US009622691B2

(12) **United States Patent**
Budiman

(10) **Patent No.: US 9,622,691 B2**
(45) **Date of Patent: Apr. 18, 2017**

(54) **MODEL BASED VARIABLE RISK FALSE GLUCOSE THRESHOLD ALARM PREVENTION MECHANISM**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 767 days.

(21) Appl. No.: **14/128,583**

(22) PCT Filed: **Oct. 30, 2012**

(86) PCT No.: **PCT/US2012/062541**

§ 371 (c)(1),
(2) Date: **Dec. 20, 2013**

(87) PCT Pub. No.: **WO2013/066849**

PCT Pub. Date: **May 10, 2013**

(65) **Prior Publication Data**

US 2014/0121488 A1 May 1, 2014

Related U.S. Application Data

(60) Provisional application No. 61/553,931, filed on Oct. 31, 2011.

(51) **Int. Cl.**

A61B 5/00	(2006.01)
A61B 5/145	(2006.01)
G06F 19/00	(2011.01)

(52) **U.S. Cl.**
CPC ***A61B 5/14532*** (2013.01); ***A61B 5/7275*** (2013.01); ***A61B 5/746*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61B 5/14532; A61B 5/746
See application file for complete search history.

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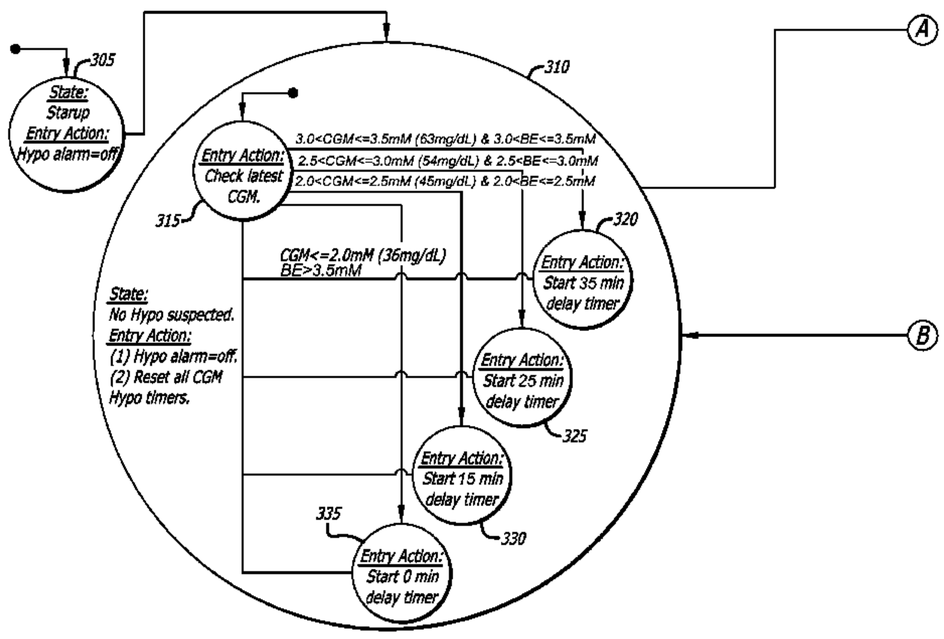
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(57) **ABSTRACT**

Methods of determining when to activate an analyte, e.g. glucose, related alarm, such as a hypoglycemia alarm, of a continuous analyte monitor is provided. Also provided are systems, devices and kits. Embodiments include methods for determining when to activate an analyte alarm of a continuous analyte monitor. The methods may include receiving information from the continuous analyte monitor related to the user's analyte concentration, wherein the information is received at a data processing component. The methods may also include receiving information that is input by the user, and the information is related to the user's analyte concentration.

27 Claims, 6 Drawing Sheets



(52) **U.S. Cl.**
CPC *A61B 5/002* (2013.01); *A61B 5/0031* (2013.01); *G06F 19/3468* (2013.01)

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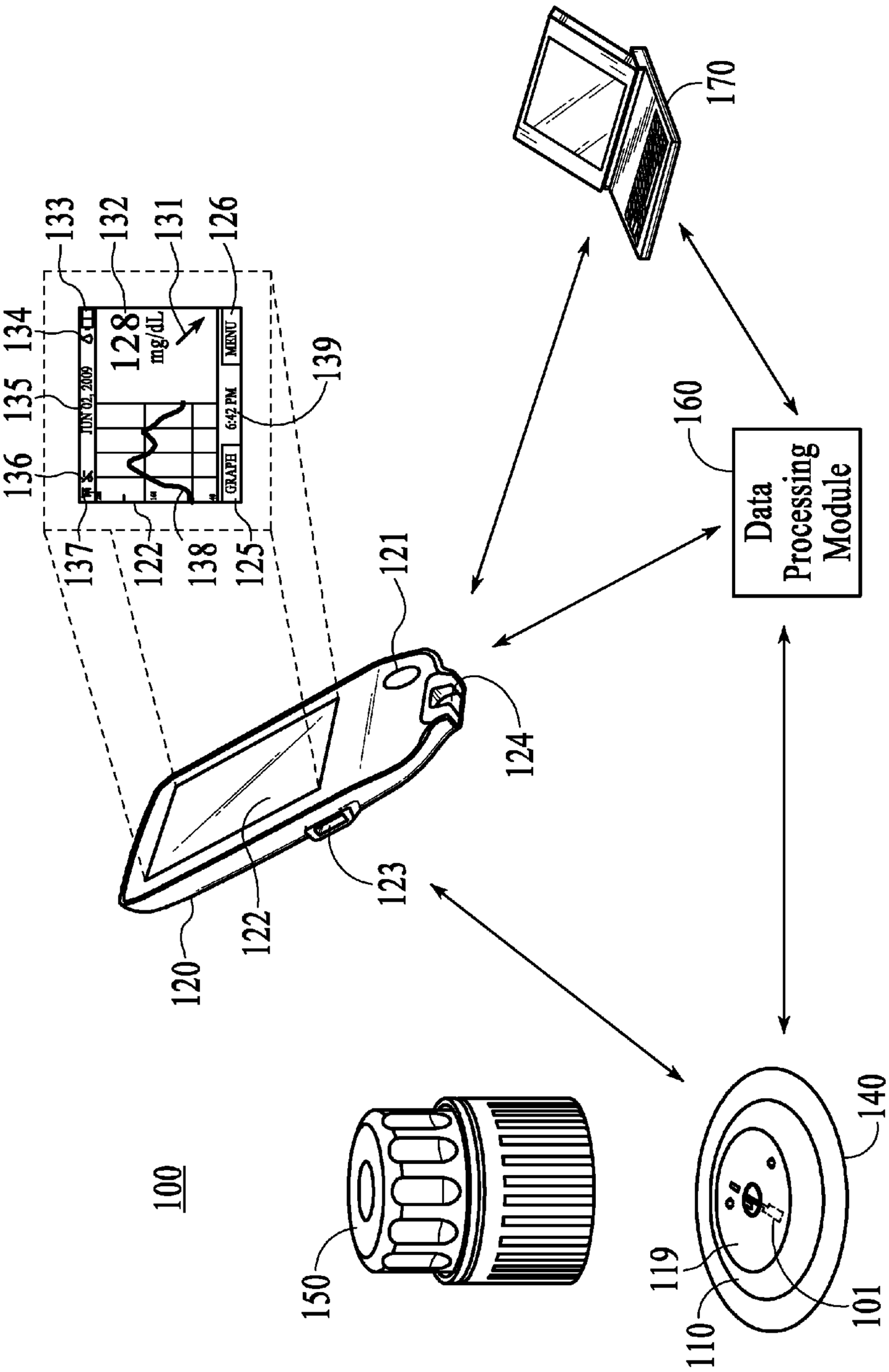

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FIG. 1

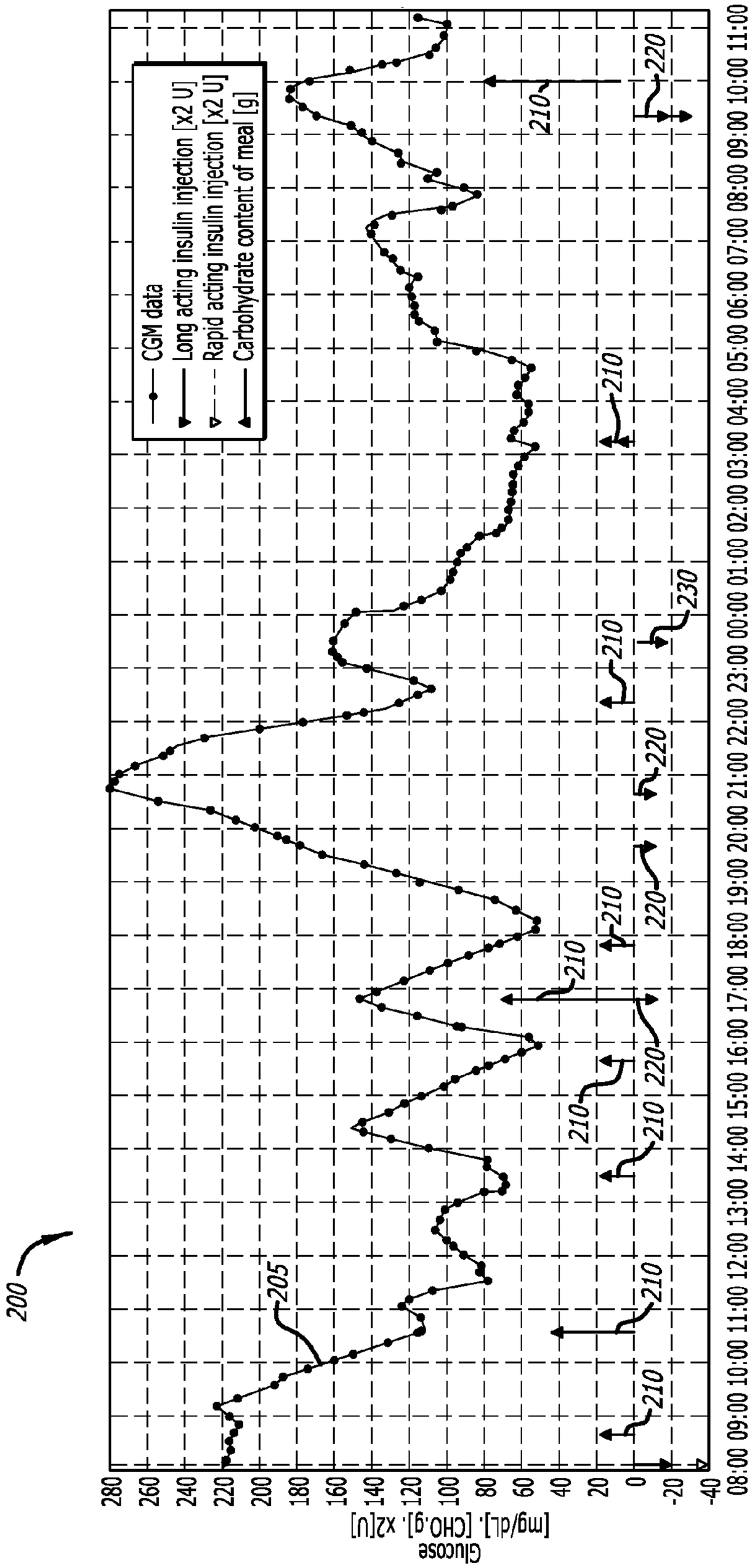

200
205
210
220
230
CGM data
Long acting insulin injection [x2 U]
Rapid acting insulin injection [x2 U]
Carbohydrate content of meal [g]
Glucose [mg/dL], [CHO.g], x2[U]
Time
280
260
240
220
200
180
160
140
120
100
80
60
40
20
0
-20
-40
08:00 09:00 10:00 11:00 12:00 13:00 14:00 15:00 16:00 17:00 18:00 19:00 20:00 21:00 22:00 23:00 00:00 01:00 02:00 03:00 04:00 05:00 06:00 07:00 08:00 09:00 10:00 11:00

