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(54) Title: NONINVASIVE HYDRATION MONITORING

(57) Abstract: Novel tools and techniques for assessing, predicting and/or estimating effectiveness of hydration of a patient and/or an amount of fluid needed for effective hydration of the patient, in some cases, noninvasively.

FIG. 1A
Noninvasive Hydration Monitoring

STATEMENT AS TO RIGHTS TO INVENTIONS MADE UNDER FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT

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FIELD

[0003] The present disclosure relates, in general, tools and techniques for medical monitoring, and more particularly, to tools and techniques that can monitor, estimate, and/or predict effectiveness of hydration efforts and/or an amount of fluid necessary for effective hydration of a patient, athlete, or other person.

BACKGROUND

[0004] Proper Hydration is important in maintaining general fitness. It is especially important during exercise or excessive environmental conditions, or in the case of various physical conditions or illness. Further, effective hydration (e.g., neither over nor under hydration) is important to optimize physical performance, for example, when engaged in sports. Two key questions need to be answered to ensure
optimal fluid intake by the body. First, if one is drinking fluids of specific kind, is this fluid leading to effective hydration. If it is not, then either the fluid needs to be changed or the current condition (either environment or the state of the body) of the individual is preventing proper hydration from taking place. Second, how much fluid should one consume in order to prevent over or under hydration?

[0005] Unfortunately, there is currently no simple way for the average person to answer these questions quickly and easily. In many cases, by the time a person becomes overtly symptomatic (e.g., headache, dry mouth, lack of perspiration), that person has already entered a state of substantial dehydration. While invasive tests can be performed in a clinical setting, such tests are infeasible in the field, for example, in the midst of an athletic contest. Anecdotal measures for how much to drink to stay hydrated are imprecise at best, and are equally likely to lead to under hydration or over hydration.

[0006] Hence, there is a need for an automated, noninvasive device for early diagnosis, real-time monitoring and tracking of hydration effectiveness, for general health and wellness, to avoid complications in the case of illness or other physical conditions, and to help optimize athletic performance.

**BRIEF SUMMARY**

[0007] Various embodiments can assess the effectiveness of fluid intake hydration, where effectiveness can be defined, but not limited to, as leading to a better hydration state or maintain an optimal hydration state. In one aspect, optimal hydration might be defined as a fluid state that maximized some performance index/measure, perhaps indicated by the patient's compensatory reserve index ("CRI," also referred to herein and in the Related Applications as "cardiac reserve index" or "hemodynamic reserve index" ("HDRI"), all of which should be considered synonymous for purposes of this disclosure). (While the term, "patient," is used herein for convenience, that descriptor should not be considered limiting, because various embodiments can be employed both in a clinical setting and outside any clinical setting, such as by an athlete before, during, or after an athletic contest or training, a person during daily activities, a soldier on the battlefield, etc. Thus, the term, "patient," as used herein, should be interpreted broadly and should be
considered to be synonymous with "person.") In other cases, the assessments might be based on raw waveform data (e.g., PPG waveform data) captured by a sensor on the patent (such as the sensors described below and the Related Applications, for example). In further cases, a combination of waveform data and calculated/estimated CRI can be used to calculate the effectiveness of hydration and/or the amount of fluid needed for effective hydration. In other aspects, such functionality can be provided by and/or integrated with systems, devices (such as a cardiac reserve monitor and/or wrist-worn sensor device), tools, techniques, methods, and software described below and in the Related Applications.

[0008] The tools provided by various embodiments include, without limitation, methods, systems, and/or software products. Merely by way of example, a method might comprise one or more procedures, any or all of which are executed by a computer system. Correspondingly, an embodiment might provide a computer system configured with instructions to perform one or more procedures in accordance with methods provided by various other embodiments. Similarly, a computer program might comprise a set of instructions that are executable by a computer system (and/or a processor therein) to perform such operations. In many cases, such software programs are encoded on physical, tangible and/or non-transitory computer readable media (such as, to name but a few examples, optical media, magnetic media, and/or the like).

[0009] For example, one set of embodiments provides methods. An exemplary method might comprise monitoring, with one or more sensors, physiological data of a patient. The method might further comprise analyzing, with a computer system, the physiological data. Many different types of physiological data can be monitored and/or analyzed by various embodiments, including without limitation, blood pressure waveform data, plethysmograph waveform data, photoplethysmograph ("PPG") waveform data (such as that generated by a pulse oximeter), and/or the like. In an aspect of some embodiments, analyzing the physiological data might comprise analyzing the data against a pre-existing model. In some cases, the method can further comprise assessing the effectiveness of hydration efforts, and/or displaying (e.g., on a display device) an assessment of the effectiveness of the hydration efforts. Such an assessment can include, without limitation, an estimate of the effectiveness at a current time, a prediction of the effectiveness at
some point in the future, an estimate and/or prediction of a volume of fluid necessary for effective hydration, an estimate of the probability a patient requires fluids, etc.

[0010] An apparatus, in accordance with yet another set of embodiments, might comprise a computer readable medium having encoded thereon a set of instructions executable by one or more computers to perform one or more operations. In some embodiments, the set of instructions might comprise instructions for performing some or all of the operations of methods provided by certain embodiments.

[0011] A system, in accordance with yet another set of embodiments, might comprise one or more processors and a computer readable medium in communication with the one or more processors. The computer readable medium might have encoded thereon a set of instructions executable by the computer system to perform one or more operations, such as the set of instructions described above, to name one example. In some embodiments, the system might further comprise one or more sensors and/or a therapeutic device, either or both of which might be in communication with the processor and/or might be controlled by the processor. Such sensors can include, but are not limited to, a blood pressure sensor, an intracranial pressure monitor, a central venous pressure monitoring catheter, an arterial catheter, an electroencephalograph, a cardiac monitor, a transcranial Doppler sensor, a transthoracic impedance plethysmograph, a pulse oximeter, a near infra-red spectrometer, a ventilator, an accelerometer, an electrooculogram, a transcutaneous glucometer, an electrolyte sensor, and/or an electronic stethoscope.

**BRIEF DESCRIPTION OF THE DRAWINGS**

[0012] A further understanding of the nature and advantages of particular embodiments may be realized by reference to the remaining portions of the specification and the drawings, in which like reference numerals are used to refer to similar components. In some instances, a sub-label is associated with a reference numeral to denote one of multiple similar components. When reference is made to a reference numeral without specification to an existing sub-label, it is intended to refer to all such multiple similar components.
[0013] Fig. 1A is a schematic diagram illustrating a system for estimating compensatory reserve, in accordance with various embodiments.

[0014] Fig. 1B is a schematic diagram illustrating a sensor system that can be worn on a patient's body, in accordance with various embodiments.

[0015] Fig. 2A is a process flow diagram illustrating a method of assessing effectiveness of hydration, in accordance with various embodiments.

[0016] Fig. 2B illustrates a technique for assessing effectiveness of hydration, in accordance with various embodiments.

[0017] Fig. 3A is a process flow diagram illustrating a method estimating a patient's compensatory reserve and/or dehydration state, in accordance with various embodiments.

[0018] Fig. 3B illustrates a technique for estimating and/or predicting a patient's compensatory reserve index, in accordance with various embodiments.

[0019] Fig. 4 is a process flow diagram illustrating a method of generating a model of a physiological state, in accordance with various embodiments.

[0020] Fig. 5 is a generalized schematic diagram illustrating a computer system, in accordance with various embodiments.

[0021] Figs. 6-8 are exemplary screen captures illustrating display features of a compensatory reserve monitor showing assessments of hydration effectiveness, in accordance with various techniques.

DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS

[0022] The following disclosure illustrates a few exemplary embodiments in further detail to enable one of skill in the art to practice such embodiments. The described examples are provided for illustrative purposes and are not intended to limit the scope of the invention.

[0023] In the following description, for the purposes of explanation, numerous specific details are set forth in order to provide a thorough understanding of the described embodiments. It will be apparent to one skilled in the art, however, that other embodiments of the present may be practiced without some of these specific
details. In other instances, certain structures and devices are shown in block diagram form. Several embodiments are described herein, and while various features are ascribed to different embodiments, it should be appreciated that the features described with respect to one embodiment may be incorporated with other embodiments as well. By the same token, however, no single feature or features of any described embodiment should be considered essential to every embodiment of the invention, as other embodiments of the invention may omit such features.

[0024] Unless otherwise indicated, all numbers used herein to express quantities, dimensions, and so forth should be understood as being modified in all instances by the term "about." In this application, the use of the singular includes the plural unless specifically stated otherwise, and use of the terms "and" and "or" means "and/or" unless otherwise indicated. Moreover, the use of the term "including," as well as other forms, such as "includes" and "included," should be considered non-exclusive. Also, terms such as "element" or "component" encompass both elements and components comprising one unit and elements and components that comprise more than one unit, unless specifically stated otherwise.

[0025] **Overview**

[0026] A set of embodiments provides methods, systems, and software that can be used, in many cases noninvasively, to quickly and accurately assess the effectiveness of hydration of a patient. Such an assessment can include, without limitation, an estimate of the effectiveness at a current time, a prediction of the effectiveness at some point in the future, an estimate and/or prediction of a volume of fluid necessary for effective hydration, an estimate of the probability a patient requires fluids, etc. In a particular set of embodiments, a device, which can be worn on the patient's body, can include one or more sensors that monitor a patient's physiological parameters. The device (or a computer in communication with the device) can analyze the data captured by the sensors and compare such data with a model (which can be generated in accordance with other embodiments) to assess the effectiveness of hydration, as described in further detail below.

[0027] Different embodiments can measure a number of different physiological parameters from the patient, and the analysis of those parameters can vary according to which parameters are measured (and which, according to the
generated model, are found to be most predictive of the effectiveness of hydration, including the probability of the need for hydration and/or the volume of fluids needed. In some cases, the parameters themselves (e.g., continuous waveform data captured by a photoplethysmograph) can be analyzed against the model to make assessments of hydration effectiveness. In other cases, physiological parameters can be derived from the captured data, and these parameters can be used. Merely by way of example, as described further below and the '483 Application (already incorporated by reference), direct physiological data (captured by sensors) can be used to estimate a value of CRI, and this value of CRI can be used to assess the effectiveness of hydration. In yet other cases, the derived CRI values and raw sensor data can be used together to perform such an assessment.

[0028] For example, the '483 Application describes a compensatory reserve monitor (also described as a cardiac reserve monitor or hemodynamic reserve monitor) that is able to estimate the compensatory reserve of a patient. In an aspect, this monitor quickly, accurately and/or in real-time can determine the probability of whether a patient is bleeding. In another aspect, the device can simultaneously monitor the patient's compensatory reserve by tracking the patient's CRI, to appropriately and effectively guide hydration and ongoing patient care. The same device (or a similar device) can also include advanced functionality to assess the effectiveness of hydration, based on the monitored CRI values, as explained in further detail below.

