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Grudic et al.

(10) Patent No.: **US 9,757,041 B2**
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(54) **HEMODYNAMIC RESERVE MONITOR AND HEMODIALYSIS CONTROL**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1189 days.

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(22) Filed: **Jul. 20, 2012**

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Related U.S. Application Data

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(51) **Int. Cl.**
A61B 5/0205 (2006.01)
A61B 5/02 (2006.01)
(Continued)

(52) **U.S. Cl.**
CPC ***A61B 5/02028*** (2013.01); ***A61B 5/021*** (2013.01); ***A61B 5/02042*** (2013.01);
(Continued)

(58) **Field of Classification Search**
CPC A61B 5/14551; A61B 5/02416; A61B 5/0205; A61B 5/021
See application file for complete search history.

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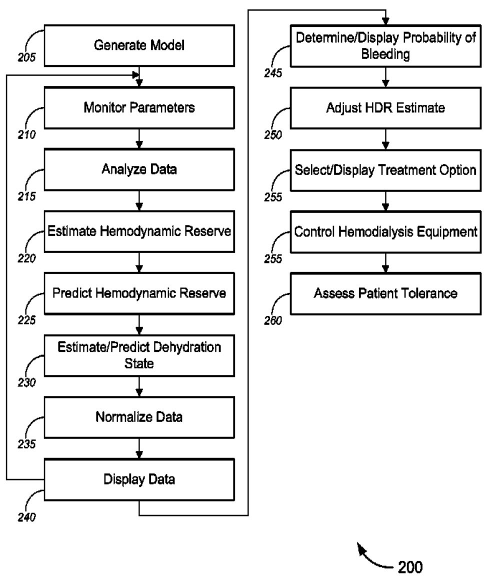
Primary Examiner — Patricia Mallari
Assistant Examiner — Michael Catina
(74) *Attorney, Agent, or Firm* — Swanson & Bratschun, L.L.C.

(57) **ABSTRACT**

Tools and techniques for estimating a probability that a patient is bleeding or has sustained intravascular volume loss (e.g., due to hemodialysis or dehydration) and/or to estimate a patient's current hemodynamic reserve index, track the patient's hemodynamic reserve index over time, and/or predict a patient's hemodynamic reserve index in the future. Tools and techniques for estimating and/or predicting a patient's dehydration state. Tools and techniques for controlling a hemodialysis machine based on the patient's estimated and/or predicted hemodynamic reserve index.

57 Claims, 15 Drawing Sheets



Related U.S. Application Data

application No. 13/028,140, filed on Feb. 15, 2011, now Pat. No. 8,512,260, and a continuation-in-part of application No. PCT/US2009/062119, filed on Oct. 26, 2009.

(60) Provisional application No. 61/510,792, filed on Jul. 22, 2011, provisional application No. 61/614,426, filed on Mar. 22, 2012, provisional application No. 61/310,583, filed on Mar. 4, 2010, provisional application No. 61/305,110, filed on Feb. 16, 2010, provisional application No. 61/252,978, filed on Oct. 19, 2009, provisional application No. 61/166,499, filed on Apr. 3, 2009, provisional application No. 61/166,486, filed on Apr. 3, 2009, provisional application No. 61/166,472, filed on Apr. 3, 2009, provisional application No. 61/109,490, filed on Oct. 29, 2008.

(51) **Int. Cl.**

A61B 5/021	(2006.01)
A61B 5/00	(2006.01)
A61B 5/029	(2006.01)
A61B 5/0402	(2006.01)
A61B 5/1455	(2006.01)

(52) **U.S. Cl.**

CPC ***A61B 5/7275*** (2013.01); *A61B 5/029* (2013.01); *A61B 5/0402* (2013.01); *A61B 5/14551* (2013.01)

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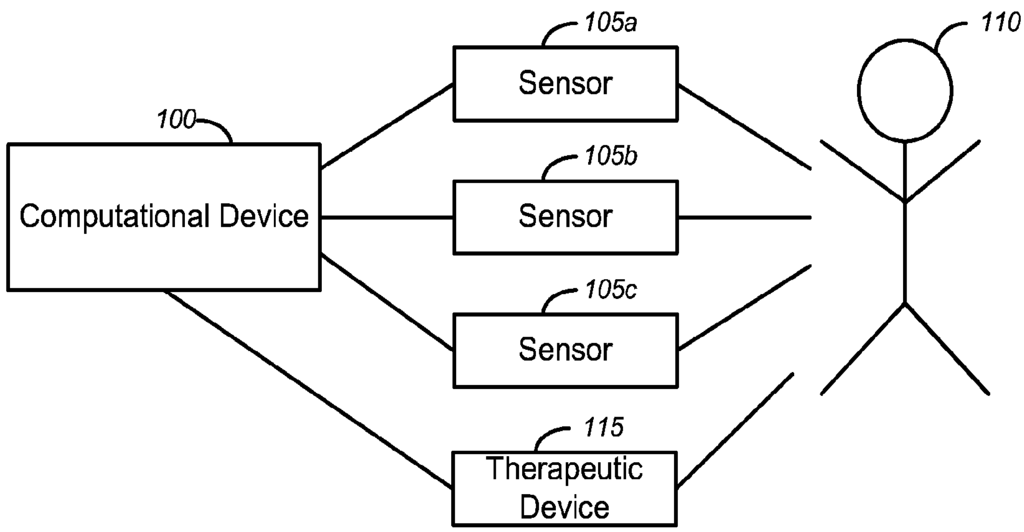