FIG. 2

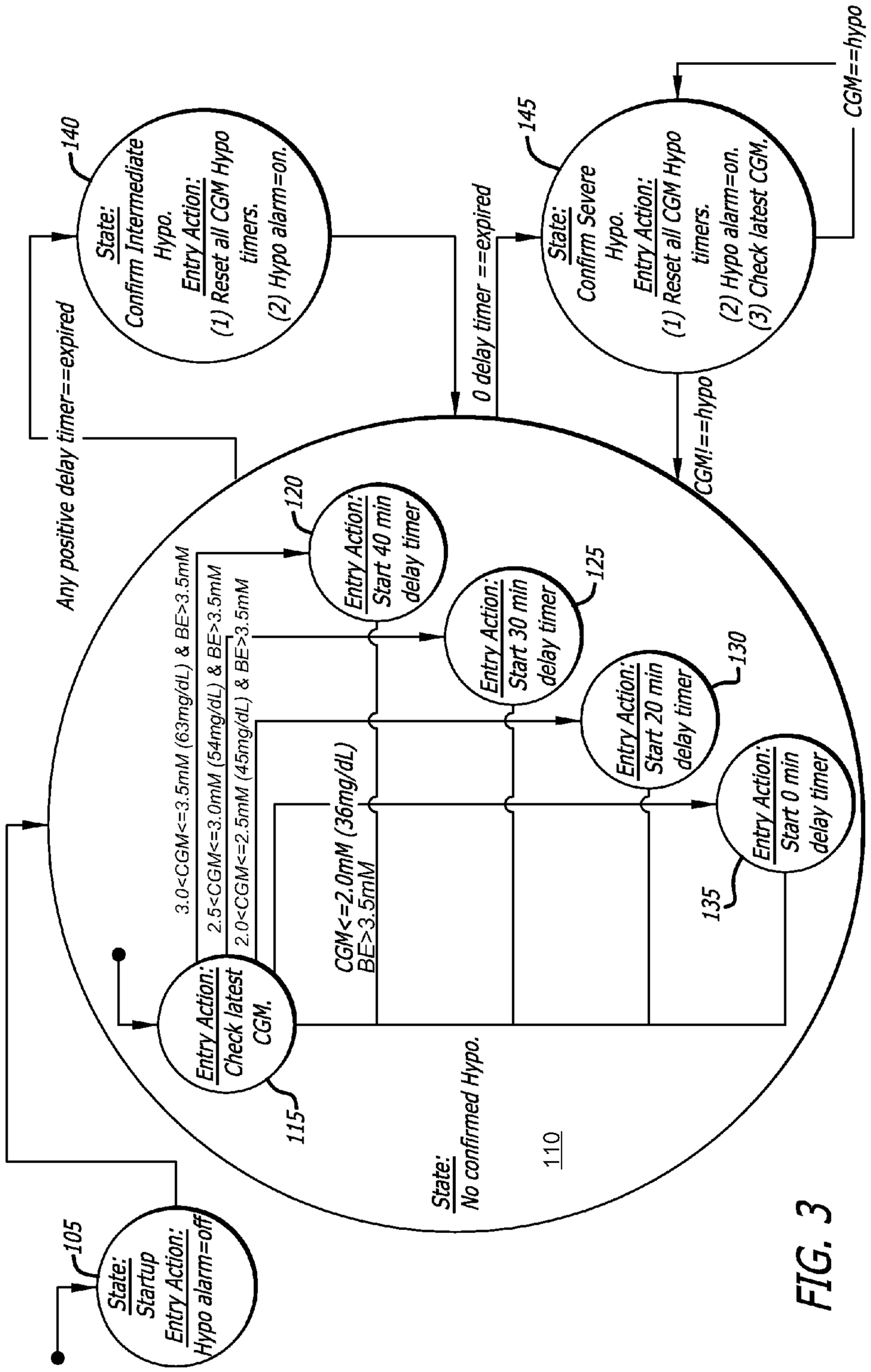
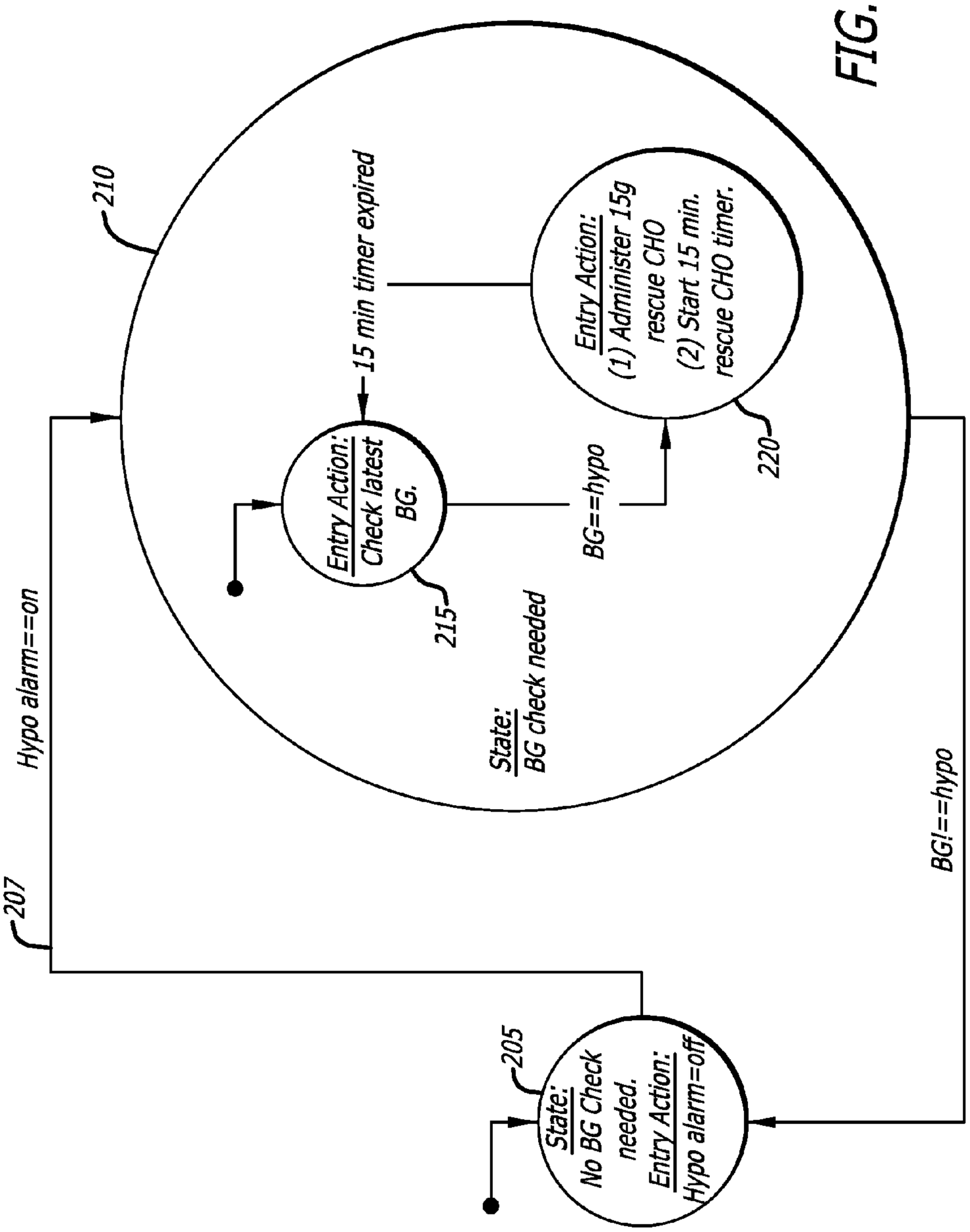

105
State:
Startup
Entry Action:
Hypo alarm=off
State:
No confirmed Hypo.
110
115
Entry Action:
Check latest CGM.
CGM<=2.0mM (36mg/dL)
BE>3.5mM
3.0<CGM<=3.5mM (63mg/dL) & BE>3.5mM
2.5<CGM<=3.0mM (54mg/dL) & BE>3.5mM
2.0<CGM<=2.5mM (45mg/dL) & BE>3.5mM
120
Entry Action:
Start 40 min delay timer
125
Entry Action:
Start 30 min delay timer
130
Entry Action:
Start 20 min delay timer
135
Entry Action:
Start 0 min delay timer
Any positive delay timer==expired
140
State:
Confirm Intermediate Hypo.
Entry Action:
(1) Reset all CGM Hypo timers.
(2) Hypo alarm=on.
0 delay timer ==expired
145
State:
Confirm Severe Hypo.
Entry Action:
(1) Reset all CGM Hypo timers.
(2) Hypo alarm=on.
(3) Check latest CGM.
CGM==hypo
CGM!==hypo

FIG. 3

FIG. 4


207
Hypo alarm==on
210
State:
BG check needed
215
Entry Action:
Check latest BG.
15 min timer expired
BG==hypo
220
Entry Action:
(1) Administer 15g rescue CHO
(2) Start 15 min. rescue CHO timer.
BG!==hypo
205
State:
No BG Check needed.
Entry Action:
Hypo alarm=off

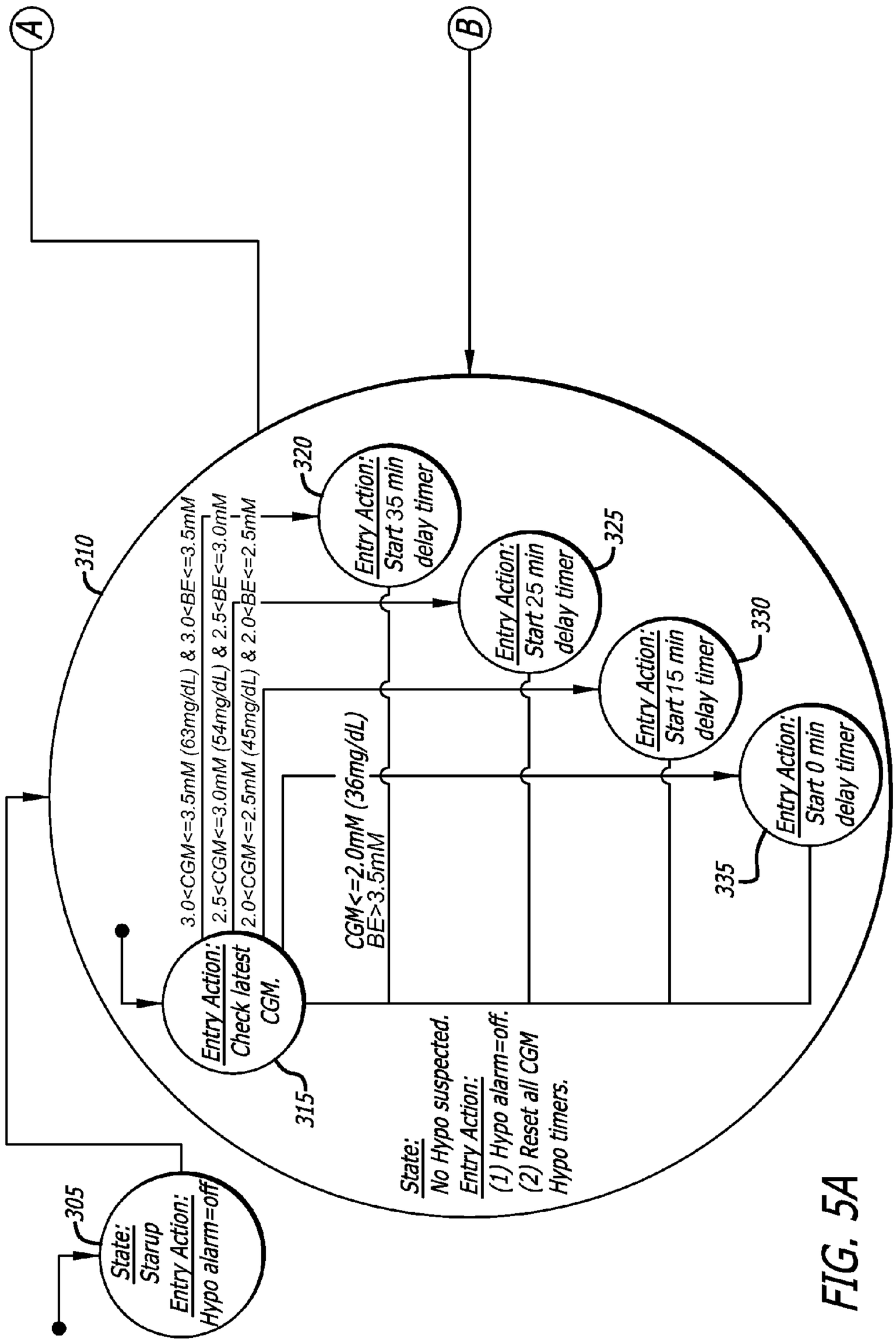
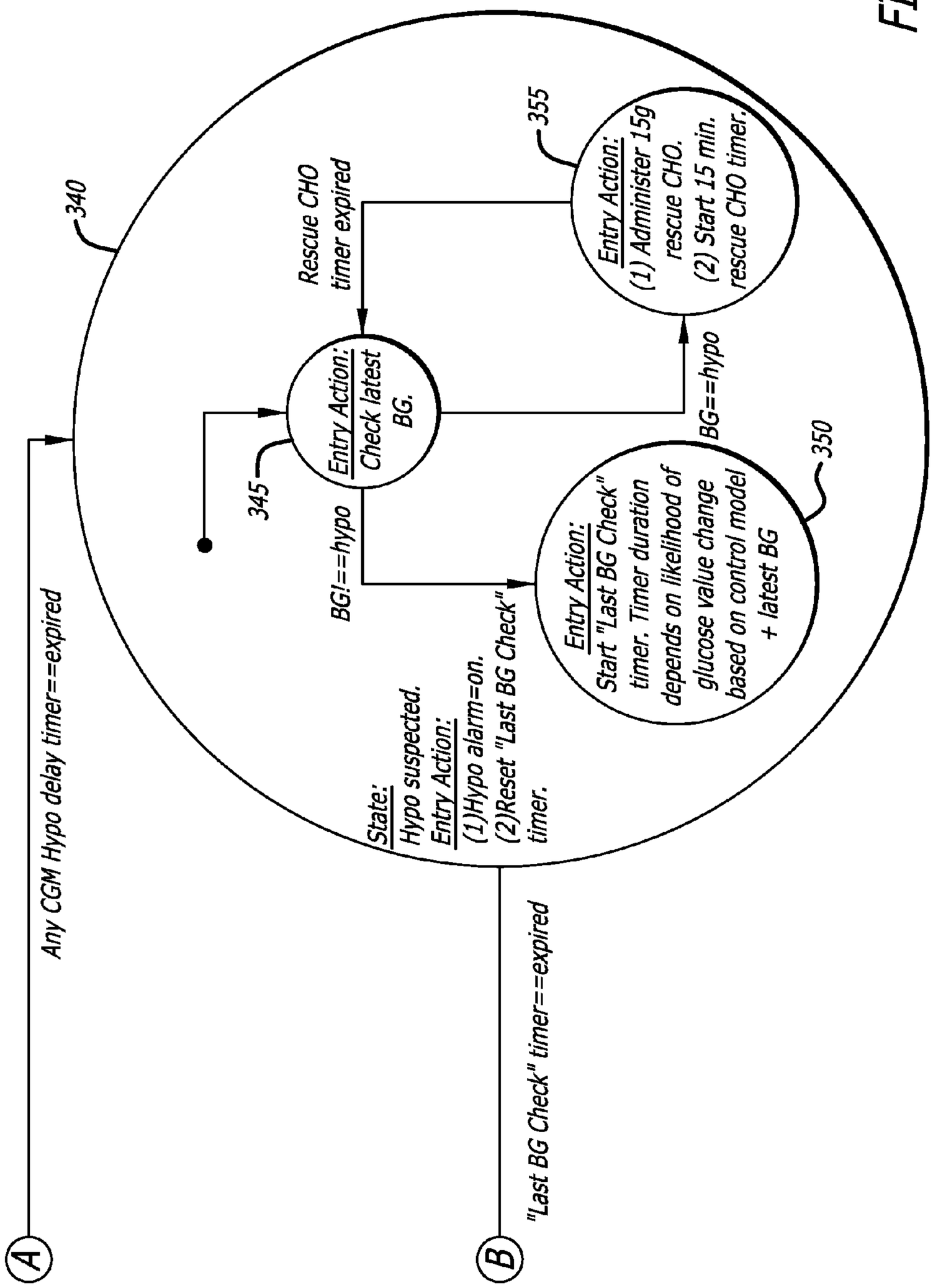

