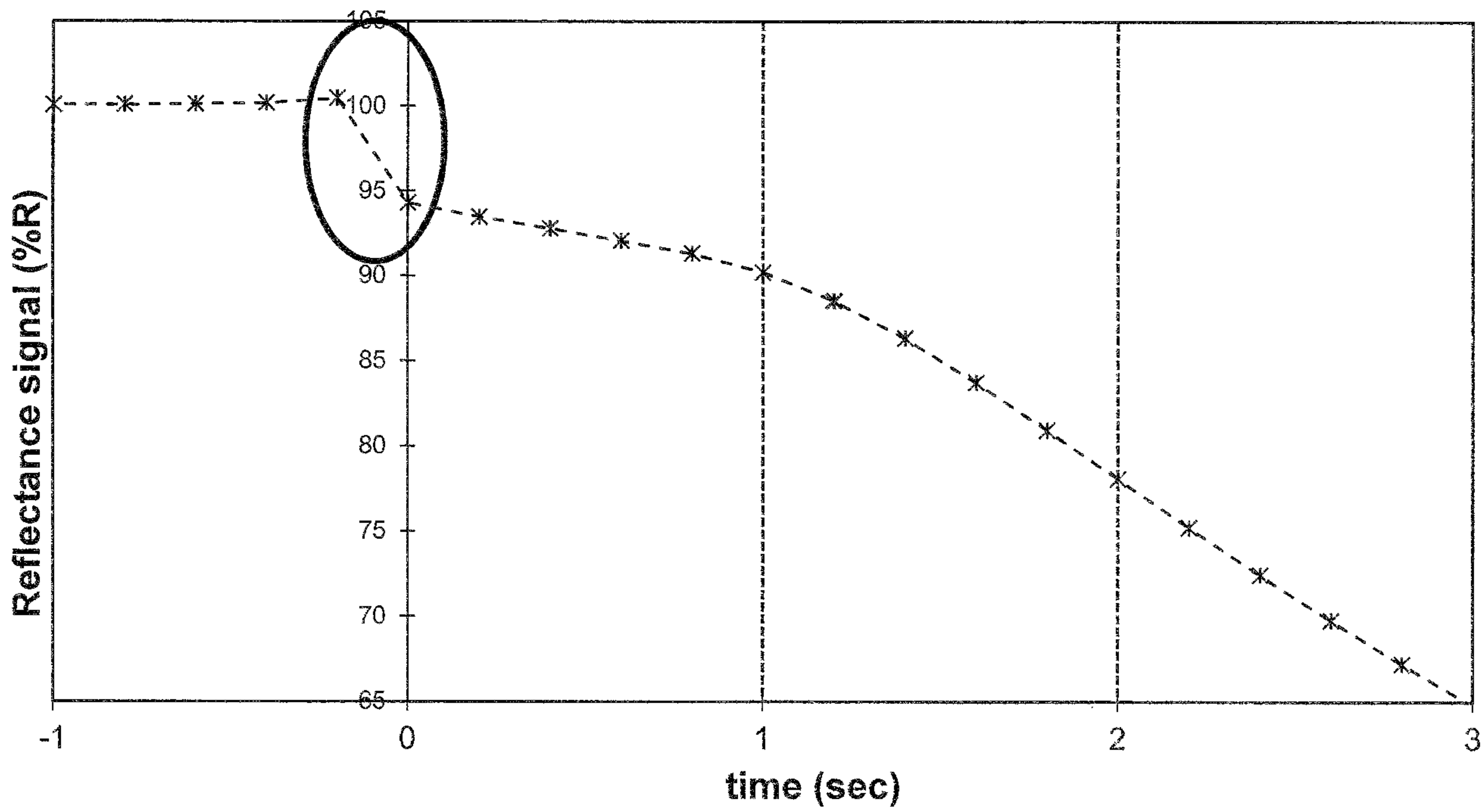
Fig. 1


Reflectance signal (%R)
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100
95
90
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80
75
70
65
-1
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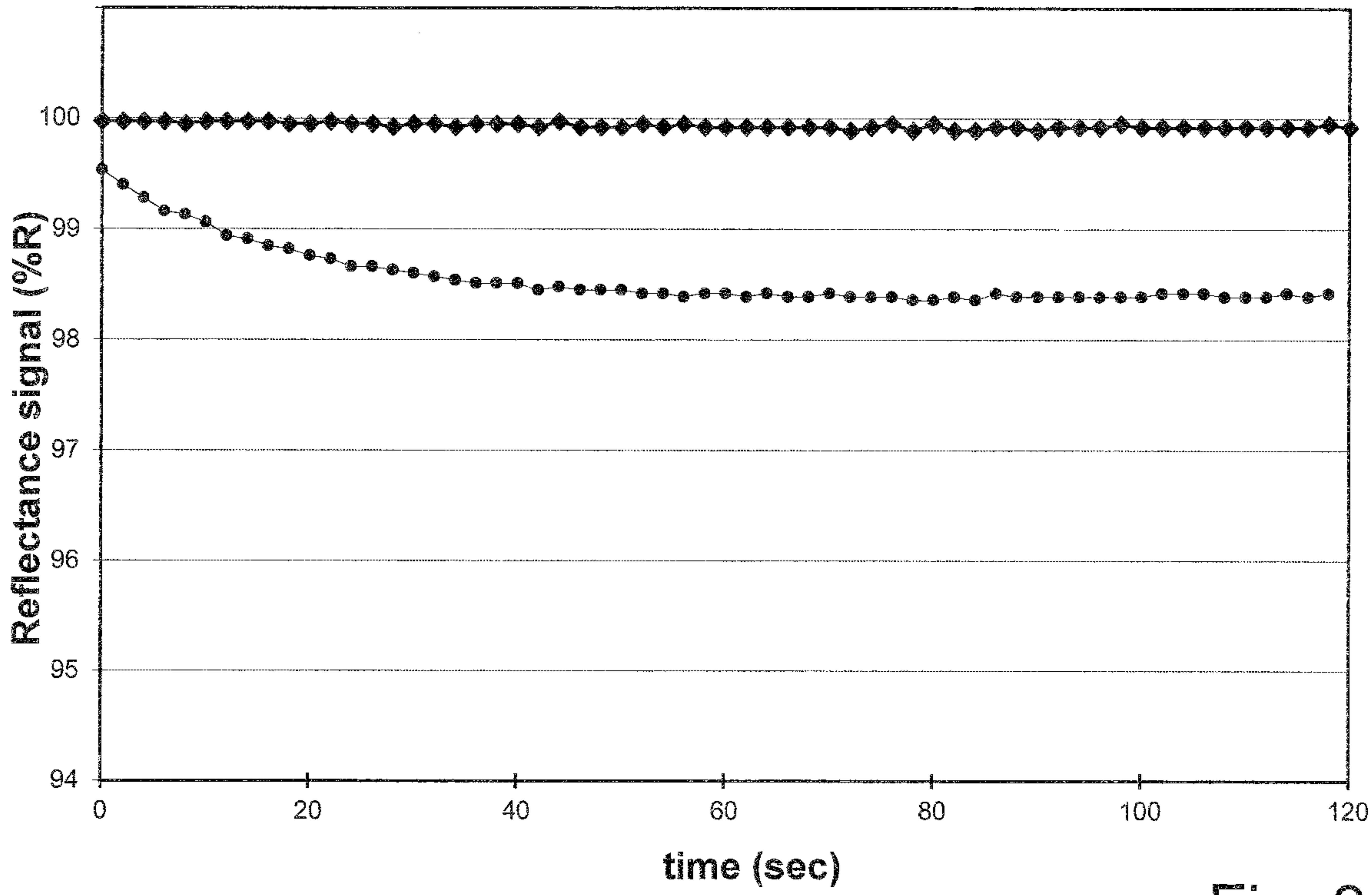
time (sec)

Fig. 2


Reflectance signal (%R)
100
99
98
97
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94
0
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100
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time (sec)