[0029] CRI is a hemodynamic parameter that is indicative of the individual-specific proportion of intravascular fluid reserve remaining before the onset of hemodynamic decompensation. CRI has values that range from 1 to 0, where values near 1 are associated with normovolemia (normal circulatory volume) and values near 0 are associated with the individual specific circulatory volume at which hemodynamic decompensation occurs.

[0030] The mathematical formula of CRI, at some time "t" is given by the following equation:

$$CRI(t) = 1 - \frac{BLV(t)}{BLV_{HDD}}$$  \hspace{1cm} (Eq. 1)
Where $BLV(t)$ is the intravascular volume loss ("BLV," also referred to as "blood loss volume" in the Related Applications) of a person at time "t," and $BLV_{HDD}$ is the intravascular volume loss of a person when they enter hemodynamic decompensation ("HDD"). Hemodynamic decompensation is generally defined as occurring when the systolic blood pressure falls below 70 mmHg. This level of intravascular volume loss is individual specific and will vary from subject to subject.

Lower body negative pressure (LBNP) in some linear or nonlinear relationship $\lambda$ with intravascular volume loss:

$$BLV = \lambda \cdot LBNP$$  \hspace{1cm} (Eq. 2)

can be used in order to estimate the CRI for an individual undergoing a LBNP experiment as follows:

$$CRI = I - \frac{BLV(t)}{BLV_{HDD}} \approx 1 - \frac{\lambda \cdot LBN(t)}{\lambda \cdot LBN_{HDD}} = 1 - \frac{LBN_{P}W}{LBN_{HDD}}$$  \hspace{1cm} (Eq. 3)

Where LBNP(t) is the LBNP level that the individual is experiencing at time "t", and, LBNP_{HDD} is the LNPB level that the individual will enter hemodynamic decompensation.

Using either CRI data, raw (or otherwise processed) sensor data, or both, various embodiments can assess the effectiveness of hydration. In one embodiment, the effectiveness of hydration ("HE") can be expressed as a value between 0 and 1; when $HE = 1$, hydration is proceeding effectively, when $HE = 0$, hydration is not producing the desired result, perhaps due to ongoing bleeding. (Of course, other embodiments can scale the value of HE differently). In an aspect of some embodiments, a general expression for the estimate of as follows:

$$HE = f_{HE}(CRI_t, FV_t, S_t)$$  \hspace{1cm} (Eq. 4)

Where $HE$ is a measure of hydration effectiveness, $f_{HE}(CRI_t, FV_t, S_t)$ is an algorithm embodied by a model generated empirically, e.g., using the techniques described with respect to Fig. 4 below, and/or in the Related Applications, $CRI_t$ is a time history of CRI values (which can range from a single CRI value to many hours of CRI values), $FV_t$ is a time history of fluid volume being given to the patient (which can range from a single value to many hours of values), and $S_t$ is a time history of raw...
sensor values, such as physiological data measured by the sensors, as described elsewhere herein (which can range from one value to many hours of values).

[0037] The functional form of Eq. 4 is similar to but not limited to the form of the CRI model in the sense that time histories of \((CRI_t, FV_t, S_t)\) data gathered from human subjects at various levels of HE are compared to time histories of \((CRI_t, FV_t, S_t)\) for the current patient being monitored. The estimated HE for the current patient is then that which is the closest in \((CRI_t, FV_t, S_t)\) space to the previously gathered data.

[0038] While Eq. 4 is the general expression for HE, various embodiments might use subsets of the parameters considered in Eq. 4. For instance, in one embodiment, a model might consider only the volume of fluid and CRI data, without accounting for raw sensor input. In that case, HE can be calculated as follows:

\[
HE = f_{HE}(CRI_t, FV_t)
\]  
(Eq. 5)

[0039] Similarly, some models might estimate HE based on sensor data, rather than first estimating CRI, in which case, HE can be expressed thusly:

\[
HE = f_{HE}(FV_t, S_t)
\]  
(Eq. 6)

[0040] The choice of parameters to use in modeling HE is discretionary, and it can depend on what parameters are shown (e.g., using the techniques of Fig. 4, below) to result in the best prediction of HE.

[0041] In another aspect, the effectiveness of hydration can be assessed by estimating or predicting the volume, \(V\), of fluid necessary for effective hydration of the patient. This volume, \(V\), can indicate a volume of fluid needed for full hydration if therapy has not yet begun, and/or it can indicate a volume remaining for fully effective hydration if therapy is underway. Like HE, the value of \(V\) can be estimated/predicted using the modeling techniques described herein and in the Related Applications. In a general case, \(V\) can be expressed as the following:

\[
V = f_v(CRI_t, FV_t, S_t)
\]  
(Eq. 7)

where \(V\) is an estimated volume of fluid needed by a patient need to prevent over or under hydration, \(f_v(CRI_t, FV_t, S_t)\) is an algorithm embodied by a model generated empirically, e.g., using the techniques described with respect to Fig. 4 below, and/or in the Related Applications., \(CRI_t\) is a time history of CRI values, \(FV_t\) is a time
history of fluid volume being given to the patient, and \( S_t \) is a time history of physiological data received from the one or more sensors.

[0042] As with the estimate of HE, various embodiments can employ subsets of the parameters used in the general expression of Eq.7. Thus, different embodiments might calculate \( V \) as follows:

\[
V = f_v(CRI_t, FV_t) \quad \text{(Eq. 8)}
\]

or

\[
V = f_v(FV_t, S_t) \quad \text{(Eq. 9)}
\]

[0043] Yet another way of assessing effectiveness of hydration (which can even include assessing the need for hydration) is estimating the probability \( P_f \) that the patient requires fluids; this probability can estimate the likelihood that the patient requires hydration if therapy has not been initiated, and/or, if hydration therapy is underway, the probability can estimate the likelihood that further hydration is necessary. The value of this probability, which can be expressed, e.g., as a percentage, as a decimal value between 0 and 1, etc. can be estimated using the following expression:

\[
P_f = f_{pf}(CRI_t, S_t) \quad \text{(Eq. 10)}
\]

where \( P_f \) is the estimated probability that the patient requires fluid, \( f_{pf}(CRI_t, S_t) \) is a relationship derived based on empirical study, \( CRI_t \) is a time history of CRI values, and \( S_t \) is a time history of physiological data received from the one or more sensors.

Once again, this general expression can be employed, in various embodiments, using subsets of the parameters in the general expression, such as the following:

\[
P_f = f_{pf}(CRI_t) \quad \text{(Eq. 11)}
\]

or

\[
P_f = f_{pf}(S_t) \quad \text{(Eq. 12)}
\]

[0044] In the estimate of any of HE, \( V \), or \( P_f \), the function expresses a relationship that is derived based on empirical study. In a set of embodiments, for example, various sensor data can be collected from test subjects before, during, and/or after hydration efforts, during hemorrhaging, or under other conditions that might simulate such situations. This sensor data can be analyzed to develop models, using
techniques similar to those of Fig. 4 below, which can then be used to estimate various assessments of hydration effectiveness, using, e.g., the methods described below with respect to Figs. 2 and 3.

[0045] A measure of CRI, HE, V, and/or P_r can be useful in a variety of clinical settings, including but not limited to: 1) acute blood loss volume due to injury or surgery; 2) acute circulatory volume loss due to hemodialysis (also called intradialytic hypotension); and 3) acute circulatory volume loss due to various causes of dehydration (e.g. reduced fluid intake, vomiting, dehydration, etc.). A change in CRI can also herald other conditions, including without limitation changes in blood pressure, general fatigue, overheating and certain types of illnesses. Accordingly, the tools and techniques for estimating and/or predicting CRI can have a variety of applications in a clinical setting, including without limitation diagnosing such conditions.

[0046] Moreover, measures of CRI, HE, V, and/or P_r can have applicability outside the clinical setting. For example, an athlete can be monitored (e.g., using a wrist-wearable hydration monitor) before, during, or after competition or training to ensure optimal performance (and overall health and recovery). In other situations, a person concerned about overall wellbeing can employ a similar hydration monitor to ensure that he or she is getting enough (but not too much) fluid, ill infants or adults can be monitored while ill to ensure that symptoms (e.g., vomiting, diarrhea) do not result in dehydration, and the like. Similarly, soldiers in the field (particularly in harsh conditions) can be monitored to ensure optimal operational readiness.

[0047] In various embodiments, a hydration monitor, compensatory reserve monitor, a wrist-wearable sensor device, and/or another integrated system can include, but is not limited to, some or all of the following functionality, as described in further detail herein and in the Related Applications:

[0048] A. Estimating and/or displaying intravascular volume loss to hemodynamic decompensation (or cardiovascular collapse).

[0049] B. Estimating, predicting and/or displaying a patient's compensatory reserve as an index that is proportional to an approximate measure of intravascular volume loss to CV collapse, recognizing that each patient has a unique reserve capacity.
C. Estimating, predicting and/or displaying a patient's compensatory reserve as an index with a normative value at euvolemia (for example, \( \text{CRI} = 1 \)), representing a state in which the patient is normovolemic; a minimum value (for example, \( \text{CRI} = 0 \)) which implies no circulatory reserve and that the patient is experiencing CV collapse; and/or an excess value (for example, \( \text{CRI} > 1 \)) representing a state in which the patient is hypervolemic; the patient's normalized compensatory reserve can be displayed on a continuum between the minimum and maximum values (perhaps labeled by different symbols and/or colors depending on where the patient falls on the continuum).

D. Determining and/or displaying a probability that bleeding or intravascular volume loss has occurred.

E. Displaying an indicator that intravascular volume loss has occurred and/or is ongoing; as well as other measures of reserve, such as trend lines.

F. Estimating a patient's current blood pressure and/or predicting a patient's future blood pressure.

G. Predicting the future effectiveness of fluid resuscitation efforts.

H. Estimating and/or predicting a volume of fluid necessary for effective resuscitation.

I. Estimating a probability that a patient needs fluids.

J. Estimating a hydration state of a patient or user.

K. Predicting a future hydration state of a patient or user.

L. Estimate and/or predicting a volume of fluid intake necessary for adequate hydration of a patient or user.

M. Estimating a probability that a patient is dehydrated.

In various embodiments, CRI, HE, V, and/or P\( f \) estimates can be (i) based on a fixed time history of patient monitoring (for example a 30 second or 30 heart beat window); (ii) based on a dynamic time history of patient monitoring (for example monitoring for 200 minutes, the system may use all sensor information
gathered during that time to refine and improve CRI estimates, hydration effectiveness assessments, etc.; (iii) based on either establishing baseline estimates when the patient is normovolemic (no volume loss has occurred); and/or (iv) based on NO baselines estimates when patient is normovolemic.