A
B
310
State:
No Hypo suspected.
Entry Action:
(1) Hypo alarm=off.
(2) Reset all CGM
Hypo timers.
315
Entry Action:
Check latest
CGM.
3.0<CGM<=3.5mM (63mg/dL) & 3.0<BE<=3.5mM
2.5<CGM<=3.0mM (54mg/dL) & 2.5<BE<=3.0mM
2.0<CGM<=2.5mM (45mg/dL) & 2.0<BE<=2.5mM
CGM<=2.0mM (36mg/dL)
BE>3.5mM
320
Entry Action:
Start 35 min
delay timer
325
Entry Action:
Start 25 min
delay timer
330
Entry Action:
Start 15 min
delay timer
335
Entry Action:
Start 0 min
delay timer
305
State:
Starup
Entry Action:
Hypo alarm=off

FIG. 5A

FIG. 5B


A
Any CGM Hypo delay timer==expired
340
345
Entry Action:
Check latest BG.
BG!==hypo
State:
Hypo suspected.
Entry Action:
(1)Hypo alarm=on.
(2)Reset "Last BG Check" timer.
Rescue CHO timer expired
BG==hypo
350
Entry Action:
Start "Last BG Check" timer. Timer duration depends on likelihood of glucose value change based on control model + latest BG
355
Entry Action:
(1) Administer 15g rescue CHO.
(2) Start 15 min. rescue CHO timer.
B
"Last BG Check" timer==expired

MODEL BASED VARIABLE RISK FALSE GLUCOSE THRESHOLD ALARM PREVENTION MECHANISM

PRIORITY

The present application claims priority to U.S. provisional application No. 61/553,931 filed Oct. 31, 2011, entitled "Model Based Variable Risk False Glucose Threshold Alarm Prevention Mechanism", the disclosure of which is incorporated herein by reference for all purposes.

BACKGROUND

The detection of the level of glucose or other analytes, such as lactate, oxygen or the like, in certain individuals is vitally important to their health. For example, the monitoring of glucose is particularly important to individuals with diabetes. Diabetics may need to monitor glucose levels to determine when insulin is needed to reduce glucose levels in their bodies or when additional glucose is needed to raise the level of glucose in their bodies.

Devices have been developed for continuous or automatic monitoring of analytes, such as glucose, in bodily fluid such as in the blood stream or in interstitial fluid. Some of these analyte measuring devices are configured so that at least a portion of the devices are positioned below a skin surface of a user, e.g., in a blood vessel or in the subcutaneous tissue of a user.

Ease of insertion and use, including minimal user intervention and on-body size and height (or thickness) of such transcutaneous or percutaneous medical devices that are worn on the body are important in usability, wearability, and comfort during the device usage. Moreover, for many of such medical devices that require a battery or a similar power source to perform the device specific operations, power management as well as shelf life is important.

SUMMARY

Embodiments include methods for determining when to activate an analyte alarm of a continuous analyte monitor. The methods may include receiving information from the continuous analyte monitor related to the user's analyte concentration, wherein the information is received at a data processing component. The methods may also include receiving information that is input by the user, and the information is related to the user's analyte concentration. The information that is input by the user can also be received at the data processing component. In addition, the methods may also include that the data processing component determines the best-estimate (BE) of the user's analyte concentration based upon the information from the continuous analyte monitor and information from the user. Further, the methods may include that at least one condition for activating the analyte alarm is determined by the data processing component. Furthermore, if the information related to the user's analyte concentration converges with the best-estimate of the user's analyte concentration then the data processing component can modify the at least one condition for activating the analyte alarm.

Embodiments further include an integrated analyte monitoring device assembly, that includes an analyte sensor for transcutaneous positioning through a skin layer and maintained in fluid contact with an interstitial fluid under the skin layer during a predetermined time period, the analyte sensor having a proximal portion and a distal portion, and sensor electronics coupled to the analyte sensor. The sensor electronics can include the sensor electronics comprising a circuit board having a conductive layer and a sensor antenna disposed on the conductive layer, one or more electrical contacts provided on the circuit board and coupled with the proximal portion of the analyte sensor to maintain continuous electrical communication, and a data processing component provided on the circuit board and in signal communication with the analyte sensor. The data processing component can be configured to execute one or more routines for processing signals received from the analyte sensor, control the transmission of data associated with the processed signals received from the analyte sensor to a remote location using the sensor antenna in response to a request signal received from the remote location. The data processing component may be further configured to receive information from the continuous analyte monitor related to the user's analyte concentration, receive data from the user related to the user's analyte concentration, determine a best-estimate of the user's analyte concentration based upon the data signal and user data received at the processor, determine at least one condition for activating an analyte alarm, modify the at least one condition for activating the analyte alarm if the information related to the user's analyte concentration converges with the best-estimate of the user's analyte concentration.

Additional embodiments include an integrated analyte monitoring device that can include a data processing component provided on the circuit board and in signal communication with an analyte sensor. The data processing component of the integrated analyte monitoring device may be configured to execute one or more routines for processing signals received from the analyte sensor, and control the transmission of data associated with the processed signals received from the analyte sensor to a remote location using the sensor antenna in response to a request signal received from the remote location. The data processing component may be additionally configured to receive information from the continuous analyte monitor related to the user's analyte concentration, as well as data from the user related to the user's analyte concentration. A determination of the best-estimate of the user's analyte concentration based upon the data signal and user data received at the processor, as well as at least one condition for activating an analyte, can also be accomplished using the data processing component. Still further, the data processing component can be configured to modify the at least one condition for activating the analyte alarm if the information related to the user's analyte concentration converges with the best-estimate of the user's analyte concentration.

These and other features, objects and advantages of the present disclosure will become apparent to those persons skilled in the art upon reading the details of the present disclosure as more fully described below.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** shows a data monitoring and management system such as, for example, an analyte (e.g., glucose) monitoring system in accordance with certain embodiments of the present disclosure;

FIG. **2** is a graphical representation of a glucose profile showing a user's glucose level measured using a CGM sensor as a function of time, and also depicting the variation of the glucose level as a function of carbohydrate intake and insulin administration;

FIG. **3** is a schematic diagram of a continuous glucose monitor based subsystem, illustrated in terms of a state machine;

FIG. **4** is a schematic diagram of a glucose level based subsystem illustrated in terms of a state machine coupled to the continuous glucose monitor subsystem FIG. **3**; and

FIGS. **5**A and **5**B are schematic diagrams of an embodiment of the disclosure wherein the continuous glucose monitor and glucose level state machines are coupled to a stronger degree than the embodiments shown in FIGS. **3** and **4**, and also showing an additional delay timer asserted after glucose level confirmation.

INCORPORATION BY REFERENCE

Patents, applications and/or publications described herein, including the following patents, applications and/or publications are incorporated herein by reference for all purposes: U.S. Pat. Nos. 4,545,382, 4,711,245, 5,262,035, 5,262,305, 5,264,104, 5,320,715, 5,356,786, 5,509,410, 5,543,326, 5,593,852, 5,601,435, 5,628,890, 5,820,551, 5,822,715, 5,899,855, 5,918,603, 6,071,391, 6,103,033, 6,120,676, 6,121,009, 6,134,461, 6,143,164, 6,144,837, 6,161,095, 6,175,752, 6,270,455, 6,284,478, 6,299,757, 6,338,790, 6,377,894, 6,461,496, 6,503,381, 6,514,460, 6,514,718, 6,540,891, 6,560,471, 6,579,690, 6,591,125, 6,592,745, 6,600,997, 6,605,200, 6,605,201, 6,616,819, 6,618,934, 6,650,471, 6,654,625, 6,676,816, 6,730,200, 6,736,957, 6,746,582, 6,749,740, 6,764,581, 6,773,671, 6,881,551, 6,893,545, 6,932,892, 6,932,894, 6,942,518, 7,041,468, 7,167,818, 7,299,082, and 7,866,026, and U.S. Patent Publication Nos. 2004/0186365, now U.S. Pat. No. 7,811,231, 2005/0182306, now U.S. Pat. No. 8,771,183, 2006/0025662, now U.S. Pat. No. 7,740,581, 2006/0091006, 2007/0056858, now U.S. Pat. No. 8,298,389, 2007/0068807, now U.S. Pat. No. 7,846,311, 2007/0095661, 2007/0108048, now U.S. Pat. No. 7,918,975, 2007/0199818, now U.S. Pat. No. 7,811,430, 2007/0227911, now U.S. Pat. No. 7,887,682, 2007/0233013, 2008/0066305, now U.S. Pat. No. 7,895,740, 2008/0081977, now U.S. Pat. No. 7,618,369, 2008/0102441, now U.S. Pat. No. 7,822,557, 2008/0148873, now U.S. Pat. No. 7,802,467, 2008/0161666, 2008/0267823, 2009/0054748, now U.S. Pat. No. 7,885,698, 2009/0294277, 2010/0213057, 2010/0081909, now U.S. Pat. No. 8,219,173, 2009/0247857, now U.S. Pat. No. 8,346,335, 2011/0106126, 2011/0082484, 2010/0326842, 2010/0198034, 2010/0324392, now U.S. Pat. No. 9,402,544, 2010/0230285, 2010/0313105, now U.S. Pat. No. 8,595,607, 2011/0213225, 2011/0021889, 2011/0193704, now U.S. Pat. No. 8,514,086, 2011/0190603, 2010/0317952, 2011/0191044, now U.S. Pat. No. 9,351,669, 2011/0257495, now U.S. Pat. No. 8,965,477, 2011/0288574, now U.S. Pat. No. 9,265,453, 2011/0319729, now U.S. Pat. No. 9,215,992, and 2012/0010642, now U.S. Pat. No. 9,186,098.

DETAILED DESCRIPTION

Within the scope of the present disclosure, there are provided devices, systems, kits and methods for providing compact, low profile, on-body physiological parameter monitoring device (physiological parameters such as for example, but not limited to analyte levels, temperature levels, heart rate, etc), configured for single or multiple use over a predetermined time period, which provide a low profile geometry, effective power management, improved shelf life, and ease and comfort of use including device positioning, and activation. Embodiments include an on-body assembly including a transcutaneously positioned analyte sensor and sensor electronics in a compact, low profile integrated assembly and coupled to an insertion device for deployment.

Before the present disclosure is described in additional detail, it is to be understood that this disclosure is not limited to particular embodiments described, as such may, of course, vary. It is also to be understood that the terminology used herein is for the purpose of describing particular embodiments only, and is not intended to be limiting, since the scope of the present disclosure will be limited only by the appended claims.

Where a range of values is provided, it is understood that each intervening value, to the tenth of the unit of the lower limit unless the context clearly dictates otherwise, between the upper and lower limit of that range and any other stated or intervening value in that stated range, is encompassed within the disclosure. The upper and lower limits of these smaller ranges may independently be included in the smaller ranges is also encompassed within the disclosure, subject to any specifically excluded limit in the stated range. Where the stated range includes one or both of the limits, ranges excluding either or both of those included limits are also included in the disclosure.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure belongs. Although any methods and materials similar or equivalent to those described herein can also be used in the practice or testing of the present disclosure, the preferred methods and materials are now described. All publications mentioned herein are incorporated herein by reference to disclose and describe the methods and/or materials in connection with which the publications are cited.