Fig. 3

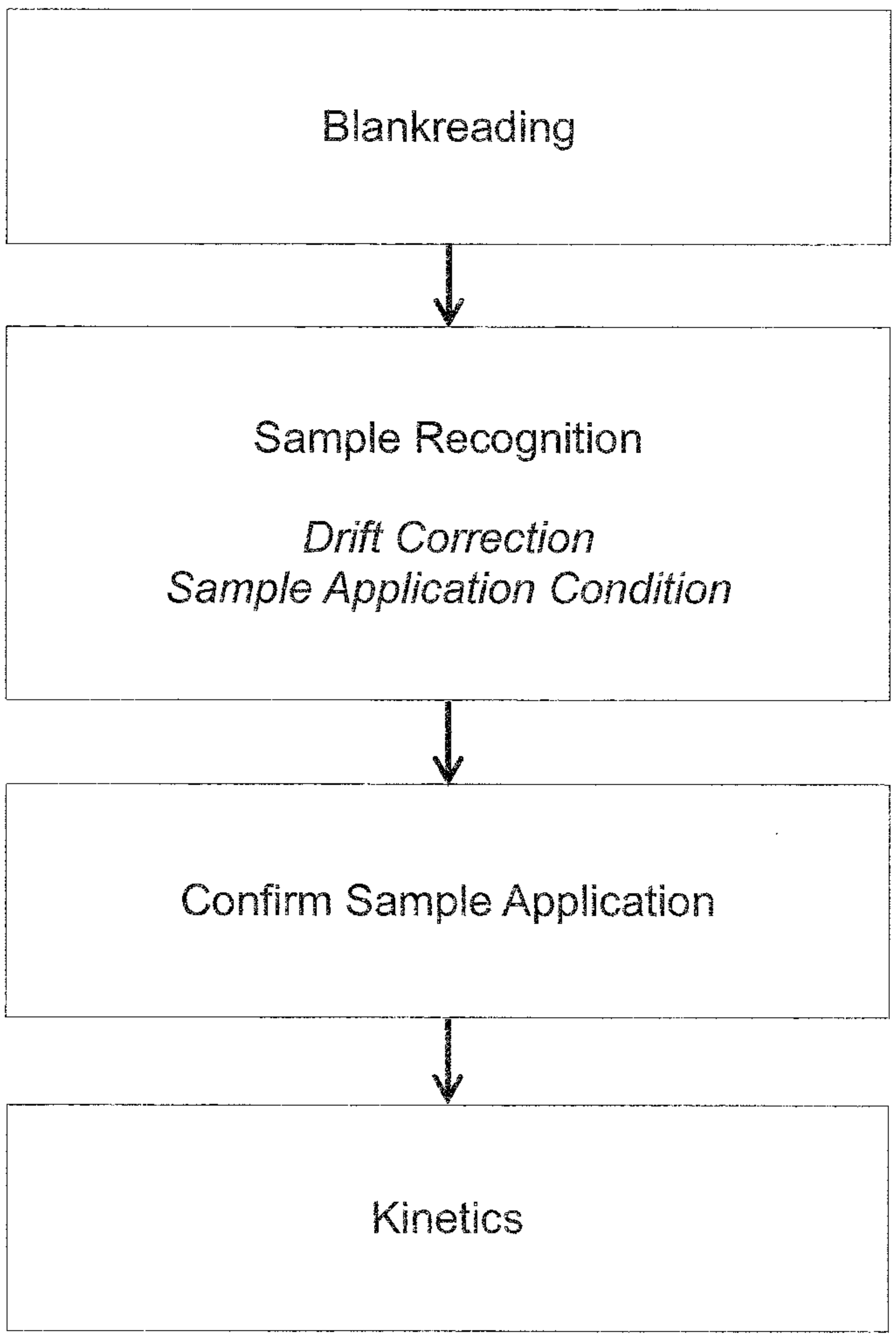

Blankreading
Sample Recognition
Drift Correction
Sample Application Condition
Confirm Sample Application
Kinetics