[C0063]  Certain embodiments can also recommend treatment options, based on the analysis of the patient's condition (including the estimated/predicted blood pressure, probability of bleeding, state of dehydration, and/or the patient's estimated and/or predicted CRI). Treatment options can include, without limitation, such things as optimizing hemodynamics, ventilator adjustments, IV fluid adjustments (e.g., controlling the flow rate of an IV pump or the drip rate of an IV drip), transfusion of blood or blood products, infusion of volume expanders, medication changes, changes in patient position and surgical therapy.

[C0064]  As one example, certain embodiments can be used to control an IV drip, IV pump, or rapid infuser. For instance, an embodiment might estimate the probability that a patient requires fluids and activate such a device in response to that estimate (or instruct a clinician to attach such a device to the patient and activate the device). The system might then monitor the progress of the hydration effort (through continual or periodic assessment of the effectiveness of hydration) and increase/decrease drip or flow rates accordingly.

[C0065]  As another example, certain embodiments can be used as an input for a hemodialysis procedure. For example, certain embodiments can predict how much intravascular (blood) volume can be safely removed from a patient during a hemodialysis process. For example, an embodiment might provide instructions to a human operator of a hemodialysis machine, based on estimates or predictions of the patient's CRI. Additionally and/or alternatively, such embodiments can be used to continuously self-adjust the ultra-filtration rate of the hemodialysis equipment, thereby completely avoiding intradialytic hypotension and its associated morbidity.

[C0066]  As yet another example, certain embodiments can be used to estimate and/or predict a dehydration state (and/or the amount of dehydration) in an individual (e.g., a trauma patient, an athlete, an elder living at home, etc.) and/or to provide treatment (either by providing recommendations to treating personnel or by directly controlling appropriate therapeutic equipment). For instance, if an analytical model
indicates a relationship between CRI (and/or any other physiological phenomena that can be measured and/or estimated using the techniques described herein and in the Related Applications) and dehydration state, an embodiment can apply that model, using the techniques described herein, to estimate a dehydration state of the patient.

[0067] **Exemplary Systems and Methods**

[0068] Fig. 1A provides a general overview of a system provided by certain embodiments. The system includes a computer system 100 in communication with one or more sensors 105, which are configured to obtain physiological data from the subject (e.g., animal or human test subject or patient) 110. In one embodiment, the computer system 100 comprises a Lenovo THINKPAD X200, 4GB of RAM with Microsoft WINDOWS 7 operating system and is programmed with software to execute the computational methods outlined herein. The computational methods can be implemented in MATLAB 2009b and C++ programming languages. A more general example of a computer system 100 that can be used in some embodiments is described in further detail below. Even more generally, however, the computer system 100 can be any system of one or more computers that are capable of performing the techniques described herein. In a particular embodiment, for example, the computer system 100 is capable of reading values from the physiological sensors 105, generating models of physiological state from those sensors, and/or employing such models to make individual-specific estimations, predictions, or other diagnoses, displaying the results, recommending and/or implementing a therapeutic treatment as a result of the analysis, and/or archiving (learning) these results for use in future, model building and predictions.

[0069] The sensors 105 can be any of a variety of sensors (including without limitation those described herein) for obtaining physiological data from the subject. An exemplary sensor suite might include a Finometer sensor for obtaining a noninvasive continuous blood pressure waveform, a pulse oximeter sensor, an Analog to Digital Board (National Instruments USB-9215A 16-Bit, 4 channel) for connecting the sensors (either the pulse oximeter and/or the finometer) to the computer system 100. More generally, in an embodiment one or more sensors 105 might obtain, e.g., using one or more of the techniques described herein, continuous physiological waveform data, such as continuous blood pressure. Input from the sensors 105 can
constitute continuous data signals and/or outcomes that can be used to generate, and/or can be applied to, a predictive model as described below.

[0070] In some cases, the structure might include a therapeutic device 115 (also referred to herein as a "physiological assistive device"), which can be controlled by the computer system 100 to administer therapeutic treatment, in accordance with the recommendations developed by analysis of a patient's physiological data. In a particular embodiment, the therapeutic device might comprise hemodialysis equipment (also referred to as a hemodialysis machine), which can be controlled by the computer system 100 based on the estimated CRI of the patient, as described in further detail below. Further examples of therapeutic devices in other embodiments can include a cardiac assist device, a ventilator, an automatic implantable cardioverter defibrillator ("AICD"), pacemakers, an extracorporeal membrane oxygenation circuit, a positive airway pressure ("PAP") device (including without limitation a continuous positive airway pressure ("cPAP") device or the like), an anesthesia machine, an integrated critical care system, a medical robot, intravenous and/or intra-arterial pumps that can provide fluids and/or therapeutic compounds (e.g., through intravenous injection), intravenous drips, a rapid infuser, a heating/cooling blanket, and/or the like.

[0071] Fig. 1B illustrates in more detail an exemplary sensor device 105, which can be used in the system 100 described above. (It should be noted, of course, that the depicted sensor device 105 of Fig. 1B is not intended to be limiting, and different embodiments can employ any sensor that captures suitable data, including without limitation sensors described elsewhere in this disclosure and in the Related Applications.) The illustrated sensor device 105 is designed to be worn on a patient's wrist and therefore can be used both in clinical settings and in the field (e.g., on any person for whom monitoring might be beneficial, for a variety of reasons, including without limitation assessment of blood pressure and/or hydration during athletic competition or training, daily activities, military training or action, etc.). In one aspect, the sensor device 105 can serve as an integrated hydration monitor, which can assess hydration as described herein, display an indication of the assessment, recommend therapeutic action based on the assessment, or the like, in a form factor that can be worn during athletic events and/or daily activities.
Hence, the exemplary sensor 105 device (hydration monitor) includes a finger cuff 125 and a wrist unit 130. The finger cuff 125 includes a fingertip sensor 135 (in this case, a PPG sensor) that captures data based on physiological conditions of the patient, such as PPG waveform data. The sensor 135 communicates with an input/output unit 140 of the wrist unit 130 to provide output from the sensor 135 to a processing unit 145 of the wrist unit 130. Such communication can be wired (e.g., via a standard—such as USB—or proprietary connector on the wrist unit 130) and/or wireless (e.g., via Bluetooth, such as Bluetooth Low Energy ("BTLE"), near field connection ("NFC"), WiFi, or any other suitable radio technology).

In different embodiments, the processing unit can have different types of functionality. For example, in some cases, the processing unit might simply act to store and/or organize data prior to transmitting the data through the I/O unit 140 to a monitoring computer 100, which might perform data analysis, control a therapeutic device 115, etc. In other cases, however, the processing unit 145 might act as a specialized computer (e.g., with some or all of the components described in connection with Fig. 5, below and/or some or all of the functionality ascribed to the computer 100 of Figs. 1A and 1B), such that the processing unit can perform data analysis onboard, e.g., to estimate and/or predict a patient's current and/or future blood pressure. As such, the wrist unit 105 might include a display, which can display any output described herein, including without limitation estimated and/or predicted values (e.g., of CRI, blood pressure, hydration status, etc.), data captured by the sensor (e.g., heart rate, pulse ox, etc.), and/or the like.

In some cases, the wrist unit 130 might include a wrist strap 155 that allows the unit to be worn on the wrist, similar to a watch. Of course, other options are available to facilitate transportation of the sensor device 105 with a patent. More generally, the sensor device 105 might not include all of the components described above, and/or various components might be combined and/or reorganized; once again, the embodiment illustrated by Fig. 1B should be considered only illustrative, and not limiting, in nature.

Figs. 2A, 2B, 3A, 3B and 4 illustrate methods and screen displays in accordance with various embodiments. While the methods of Figs. 2A, 2B, 3A, 3B and 4 are illustrated, for ease of description, as different methods, it should be appreciated that the various techniques and procedures of these methods can be
combined in any suitable fashion, and that, in some embodiments, the methods
depicted by Figs. 2A, 2B, 3A, 3B and 4 can be considered interoperable and/or as
portions of a single method. Similarly, while the techniques and procedures are
depicted and/or described in a certain order for purposes of illustration, it should be
appreciated that certain procedures may be reordered and/or omitted within the scope
of various embodiments. Moreover, while the methods illustrated by Figs. 2A, 2B,
3A, 3B and 4 can be implemented by (and, in some cases, are described below with
respect to) the computer system 100 of Fig. 1 (or other components of the system,
such as the sensor 105 of Figs. 1A and 1B), these methods may also be implemented
using any suitable hardware implementation. Similarly, while the computer system
100 of Fig. 1 (and/or other components of such a system) can operate according to the
methods illustrated by Figs. 2A, 2B, 3A, 3B and 4 (e.g., by executing instructions
embodied on a computer readable medium), the system 100 can also operate
according to other modes of operation and/or perform other suitable procedures.

Merely by way of example, a method might comprise one or more
procedures, any or all of which are executed by a computer system. Correspondingly,
an embodiment might provide a computer system configured with instructions to
perform one or more procedures in accordance with methods provided by various
other embodiments. Similarly, a computer program might comprise a set of
instructions that are executable by a computer system (and/or a processor therein) to
perform such operations. In many cases, such software programs are encoded on
physical, tangible and/or non-transitory computer readable media (such as, to name
but a few examples, optical media, magnetic media, and/or the like).

By way of non-limiting example, various embodiments can comprise a
method for using sensor data to assess the effectiveness of fluid resuscitation of a
patient and/or the hydration of a patient. Fig. 2 illustrates an exemplary method 200
in accordance with various embodiments. The method 200 might comprise
generating a model, e.g., with a computer system, against which patient data can be
analyzed to estimate and/or predict various physiological states (block 205). In a
general sense, generating the model can comprise receiving data pertaining to a
plurality of more physiological parameters of a test subject to obtain a plurality of
physiological data sets. Such data can include PPG waveform data to name one
example, and/or any other type of sensor data including without limitation data captured by other sensors described herein and in the Related Applications.

[0078] Generating a model can further comprise directly measuring one or more physiological states of the test subject with a reference sensor to obtain a plurality of physiological state measurements. The one or more physiological states can include, without limitation, states of various volumes of blood loss and/or fluid resuscitation, and/or various states of hydration and/or dehydration. (In other embodiments, different states can include a state of hypovolemia, a state of euvolemia, and/or a state of cardiovascular collapse (or near-cardiovascular collapse), and/or can include states that have been simulated, e.g., through use of an LBNP apparatus). Other physiological states that can be used to generate a model are described elsewhere herein and in the Related Applications.