100
Computational Device
105a
Sensor
105b
Sensor
105c
Sensor
115
Therapeutic Device
110

FIG. 1

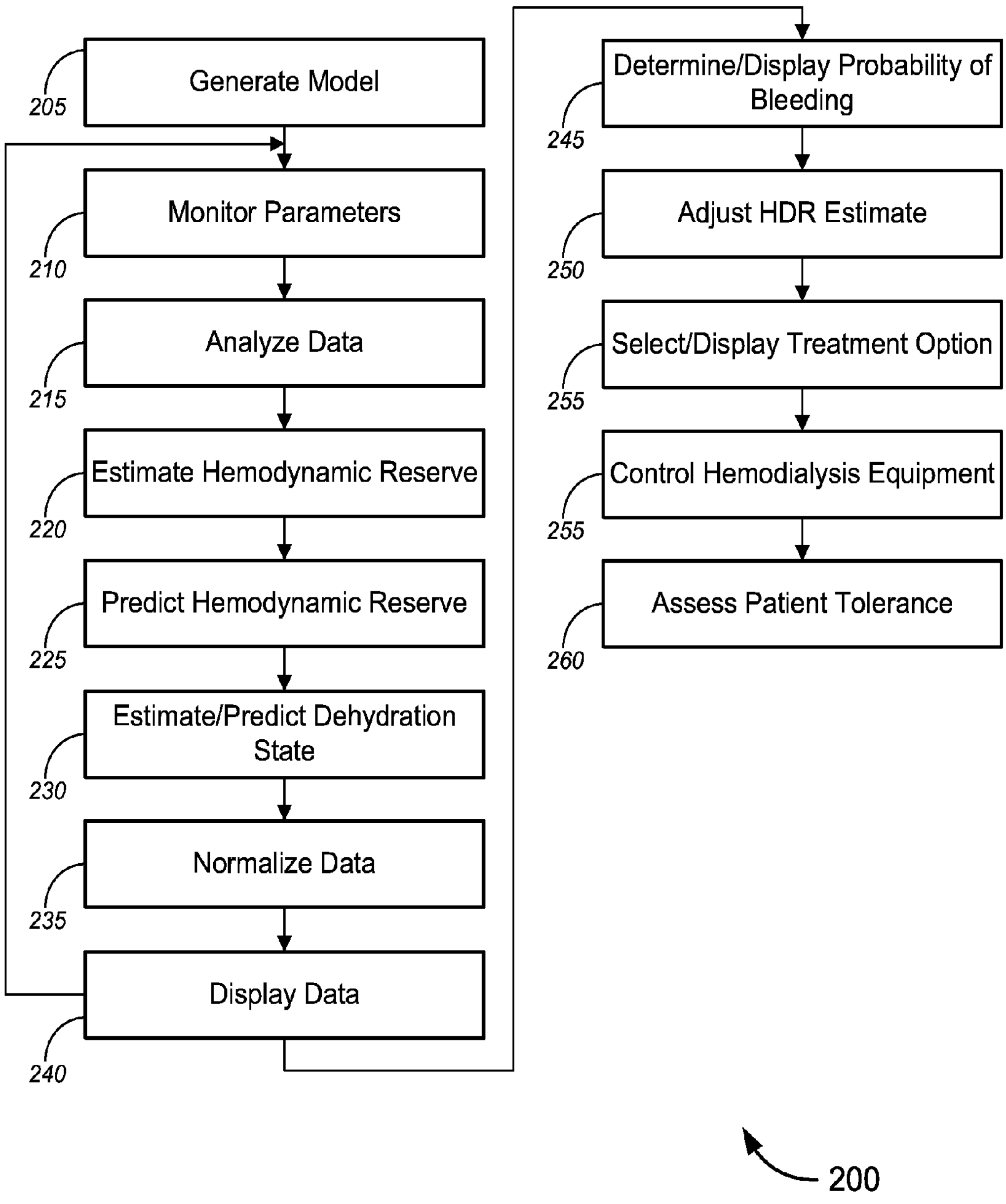

Generate Model
205
Monitor Parameters
210
Analyze Data
215
Estimate Hemodynamic Reserve
220
Predict Hemodynamic Reserve
225
Estimate/Predict Dehydration State
230
Normalize Data
235
Display Data
240
Determine/Display Probability of Bleeding
245
Adjust HDR Estimate
250
Select/Display Treatment Option
255
Control Hemodialysis Equipment
255
Assess Patient Tolerance
260
200