Fig. 4

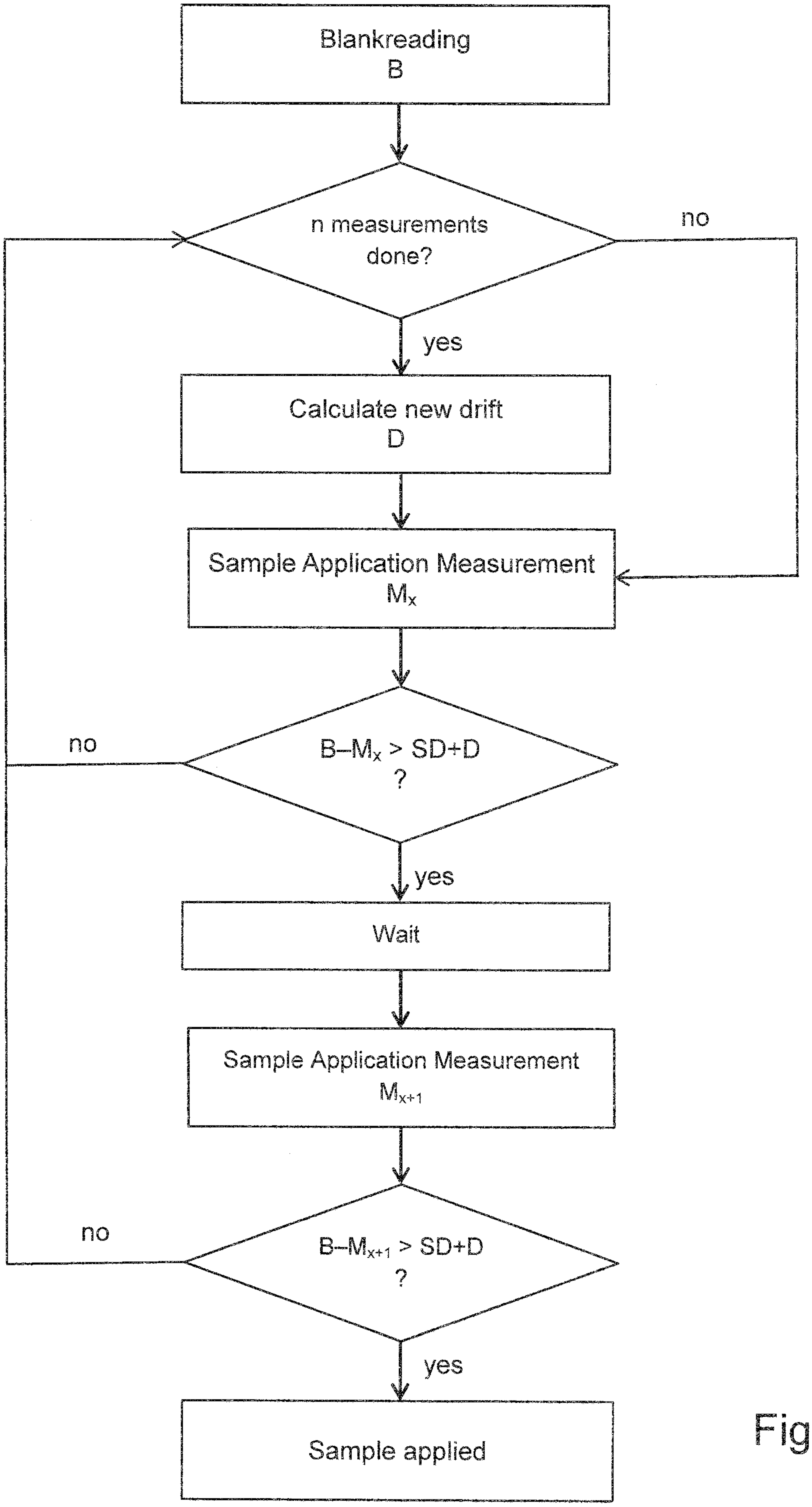