[0079] Generating the model can further comprise correlating the physiological state(s) with the measured physiological parameters. There are a variety of techniques for generating a model in accordance with different embodiments, using these general functions. One exemplary technique for generating a model of a generic physiological state is described below with respect to Fig. 4, below, which provides a technique using a machine-learning algorithm to optimize the correlation between measured physiological parameters (such as PPG waveform data, to name one example) and physical states (e.g., various blood volume states, including states where a known volume of blood loss has occurred and/or a known volume of fluid resuscitation has been administered, various states of hydration and/or dehydration, etc.). It should be appreciated, however, that any suitable technique or model may be employed in accordance with various embodiments.

[0080] A number of physiological states can be modeled, and a number of different conditions can be imposed on test subjects as part of the model generation. For example, physiological states that can be induced (or monitored when naturally occurring) in test subjects include, without limitation, reduced circulatory system volume, known volume of blood loss, specified amounts of fluids added to blood volume, dehydration, cardiovascular collapse or near-cardiovascular collapse, euvolemia, hypervolemia, low blood pressure, high blood pressure, normal blood pressure, and/or the like.
Merely by way of example, in one set of embodiments, a number of physiological parameters of a plurality of test subjects might be measured. In some cases, a subject might undergo varying, measured levels of blood loss (either real or simulated) or intravenous fluid addition. Using the method described below with respect to Fig. 4 (or other, similar techniques, many of which are described in the Related Applications), the system can determine which sensor information most effectively differentiates between subjects at different blood loss/addition volume levels.

Additionally and/or alternatively to using direct (e.g., raw) sensor data to build such models, some embodiments might construct a model based on data that is derived from sensor data. Merely by way of example, one such model might use, as input values, CRI values of test subjects in different blood loss and/or volume addition conditions. Accordingly, the process of generating a model might first comprise building a model of CRI, and then, from that model, building a model of hydration effectiveness. (In other cases, a hybrid model might consider both raw sensor data and CRI data.)

A CRI model can be generated in different ways. For example, in some cases, one or more test subjects might be subjected to LBNP. In an exemplary case, LBNP data is collected from human subjects being exposed to progressively lower levels of LBNP, until hemodynamic decompensation, at which time LBNP is released and the subject recovers. Each level of LBNP represents an additional amount of blood loss. During these tests, physiological data (including without limitation waveform data, such as continuous non-invasive blood pressure data)) can be collected before, during, and/or after the application of the LBNP. As noted above, a relationship (as expressed by Equation 2) can be identified between LBNP and intravascular volume loss, and this relationship can be used to estimate CRI. Hence, LBNP studies form a framework (methodology) for the development of the hemodynamic parameter referred to herein as CRI and can be used to generate models of this parameter.

More generally, several different techniques that induce a physiological state of reduced volume in the circulatory system, e.g., to a point of cardiovascular collapse (hemodynamic decompensation) or to a point near cardiovascular collapse, can be used to generate such a model. LBNP can be used to
induce this condition, as noted above. In some cases, such as in a study described below, dehydration can be used to induce this condition as well. Other techniques are possible as well. Similarly, data collected from a subject in a state of euvolemia, dehydration, hypervolemia, and/or other states might be used to generate a CRI model in different embodiments.

[0085] At block 210, the method 200 comprises monitoring, with one or more sensors, physiological data of a patient. As noted above, a variety of physical parameters can be monitored, invasively and/or non-invasively, depending on the nature of the anticipated physiological state of the patient. In an aspect, monitoring the one or more physical parameters might comprise receiving, e.g., from a physiological sensor, continuous waveform data, which can be sampled as necessary. Such data can include, without limitation, plethysmograph waveform data, PPG waveform data (such as that generated by a pulse oximeter), and/or the like.

[0086] The method 200 might further comprise analyzing, with a computer system (e.g., a monitoring computer 100 and/or a processing unit 135 of a sensor unit, as described above), the physiological data (block 215). In some cases, the physiological data is analyzed against a pre-existing model (which might be generated as described above and which in turn, can be updated based on the analysis, as described in further detail below and in the Related Applications).

[0087] Merely by way of example, in some cases, sensor data can be analyzed directly against a generated model to assess the effectiveness of hydration (which can include estimating current values, and/or predicting future values for any or all of HE, V, and/or P_f as expressed above. For example, the sensor data can be compared to determine similarities with models that estimate and/or predict any of these values. Merely by way of example, an input waveform captured by a sensor from a patient might be compared with sample waveforms generated by models for each of these values.

[0088] For example, the technique 265 provides one method for deriving an estimate of HE in accordance with some embodiments. It should be noted that the technique 265 is presented as an example only, and that while this technique 265 estimates HE from raw sensor data, similar techniques can be used to estimate or predict HE, V, and/or P_f from raw sensor data, CRI data, and/or a combination of
both. For example, one model might produce a first estimate of HE from raw sensor data, produce a second estimate of HE from estimated CRI values, and then combine those estimates (in either weighted or unweighted fashion) to produce a hybrid HE estimate.

The illustrated technique 265 comprises sampling waveform data (e.g., any of the data described herein and in the Related Applications, including without limitation arterial waveform data, such as continuous PPG waveforms and/or continuous noninvasive blood pressure waveforms) for a specified period, such as 32 heartbeats (block 270). That sample is compared with a plurality of waveforms of reference data corresponding to HE values (block 275), which in this case range from 0 to 1 using the scale described above (but alternatively might use any appropriate scale). These reference waveforms are derived as part of the model developed using the algorithms described in this and the Related Applications, might be the result of experimental data, and/or the like. In effect, these reference waveforms reflect the relationship from Eq. 6, above.

According to the technique 265, the sample might be compared with waveforms corresponding to a HE=0 (block 275a), HE=0.5 (block 275b), and HE=1 (block 275c), as illustrated. (As illustrated by the ellipses on Fig. 2B, any number of sample waveforms can be used for the comparison; for example, if there is a nonlinear relationship between the measured sensor data and the HE values, more sample waveforms might provide for a better comparison.) From the comparison, a similarity coefficient is calculated (e.g., using a least squares or similar analysis) to express the similarity between the sampled waveform and each of the reference waveforms (block 280). These similarity coefficients can be normalized (if appropriate) (block 285), and the normalized coefficients can be summed (block 390) to produce an estimated HE value of the patient.

In other cases, similar techniques can be used to analyze data against a model based on parameters derived from direct sensor measurements. (In one aspect, such operations can be iterative in nature, by generating the derived parameters—such as CRI, to name one example—by analyzing the sensor data against a first model, and then analyzing the derived parameters against a second model.)
For example, Fig 3A illustrates a method 300 of calculating a patient's CRI, which can be used (in some embodiments) as a parameter that can be analyzed to assess the effectiveness of hydration (including the probability that fluids are needed and/or the estimated volume of fluid necessary for effective hydration). The method 300 includes generating a model of CRI (block 305), monitoring physiological parameters (310) and analyzing the monitored physical parameters (block 315), using techniques such as those described above and in the '483 Application, for example.

Based on this analysis, the method 300, in an exemplary embodiment, includes estimating, with the computer system, a compensatory reserve of the patient, based on analysis of the physiological data (block 320). In some cases, the method might further comprise predicting, with the computer system, the compensatory reserve of the patient at one or more time points in the future, based on analysis of the physiological data (block 325). The operations to predict a future value of a parameter can be similar to those for estimating a current value; in the prediction context, however, the applied model might correlate measured data in a test subject with subsequent values of the diagnostic parameter, rather than contemporaneous values. It is worth noting, of course, that in some embodiments, the same model can be used to both estimate a current value and predict future values of a physiological parameter.

The estimated and/or predicted compensatory reserve of the patient can be based on several factors. Merely by way of example, in some cases, the estimated/predicted compensatory reserve can be based on a fixed time history of monitoring the physiological data of the patient and/or a dynamic time history of monitoring the physiological data of the patient. In other cases, the estimated/predicted compensatory reserve can be based on a baseline estimate of the patient's compensatory reserve established when the patient is euvoletic. In still other cases, the estimate and/or prediction might not be based on a baseline estimate of the patient's compensatory reserve established when the patient is euvoletic.

Merely by way of example, Fig. 3B illustrates one technique 365 for deriving an estimate of CRI in accordance with some embodiments similar to the technique 265 described above with respect to Fig. 2B for deriving an assessment of hydration effectiveness directly from sensor data (and, in fact, CRI can be derived as
described herein, and that derived value can be used, alone or with raw sensor data, to assess such effectiveness). The illustrated technique comprises sampling waveform data (e.g., any of the data described herein and in the Related Applications, including without limitation arterial waveform data, such as continuous PPG waveforms and/or continuous noninvasive blood pressure waveforms) for a specified period, such as 32 heartbeats (block 370). That sample is compared with a plurality of waveforms of reference data corresponding to different CRI values (block 375). (These reference waveforms might be derived using the algorithms described in the Related Applications, might be the result of experimental data, and/or the like). Merely by way of example, the sample might be compared with waveforms corresponding to a CRI of 1 (block 375a), a CRI of 0.5 (block 375b), and a CRI of 0 (block 375c), as illustrated. From the comparison, a similarity coefficient is calculated (e.g., using a least squares or similar analysis) to express the similarity between the sampled waveform and each of the reference waveforms (block 380). These similarity coefficients can be normalized (if appropriate) (block 385), and the normalized coefficients can be summed (block 390) to produce an estimated value of the patient's CRI.

Returning to Fig. 3A, the method 300 can comprise estimating and/or predicting a patient's dehydration state (block 330). The patient's state of dehydration can be expressed in a number of ways. For instance, the state of dehydration might be expressed as a normalized value (for example, with 1.0 corresponding to a fully hydrated state and 0.0 corresponding to a state of morbid dehydration). In other cases, the state of dehydration might be expressed as a missing volume of fluid or as a volume of fluid present in the patient's system, or using any other appropriate metric.

A number of techniques can be used to model dehydration state. Merely by way of example, as noted above (and described in further detail below), the relationship between a patient's compensatory reserve and level of dehydration can be modeled. Accordingly, in some embodiments, estimating a dehydration state of the patient might comprise estimating the compensatory reserve (e.g., CRI) of the patient, and then, based on that estimate and the known relationship, estimating the dehydration state. Similarly, a predicted value of compensatory reserve at some point in the future can be used to derive a predicted dehydration state at that point in the
future. Other techniques might use a parameter other than CRI to model dehydration state.