It must be noted that as used herein and in the appended claims, the singular forms "a", "an", and "the" include plural referents unless the context clearly dictates otherwise.

The publications discussed herein are provided solely for their disclosure prior to the filing date of the present application. Nothing herein is to be construed as an admission that the present disclosure is not entitled to antedate such publication by virtue of prior disclosure. Further, the dates of publication provided may be different from the actual publication dates which may need to be independently confirmed.

As will be apparent to those of skill in the art upon reading this disclosure, each of the individual embodiments described and illustrated herein has discrete components and features which may be readily separated from or combined with the features of any of the other several embodiments without departing from the scope or spirit of the present disclosure.

The figures shown herein are not necessarily drawn to scale, with some components and features being exaggerated for clarity.

Generally, embodiments of the present disclosure relate to methods and devices for detecting at least one analyte, such as glucose, in body fluid. In certain embodiments, the present disclosure relates to the continuous and/or automatic in vivo monitoring of the level of an analyte using an analyte sensor.

Accordingly, embodiments include analyte monitoring devices and systems that include an analyte sensor—at least a portion of which is positionable beneath the skin of the user—for the in vivo detection of an analyte, such as glucose, lactate, and the like, in a body fluid. Embodiments

include wholly implantable analyte sensors and analyte sensors in which only a portion of the sensor is positioned under the skin and a portion of the sensor resides above the skin, e.g., for contact to a transmitter, receiver, transceiver, processor, etc. The sensor may be, for example, subcutaneously positionable in a patient for the continuous or periodic monitoring of a level of an analyte in a patient's interstitial fluid.

For the purposes of this description, continuous monitoring and periodic monitoring will be used interchangeably, unless noted otherwise. Discrete monitoring as used herein includes the acquisition or reception of monitored analyte data where real time monitored analyte level information is received or acquired on demand or in response to a request to an analyte monitoring device including sensor and sensor electronics. That is, embodiments include analyte sensors and sensor electronics which sample and process analyte related information based on a programmed or programmable schedule such as every minute, every five minutes and so on. Such analyte monitoring routines may be reported or transmitted in real time to a receiver unit/reader device at the time of data sampling and processing. Alternatively, as discussed, the continuously sampled analyte data and processed analyte related signals may be stored and transmitted to a remote location such as the receiver unit, data processing module, the data processing terminal, the reader device or the remote terminal in response to a request for such information from the remote location. The analyte level may be correlated and/or converted to analyte levels in blood or other fluids. In certain embodiments, an analyte sensor may be positioned in contact with interstitial fluid to detect the level of glucose, and the detected glucose may be used to infer the glucose level in the patient's bloodstream. Analyte sensors may be insertable into a vein, artery, or other portion of the body containing fluid. Embodiments of the analyte sensors of the subject disclosure may be configured for monitoring the level of the analyte over a time period which may range from minutes, hours, days, weeks, or longer.

Of interest are analyte sensors, such as glucose sensors, that are capable of in vivo detection of an analyte for about one hour or more, e.g., about a few hours or more, e.g., about a few days of more, e.g., about three or more days, e.g., about five days or more, e.g., about seven days or more, e.g., about several weeks or at least one month. Future analyte levels may be predicted based on information obtained, e.g., the current analyte level at time t_0, the rate of change of the analyte, etc. Predictive alarms may notify the user of predicted analyte levels that may be of concern prior in advance of the analyte level reaching the future level. This enables the user an opportunity to take corrective action. Embodiments include transmission of the acquired real time analyte information on-demand from the user (using for example, the reader device/receiver unit positioned in close proximity to the low profile on-body patch device), storage of the acquired real time analyte information, and subsequent transmission based on retrieval from the storage device (such as a memory device).

FIG. **1** shows an exemplary in vivo-based analyte monitoring system **100** in accordance with embodiments of the present disclosure. As shown, in certain embodiments, analyte monitoring system **100** includes on body electronics **110** electrically coupled to in vivo analyte sensor **101** (a proximal portion of which is shown in FIG. **1**) and attached to adhesive layer **140** for attachment on a skin surface on the body of a user. On body electronics **110** includes on body housing **119**, that defines an interior compartment. Also shown in FIG. **1** is insertion device **150** that, when operated, transcutaneously positions a portion of analyte sensor **101** through a skin surface and in fluid contact with ISF, and positions on body electronics **110** and adhesive layer **140** on a skin surface. In certain embodiments, on body electronics **110**, analyte sensor **101** and adhesive layer **140** are sealed within the housing of insertion device **150** before use, and in certain embodiments, adhesive layer **140** is also sealed within the housing or itself provides a terminal seal of the insertion device **150**. Devices, systems and methods that may be used with embodiments herein are described, e.g., in U.S. patent application Ser. Nos. 12/698,129, now U.S. Pat. No. 9,402,544, 13/071,461, now U.S. Pat. No. 9,215,992, 13/071,487, now U.S. Pat. No. 9,265,453, and 13/071,497, now U.S. Pat. No. 9,186,098, the disclosures of each of which are incorporated herein by reference for all purposes.

Referring back to the FIG. **1**, analyte monitoring system **100** includes display device **120** or receiver/reader unit, which includes a display **122** to output information to the user, an input component **121** such as a button, actuator, a touch sensitive switch, a capacitive switch, pressure sensitive switch, jog wheel or the like, to input data or command to display device **120** or otherwise control the operation of display device **120**. It is noted that some embodiments may include display-less devices or devices without any user interface components. These devices may be functionalized to store data as a data logger and/or provide a conduit to transfer data from on body electronics and/or a display-less device to another device and/or location. Embodiments will be described herein as display devices for exemplary purposes which are in no way intended to limit the embodiments of the present disclosure. It will be apparent that display-less devices may also be used in certain embodiments.

In certain embodiments, on body electronics **110** may be configured to store some or all of the monitored analyte related data received from analyte sensor **101** in a memory during the monitoring time period, and maintain it in memory until the usage period ends. In such embodiments, stored data is retrieved from on body electronics **110** at the conclusion of the monitoring time period, for example, after removing analyte sensor **101** from the user by detaching on body electronics **110** from the skin surface where it was positioned during the monitoring time period. In such data logging configurations, real time monitored analyte level is not communicated to display device **120** during the monitoring period or otherwise transmitted from on body electronics **110**, but rather, retrieved from on body electronics **110** after the monitoring time period.

In certain embodiments, input component **121** of display device **120** may include a microphone and display device **120** may include software configured to analyze audio input received from the microphone, such that functions and operation of the display device **120** may be controlled by voice commands. In certain embodiments, an output component of display device **120** includes a speaker for outputting information as audible signals. Similar voice responsive components such as a speaker, microphone and software routines to generate, process and store voice driven signals may be provided to on body electronics **110**.

In certain embodiments, display **122** and input component **121** may be integrated into a single component, for example a display that can detect the presence and location of a physical contact touch upon the display such as a touch screen user interface. In such embodiments, the user may control the operation of display device **120** by utilizing a set of pre-programmed motion commands, including, but not limited to, single or double tapping the display, dragging a

finger or instrument across the display, motioning multiple fingers or instruments toward one another, motioning multiple fingers or instruments away from one another, etc. In certain embodiments, a display includes a touch screen having areas of pixels with single or dual function capacitive elements that serve as LCD elements and touch sensors.

Display device **120** also includes data communication port **123** for wired data communication with external devices such as remote terminal (personal computer) **170**, for example. Example embodiments of the data communication port **123** include USB port, mini USB port, RS-232 port, Ethernet port, FireWire™ (IEEE 1394) port, or other similar data communication ports configured to connect to the compatible data cables. Display device **120** may also include an integrated in vitro glucose meter, including in vitro test strip port **124** to receive an in vitro glucose test strip for performing in vitro blood glucose measurements.

Referring still to FIG. **1**, display **122** in certain embodiments is configured to display a variety of information—some or all of which may be displayed at the same or different time on display **122**. In certain embodiments the displayed information is user-selectable so that a user can customize the information shown on a given display screen. Display **122** may include but is not limited to graphical display **138**, for example, providing a graphical output of glucose values over a monitored time period (which may show important markers such as meals, exercise, sleep, heart rate, blood pressure, etc), a numerical display **132**, for example, providing monitored glucose values (acquired or received in response to the request for the information), and trend or directional arrow display **131** that indicates a rate of analyte change and/or a rate of the rate of analyte change, e.g., by moving locations on display **122**. Additionally, display **122** may include an alarm display that annunciates.

As further shown in FIG. **1**, display **122** may also include date display **135** providing for example, date information for the user, time of day information display **139** providing time of day information to the user, battery level indicator display **133** which graphically shows the condition of the battery (rechargeable or disposable) of the display device **120**, sensor calibration status icon display **134** for example, in monitoring systems that require periodic, routine or a predetermined number of user calibration events, notifying the user that the analyte sensor calibration is necessary, audio/vibratory settings icon display **136** for displaying the status of the audio/vibratory output or alarm state, and wireless connectivity status icon display **137** that provides indication of wireless communication connection with other devices such as on body electronics, data processing module **160**, and/or remote terminal **170**. As additionally shown in FIG. **1**, display **122** may further include simulated touch screen button **125**, **126** for accessing menus, changing display graph output configurations or otherwise for controlling the operation of display device **120**.

Referring back to FIG. **1**, in certain embodiments, display **122** of display device **120** may be additionally, or instead of visual display, configured to output alarm notifications such as alarm and/or alert notifications, glucose values etc, which may be audible, tactile, or any combination thereof. In one aspect, the display device **120** may include other output components such as a speaker, vibratory output component and the like to provide audible and/or vibratory output indication to the user in addition to the visual output indication provided on display **122**. Further details and other display embodiments can be found in, e.g., U.S. patent application Ser. No. 12/871,901, now U.S. Pat. No. 8,514,086, and U.S. provisional application Nos. 61/238,672, 61/247,541, 61/297,625, the disclosures of each of which are incorporated herein by reference for all purposes.

After the positioning of on body electronics **110** on the skin surface and analyte sensor **101** in vivo to establish fluid contact with ISF (or other appropriate body fluid), on body electronics **110** in certain embodiments is configured to wirelessly communicate analyte related data (such as, for example, data corresponding to monitored analyte level and/or monitored temperature data, and/or stored historical analyte related data) when on body electronics **110** receives a command or request signal from display device **120**. In certain embodiments, on body electronics **110** may be configured to at least periodically broadcast real time data associated with a monitored analyte level received by display device **120**, when display device **120** is within communication range of the data broadcast from on body electronics **110**, i.e., it does not need a command or request from display device **120** to send information.

For example, when within a communication range, display device **120** may be configured to automatically transmit one or more commands to on body electronics **110** to initiate data transfer, and in response, on body electronics **110** may be configured to wirelessly transmit stored analyte related data collected during the monitoring time period to display device **120**. In certain embodiments, the data transfer may be user initiated. Display device **120** may in turn be connected to a remote terminal **170**, such as a personal computer, and functions as a data conduit to transfer the stored analyte level information from the on body electronics **110** to remote terminal **170**. In certain embodiments, the received data from the on body electronics **110** may be stored (permanently or temporarily) in one or more memory of the display device **120**. In certain other embodiments, display device **120** is configured as a data conduit to pass the data received from on body electronics **110** to remote terminal **170** that is connected to display device **120**.

Referring still to FIG. **1**, also shown in analyte monitoring system **100** are data processing module **160** and remote terminal **170**. Remote terminal **170** may include a personal computer, a server terminal, a laptop computer or other suitable data processing devices including software for data management and analysis and communication with the components in the analyte monitoring system **100**. For example, remote terminal **170** may be connected to a local area network (LAN), a wide area network (WAN), or other data network for uni-directional or bi-directional data communication between remote terminal **170** and display device **120** and/or data processing module **160**.

Remote terminal **170** in certain embodiments may include one or more computer terminals located at a physician's office or a hospital. For example, remote terminal **170** may be located at a location other than the location of display device **120**. Remote terminal **170** and display device **120** could be in different rooms or different buildings. Remote terminal **170** and display device **120** could be at least about one mile apart, e.g., at least about 10 miles apart, e.g., at least about 100 miles apart. For example, remote terminal **170** could be in the same city as display device **120**, remote terminal **170** could be in a different city than display device **120**, remote terminal **170** could be in the same state as display device **120**, remote terminal **170** could be in a different state than display device **120**, remote terminal **170** could be in the same country as display device **120**, or remote terminal **170** could be in a different country than display device **120**, for example.

In certain embodiments, a separate, optional data communication/processing device such as data processing mod-

ule **160** may be provided in analyte monitoring system **100**. Data processing module **160** may include components to communicate using one or more wireless communication protocols such as, for example, but not limited to, infrared (IR) protocol, Bluetooth® protocol, Zigbee® protocol, and 802.11 wireless LAN protocol. Additional description of communication protocols including those based on Bluetooth® protocol and/or Zigbee® protocol can be found in U.S. Patent Publication No. 2006/0193375 incorporated herein by reference for all purposes. Data processing module **160** may further include communication ports, drivers or connectors to establish wired communication with one or more of display device **120**, on body electronics **110**, or remote terminal **170** including, for example, but not limited to USB connector and/or USB port, Ethernet connector and/or port, FireWire™ (IEEE 1394) connector and/or port, or RS-232 port and/or connector.