FIG. 2

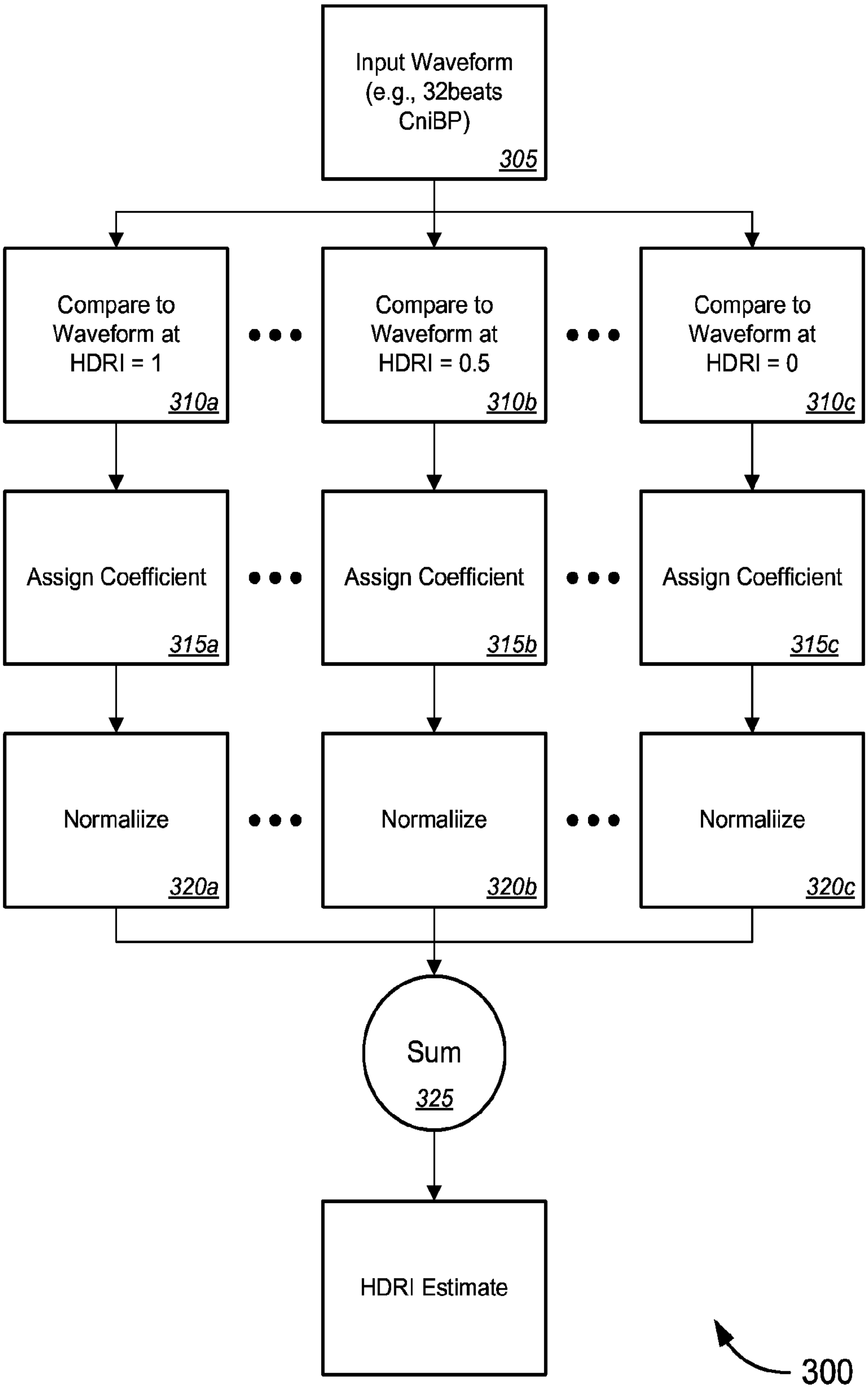

Input Waveform
(e.g., 32beats
CniBP)
305
Compare to
Waveform at
HDRI = 1
310a
Compare to
Waveform at
HDRI = 0.5
310b
Compare to
Waveform at
HDRI = 0
310c
Assign Coefficient