[0098] The method 300 might further comprise normalizing the results of the analysis (block 335), such as the compensatory reserve, dehydration state, and/or probability of bleeding, to name a few examples. Merely by way of example, the estimated/predicted compensatory reserve of the patient can be normalized relative to a normative normal blood volume value corresponding to euvoelmia, a normative excess blood volume value corresponding to circulatory overload, and a normative minimum blood volume value corresponding to cardiovascular collapse. Any values can be selected as the normative values. Merely by way of example, in some embodiments, the normative excess blood volume value is >1, the normative normal blood volume value is 1, and the normative minimum blood volume value is 0. As an alternative, in other embodiments, the normative excess blood volume value might be defined as 1, the normative normal blood volume value might be defined as 0, and the normative minimum blood volume value at the point of cardiovascular collapse might be defined as -1. As can be seen from these examples, different embodiments might use a number of different scales to normalize CRI and other estimated parameters.

[0099] In an aspect, normalizing the data can provide benefits in a clinical setting, because it can allow the clinician to quickly make a qualitative judgment of the patient's condition, while interpretation of the raw estimates/predictions might require additional analysis. Merely by way of example, with regard to the estimate of the compensatory reserve of the patient, that estimate might be normalized relative to a normative normal blood volume value corresponding to euvoelmia and a normative minimum blood volume value corresponding to cardiovascular collapse. Once again, any values can be selected as the normative values. For example, if the normative normal blood volume is defined as 1, and the normative minimum blood volume value is defined as 0, the normalized value, falling between 0.0 and 1.0 can quickly apprise a clinician of the patient's location on a continuum between euvoelmia and cardiovascular collapse. Similar normalizing procedures can be implemented for other estimated data (such as probability of bleeding, dehydration, and/or the like).

[0100] The method 300 might further comprise displaying data with a display device (block 340). Such data might include an estimate and/or prediction of the compensatory reserve of the patient and/or an estimate and/or prediction of the
patient's dehydration state. A variety of techniques can be used to display such data. Merely by way of example, in some cases, displaying the estimate of the compensatory reserve of the patient might comprise displaying the normalized estimate of the compensatory reserve of the patient. Alternatively and/or additionally, displaying the normalized estimate of the compensatory reserve of the patient might comprise displaying a graphical plot showing the normalized excess blood volume value, the normalized normal blood volume value, the normalized minimum blood volume value, and the normalized estimate of the compensatory reserve (e.g., relative to the normalized excess blood volume value, the normalized normal blood volume value, the normalized minimum blood volume value).

[0101] In some cases, the method 300 might comprise repeating the operations of monitoring physiological data of the patient, analyzing the physiological data, and estimating (and/or predicting) the compensatory reserve of the patient, to produce a new estimated (and/or predicted) compensatory reserve of the patient. Thus, displaying the estimate (and/or prediction) of the compensatory reserve of the patient might comprises updating a display of the estimate of the compensatory reserve to show the new estimate (and/or prediction) of the compensatory reserve, in order to display a plot of the estimated compensatory reserve over time. Hence, the patient's compensatory reserve can be repeatedly estimated and/or predicted on any desired interval (e.g., after every heartbeat), on demand, etc.

[0102] In further embodiments, the method 300 can comprise determining a probability that the patient is bleeding, and/or displaying, with the display device, an indication of the probability that the patient is bleeding (block 345). For example, some embodiments might generate a model based on data that removes fluid from the circulatory system (such as LBNP, dehydration, etc.). Another embodiment might generate a model based on fluid removed from a subject voluntarily, e.g., during a blood donation, based on the known volume (e.g., 500cc) of the donation. Based on this model, using techniques similar to those described above, a patient's physiological data can be monitored and analyzed to estimate a probability that the patient is bleeding (e.g., internally).

[0103] In some cases, the probability that the patient is bleeding can be used to adjust the patient's estimated CRI. Specifically, give a probability of bleeding expressed as $Pr_{Bleed}$ at a time $t$, the adjusted value of CRI can be expressed as:
\[ CRI_{Adjusted} (t) = 1 - ((1 - CRI(t)) \times \text{Pr}_{\text{Bleed}}(t)) \] (Eq. 13)

[0105] Given this relationship, the estimated CRI can be adjusted to produce a more accurate diagnosis of the patient's condition at a given point in time.

[0106] The method 300 might comprise selecting, with the computer system, a recommended treatment option for the patient, and/or displaying, with the display device, the recommended treatment option (block 355). The recommended treatment option can be any of a number of treatment options, including without limitation, optimizing hemodynamics of the patient, a ventilator adjustment, an intravenous fluid adjustment, transfusion of blood or blood products to the patient, infusion of volume expanders to the patient, a change in medication administered to the patient, a change in patient position, and surgical therapy.

[0107] In a specific example, the method 300 might comprise controlling operation of hemodialysis equipment (block 360), based at least in part on the estimate of the patient's compensatory reserve. Merely by way of example, a computer system that performs the monitoring and estimating functions might also be configured to adjust an ultra-filtration rate of the hemodialysis equipment in response to the estimated CRI values of the patient. In other embodiments, the computer system might provide instructions or suggestions to a human operator of the hemodialysis equipment, such as instructions to manually adjust an ultra-filtration rate, etc.

[0108] In some embodiments, the method 300 might include assessing the tolerance of an individual to blood loss, general volume loss, and/or dehydration (block 365). For example, such embodiments might include estimating a patient's CRI based on the change in a patient's position (e.g., from lying prone to standing, lying prone to sitting, and/or sitting to standing). Based on changes to the patient's CRI in response to these maneuvers, the patient's sensitivity to blood loss, volume loss, and/or dehydration can be measured. In an aspect, this measurement can be performed using a CRI model generated as described above; the patient can be monitored using one or more of the sensors described above, and the changes in the sensor output when the subject changes position can be analyzed according to the model (as described above, for example) to assess the tolerance of the individual to volume loss. Such monitoring and/or analysis can be performed in real time.
Returning to Fig. 2, based on the analysis of the data (whether data collected directly by sensors or derived data, such as CRI, or both) against a model (which might include multiple submodels, such as a model of HE against raw data and a model of HE against CRI), the method 200 can include assessing the effectiveness of hydration of the patient (block 220), based on analysis of the patient's physiological data against the model. As noted above, assessing effectiveness of hydration can include estimating or predicting a number of values, such as the estimated effectiveness, HE, of the hydration effort, the volume, V, of fluid necessary for effective hydration, the probability, P_n, that the patient needs fluids, and/or the like.

In some cases, the assessment of the effectiveness of hydration will be based on the analysis of a plurality of measured (or derived) values of a particular physiological parameter (or plurality of parameters). Hence, in some cases, the analysis of the data might be performed on a continuous waveform, either during or after measurement of the waveform with a sensor (or both), and the assessment of the effectiveness can be updated as hydration efforts continue. Further, the amount of fluids added to the patient's blood volume can be measured directly, and these direct measurements (at block 235) can be fed back into the model to update the model and thereby improve performance of the algorithms in the model (e.g., by refining the weights given to different parameters in terms of estimative or predictive value). The updated model can then be used to continue assessing the treatment (in the instant patient and/or in a future patient), as shown by the broken lines on Fig. 2A.

In some cases, the method 200 comprises displaying data (block 230) indicating the assessment of the effectiveness of hydration. In some cases, the data might be displayed on a display of a sensor device (such as the device 105 illustrated by Fig. 1B). Alternatively and/or additionally the data might be displayed on a dedicated machine, such as a compensatory reserve monitor, or on a monitor of a generic computer system. The data might be displayed alphanumerically, graphically, or both. Figs. 6-8, described below, illustrate several possible exemplary displays of assessments of hydration effectiveness. There are many different ways that the data can be displayed, and any assessments, estimates or predictions generated by the method 200 can be displayed in any desired way, in accordance with various embodiments.
In certain embodiments, the method 200 can include selecting and/or displaying treatment options for the patient (block 235) and/or controlling a therapeutic device (block 240) based on the assessment of the effectiveness of hydration of the patient. For example, a display might indicate to a clinician or the patient him or herself that the patient is becoming (or has become) dehydrated, that fluid resuscitation therapy should be initiated, an estimated volume of fluid to drink, infuse, or otherwise consume, a drip rate for an IV drip, a flow rate for an IV pump or infuser, or the like. Similarly, the system might be configured to control operation of a therapeutic device, such as dispensing a fluid to drink from an automated dispenser, activating or adjusting the flow rate of an IV pump or infuser, adjusting the drip rate of an IV drip, and/or the like, based on the assessment of the effectiveness of hydration. As another example, certain embodiments might include a water bladder (e.g., a backpack-based hydration pack, such as those available from Camelbak Products LLC) or a water bottle, and the hydration monitor could communicate with and/or control operation of such a dispensing device (e.g., to cause the device to dispense a certain amount of fluid, to cause the device to trigger an audible alarm, etc.).

Further, in certain embodiments, the method 200 can include functionality to help a clinician (or other entity) to monitor hydration, fluid resuscitation and/or blood volume status. For example, in some cases, any measure of effectiveness outside of the normal range (such as a value of Pf higher than a certain threshold value, a value of HE lower than a threshold value, etc.) would set off various alarm conditions, such as an audible alarm, a message to a physician, a message to the patient, an update written automatically to a patient's chart, etc. Such messaging could be accomplished by electronic mail, text message, etc., and a sensor device or monitoring computer could be configured with, e.g., an SMTP client, text messaging client, or the like to perform such messaging.

In some cases, feedback and/or notifications might be sent to a third party, regardless of whether any alarm condition were triggered. For example, a hydration monitor might be configured to send monitoring results (e.g., any of the assessments, estimates and/or predictions described herein) to another device or computer, either for personal monitoring by the patient or for monitoring by another. Examples could include transmitting such alarms or data (e.g., by Bluetooth, NFC,
WiFi, etc.) to a wireless phone, wearable device (e.g., smart watch or glasses) or other personal device of the patient, e.g., for inclusion in a health monitoring application. Additionally and/or alternatively, such information could be sent to a specified device or computer (e.g., via any available IP connection), for example to allow a parent to monitor a child's (or a child to monitor an elderly parent's) hydration remotely, to allow a coach to monitor a player's hydration remotely, and/or to allow a superior officer to monitor a soldier's hydration remotely. In some cases (e.g., a coach or superior officer), an application might aggregate results from a plurality of hydration monitors, to allow the supervisor to view (e.g., in a dashboard-type configuration), hydration effectiveness (and/or any other data, such as CRI, blood pressure, etc.) for a group of people. Such a display might employ, for example, a plurality of "fuel gauge" displays, one (or more) for each person in the group, allowing the supervisor to quickly ascertain any unusual results (e.g., based on the color of the gauge, etc.).