In certain embodiments, data processing module **160** is programmed to transmit a polling or query signal to on body electronics **110** at a predetermined time interval (e.g., once every minute, once every five minutes, or the like), and in response, receive the monitored analyte level information from on body electronics **110**. Data processing module **160** stores in its memory the received analyte level information, and/or relays or retransmits the received information to another device such as display device **120**. More specifically in certain embodiments, data processing module **160** may be configured as a data relay device to retransmit or pass through the received analyte level data from on body electronics **110** to display device **120** or a remote terminal (for example, over a data network such as a cellular or WiFi data network) or both.

In certain embodiments, on body electronics **110** and data processing module **160** may be positioned on the skin surface of the user within a predetermined distance of each other (for example, about 1-12 inches, or about 1-10 inches, or about 1-7 inches, or about 1-5 inches) such that periodic communication between on body electronics **110** and data processing module **160** is maintained. Alternatively, data processing module **160** may be worn on a belt or clothing item of the user, such that the desired distance for communication between the on body electronics **110** and data processing module **160** for data communication is maintained. In a further aspect, the housing of data processing module **160** may be configured to couple to or engage with on body electronics **110** such that the two devices are combined or integrated as a single assembly and positioned on the skin surface. In further embodiments, data processing module **160** is detachably engaged or connected to on body electronics **110** providing additional modularity such that data processing module **160** may be optionally removed or reattached as desired.

Referring again to FIG. **1**, in certain embodiments, data processing module **160** is programmed to transmit a command or signal to on body electronics **110** at a predetermined time interval such as once every minute, or once every 5 minutes or once every 30 minutes or any other suitable or desired programmable time interval to request analyte related data from on body electronics **110**. When data processing module **160** receives the requested analyte related data, it stores the received data. In this manner, analyte monitoring system **100** may be configured to receive the continuously monitored analyte related information at the programmed or programmable time interval, which is stored and/or displayed to the user. The stored data in data processing module **160** may be subsequently provided or transmitted to display device **120**, remote terminal **170** or the like for subsequent data analysis such as identifying frequency of periods of glycemic level excursions over the monitored time period, or the frequency of the alarm event occurrence during the monitored time period, for example, to improve therapy related decisions. Using this information, the doctor, healthcare provider or the user may adjust or recommend modification to the diet, daily habits and routines such as exercise, and the like.

In another embodiment, data processing module **160** transmits a command or signal to on body electronics **110** to receive the analyte related data in response to a user activation of a switch provided on data processing module **160** or a user initiated command received from display device **120**. In further embodiments, data processing module **160** is configured to transmit a command or signal to on body electronics **110** in response to receiving a user initiated command only after a predetermined time interval has elapsed. For example, in certain embodiments, if the user does not initiate communication within a programmed time period, such as, for example about 5 hours from last communication (or 10 hours from the last communication, or 24 hours from the last communication), the data processing module **160** may be programmed to automatically transmit a request command or signal to on body electronics **110**. Alternatively, data processing module **160** may be programmed to activate an alarm to notify the user that a predetermined time period of time has elapsed since the last communication between the data processing module **160** and on body electronics **110**. In this manner, users or healthcare providers may program or configure data processing module **160** to provide certain compliance with analyte monitoring regimen, so that frequent determination of analyte levels is maintained or performed by the user.

In certain embodiments, when a programmed or programmable alarm condition is detected (for example, a detected glucose level monitored by analyte sensor **101** that is outside a predetermined acceptable range indicating a physiological condition which requires attention or intervention for medical treatment or analysis (for example, a hypoglycemic condition, a hyperglycemic condition, an impending hyperglycemic condition or an impending hypoglycemic condition)), the one or more output indications may be generated by the control logic or processor of the on body electronics **110** and output to the user on a user interface of on body electronics **110** so that corrective action may be timely taken. In addition to or alternatively, if display device **120** is within communication range, the output indications or alarm data may be communicated to display device **120** whose processor, upon detection of the alarm data reception, controls the display **122** to output one or more notification.

In certain embodiments, control logic or microprocessors of on body electronics **110** include software programs to determine future or anticipated analyte levels based on information obtained from analyte sensor **101**, e.g., the current analyte level, the rate of change of the analyte level, the acceleration of the analyte level change, and/or analyte trend information determined based on stored monitored analyte data providing a historical trend or direction of analyte level fluctuation as function time during monitored time period. Predictive alarm parameters may be programmed or programmable in display device **120**, or the on body electronics **110**, or both, and output to the user in advance of anticipating the user's analyte level reaching the future level. This provides the user an opportunity to take timely corrective action.

Information, such as variation or fluctuation of the monitored analyte level as a function of time over the monitored

time period providing analyte trend information, for example, may be determined by one or more control logic or microprocessors of display device **120**, data processing module **160**, and/or remote terminal **170**, and/or on body electronics **110**. Such information may be displayed as, for example, a graph (such as a line graph) to indicate to the user the current and/or historical and/or and predicted future analyte levels as measured and predicted by the analyte monitoring system **100**. Such information may also be displayed as directional arrows (for example, see trend or directional arrow display **131**) or other icon(s), e.g., the position of which on the screen relative to a reference point indicated whether the analyte level is increasing or decreasing as well as the acceleration or deceleration of the increase or decrease in analyte level. This information may be utilized by the user to determine any necessary corrective actions to ensure the analyte level remains within an acceptable and/or clinically safe range. Other visual indicators, including colors, flashing, fading, etc., as well as audio indicators including a change in pitch, volume, or tone of an audio output and/or vibratory or other tactile indicators may also be incorporated into the display of trend data as means of notifying the user of the current level and/or direction and/or rate of change of the monitored analyte level. For example, based on a determined rate of glucose change, programmed clinically significant glucose threshold levels (e.g., hyperglycemic and/or hypoglycemic levels), and current analyte level derived by an in vivo analyte sensor, the system **100** may include an algorithm stored on computer readable medium to determine the time it will take to reach a clinically significant level and will output notification in advance of reaching the clinically significant level, e.g., 30 minutes before a clinically significant level is anticipated, and/or 20 minutes, and/or 10 minutes, and/or 5 minutes, and/or 3 minutes, and/or 1 minute, and so on, with outputs increasing in intensity or the like.

Referring again back to FIG. **1**, in certain embodiments, software algorithm(s) for execution by data processing module **160** may be stored in an external memory device such as an SD card, microSD card, compact flash card, XD card, Memory Stick card, Memory Stick Duo card, or USB memory stick/device including executable programs stored in such devices for execution upon connection to the respective one or more of the on body electronics **110**, remote terminal **170** or display device **120**. In a further aspect, software algorithms for execution by data processing module **160** may be provided to a communication device such as a mobile telephone including, for example, WiFi or Internet enabled smart phones or personal digital assistants (PDAs) as a downloadable application for execution by the downloading communication device.

Examples of smart phones include Windows®, Android™, iPhone® operating system, Palm® WebOS™, Blackberry® operating system, or Symbian® operating system based mobile telephones with data network connectivity functionality for data communication over an internet connection and/or a local area network (LAN). PDAs as described above include, for example, portable electronic devices including one or more microprocessors and data communication capability with a user interface (e.g., display/output unit and/or input unit, and configured for performing data processing, data upload/download over the internet, for example. In such embodiments, remote terminal **170** may be configured to provide the executable application software to the one or more of the communication devices described above when communication between the remote terminal **170** and the devices are established.

In still further embodiments, executable software applications may be provided over-the-air (OTA) as an OTA download such that wired connection to remote terminal **170** is not necessary. For example, executable applications may be automatically downloaded as software download to the communication device, and depending upon the configuration of the communication device, installed on the device for use automatically, or based on user confirmation or acknowledgement on the communication device to execute the installation of the application. The OTA download and installation of software may include software applications and/or routines that are updates or upgrades to the existing functions or features of data processing module **160** and/or display device **120**.

Referring back to remote terminal **170** of FIG. **1**, in certain embodiments, new software and/or software updates such as software patches or fixes, firmware updates or software driver upgrades, among others, for display device **120** and/or on body electronics **110** and/or data processing module **160** may be provided by remote terminal **170** when communication between the remote terminal **170** and display device **120** and/or data processing module **160** is established. For example, software upgrades, executable programming changes or modification for on body electronics **110** may be received from remote terminal **170** by one or more of display device **120** or data processing module **160**, and thereafter, provided to on body electronics **110** to update its software or programmable functions. For example, in certain embodiments, software received and installed in on body electronics **110** may include software bug fixes, modification to the previously installed software parameters (modification to analyte related data storage time interval, resetting or adjusting time base or information of on body electronics **110**, modification to the transmitted data type, data transmission sequence, or data storage time period, among others). Additional details describing field upgradability of software of portable electronic devices, and data processing are provided in U.S. application Ser. Nos. 12/698,124, 12/794,721, now U.S. Pat. No. 8,595,607, 12/699,653, and 12/699,844, now U.S. Pat. No. 8,930,203, and U.S. Provisional Application Nos. 61/359,265, and 61/325,155 the disclosure of which is incorporated by reference herein for all purposes.

Generally, the concentration of glucose in a person changes as a result of one or more external influences such as meals and exercise, and also changes resulting from various physiological mechanisms such as stress, illness, menstrual cycle and the like. In a person with diabetes, such changes can necessitate monitoring the person's glucose level and administering insulin or other glucose level altering drugs, such as, e.g., a glucose lowering or raising drug, as needed to maintain the person's glucose level with a desired range. In any of the above examples, the system **100** is thus configured to determine, based on some amount of patient-specific information, an appropriate amount, type and/or timing of insulin or other glucose level altering drug to administer in order to maintain normal glucose levels without causing hypoglycemia or hyperglycemia. In some embodiments, the system **100** is configured to control one or more external insulin pumps, such as, e.g., subcutaneous, transcutaneous or transdermal pumps, and/or implanted insulin pumps to automatically infuse or otherwise supply the appropriate amount and type of insulin to the user's body in the form of one or more insulin boluses.

In another embodiment, the system **100** is configured to display or otherwise notify the user of the appropriate amount, type, and/or timing of the insulin in the form of an

insulin delivery or administration recommendation or instruction. In such embodiments, the hardware and/or software forming system **100** allows the user to accept the recommended insulin amount, type, and/or timing, or to reject it. If the recommendation is accepted by the user, the system **100**, in one embodiment, automatically infuses or otherwise provides the appropriate amount and type of insulin to the user's body in the form of one or more insulin boluses. If, on the other hand, the user rejects the insulin recommendation, the hardware and/or software forming system **100** allows the user to override the system **100** and manually enter values for insulin bolus quantity, type, and/or timing in the system **100**. The system **100** is thus configured by the user to automatically infuse or otherwise provide the user specified amount, type, and/or timing of the insulin to the user's body in the form of one or more insulin boluses.

Alternatively, the appropriate amount and type of insulin corresponding to the insulin recommendation displayed by the system **100** may be manually injected into, or otherwise administered to, the user's body. It will be understood, however, that the system **100** may alternatively or additionally be configured in like manner to determine, recommend, and/or deliver other types of medication to a patient.

The system **100** is operable, as just described, to determine and either recommend or administer an appropriate amount of insulin or other glucose level lowering drug to the patient in the form of one or more insulin boluses. In order to determine appropriate amounts of insulin to be delivered or administered to the user to bring the user's glucose level within an acceptable range, the system **100** requires at least some information relating to one or more external influences and/or various physiological mechanisms associated with the user. For example, the system **100** may receive information if the user is about to ingest, is ingesting, or has recently ingested, a meal or snack, to determine an appropriate amount, type and/or timing of one or more meal compensation boluses of insulin. When a person ingests food in the form of a meal or snack, the person's body reacts by absorbing glucose from the meal or snack over time. For purposes of this document, any ingesting of food may be referred hereinafter as a "meal," and the term "meal" therefore encompasses traditional meals, such as, e.g., breakfast, lunch, and dinner, as well as intermediate snacks, drinks, and the like.

FIG. **2** depicts a typical glucose profile **200** for a user determined using a CGM sensor, such as sensor **101** with on body electronics **110**. The graph **205** plots the measured glucose level as a function of time. This profile shows the effect on glucose level from various actions, such as meal/carbohydrate intake **210**, and the delivery of rapid acting insulin **220** and long acting insulin **230**.

The general shape of a glucose profile for any person rises following ingestion of a meal, peaks at some measureable time following the meal, and then decreases thereafter. The speed, e.g., the rate from beginning to completion, of any one glucose absorption profile typically varies for a person by meal composition, meal type or time (e.g., breakfast, lunch, dinner, or snack), and/or according to one or more other factors, and may also vary from day-to-day under otherwise identical meal circumstances. Generally, the information relating to such meal intake information supplied by the user to the system **100** should contain, either explicitly or implicitly, an estimate of the carbohydrate content of the meal or snack, corresponding to the amount of carbohydrates that the user is about to ingest, is ingesting, or has recently ingested, as well as an estimate of the speed of overall glucose absorption from the meal by the user.