315a
Assign Coefficient
315b
Assign Coefficient
315c
Normaliize
320a
Normaliize
320b
Normaliize
320c
Sum
325
HDRI Estimate
300

FIG. 3

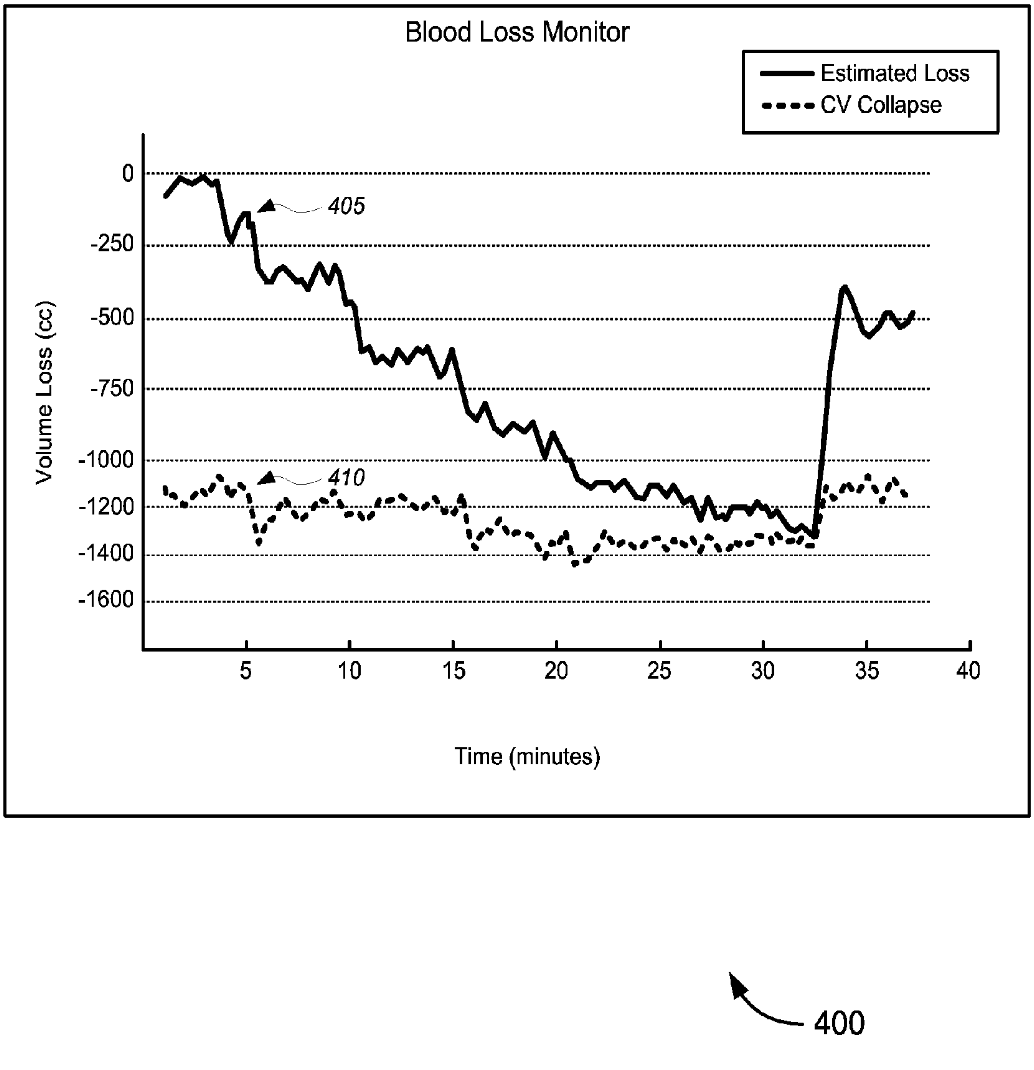
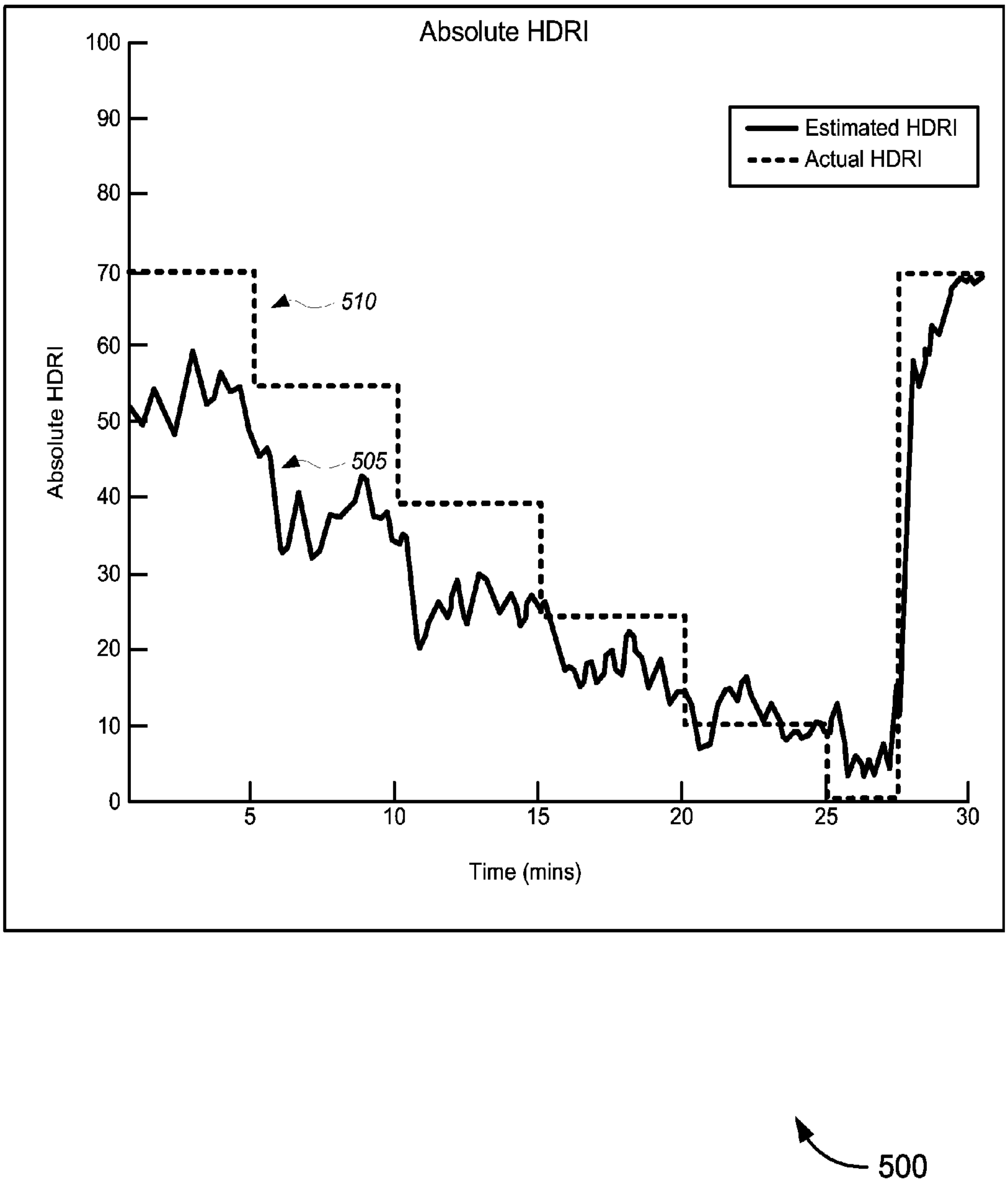