[0115] Similarly, if an alarm condition were met for another physiological parameter (such as blood pressure, which can be estimated as described in the '171 Application, for example), that alarm could trigger an assessment of hydration effectiveness via this the method 200, to determine whether the first alarm condition has merit or not. If not, perhaps there could be an automated silencing of the original alarm condition, since all is well at present. More generally, the assessment techniques could be added to an ecosystem of monitoring algorithms (including without limitation those described in the Related Applications), which would inform one another or work in combination, to inform one another about how to maintain optimal physiological stability.

[0116] Fig. 4 illustrates a method 400 of employing such a self-learning predictive model (or machine learning) technique, according to some embodiments. In particular, the method 400 can be used to correlate physiological data received from a subject sensor with a measured physiological state. More specifically, with regard to various embodiments, the method 400 can be used to generate a model for assessing, predicting and/or estimating various physiological parameters, such as blood loss volume, effectiveness of hydration or fluid resuscitation efforts, estimated and/or predicted blood pressure, CRI, the probability that a patient is bleeding, a patient's dehydration state, and/or the like, from one or more of a number of different
physiological parameters, including without limitation those described above and in the Related Applications.

[0117] The method 400 begins at block 405 by collecting raw data measurements that may be used to derive a set of $D$ data signals $s_1, ..., s_D$ as indicated at block 410 (each of the data signals $s$ being, in a particular case, input from one or many different physiological sensors). Embodiments are not constrained by the type of measurements that are made at block 405 and may generally operate on any data set. For example, data signals can be retrieved from a computer memory and/or can be provided from a sensor or other input device. As a specific example, the data signals might correspond to the output of the sensors described above (which measure the types of waveform data described above, such as continuous, non-invasive PPG data and/or blood pressure waveform data).

[0118] A set of $K$ current or future outcomes $\tilde{\sigma} = (o_1, ..., o_K)$ is hypothesized at block 415 (the outcomes $o$ being, in this case, past and/or future physiological states, such as probability that fluids are needed, volume of fluid needed for effective hydration or fluid resuscitation, HE, CRI, dehydration state, probability of bleeding, etc.). The method autonomously generates a predictive model $M$ that relates the derived data signals $\tilde{s}$ with the outcomes $\tilde{\sigma}$. As used herein, "autonomous," means "without human intervention."

[0119] As indicated at block 420, this is achieved by identifying the most predictive set of signals $S_k$, where $S_k$ contains at least some (and perhaps all) of the derived signals $s_1, ..., s_D$ for each outcome $o_k$, where $k \in \{1, ..., K\}$. A probabilistic predictive model $d_k = M_k(S_k)$ is learned at block 425, where $d_k$ is the prediction of outcome $o_k$ derived from the model $M_k$ that uses as inputs values obtained from the set of signals $S_k$, for all $k \in \{1, ..., K\}$. The method 400 can learn the predictive models $d_k = M_k(S_k)$ incrementally (block 430) from data that contains example values of signals $s_1, ..., s_D$ and the corresponding outcomes $o_1, ..., o_K$. As the data become available, the method 400 loops so that the data are added incrementally to the model for the same or different sets of signals $S_k$, for all $k \in \{1, ..., K\}$.

[0120] While the description above outlines the general characteristics of the methods, additional features are noted. A linear model framework may be used to
identify predictive variables for each new increment of data. In a specific
embodiment, given a finite set of data of signals and outcomes \{\theta_4, \hat{\theta}_1, (\tilde{s}_2, \tilde{s}_2), \ldots \},
a linear model may be constructed that has the form, for all \( k \in \{1, \ldots, K\} \),

\[
\hat{\theta}_k = f_k \left( a_0 + \sum_{j=1}^{d} a_{sj} \right) \quad \text{(Eq. 14)}
\]

where \( f_k \) is any mapping from one input to one output, and \( a_0, a_1, \ldots, a_d \)
are the linear model coefficients. The framework used to derive the linear model
coefficients may estimate which signals \( s, s_1, \ldots, s_d \) are not predictive and
accordingly sets the corresponding coefficients \( a_0, a_1, \ldots, a_d \) to zero. Using only the
predictive variables, the model builds a predictive density model of the data,
\{\{\theta_4, \hat{\theta}_1\}, (\tilde{s}_2, \tilde{s}_2), \ldots \}. For each new increment of data, a new predictive density
models can be constructed.

In some embodiments, a prediction system can be implemented that can
predict future results from previously analyzed data using a predictive model and/or
modify the predictive model when data does not fit the predictive model. In some
embodiments, the prediction system can make predictions and/or to adapt the
predictive model in real-time. Moreover, in some embodiments, a prediction system
can use large data sets not only to create the predictive model, but also predict future
results as well as adapt the predictive model.

In some embodiments, a self-learning, prediction device can include a
data input, a processor and an output. Memory can include application software that
when executed can direct the processor to make a prediction from input data based on
a predictive model. Any type of predictive model can be used that operates on any
type of data. In some embodiments, the predictive model can be implemented for a
specific type of data. In some embodiments, when data is received the predictive
model can determine whether it understands the data according to the predictive
model. If the data is understood, a prediction is made and the appropriate output
provided based on the predictive model. If the data is not understood when received,
then the data can be added to the predictive model to modify the model. In some
embodiments, the device can wait to determine the result of the specified data and can
then modify the predictive model accordingly. In some embodiments, if the data is
understood by the predictive model and the output generated using the predictive
model is not accurate, then the data and the outcome can be used to modify the
predictive model. In some embodiments, modification of the predictive model can occur in real-time.

[0125] Particular embodiments can employ the tools and techniques described in the Related Applications in accordance with the methodology described herein perform the functions of a cardiac reserve monitor, a wrist-wear able sensor device, and/or a monitoring computer, as described herein (the functionality of any or all of which can be combined in a single, integrated device, in some embodiments). These functions include, but are not limited to assessing fluid resuscitation of a patient, assessing hydration of a patient, monitoring, estimating and/or predicting a subject's (including without limitation, a patient's) current or future blood pressure and/or compensatory reserve, estimating and/or determining the probability that a patient is bleeding (e.g., internally) and/or has been bleeding, recommending treatment options for such conditions, and/or the like. Such tools and techniques include, in particular, the systems (e.g., computer systems, sensors, therapeutic devices, etc.) described in the Related Applications, the methods (e.g., the analytical methods for generating and/or employing analytical models, the diagnostic methods, etc.), and the software programs described herein and in the Related Applications, which are incorporated herein by reference.

[0126] Hence, Fig. 5 provides a schematic illustration of one embodiment of a computer system 500 that can perform the methods provided by various other embodiments, as described herein, and/or can function as a monitoring computer, CRI monitor, processing unit of sensor device, etc. It should be noted that Fig. 5 is meant only to provide a generalized illustration of various components, of which one or more (or none) of each may be utilized as appropriate. Fig. 5, therefore, broadly illustrates how individual system elements may be implemented in a relatively separated or relatively more integrated manner.

[0127] The computer system 500 is shown comprising hardware elements that can be electrically coupled via a bus 505 (or may otherwise be in communication, as appropriate). The hardware elements may include one or more processors 510, including without limitation one or more general-purpose processors and/or one or more special-purpose processors (such as digital signal processing chips, graphics acceleration processors, and/or the like); one or more input devices 515, which can include without limitation a mouse, a keyboard and/or the like; and one or more
output devices 520, which can include without limitation a display device, a printer
and/or the like.

[0128] The computer system 500 may further include (and/or be in
communication with) one or more storage devices 525, which can comprise, without
limitation, local and/or network accessible storage, and/or can include, without
limitation, a disk drive, a drive array, an optical storage device, solid-state storage
device such as a random access memory ("RAM") and/or a read-only memory
("ROM"), which can be programmable, flash-updateable and/or the like. Such
storage devices may be configured to implement any appropriate data stores,
including without limitation, various file systems, database structures, and/or the like.

[0129] The computer system 500 might also include a communications
subsystem 530, which can include without limitation a modem, a network card
(wireless or wired), an infra-red communication device, a wireless communication
device and/or chipset (such as a Bluetooth™ device, an 802.11 device, a WiFi device,
a WiMax device, a WWAN device, cellular communication facilities, etc.), and/or the
like. The communications subsystem 530 may permit data to be exchanged with a
network (such as the network described below, to name one example), with other
computer systems, and/or with any other devices described herein. In many
embodiments, the computer system 500 will further comprise a working memory 535,
which can include a RAM or ROM device, as described above.

[0130] The computer system 500 also may comprise software elements, shown
as being currently located within the working memory 535, including an operating
system 540, device drivers, executable libraries, and/or other code, such as one or
more application programs 545, which may comprise computer programs provided by
various embodiments, and/or may be designed to implement methods, and/or
configure systems, provided by other embodiments, as described herein. Merely by
way of example, one or more procedures described with respect to the method(s)
discussed above might be implemented as code and/or instructions executable by a
computer (and/or a processor within a computer); in an aspect, then, such code and/or
instructions can be used to configure and/or adapt a general purpose computer (or
other device) to perform one or more operations in accordance with the described
methods.
[0131] A set of these instructions and/or code might be encoded and/or stored on a non-transitory computer readable storage medium, such as the storage device(s) 525 described above. In some cases, the storage medium might be incorporated within a computer system, such as the system 500. In other embodiments, the storage medium might be separate from a computer system (i.e., a removable medium, such as a compact disc, etc.), and/or provided in an installation package, such that the storage medium can be used to program, configure and/or adapt a general purpose computer with the instructions/code stored thereon. These instructions might take the form of executable code, which is executable by the computer system 500 and/or might take the form of source and/or installable code, which, upon compilation and/or installation on the computer system 500 (e.g., using any of a variety of generally available compilers, installation programs, compression/decompression utilities, etc.) then takes the form of executable code.

[0132] It will be apparent to those skilled in the art that substantial variations may be made in accordance with specific requirements. For example, customized hardware (such as programmable logic controllers, field-programmable gate arrays, application-specific integrated circuits, and/or the like) might also be used, and/or particular elements might be implemented in hardware, software (including portable software, such as applets, etc.), or both. Further, connection to other computing devices such as network input/output devices may be employed.