The estimate of the amount of carbohydrates that the patient is about to ingest, is ingesting, or has recently ingested, may be provided by the user in any of the various forms. Examples include, but are not limited to, a direct estimate or carbohydrate weight (e.g., in units of grams or other convenient weight measure), an amount of carbohydrates relative to a reference amount (e.g., a dimensionless amount), an estimate of meal or snack size (e.g., a dimensionless amount or units of serving), and an estimate of meal or snack size relative to a reference snack size (e.g., a dimensionless amount). Other forms of providing for user input of carbohydrate content of a meal or snack will occur to those skilled in the art, and any such other forms are contemplated by this disclosure.

The estimate of the speed of overall glucose absorption from the meal by the user may likewise be provided by the user in any of various forms. For example, for a specified value of the expected speed of overall glucose absorption, the glucose absorption profile captures the speed of absorption of the meal taken by the user. As another example, the speed of overall glucose absorption from the meal by the user also includes time duration between ingesting of the meal by a user and the peak glucose absorption of the meal by that user, which captures the duration of the meal taken by the user. The speed of overall glucose absorption may thus be expressed in the form of meal speed or duration. Examples of the expected speed of overall glucose absorption parameter in this case may include, but are not limited to, a compound parameter corresponding to an estimate of the meal speed or duration (e.g., units of time), a compound parameter corresponding to meal speed or duration relative to a reference meal speed or duration (e.g., dimensionless), or the like.

As another example of providing the estimate of the expected speed of overall glucose absorption parameter, the shape and duration of the glucose absorption profile may be mapped to the composition of the meal. Examples of the expected speed of overall glucose absorption parameter in this case may include, but are not limited to, an estimate of fat amount, protein amount, and carbohydrate amount (e.g., in units of grams) in conjunction with a carbohydrate content estimate in the form of meal size or relative meal size, an estimate of fat amount and carbohydrate amount relative to reference fat, protein, and carbohydrate amounts in conjunction with a carbohydrate content estimate in the form of meal size or relative meal size, and an estimate of total glycemic index of the meal or snack (e.g., dimensionless), wherein the term "total glycemic index" is defined for purposes of this disclosure as a parameter that ranks meals and snacks by the speed at which the meals or snacks cause the user's glucose level to rise. Thus, for example, a meal or snack having a low glycemic index produces a gradual rise in glucose level whereas a meal or snack having a high glycemic index produces a fast rise in glucose level. One exemplary measure of total glycemic index may be, but is not limited to, the ratio of carbohydrates absorbed from the meal and a reference value, such as derived from pure sugar or white bread, over a specified time period (e.g., 2 hours). Other forms of providing for user input of the expected overall speed of glucose absorption from the meal by the patient, and/or for providing for user input of the expected shape and duration of the glucose absorption profile generally will occur to those skilled in the art, and any such other forms are contemplated by this disclosure.

Generally, the concentration of glucose in a person with diabetes changes as a result of one or more external influences such as meals and/or exercise, and may also change

resulting from various physiological mechanisms such as stress, menstrual cycle and/or illness. In any of the above examples, the system **100** responds to the measured glucose by determining the appropriate amount of insulin to administer in order to maintain normal glucose levels without causing hypoglycemia. In some embodiments, the system **100** is implemented as a discreet system with an appropriate sampling rate, which may be periodic, aperiodic, or triggered, although other continuous systems or hybrid systems may alternatively be implemented as described above.

As one example of a conventional diabetes control system, one or more software algorithms may include a collection of rule sets which use (1) glucose information, (2) insulin delivery information, and/or (3) user inputs such as mean intake, exercise, stress, illness and/or other physiological properties to provide therapy, and the like, to manage the user's glucose level. The rule sets are generally based on observations and clinical practices as well as mathematical models derived through or based on analysis of physiological mechanisms obtained from clinical studies. In the exemplary system, models of insulin pharmacokinetics, pharmacodynamics, glucose dynamics, meal absorption and exercise responses of individual patients are used to determine the timing and the amount of insulin to be delivered. A learning module may be provided to allow adjustment of the model parameters when the patient's overall performance metric degrades such as, for example, adaptive algorithms, using Bayesian estimates, may be implemented. An analysis model may also be incorporated which oversees the learning to accept or reject learning. Adjustments are achieved utilizing heuristics, rules, formulae, minimization of cost function(s) or tables (such as, for example, gain scheduling).

Model-based methods, such as a Kalman filter, can be programmed into the processor(s) of the system using appropriate embedded or inputted software to predict the outcome of adding a controlled amount of insulin or other drug to a user in terms of the expected glucose value. The structures and parameters of the models define the anticipated behavior.

Any of a variety of conventional controller design methodologies, such as PID (Proportional-Integral-Derivative) systems, full state feedback systems with state estimators, output feedback systems, LQG (Linear-Quadratic-Guassian) controllers, LQR (Linear-Quadratic-Regulator) controllers, eigenvalue/eigenstructure controller systems, and the like, could be used to design algorithms to perform physiological control. They typically function by using information derived from physiological measurements and/or user inputs to determine the appropriate control action to use. While the simpler forms of fixed controllers use fixed parameters (and therefore rules) for computing the magnitude of control action, the parameters in more sophisticated forms of such controllers may use one of more dynamic parameters. The one or more dynamic parameters could, for example, take the form of one or more continuously or discretely adjustable gain values. Specific rules for adjusting such gains could, for example, be defined either on an individual basis or on the basis of a user population, and in either case will typically be derived according to one or more mathematical models. Such gains are typically scheduled according to one or more rule sets designed to cover the expected operating ranges in which operation is typically nonlinear and variable, thereby reducing sources of error.

Model based control systems, such as those utilizing model predictive control algorithms, can be constructed as a black box wherein equations and parameters have no strict analogs in physiology. Rather, such models may instead be representations that are adequate for the purpose of physiological control. The parameters are typically determined from measurements of physiological parameters such as glucose level, insulin concentration, and the like, and from physiological inputs such as food intake, alcohol intake, insulin dose, and the like, and also from physiological states such as stress level, exercise intensity and duration, menstrual cycle phase, and the like. These models are used to estimate current glucose level or to predict future glucose levels. Such models may also take into account unused insulin remaining in the user after a bolus of insulin is given, for example, in anticipation of a meal. Such unused insulin will be variously described as unused, remaining, or "insulin on board."

A model based control system can perform a prediction of a user's blood glucose concentration in terms of a "best-estimate" as well as upper and/or lower bounds of the estimate for the present time and up to a finite time in the future. A Kalman filter can be implemented by the model based control system to estimate, predict, and model the best-estimate and the variance (i.e., upper and/or lower bounds) of a user's blood analyte concentration. A Kalman filter produces estimates of the true values of measurements of the user's blood glucose concentration by predicting a value, estimating the uncertainty of the predicted value, and computing a weighted average of the predicted value and the measured value. The most weight is given to the value with the least uncertainty. The estimates produced by the Kalman filter tend to be closer to the true values than the original measurements because the weighted average has a better estimated uncertainty than either of the values that went into the weighted average. The Kalman filter model assumes the true state at time k is evolved from the state at (k−1) according to $x_k=F_k x_{k-1}+B_k u_k+w_k$, where:

- F_k is the state transition model which is applied to the previous state x_{k-1};
- B_k is the control-input model which is applied to the control vector u_k;
- w_k is the process which is assumed to be drawn from a zero mean multivariate normal distribution with covariance Q_k.

The Kalman filter is a recursive estimator, which means that only the estimated state from the previous time step and the current measurement are needed to compute the estimate for the current state. In contrast to batch estimation techniques, no history of observations and/or estimates is required. In what follows, the notation $\hat{x}_{n|m}$ represents the estimate of x at time n given observations up to, and including time m. The state of the filter is represented by two variables:

1. $\hat{x}_{k|k}$, the a posteriori state estimate at time k given observations up to and including time k; and
2. $P_{k|k}$, the a posteriori error covariance matrix (e.g., a measure of the estimated accuracy of the state estimate.

The Kalman filter can be written as a single equation; however it is most often conceptualized as two distinct phases: "predict" and "update." The predict phase uses the state estimate from the previous timestep to produce an estimate of the state at the current timestep. The predicted state estimate is also known as the a priori state estimate because, although it is an estimate of the state at the current timestep, it does not include observation information from the current timestep. In the update phase, the current a priori prediction is combined with current observation information to refine the state estimate. The improved estimate is termed the a posteriori state estimate. Typically, the two phases

alternate, with the prediction advancing the state until the next scheduled observation, and the update incorporating the observation. However, this is not necessary. If an observation is unavailable for some reason, the update may be skipped and multiple prediction steps performed. Likewise, if multiple independent observations are available at the same time, multiple update steps may be performed. The formula for the updated estimate and covariance of the Kalman filter can be seen below.

Predicted (i.e., a Priori) State Estimate:

$$\hat{x}_{k|k-1}=F_k\hat{x}_{k-1|k-1}+B_k u_k$$

Predicted (i.e., a Priori) Estimate Covariance:

$$P_{k|k-1}F_kP_{k=-1|k-1}F_k{}^T+Q_k$$

Measurement Residual:

$$\hat{y}=z_k-H_k\hat{x}_{k|k-1}$$

Residual Covariance:

$$S_k=H_kP_{k|k-1}H_k{}^T+R_k$$

Optimal Kalman Gain:

$$K_k=P_{k|k-1}H_k{}^TS_k{}^{-1}$$

Updated (i.e., a Posteriori) State Estimate:

$$\hat{x}_{k|k}=\hat{x}_{k|k-1}+K_k\hat{y}_k;\text{ and}$$

Updated (i.e., a Posteriori) Estimate Covariance:

$$P_{k|k}=(I-K_kH_k)/P_{k|k-1}$$

More specifically, the Kalman filter of the model based control system can use the known user inputs described above and the user's blood analyte readings taken from the on-body sensor to determine a best-estimate of the user's actual blood analyte readings.

Insulin therapy is derived by the system based on the model's ability to predict glucose levels for various inputs. Other conventional modeling techniques may be additionally or alternatively used to predict glucose levels, including for example, but not limited to, building models from first principles.

In a system as described above, the controller is typically programmed to provide a "basal rate" of insulin deliver or administration. Such a basal rate is the rate of continuous supply of insulin by an insulin delivery device such as a pump that is used to maintain a desired glucose level in the user. Periodically, due to various events that affect the metabolism of a user, such as eating a meal or engaging in exercise, a "bolus" delivery of insulin is required. A "bolus" is defined as a specific amount of insulin that is required to raise the blood concentration of insulin to an effective level to counteract the effects of the ingestion of carbohydrates during a meal and also takes into account the effects of exercise on the glucose level of the user.

As described above, an analyte monitor may be used to continuously monitor the glucose level of a user. The controller is programmed with appropriate software and uses models as described above to predict the effect of carbohydrate ingestion and exercise, among other factors, on the predicted level of glucose of the user at a selected time. Such a model must also take into account the amount of insulin remaining in the blood stream from a previous bolus or basal rate infusion of insulin when determining whether or not to provide a bolus of insulin to the user.

Continuous glucose monitoring (CGM) systems occasionally exhibit non-zero-mean signal artifacts commonly called "dropout," where the sensor signal output is momentarily lower than it should be given an interstitial glucose value. From a closed-loop control perspective, this measurement error poses an annoyance in that the falsely lower signal could trigger a momentary reduction or cessation of insulin delivery commands due to the perceived hypoglycemic event. This can result in a false alarm based either on a perceived current glucose level or a computed future glucose level.

In certain embodiments of the present disclosure, techniques including computer implemented algorithms for reducing false hypoglycemic alarms due to a combination of a user's glucose range being mostly euglycemic (normal) and CGM system signal artifacts such as dropouts which tend to negatively bias the glucose display is provided. In such embodiments, the threshold for detecting a hypoglycemic threshold is modified by introducing a conditional time delay such that most dropouts are shorter in duration than the time delay so that the dropouts do not trigger an alarm. Additionally, the threshold is modified appropriately so that detection of true hypoglycemic events is not delayed beyond what has been determined to be clinically safe.

It is possible, using clinical data and insulin delivery information, to trust a CGM system to provide a balance between hypoglycemic detection sensitivity and reasonable specificity that minimizes false alarms under a wide range of glucose profiles. With good glycemic control, the proportion of true-hypoglycemia may be reduced significantly enough that signal artifacts of the CGM system become an important factor in causing false alarm rates.

In one embodiment of the present system, a combination of glucose level measurements, known as CGM signal artifact characteristics, and the best-estimate of relevant physiological states, such as, for example, plasma glucose, interstitial glucose, insulin on board, and effective insulin, are used to delay the enunciation of a CGM based hypoglycemic alarm and determine whether or not the alarm should persist. In this embodiment, instead of using an artifact detector which relies on a mechanism that is sensitive to the artifacts in the signal, the alarm instead is tuned to be insensitive to the artifacts, yet at the same time maintain a safe level of sensitivity to hypoglycemic events.

The CGM based hypoglycemic alarm of the one embodiment of the disclosure comprises several hypoglycemic thresholds. For each threshold, there exists a timer that may potentially annunciate a hypoglycemic alarm. The lower the threshold, the shorter the amount of delay between the time the CGM measurement value is obtained and when the alarm is sounded. The amount of delay depends primarily on the level of risk associated with the delayed response to a true hypoglycemic event at a given glucose level as well as the probability of the duration of false alarms due to the presence of CGM signal artifacts at a given glucose level.