Blood Loss Monitor
Estimated Loss
CV Collapse
405
410
0
-250
-500
-750
-1000
-1200
-1400
-1600
Volume Loss (cc)
5
10
15
20
25
30
35
40
Time (minutes)
400

FIG. 4



Absolute HDRI
Estimated HDRI
Actual HDRI
Absolute HDRI
100
90
80
70
60
50
40
30
20
10
0
5
10
15
20
25
30
Time (mins)
510
505
500

FIG. 5

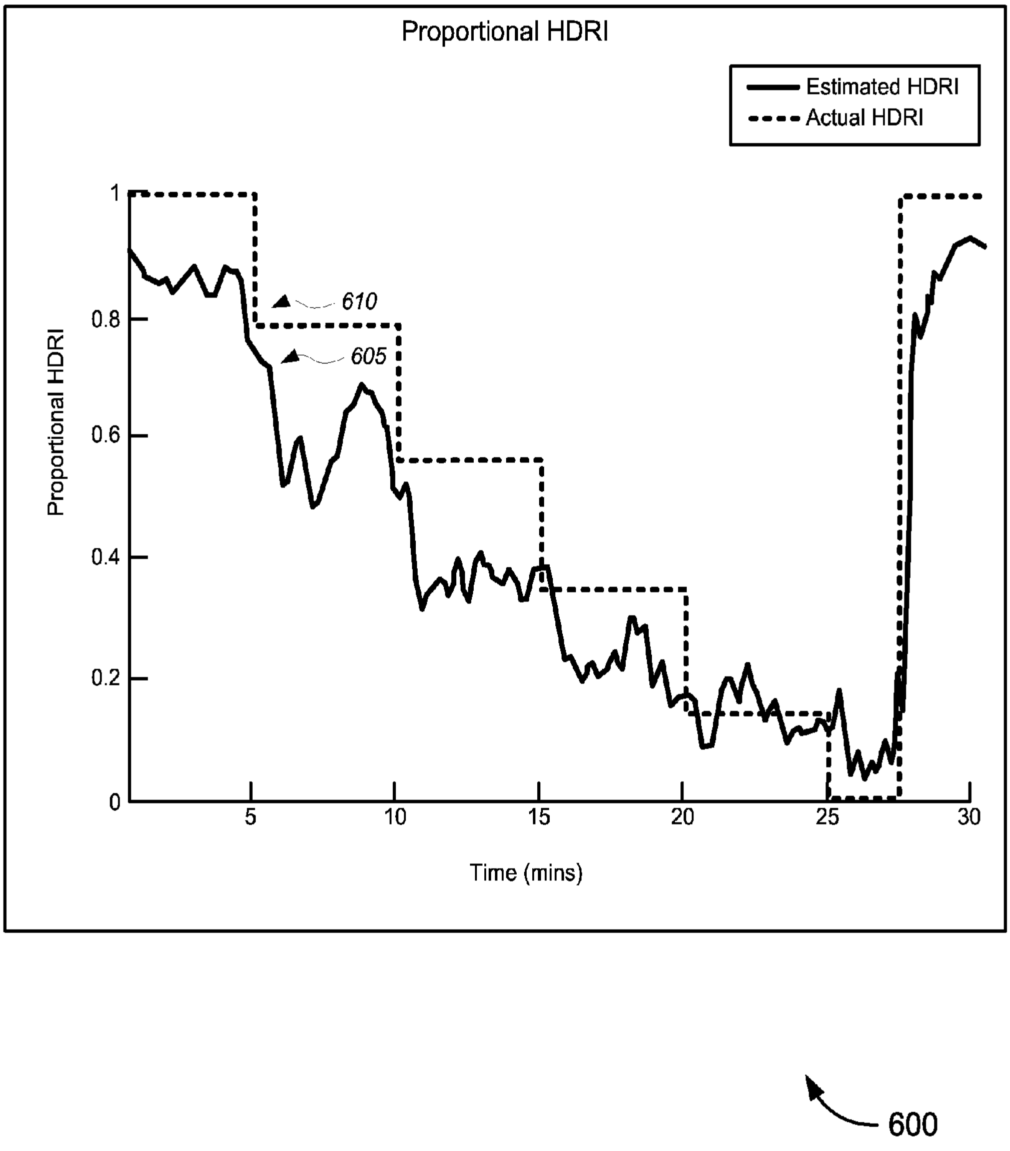

Proportional HDRI
Estimated HDRI
Actual HDRI
1
0.8
0.6
0.4
0.2
0
Proportional HDRI
610
605
5
10
15
20
25
30
Time (mins)
600

FIG. 6

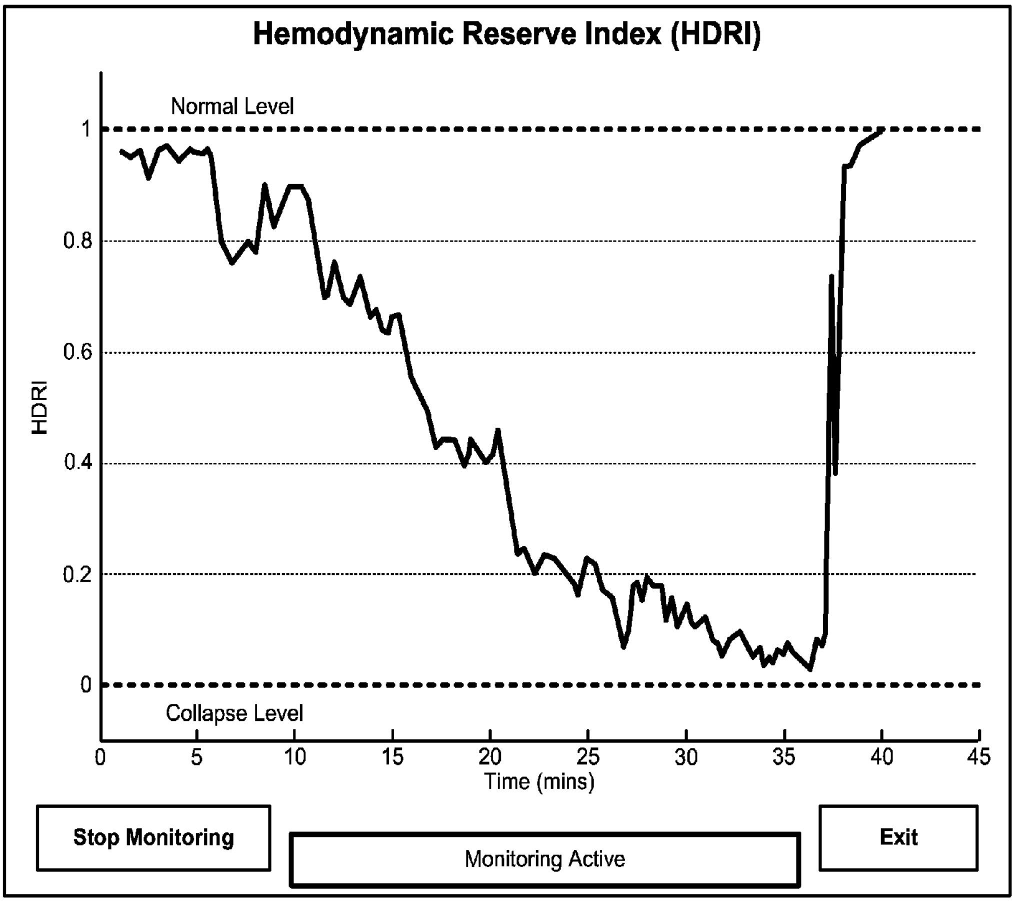

Hemodynamic Reserve Index (HDRI)
Normal Level
1
0.8
0.6
0.4
0.2
0
HDRI
Collapse Level
0
5
10
15
20
25
30
35
40
45
Time (mins)
Stop Monitoring
Monitoring Active
Exit