[0133] As mentioned above, in one aspect, some embodiments may employ a computer system (such as the computer system 500) to perform methods in accordance with various embodiments of the invention. According to a set of embodiments, some or all of the procedures of such methods are performed by the computer system 500 in response to processor 510 executing one or more sequences of one or more instructions (which might be incorporated into the operating system 540 and/or other code, such as an application program 545) contained in the working memory 535. Such instructions may be read into the working memory 535 from another computer readable medium, such as one or more of the storage device(s) 525. Merely by way of example, execution of the sequences of instructions contained in the working memory 535 might cause the processor(s) 510 to perform one or more procedures of the methods described herein.
The terms "machine readable medium" and "computer readable medium," as used herein, refer to any medium that participates in providing data that causes a machine to operation in a specific fashion. In an embodiment implemented using the computer system 500, various computer readable media might be involved in providing instructions/code to processor(s) 510 for execution and/or might be used to store and/or carry such instructions/code (e.g., as signals). In many implementations, a computer readable medium is a non-transitory, physical and/or tangible storage medium. Such a medium may take many forms, including but not limited to, non-volatile media, volatile media, and transmission media. Non-volatile media includes, for example, optical and/or magnetic disks, such as the storage device(s) 525. Volatile media includes, without limitation, dynamic memory, such as the working memory 535. Transmission media includes, without limitation, coaxial cables, copper wire and fiber optics, including the wires that comprise the bus 505, as well as the various components of the communication subsystem 530 (and/or the media by which the communications subsystem 530 provides communication with other devices). Hence, transmission media can also take the form of waves (including without limitation radio, acoustic and/or light waves, such as those generated during radio-wave and infra-red data communications).

Common forms of physical and/or tangible computer readable media include, for example, a floppy disk, a flexible disk, a hard disk, magnetic tape, or any other magnetic medium, a CD-ROM, any other optical medium, a RAM, ROM, a PROM, and EPROM, a FLASH-EPROM, any other memory chip or cartridge, a carrier wave as described hereinafter, or any other medium from which a computer can read instructions and/or code.

Various forms of computer readable media may be involved in carrying one or more sequences of one or more instructions to the processor(s) 510 for execution. Merely by way of example, the instructions may initially be carried on a magnetic disk and/or optical disc of a remote computer. A remote computer might load the instructions into its dynamic memory and send the instructions as signals over a transmission medium to be received and/or executed by the computer system 500. These signals, which might be in the form of electromagnetic signals, acoustic signals, optical signals and/or the like, are all examples of carrier waves on which
instructions can be encoded, in accordance with various embodiments of the invention.

[0137] The communications subsystem 530 (and/or components thereof) generally will receive the signals, and the bus 505 then might carry the signals (and/or the data, instructions, etc. carried by the signals) to the working memory 535, from which the processor(s) 505 retrieves and executes the instructions. The instructions received by the working memory 535 may optionally be stored on a storage device 525 either before or after execution by the processor(s) 510.

[0138] Figs. 6-8 illustrate exemplary screen captures from a display device of a compensatory reserve monitor, showing various features that can be provided by one or more embodiments. Similar screens could be shown by other monitoring devices, such as a display of a wrist-wearable sensor device, a display of a monitoring computer, and/or the like. While Figs. 6-8 use HE as an example condition for illustrative purposes, other embodiments might also display values for the volume, V, the volume of fluid necessary for effective hydration, or the probability, Pf, that the patient needs fluid (including additional fluid, if hydration efforts already are in underway).

[0139] Fig. 6 illustrates an exemplary display 600 of a compensatory reserve monitor implementation where a normalized hydration effectiveness ("HE") of "1" implies that the hydration efforts have are completely effective, and "0" implies that the hydration efforts are completely ineffective. Values in between "0" and "1" imply a continuum of effectiveness.

[0140] Fig. 7A illustrates four screen captures 700 of a display of a compensatory reserve monitor implementation that displays HE as a "fuel gauge" type bar graph for a person undergoing central volume blood loss and subsequent hydration efforts. While Fig. 6 illustrates a trace of HE over time, the bar graphs of Figure 7A provide snapshots of HE at the time of each screen capture. (In the illustrated implementation, the bar graphs are continuously and/or periodically updated, such that each bar graph could correspond to a particular position on the X-axis of Figure 6.)

[0141] A variety of additional features are possible. Merely by way of example Fig. 7B illustrates similar "fuel gauge" type displays, but the displays 705 of Fig. 7B
feature bars of different colors - for example, green (illustrated by diagonal cross-hatching), yellow (illustrated by a checked pattern) and red illustrated by gray shading) corresponding to different levels of HE, along with arrows 710 indicating trending in the HE values (e.g., rising, declining, or remaining stable).

[0142] In some embodiments, such a "fuel gauge" display (or other indicator of HE and/or different physiological parameters) can be incorporated in a more comprehensive user interface. Merely by way of example, Fig. 8 illustrates an exemplary display 800 of a monitoring system. The display 800 includes a graphical, color-coded "fuel gauge" type display 805 of the current estimated HE (similar to the displays illustrated by Fig. 8B), along with a historical display 810 of recent CRI estimates; in this example, each bar on the historical display 810 might correspond to an estimate performed every minute, but different estimate frequencies are possible, and in some embodiments, the operator can be given the option to specify a different frequency. In the illustrated embodiment, the display 800 also includes numerical display 815 of the current HE as well as a trend indicator 820 (similar to that indicated above).

[0143] In particular embodiments, the display 800 can include additional information (and, in some cases, the types of information displayed and/or the type of display can be configured by the operator). For instance, the exemplary display 800 includes an indicator 825 of the patient's current heart rate and an indicator 830 of the patient's blood oxygen saturation level (Sp02). The exemplary display 800 also includes an indicator of the estimated volume, V, necessary for effective hydration, as well as a numerical indicator 840, a trend indicator 845, and a similar color coded "fuel gauge" display 850 of the current CRI Other monitored parameters might be displayed as well, such as an ECG tracing, blood pressure, probability of bleeding estimates, and/or the like.

[0144] Conclusion

[0145] This document discloses novel tools and techniques for estimating hydration effectiveness, fluid resuscitation effectiveness, compensatory reserve and similar physiological states. While certain features and aspects have been described with respect to exemplary embodiments, one skilled in the art will recognize that numerous modifications are possible. For example, the methods and processes
described herein may be implemented using hardware components, software components, and/or any combination thereof. Further, while various methods and processes described herein may be described with respect to particular structural and/or functional components for ease of description, methods provided by various embodiments are not limited to any particular structural and/or functional architecture but instead can be implemented on any suitable hardware, firmware and/or software configuration. Similarly, while certain functionality is ascribed to certain system components, unless the context dictates otherwise, this functionality can be distributed among various other system components in accordance with the several embodiments.

Moreover, while the procedures of the methods and processes described herein are described in a particular order for ease of description, unless the context dictates otherwise, various procedures may be reordered, added, and/or omitted in accordance with various embodiments. Moreover, the procedures described with respect to one method or process may be incorporated within other described methods or processes; likewise, system components described according to a particular structural architecture and/or with respect to one system may be organized in alternative structural architectures and/or incorporated within other described systems. Hence, while various embodiments are described with—or without—certain features for ease of description and to illustrate exemplary aspects of those embodiments, the various components and/or features described herein with respect to a particular embodiment can be substituted, added and/or subtracted from among other described embodiments, unless the context dictates otherwise. Consequently, although several exemplary embodiments are described above, it will be appreciated that the invention is intended to cover all modifications and equivalents within the scope of the following claims.
WHAT IS CLAIMED IS:

1. A hydration monitor, comprising:
   one or more sensors to obtain physiological data from a patient; and
   a computer system in communication with the one or more sensors, the
   computer system comprising:
   one or more processors; and
   a computer readable medium in communication with the one or more
   processors, the computer readable medium having encoded thereon
   a set of instructions executable by the computer system to perform
   one or more operations, the set of instructions comprising:
   instructions for receiving the physiological data from the one or
   more sensors;
   instructions for analyzing the physiological data against a pre-
   existing model;
   instructions for assessing effectiveness hydration of the patient
   based on analysis of the physiological data against the pre-
   existing model; and
   instructions for displaying, on a display device, an assessment
   of the effectiveness of hydration of the patient.

2. The hydration monitor of claim 1, further comprising a therapeutic
device, wherein the set of instructions further comprises instructions for controlling
the therapeutic device based at least in part on the assessment of the effectiveness of
hydration of the patient.

3. The hydration monitor of claim 1, wherein the one or more sensors
comprise a finger cuff comprising a fingertip photoplethysmograph and wherein the
computer system comprises a wrist unit in communication with the fingertip
photoplethysmograph, the wrist unit further comprising a wrist strap.

4. A method, comprising:
   monitoring, with one or more sensors, physiological data of a patient;
   analyzing, with a computer system, the physiological data against a pre-
   existing model;
assessing effectiveness of hydration of the patient based on analysis of the physiological data; and
displaying, on a display device, an assessment of the effectiveness of hydration of the patient.

5. The method of claim 4, wherein assessing effectiveness of hydration of the patient comprises estimating the effectiveness of hydration of the patient at a current time.

6. The method of claim 4, wherein assessing effectiveness of hydration of the patient comprises predicting the effectiveness of hydration of the patient at a future time.

7. The method of claim 4, wherein assessing effectiveness of hydration of the patient comprises estimating an amount of fluid needed for effective hydration of the patient.

8. The method of claim 4, wherein assessing effectiveness of hydration of the patient comprises estimating a probability that the patient requires fluids.

9. The method of claim 4, further comprising:
   controlling operation of a therapeutic device based on the assessment of the effectiveness of hydration of the patient.

10. The method of claim 9, wherein controlling operation of a therapeutic device comprises controlling dispensation of a drink from a drink dispenser, controlling an alarm on a drink dispenser, controlling a flow rate of an intravenous pump, controlling a drip rate of an intravenous drip, or controlling a rapid infuser.

11. The method of claim 4, wherein assessing effectiveness of hydration of the patient comprises assessing effectiveness of hydration of the patient based at least in part on one or more compensatory reserve index ("CRI") values of the patient.

12. The method of claim 11, where assessing effectiveness of hydration of the patient comprises calculating a measure of effectiveness $HE$, based on the following formula:

\[ HE = f_{HE}(CRI_t, FV_t) \]
where,

$HE$ is a measure of hydration effectiveness, $f_{HE}(CRI_t, FV_t)$ is a relationship derived based on empirical study, $CRI_t$ is a time history of CRI values, and $FV_t$ is a time history of fluid volume being given to the patient.

13. The method of claim 12, wherein $HE$ ranges in value from 0 to 1.

14. The method of claim 13, wherein when $HE=1$, hydration is proceeding effectively, when $HE=0$, hydration is not producing the desired result.

15. The method of claim 11, where assessing effectiveness of hydration of the patient comprises calculating a measure of effectiveness $HE$, based on the following formula:

$$HE = f_{HE}(CRI_t, FV_t, S_t)$$

where,

$HE$ is a measure of hydration effectiveness, $f_{HE}(CRI_t, FV_t)$ is a relationship derived based on empirical study, $CRI_t$ is a time history of CRI values, $FV_t$ is a time history of fluid volume being given to the patient, and $S_t$ is a time history of physiological data received from the one or more sensors.