The CGM based hypoglycemic alarm may result in the system recommending that a finger stick glucose level measurement request. If the glucose level measurement resulting from the finger stick indicates that the CGM measure hypoglycemia does not exist, the system can turn off the alarm. Alternatively, if the finger stick glucose level measurement confirms the presence of hypoglycemia, then the controller may indicate to the user that certain actions, such as taking rescue carbohydrates and/or checking glucose level frequently thereafter until the condition has been resolved, may be required.

A user with a well-controlled glucose level, using either a fully automatic closed loop system, a partial closed loop system or intensive open loop treatment, may have a glucose profile and distribution that is altered enough that the amount of false hypoglycemic alarms from the system is

significantly larger than found in the general population of clinical data used to tune and confirm the hypoglycemic alarm response. The primary reason for this is that in the lower glucose range, the effect of signal artifacts from the CGM device become more dominant.

The CGM signal artifacts that reduce the effectiveness of the CGM based hypoglycemic alarm have been found to have an a priori distribution of severity, duration, and trajectory profile. Given a user's history of glucose levels, insulin delivery, and other relevant physiological information, a particular level of hypoglycemia carries a particular level of risk in terms of the maximum delay allowed before treatment should begin to avoid the effects of sever hypoglycemia. Delaying a hypoglycemic alarm to the extent that it is still clinically safe and yet as long as possible can reduce the false alarms due to the CGM signal artifacts.

Given a glucose level confirmation and possibly a corrective action such as administering rescue carbohydrates, glucose can be estimated with sufficient confidence such that for a finite horizon in the future, there is no need to activate the CGM based hypoglycemic alarm. This further decreases the likelihood of false alarms.

In one embodiment of the disclosure, the controller is programmed using appropriate software so as to set up two separate subsystems for decision making. While these subsystems will be described in terms of one or more state machines, those skilled in the art of control theory and engineering will understand that other embodiments may be contemplated. Thus, skilled artisans will understand how to program the processor to implement such a state machine.

FIG. **3** illustrates a state machine which governs the behavior of the assertion of the CGM based hypoglycemic detector. FIG. **3** also depicts a state machine which governs how and when confirmatory glucose level measurements, such as by a finger stick, should be taken, how and when rescue carbohydrates should be administered, and when to de-assert the CGM based hypoglycemic detector.

Referring now to FIG. **3**, in certain embodiments the CGM state machine is configured to determine when a hypoglycemic alarm should be asserted relative to a CGM threshold reading and a best-estimate of the user's BG concentration that is determined by the system. The CGM state machine begins at **105**. When the CGM measurements become available, the state machine enters the "no hypoglycemia confirmed" state **110**. Within this state, the controller obtains a current CGM value and also obtains a best-estimate of the user's blood glucose value, and dependent on the value of the measurements, controls the analysis along one of several paths. For example, if the latest CGM value (i.e., the CGM **115**) is less than or equal to 3.5 mMol/L (63 mg/dL) but greater than 3.0 mMol/L (54 mg/dL), but the best-estimate determines that the BG concentration is above 3.5 mMol/L a delay timer of 40 minutes is implemented at state **120**. If the detected CGM value is greater than 2.5 mMol/L (45 mg/dL) but less than or equal to 3.0 mMol/L (54 mg/dL), but the best-estimate determines that the BG concentration is above 3.5 mMol/L a delay of 30 minutes is implemented at state **125**. Similarly, if the detected CGM value is greater than 2.0 mMol/L (36 mg/dL) but less than or equal to 2.5 mMol/L (45 mg/dL), but the best-estimate determines that the BG concentration is above 3.5 mMol/L a delay of 20 minutes is implemented at state **130**.

When any of the timer set at states **120**, **125**, or **130** expire, and the latest CGM value is still no higher than the corresponding upper limits for the delayed timer module states **120**, **125**, or **130**, the state changes to "confirm intermediate hypoglycemia" at state **140**. In this state, the controller resets all the timers of states **120**, **125**, and **130**, and sets the hypoglycemia alarm to on. This state prevents the alarm from sounding unnecessarily when a user's glucose level is still within a range where the annoyance of an alarm outweighs the risk that the user is actually in a hypoglycemic condition that requires immediate attention. Once the alarm is sounded, the CGM state machine returns to the "no confirmed hypoglycemia" state **110**.

Where the detected CGM value is less than or equal to 2.0 mMol/L (36 mg/dL), which is indicative of severe hypoglycemia, no delay is implemented, and the machine exits from the "no confirmed hypoglycemia" state **110** to state **145**. In this state, all of the timers of states **120**, **125**, and **130** are reset, the hypoglycemia alarm is set to on, thus sounding an alarm, and the controller continues to check the current CGM value and the best-estimate value. In this state the system cannot return to the "no confirmed hypoglycemia" state **110** until the latest CGM value rises above 3.5 mMol/L (63 mg/dL). The hypoglycemia alarm, which was already activated, is related to the glucose level subsystem. When the latest CGM value rises above 3.5 mMol/L, the CGM subsystem state machine returns to "no confirmed hypoglycemia" state **110**, whether or not the latest alarm has been confirmed by a separate glucose level reading.

Referring now to FIG. **4**, the controller is programmed to set up a separate blood glucose (BG) level subsystem, which will be described in terms of a state machine. This state machine de-asserts the hypoglycemic alarm upon non-hypoglycemic confirmation using a glucose level at a fixed threshold and/or a best-estimate of the glucose level, such as when the glucose level is equal and/or estimated to 3.5 mMol/L (63 mg/dL). When the system starts, the BG state machine initializes into state **205**. In this state, no glucose level check is needed, and the hypoglycemia alarm is set to off.

When the CGM state machine asserts the hypoglycemic alarm at states **140** or **145**, the BG state machine performs a transition **207**, where the BG state machine enters a "BG check needed" state **210**. In this state, the system requests and waits for a finger stick glucose level measurement at **215**, and if a "BG equals hypoglycemia" confirmation results from the finger stick, the controller alerts the user at state **220**. The hypoglycemia confirmation based on the BG finger stick may be set at the uppermost limit of the CGM state machine's limits, which may be equal to 3.5 mMol/L (63 mg/dL) as depicted in FIG. **2**, or any other suitable value. The user may then address the low glucose level measurement by taking rescue carbohydrates at state **220**. This action may be recommended by the controller. The controller also requests another glucose level be measured in 15 minutes. This process continues until the latest glucose level indicates that the user is no longer in a hypoglycemic state.

The previous embodiments illustrated in FIGS. **3** and **4** may be generalized further by removing the actions "confirm intermediate hypoglycemia" (FIG. **3**, reference number **140**) and "confirm severe hypoglycemia" (FIG. **3**, reference number **145**) from the CGM state machine. In this embodiment, no CGM hypoglycemia timers are reset until the timers expire and the hypoglycemia alarm is annunciated. This allows for several alarm mechanisms to occur simultaneously.

In certain embodiments, if the current CGM glucose value rises above 3.5 mMol/L at any time while the CGM state machine is in the "no confirmed hypoglycemia" state **110**, the alarm may be reset and the controller returns to processing incoming CGM data as before. In this case, no alarm will be sounded.

Referring now to FIG. **5**A and FIG. **5**B, another embodiment utilizes prior knowledge of various factors such as glucose level, CGM value, insulin on board, and the like, to further minimize false alarms by modifying the length of the delay timer if there is a convergence in the information gathered from the CGM sensor and the best-estimate of the

user's BG level. As in the embodiment depicted in FIG. **3**, the CGM state machine asserts the hypoglycemic alarm, and the BG state machine de-asserts the alarm. However, the two state machines are coupled even further with the assumption that while the system is set at a "hypoglycemia suspected" state **340**, no CGM based hypoglycemic threshold shall matter. In addition, depending on the control model and the value from the latest finger stick glucose level check, a variable time can be added to delay the return into the periodic CGM based hypoglycemic detection "no hypoglycemia suspected" state **310**.

For example, if the latest finger stick BG value is 4.0 mMol/L (72 mg/dL), and the control model predicts a rapidly rising glucose level, then a relatively short delay timer might be activated before the system transitions from "hypoglycemia suspected" state **340** to the "no hypoglycemia suspected" state **310**. On the other hand, if the latest finger stick BG check indicates a glucose level value of 4.0 mMol/L (72 mg/dL) and the control model programmed into the controller predicts a rapidly dropping glucose level profile, then the system immediately transitions from the "hypoglycemia suspected" state **340** to "no hypoglycemia suspected" state **310**, but the CGM based hypoglycemia detector will be given the fastest opportunity to trigger. Using the control model and relative value of the latest finger stick BG check allows the system to apply a state transition rule that is decoupled from which CGM based hypoglycemic detector triggered the state transition, thus preventing false hypoglycemia alarms.

Referring to FIG. **5**B, when the "hypoglycemia suspected" state **340** is entered, a finger stick BG value is requested at state **345**. Depending on the glucose level profile of the user, that is, the profile due to prior insulin deliveries, insulin sensitivity, exercise and the like, the controller may enter either state **355**, where rescue carbohydrates are administered and the finger stick BG is again measured after fifteen minutes, or state **350**, where a timer indicating when the next finger stick BG confirmation is to be performed is started. The duration of this timer is dependent upon a determination of the likelihood of glucose value changes based on the future glucose level profile determined by the control model being used by the controller and the latest finger stick glucose level value.

In this embodiment, the system checks the CGM value at every sample time, instead of using four or more distinct hypoglycemia thresholds with specific time delay amounts, and continues to count-down the timer until it is larger than a latest-glucose-dependent timer.

In certain embodiments, a table of delay values as a function of glucose level is used by the processor to modify the timer delay, where crossing a lower glucose value results in a shorter alarm delay. An alarm will be annunciated whenever any timer expires (e.g., the glucose value remains below that threshold value for the duration of the timer delay). Table 1 below depicts a table that can be used by the processor to modify the timer delay.

TABLE 1

Table implemented by the processor to determine the timer delay based upon a user's glucose concentration.

Glucose Concentration (mg/dL)	Time (minutes)
60	30
50	15
45	0

For example, if the CGM sensor detects a drop in the user's blood glucose concentration to a hypoglycemic level, but the best-estimate predicts that the user's blood glucose is at a euglycemic level, then the likelihood of an actual hypoglycemic event is low. Various reasons could cause such a divergence, such as a CGM calibration error or CGM signal distortion errors such as night-time drop outs. When the user's glucose level falls below 60 mg/dL, but is above 50 mg/dL, the alarm will be delayed for 30 minutes. When the CGM sensor detects a glucose level between 50 mg/dL and 45 mg/dL, the alarm is delayed 15 minutes prior to annunciating. If the user's glucose level falls below 45 mg/dL, then the alarm annunciates immediately.

However if there is agreement between the user's blood glucose concentration determined by the CGM sensor and the best-estimate prediction that a hypoglycemic event is likely, then the system can modify the alarm mechanism to thereby decrease the likelihood of imposing unnecessary risk to the user. As the likelihood of a hypoglycemic event increases to a higher risk, the mechanism described above with respect to Table 1 can be implemented with a 50% shortening of the alarm delay, as seen below in Table 2. In this embodiment, the alarm delay is shortened to 15 minutes when the detected CGM value crosses the 60 mg/dL threshold. The alarm delay is shortened to 7.5 minutes when the detected CGM value crosses the 50 mg/dL threshold. However, the alarm is still annunciated immediately when the detected CGM value crosses the 45 mg/dL threshold.

TABLE 2

Table implemented by the processor with a shortened alarm delay based upon an increased risk of a hypoglycemic event.

Glucose Concentration (mg/dL)	Time (minutes)
60	15
50	7.5
45	0

In certain embodiments, as the likelihood of a hypoglycemic event increases, the same delay times as seen in Table 1 are retained, but the threshold values for blood analyte concentration are increased. For example, Table 3 illustrates that the alarm delay is set for 30 minutes when the detected CGM value crosses the 65 mg/dL threshold, that the alarm delay is set for 15 minutes when the detected CGM value crosses the 55 mg/dL threshold, and the alarm is annunciated immediately when the detected CGM value crosses the 50 mg/dL threshold.

TABLE 3

Table implemented by the processor with an increased blood glucose concentration based upon an increased risk of a hypoglycemic event.

Glucose Concentration (mg/dL)	Time (minutes)
65	30
55	15
50	0

In certain embodiments, a hybrid between the two previously described embodiments is implemented, wherein both threshold values and time delays are adjusted if the best-estimate glucose range determined by the model determines a heightened risk of a hypoglycemic event. As seen in Table 4 below, both the glucose threshold and the time delay are modified to avoid imposing unnecessary risk to the user.

TABLE 4

Table implemented by the processor with an increased blood glucose concentration and shortened alarm delay based upon an increased risk of a hypoglycemic event.

Glucose Concentration (mg/dL)	Time (minutes)
65	15
55	7.5
50	0

In further embodiments, the same principles of the previous three embodiments can be applied to hyperglycemia detection, such that the tiered thresholds increase in the order of the threshold values. For example, if the information received from the analyte sensor and the best-estimate of the user's analyte concentration are in divergence with one another the system waits 30 minutes when the detected CGM value reaches a 180 mg/dL threshold and remains at that threshold before triggering the alarm, the system waits 15 minutes when the detected CGM value crosses a 200 mg/dL threshold and remains at that threshold before triggering the alarm, and the system waits 7.5 minutes once the detected CGM value reaches a 220 mg/dL threshold and remains at that threshold before triggering the alarm. However, as illustrated below in Table 5, if there is convergence between the data received from the detected CGM value and the best-estimate of the user's blood glucose concentration, then the system can modify one or both of the glucose concentration threshold and the length of time the system waits before asserting the hyperglycemia alarm.