FIG. 7

700

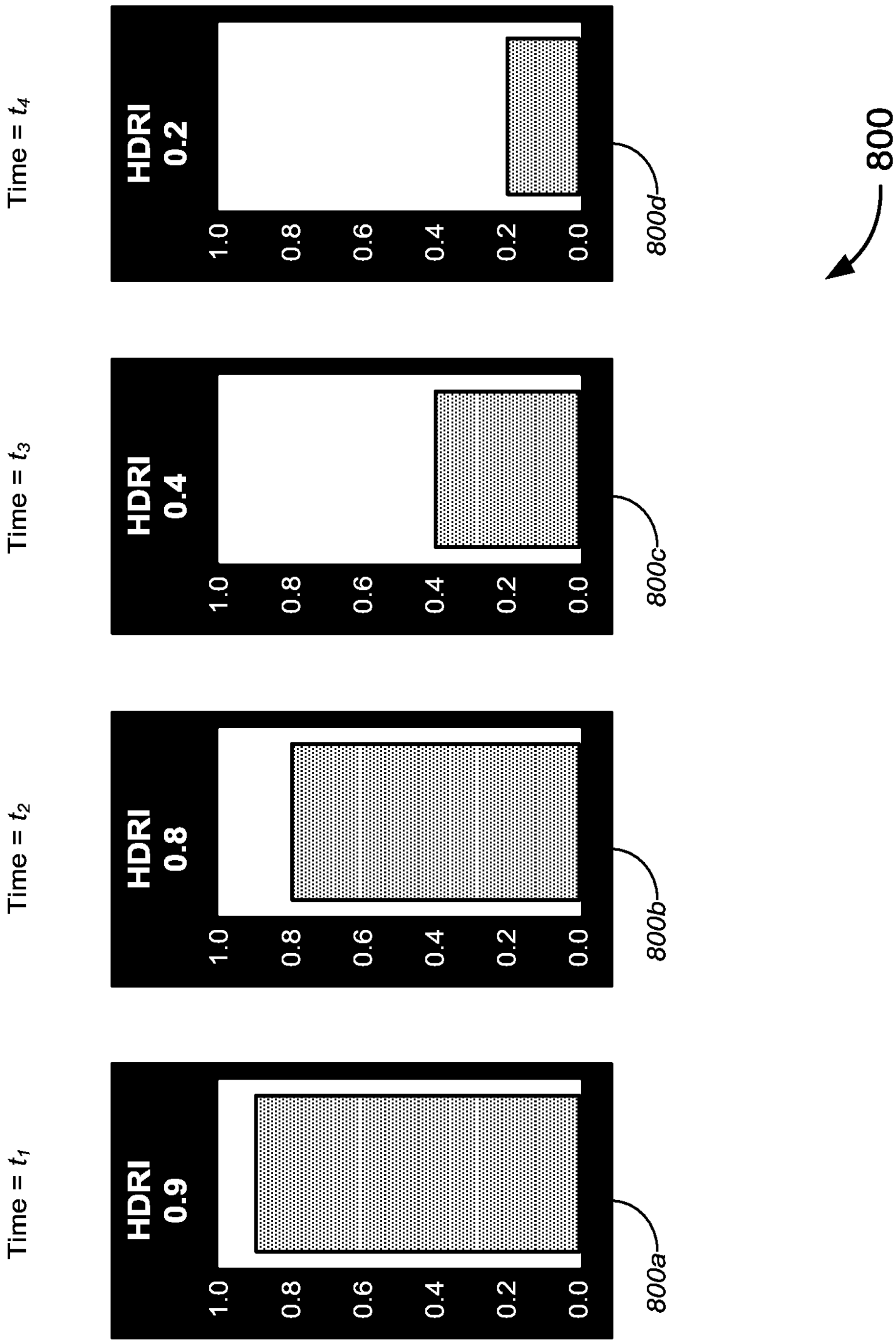

Time = t_1
HDRI 0.9
1.0
0.8
0.6
0.4
0.2
0.0
800a
Time = t_2
HDRI 0.8
1.0
0.8
0.6
0.4
0.2
0.0
800b
Time = t_3
HDRI 0.4
1.0
0.8
0.6
0.4
0.2
0.0
800c
Time = t_4
HDRI 0.2
1.0
0.8
0.6
0.4
0.2
0.0
800d
800