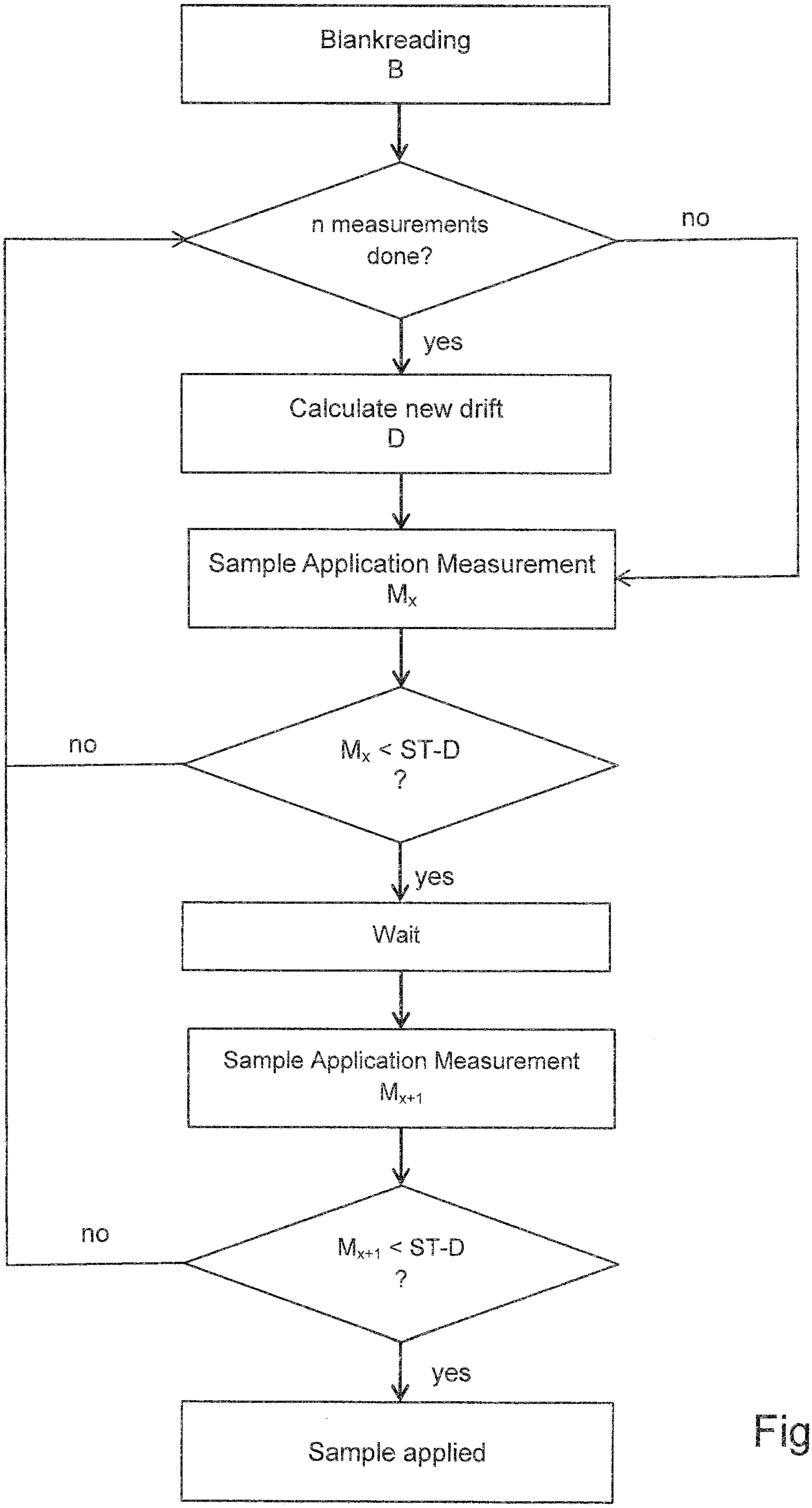