TABLE 5

Table implanted by the processor with a decrease in the hyperglycemic alarm delay based upon an increased risk of a hyperglycemic event.

Glucose Concentration (mg/dL)	Time (minutes)
180	15
200	7.5
220	3.75

The embodiments described above are particularly useful in reducing or eliminating unnecessary risk to a user by implementing hypoglycemic/hyperglycemic alarms in a timely manner. While several specific embodiments have been illustrated and described, it will be apparent that various modifications can be made without departing from the spirit and scope of the disclosure. Accordingly, it is not intended that the disclosure be limited, except as by the appended claims.

In certain embodiments, a computer-implemented method for determining when to activate an alarm of a continuous analyte monitor may comprise receiving, at a data processing component, information from the continuous analyte monitor related to the user's analyte concentration, determining, at the data processing component, the user's analyte concentration using the information received from the continuous analyte monitor, receiving, at a data processing component, information from the user related to the user's analyte concentration, determining, at a data processing component, a best-estimate of the user's analyte concentration based upon the information from the continuous analyte monitor and information from the user, determining, at a data processing component, at least one condition for activating the alarm, and modifying, at a data processing component, the at least one condition for activating the alarm based on a comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration.

Certain aspects may include that a best-estimate of the user's analyte concentration includes a range of variance.

Certain aspects may include activating, at the processor, the analyte alarm if at least one of the data signal related to the user's analyte concentration satisfies the at least one determined condition.

Certain aspects may include that the best-estimate of the user's analyte concentration is at least partially determined using at least one of a Kalman filter and other state observers.

Certain aspects may include that the at least one condition for activating the analyte alarm includes receiving a data signal that indicates that the user's analyte concentration has reached a threshold value.

Certain aspects may include that the at least one condition includes that the user's analyte concentration crosses a threshold value for a predetermined length of time.

Certain aspects may include that when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration are in high agreement with each other, this suggests an increased likelihood of true physiological events such as a hypoglycemic event.

Certain aspects may include that when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration are in high agreement with each other, this suggests an increased likelihood of a true physiological events such as a hyperglycemic event.

Certain aspects may include that the modification includes increasing or decreasing the threshold value of the user's analyte concentration.

Certain aspects may include that when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration suggests an increased likelihood of a hypoglycemic event, the threshold value is increased, and wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration suggests a low likelihood of a hypoglycemic event, the threshold value is decreased.

Certain aspects may include that the modification includes increasing or decreasing the predetermined duration that the user's analyte concentration may cross the threshold value.

Certain aspects may include that the modification includes increasing or decreasing the threshold value for the user's analyte concentration, and includes increasing or decreasing the predetermined duration that the user's analyte concentration may cross the threshold value.

Certain aspects may include that the information from the continuous analyte monitor includes at least one data signal.

In certain embodiments, an integrated analyte monitoring device assembly may comprise an analyte sensor for transcutaneous positioning through a skin layer and maintained in fluid contact with an interstitial fluid under the skin layer during a predetermined time period, the analyte sensor having a proximal portion and a distal portion, and sensor electronics coupled to the analyte sensor that may comprise a circuit board having a conductive layer and a sensor antenna disposed on the conductive layer, one or more electrical contacts provided on the circuit board and coupled with the proximal portion of the analyte sensor to maintain continuous electrical communication, and a data processing component provided on the circuit board and in signal

communication with the analyte sensor, the data processing component configured to execute one or more routines for processing signals received from the analyte sensor, the data processing component configured to control the transmission of data associated with the processed signals received from the analyte sensor to a remote location using the sensor antenna in response to a request signal received from the remote location, the data processing component configured to receive information from the continuous analyte monitor related to the user's analyte concentration, the data processing unit configured to determine the user's analyte concentration using the information received from the continuous analyte monitor, the data processing component configured to receive data from the user related to the user's analyte concentration, the data processing component configured to determine a best-estimate of the user's analyte concentration based upon the information received from the continuous analyte monitor and the data received from the user at the processor, the data processing component configured to determine at least one condition for activating an alarm, the data processing component configured to modify the at least one condition for activating the alarm based on a comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration.

Certain aspects may include that the best-estimate of the user's analyte concentration includes a range of variance.

Certain aspects may include that the data processing component is further configured to activate the alarm if at least one of the data signals related to the user's analyte concentration and the best-estimate of the user's analyte concentration satisfies the at least one determined condition.

Certain aspects may include that the best-estimate of the user's analyte concentration is at least partially determined using at least one of a Kalman filter and other state observers.

Certain aspects may include that the at least one condition for activating the alarm includes receiving a data signal that indicates that the user's glucose concentration has reached a threshold value.

Certain aspects may include that the at least one condition includes that the user's analyte concentration crosses a threshold value for a predetermined length of time.

Certain aspects may include that when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration are in high agreement with each other, this suggests an increased likelihood of a hypoglycemic event.

Certain aspects may include that when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration are in high agreement with each other, this suggests an increased likelihood of true physiological events such as a hyperglycemic event.

Certain aspects may include that the modification includes increasing or decreasing the threshold value of the user's glucose concentration.

Certain aspects may include that when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration suggests an increased likelihood of a hypoglycemic event, the threshold value is increased, and wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration suggests a low likelihood of a hypoglycemic event, the threshold value is decreased.

Certain aspects may include that the modification includes increasing or decreasing the predetermined duration that the user's analyte concentration may cross the threshold value.

Certain aspects may include that the modification includes increasing or decreasing the threshold value for the user's analyte concentration, and includes increasing or decreasing the predetermined length of time that the user's analyte concentration may cross the threshold value.

Certain aspects may include that the information from the continuous analyte monitor includes at least one data signal.

In some embodiments, an integrated analyte monitoring device may comprise a data processing component provided on a circuit board and in signal communication with a continuous analyte monitor that may be configured to execute one or more routines for processing signals received from the continuous analyte monitor, control the transmission of data associated with the processed signals received from the continuous analyte monitor to a remote location using an antenna in response to a request signal received from the remote location, receive information from the continuous analyte monitor related to the user's analyte concentration, determine the user's analyte concentration using the information received from the continuous analyte monitor, receive data from the user related to the user's analyte concentration, determine a best-estimate of the user's analyte concentration based upon the information received from the continuous analyte monitor and the data received from the user at the processor, determine at least one condition for activating an alarm, and modify the at least one condition for activating the alarm based on the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration.

While the present disclosure has been described with reference to the specific embodiments thereof, it should be understood by those skilled in the art that various changes may be made and equivalents may be substituted without departing from the true spirit and scope of the present disclosure. In addition, many modifications may be made to adapt a particular situation, material, composition of matter, process, process step or steps, to the objective, spirit and scope of the present disclosure. All such modifications are intended to be within the scope of the claims appended hereto.

What is claimed is:

1. A computer-implemented method for determining when to activate an alarm of a continuous analyte monitor, comprising:

receiving, at a data processing component, information from a continuous analyte monitor related to a user's analyte concentration;

determining, at the data processing component, the user's analyte concentration using the information received from the continuous analyte monitor;

receiving, at the data processing component, information from the user related to the user's analyte concentration;

determining, at the data processing component, a best-estimate of the user's analyte concentration based upon the information from the continuous analyte monitor and information from the user;

determining, at the data processing component, at least one condition for activating alarm; and

modifying, at the data processing component, the at least one condition for activating the alarm based on a comparison between the determination of the user's

analyte concentration and the best-estimate of the user's analyte concentration.

2. The method according to claim **1**, wherein the best-estimate of the user's analyte concentration includes a range of variance.

3. The method according to claim **2**, wherein the best-estimate of the user's analyte concentration is at least partially determined using at least one of a Kalman filter and other state observers.

4. The method according to claim **1**, comprising:

activating, at the data processing component, the analyte alarm if at least one of a data signal related to the user's analyte concentration satisfies the at least one determined condition.

5. The method according to claim **1**, wherein the at least one condition for activating the analyte alarm includes receiving a data signal that indicates that the user's analyte concentration has reached a threshold value.

6. The method according to claim **1**, wherein the at least one condition includes that the user's analyte concentration crosses a threshold value for a predetermined length of time.

7. The method according to claim **1**, wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration are in high agreement with each other, this suggests an increased likelihood of true physiological events such as a hypoglycemic event.

8. The method according to claim **7**, wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration suggests an increased likelihood of a hypoglycemic event, a threshold value is increased, and wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration suggests a low likelihood of a hypoglycemic event, the threshold value is decreased.

9. The method according to claim **1**, wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration are in high agreement with each other, this suggests an increased likelihood of a true physiological events such as a hyperglycemic event.

10. The method according to claim **1**, wherein the modification includes increasing or decreasing a threshold value of the user's analyte concentration.

11. The method according to claim **1**, wherein the modification includes increasing or decreasing a predetermined duration that the user's analyte concentration may cross a threshold value.

12. The method according to claim **1**, wherein the modification includes increasing or decreasing a threshold value for the user's analyte concentration, and includes increasing or decreasing a predetermined duration that the user's analyte concentration may cross the threshold value.

13. The method according to claim **1**, wherein the information from the continuous analyte monitor includes at least one data signal.

14. An integrated analyte monitoring device assembly, comprising:

an analyte sensor for transcutaneous positioning through a skin layer and maintained in fluid contact with an interstitial fluid under the skin layer during a predetermined time period, the analyte sensor having a proximal portion and a distal portion; and

sensor electronics coupled to the analyte sensor, the sensor electronics comprising:

a circuit board having a conductive layer and a sensor antenna disposed on the conductive layer;

one or more electrical contacts provided on the circuit board and coupled with the proximal portion of the analyte sensor to maintain continuous electrical communication; and

a data processing component provided on the circuit board and in signal communication with the analyte sensor, the data processing component configured to execute one or more routines for processing signals received from the analyte sensor, the data processing component configured to control the transmission of data associated with the processed signals received from the analyte sensor to a remote location using the sensor antenna in response to a request signal received from the remote location, the data processing component configured to receive information from a continuous analyte monitor related to a user's analyte concentration, the data processing component configured to determine the user's analyte concentration using the information received from the continuous analyte monitor, the data processing component configured to receive data from the user related to the user's analyte concentration, the data processing component configured to determine a best-estimate of the user's analyte concentration based upon the information received from the continuous analyte monitor and the data received from the user at the data processing component, the data processing component configured to determine at least one condition for activating an alarm, the data processing component configured to modify the at least one condition for activating the alarm based on a comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration.

15. The assembly according to claim **14**, wherein the best-estimate of the user's analyte concentration includes a range of variance.

16. The assembly according to claim **15**, wherein the best-estimate of the user's analyte concentration is at least partially determined using at least one of a Kalman filter and other state observers.

17. The assembly according to claim **14**, wherein the data processing component is further configured to activate the alarm if at least one of the data signals related to the user's analyte concentration and the best-estimate of the user's analyte concentration satisfies the at least one determined condition.

18. The assembly according to claim **14**, wherein the at least one condition for activating the alarm includes receiving a data signal that indicates that a user's glucose concentration has reached a threshold value.

19. The assembly according to claim **14**, wherein the at least one condition includes that the user's analyte concentration crosses a threshold value for a predetermined length of time.

20. The assembly according to claim **14**, wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration are in high agreement with each other, this suggests an increased likelihood of a hypoglycemic event.

21. The assembly according to claim **20**, wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration suggests an increased likelihood of a

hypoglycemic event, the threshold value is increased, and wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration suggests a low likelihood of a hypoglycemic event, a threshold value is decreased.

22. The assembly according to claim **14**, wherein when the comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration are in high agreement with each other, this suggests an increased likelihood of true physiological events such as a hyperglycemic event.

23. The assembly according to claim **14**, wherein the modification includes increasing or decreasing a threshold value of a user's glucose concentration.

24. The assembly according to claim **14**, wherein the modification includes increasing or decreasing a predetermined duration that the user's analyte concentration may cross a threshold value.

25. The assembly according to claim **14**, wherein the modification includes increasing or decreasing a threshold value for the user's analyte concentration, and includes increasing or decreasing a predetermined length of time that the user's analyte concentration may cross the threshold value.

26. The assembly according to claim **14**, wherein the information from the continuous analyte monitor includes at least one data signal.

27. An integrated analyte monitoring device, comprising:

a data processing component provided on a circuit board and in signal communication with a continuous analyte monitor, the data processing component configured to:

execute one or more routines for processing signals received from the continuous analyte monitor;

control the transmission of data associated with the processed signals received from the continuous analyte monitor to a remote location using an antenna in response to a request signal received from the remote location;

receive information from the continuous analyte monitor related to a user's analyte concentration;

determine the user's analyte concentration using the information received from the continuous analyte monitor;

receive data from the user related to the user's analyte concentration;

determine a best-estimate of the user's analyte concentration based upon the information received from the continuous analyte monitor and data received from the user at the data processing component;

determine at least one condition for activating an alarm; and

modify the at least one condition for activating the alarm based on a comparison between the determination of the user's analyte concentration and the best-estimate of the user's analyte concentration.

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