FIG. 8A

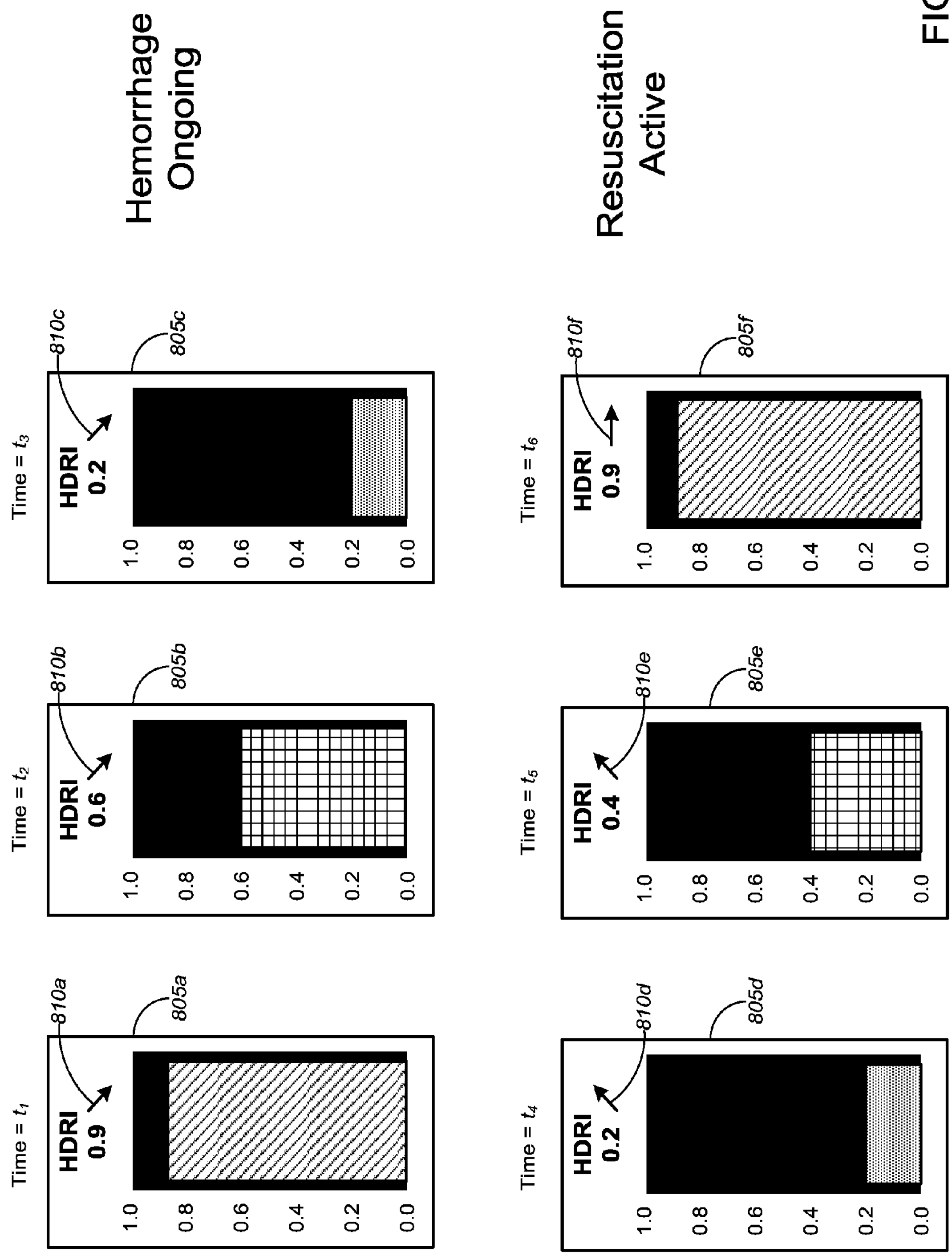

Hemorrhage
Ongoing
Resuscitation
Active
Time = t_1
HDRI
0.9
810a
805a
Time = t_2
HDRI
0.6
810b
805b
Time = t_3
HDRI
0.2
810c
805c
Time = t_4
HDRI
0.2
810d
805d
Time = t_5
HDRI
0.4
810e
805e
Time = t_6
HDRI
0.9
810f
805f
1.0
0.8
0.6
0.4
0.2
0.0

FIG. 8B

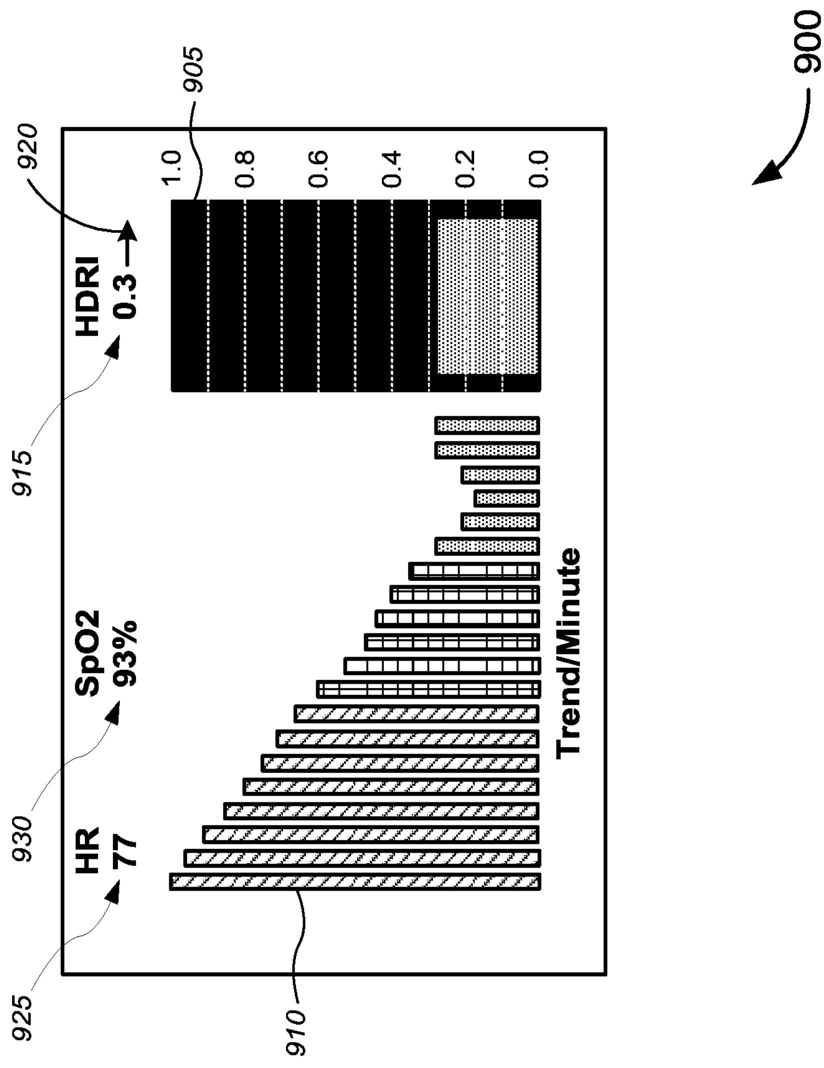

900
905
920
915
930
925
910
HDRI
0.3
SpO2
93%
HR
77
1.0
0.8
0.6
0.4
0.2
0.0
Trend/Minute