Blankreading
B
n measurements
done?
no
yes
Calculate new drift
D
Sample Application Measurement
M_x
no
$B-M_x > SD+D$
?
yes
Wait
Sample Application Measurement
M_{x+1}
no
$B-M_{x+1} > SD+D$
?
yes
Sample applied

Fig. 5


Blankreading
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n measurements
done?
no
yes
Calculate new drift
D
Sample Application Measurement
M_x
no
M_x < ST-D
?
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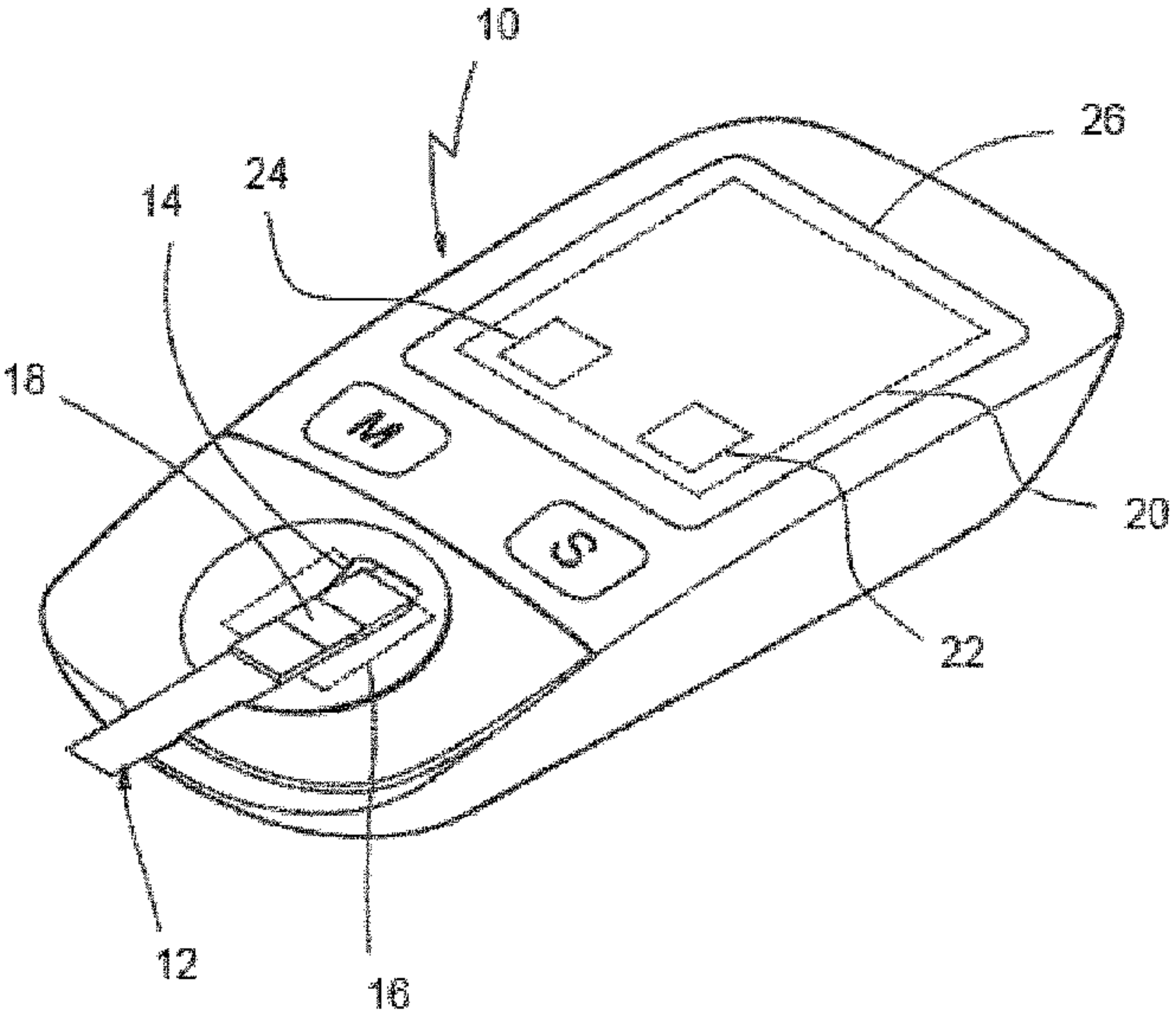
Wait
Sample Application Measurement
M_{x+1}
no
M_{x+1} < ST-D
?
yes
Sample applied

Fig. 6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