16. The method of claim 11, wherein estimating an amount of fluid needed for effective hydration of the patient comprises calculating a volume $V$ needed for effective hydration of the patient, based on the following formula:

$$V = f_v(CRI_t, FV_t)$$

where $V$ is an estimated volume of fluid needed by a patient need to prevent over or under hydration, $f_v(CRI_t, FV_t)$ is a relationship derived based on empirical study, $CRI_t$ is a time history of CRI values, and $FV_t$ is a time history of fluid volume being given to the patient.

17. The method of claim 11, wherein estimating an amount of fluid needed for effective hydration of the patient comprises calculating a volume $V$ needed for effective hydration of the patient, based on the following formula:

$$V = f_v(CRI_t, FV_t, S_t)$$

where $V$ is an estimated volume of fluid needed by a patient need to prevent over or under hydration, $f_v(CRI_t, FV_t, S_t)$ is a relationship derived based on empirical study, $CRI_t$ is a time history of CRI values, and $FV_t$ is a time history of fluid volume being given to the patient.
on empirical study, \( CRI_t \) is a time history of CRI values, \( FV_t \) is a time history of fluid volume being given to the patient, and \( S_i \) is a time history of physiological data received from the one or more sensors.

18. The method of claim 11, wherein estimating effectiveness of hydration of the patient comprises estimating a probability \( P_f \) that the patient requires fluids, based on the following formula:

\[
P_f = f_{P_f}(CRI_t, S_i)
\]

where \( P_f \) is the estimated probability that the patient requires fluid, \( f_{P_f}(CRI_t, S_i) \) is a relationship derived based on empirical study, \( CRI_t \) is a time history of CRI values, and \( S_i \) is a time history of physiological data received from the one or more sensors.

19. The method of claim 11, wherein assessing effectiveness of hydration of a patient comprises estimating the one or more CRI values.

20. The method of claim 19, wherein assessing effectiveness of hydration of a patient comprises estimating a plurality of values of CRI over time and assessing effectiveness of hydration of a patient based on changes in values of CRI over time.

21. The method of claim 19, wherein estimating one or more CRI values of the patient comprises estimating one or more CRI values by comparing the physiological data to the pre-existing model, which is constructed using the following formula:

\[
CRI(t) = t \cdot \frac{BLV(t)}{BLV_{HDD}}
\]

where \( CRI(t) \) is the compensatory reserve at time \( t \), \( BLV(t) \) is an intravascular volume loss of a test subject at time \( t \), and \( BLV_{HDD} \) is an intravascular volume loss at a point of hemodynamic decompensation of the test subject.

22. The method of claim 19, wherein the physiological data comprises waveform data and wherein estimating each of the one or more CRI values of the patient comprises comparing the waveform data with one or more sample waveforms generated by exposing one or more test subjects to state of hemodynamic decompensation or near hemodynamic decompensation, or a series of states.
progressing towards hemodynamic decompensation, and monitoring physiological data of the test subjects.

23. The method of claim 19, wherein the physiological data comprises waveform data, and wherein estimating each of the one or more CRI values comprises:
   comparing the waveform data with a plurality of sample waveforms, each of the sample waveforms corresponding to a different value of the compensatory reserve index to produce a similarity coefficient expressing a similarity between the waveform data and each of the sample waveforms;
   normalizing the similarity coefficients for each of the sample waveforms; and
   summing the normalized similarity coefficients to produce an estimated CRI value for the patient.


26. The method of claim 4, wherein at least one of the one or more sensors is selected from the group consisting of a blood pressure sensor, an intracranial pressure monitor, a central venous pressure monitoring catheter, an arterial catheter, an electroencephalograph, a cardiac monitor, a transcranial Doppler sensor, a transthoracic impedance plethysmograph, a pulse oximeter, a near infrared spectrometer, a ventilator, an accelerometer, an electrooculogram, a transcutaneous glucometer, an electrolyte sensor, and an electronic stethoscope.

27. The method of claim 4, wherein the physiological data comprises blood pressure waveform data.

28. The method of claim 4, wherein the physiological data comprises plethysmograph waveform data.
29. The method of claim 4, wherein the physiological data comprises photoplethysmograph (PPG) waveform data.

30. The method of claim 4, further comprising:
   generating the pre-existing model.

31. The method of claim 30, wherein generating the pre-existing model comprises:
   receiving data pertaining to one or more physiological parameters of a test subject to obtain a plurality of physiological data sets;
   directly measuring one or more physiological states of the test subject with a reference sensor to obtain a plurality of physiological state measurements;
   and
   correlating the received data with the physiological state measurements of the test subject.

32. The method of claim 31, wherein the one or more physiological states comprises one or more states selected from the group consisting of reduced circulatory system volume, blood loss, added fluids to blood volume, dehydration, cardiovascular collapse or near-cardiovascular collapse, euvoemia, hypervolemia.

33. The method of claim 31, wherein correlating the received data with the physiological state measurements of the test subject comprises:
   identifying a most predictive set of signals $S_k$ out of a set of signals $s_1, \ldots, s_D$ for each of one or more outcomes $o_k$ wherein the most-predictive set of signals $S_k$ corresponds to a first data set representing a first physiological parameter, and wherein each of the one or more outcomes $o_k$ represents a physiological state measurement;
   autonomously learning a set of probabilistic predictive models $d_k = M_k(S_k)$ where $d_k$ is a prediction of outcome $o_k$ derived from a model $M_k$ that uses as inputs values obtained from the set of signals $s_1$ and repeating the operation of autonomously learning incrementally from data that contains examples of values of signals $s_1, \ldots, s_D$ and corresponding outcomes $o_1, o_2, \ldots, o_k$. 


34. An apparatus, comprising:
   a computer readable medium having encoded thereon a set of instructions
   executable by one or more computers to perform one or more operations,
   the set of instructions comprising:
   instructions for receiving the physiological data from the one or more
   sensors;
   instructions for analyzing the physiological data against a pre-existing
   model;
   instructions for assessing effectiveness of hydration of the patient
   based on analysis of the physiological data against the pre-existing
   model; and
   instructions for displaying, on a display device, an assessment of the
   effectiveness of hydration of the patient.
Generate Model

Monitor Parameters

Analyze Data

Assess Hydration

Update Model

Display Data

Select/Display Treatment Options

Control Therapeutic Device

FIG. 2A
Input Waveform (e.g., 22 beats PPG)

Compare to Waveform at HE=1
Assign Coefficient
Normalize
Sum
HE Estimate

Compare to Waveform at HE=0.5
Assign Coefficient
Normalize

Compare to Waveform at HE=0
Assign Coefficient
Normalize

FIG. 2B
FIG. 3A
Input Waveform (e.g., 32 beats CniBP)

370

Compare to Waveform at CRI = 1
375a

Assign Coefficient
380a

Normalize
385a

Sum
390

CRI Estimate
365

Compare to Waveform at CRI = 0.5
375b

Assign Coefficient
380b

Normalize
385b

Compare to Waveform at CRI = 0
375c

Assign Coefficient
380c

Normalize
385c

FIG. 3B
Collect Data Measurements

Derive Signals From Data Measurements

Hypothesize Current or Future Outcomes

Identify Most Predictive Signal Set for Each Outcome

Learn Probabilistic Predictive Models

Learn Predictive Model Incrementally from Data

FIG. 4
Dehydration Occurring

Hydration Efforts Active

Time = t_3

HE 0.2
1.0 0.8 0.6 0.4 0.2 0.0

Time = t_4

HE 0.9
1.0 0.8 0.6 0.4 0.2 0.0

Time = t_5

HE 0.4
1.0 0.8 0.6 0.4 0.2 0.0

Time = t_6

HE 0.9
1.0 0.8 0.6 0.4 0.2 0.0

FIG. 7B
INTERNATIONAL SEARCH REPORT

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2014/065820

A. CLASSIFICATION OF SUBJECT MATTER
A61B 5/1455(2006.01)i, G06Q 50/22(2012.01)i

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

B. FIELDS SEARCHED
Minimum documentation searched (classification system followed by classification symbols)
A61B 5/1455; A61B 5/021; B01D 61/30; A61B 5/02; A61B 6/00; A61B 7/00; A61B 5/0205; A61M 16/00; A61B 5/00; G06Q 50/22

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

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: hydration, blood pressure, ppg

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
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<tbody>
<tr>
<td>X</td>
<td>US 2012-0330117 AL (GREGORY ZLATKO GRUDIC et al.) 27 December 2012</td>
<td>1-34</td>
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<tr>
<td></td>
<td>See abstract, paragraphs [0011]-[0063] and claims 1-41</td>
<td></td>
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<tr>
<td>A</td>
<td>US 2013-0261468 AL (HERBERT J. SEMLER et al.) 03 October 2013</td>
<td>1-34</td>
</tr>
<tr>
<td></td>
<td>See abstract, paragraphs [0016]-[0021] and figures 1-2</td>
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<td>A</td>
<td>US 2013-0041268 AL (STEFANO RIMOLDI et al.) 14 February 2013</td>
<td>1-34</td>
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<td></td>
<td>See abstract, paragraphs [0062]-[0064] and claims 1-2</td>
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<td>A</td>
<td>US 2010-0160795 AL (MATT BANET et al.) 24 June 2010</td>
<td>1-34</td>
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<td>See abstract, paragraphs [0076]-[0097] and claims 1-4</td>
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<td>A</td>
<td>US 2009-0272678 AL (LEIF SORNO et al.) 05 November 2009</td>
<td>1-34</td>
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<td></td>
<td>See abstract, paragraphs [0039]-[0058] and claims 1-2</td>
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</table>

Further documents are listed in the continuation of Box C. ❌ See patent family annex.

* Special categories of cited documents:
  "A" document defining the general state of the art which is not considered to be of particular relevance
  "E" earlier application or patent but published on or after the international filing date
  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
  "O" document referring to an oral disclosure, use, exhibition or other means
  "P" document published prior to the international filing date but later than the priority date claimed
  "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
  "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
  "&" document member of the same patent family

Date of the actual completion of the international search
25 February 2015 (25.02.2015)

Date of mailing of the international search report
26 February 2015 (26.02.2015)

Name and mailing address of the ISA/KR
International Application Division
Korean Intellectual Property Office
189 Cheongna-ro, Seo-gu, Daejeon Metropolitan City, 302-701, Republic of Korea
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Authorized officer
KJM, Tae Hoon
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