FIG. 9

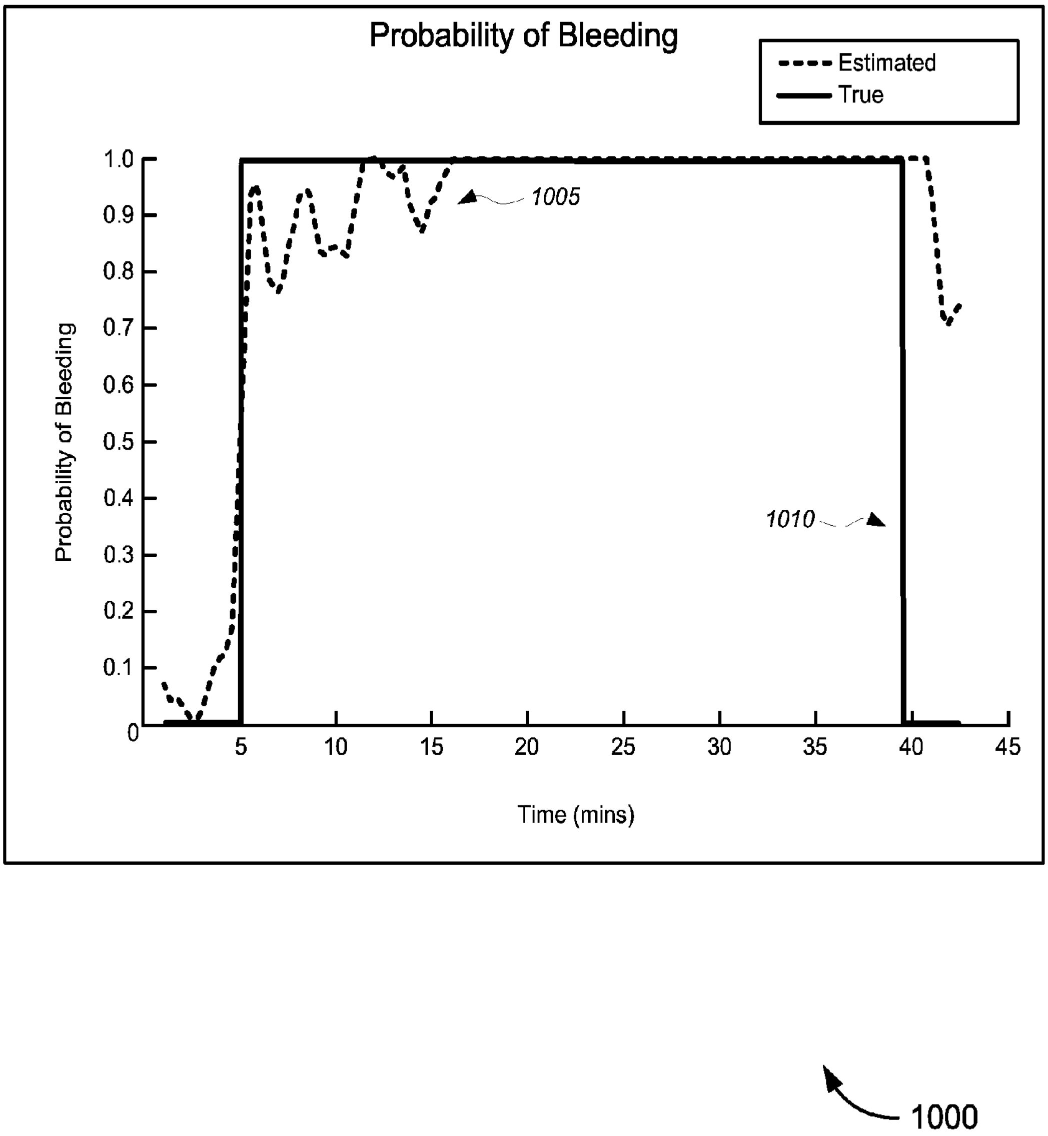

Probability of Bleeding
Estimated
True
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Probability of Bleeding
1005
1010
5
10
15
20
25
30
35
40
45
Time (mins)
1000

FIG. 10

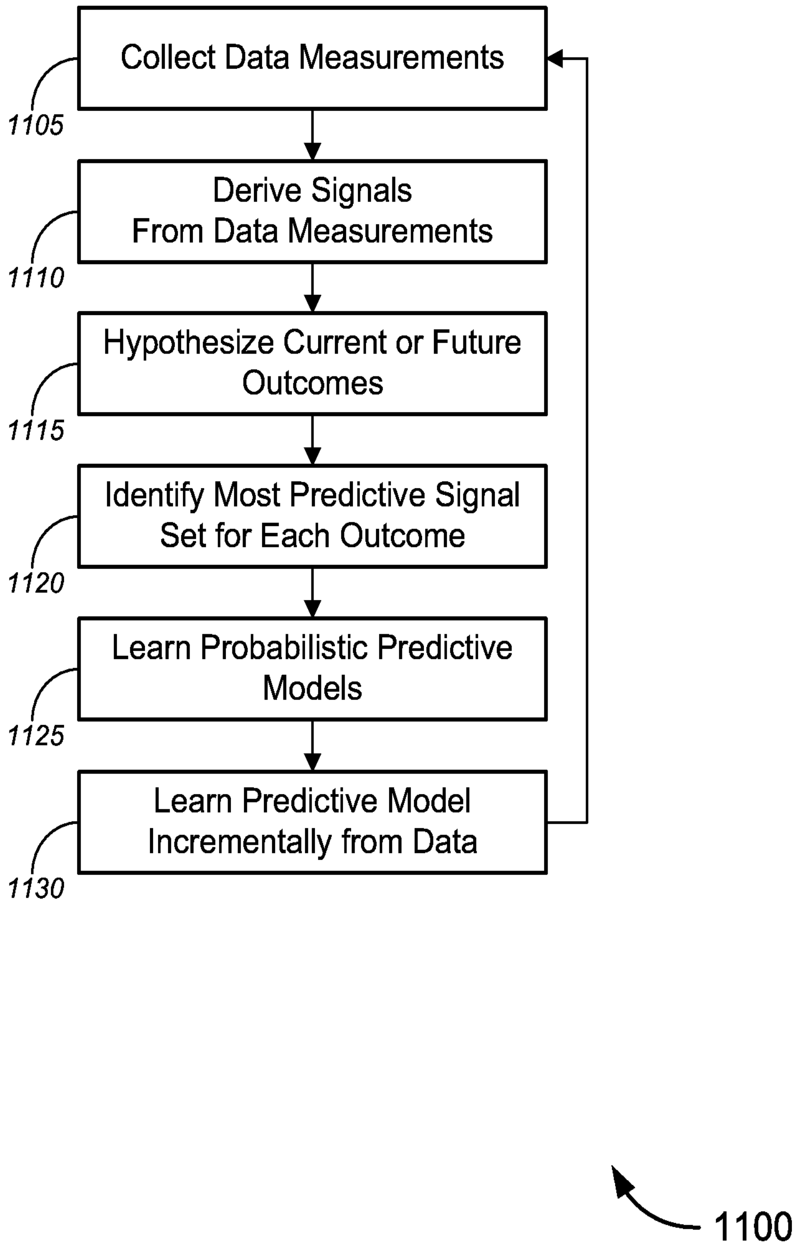

Collect Data Measurements
1105
Derive Signals From Data Measurements
1110
Hypothesize Current or Future Outcomes
1115
Identify Most Predictive Signal Set for Each Outcome
1120
Learn Probabilistic Predictive Models
1125
Learn Predictive Model Incrementally from Data
1130
1100

FIG. 11

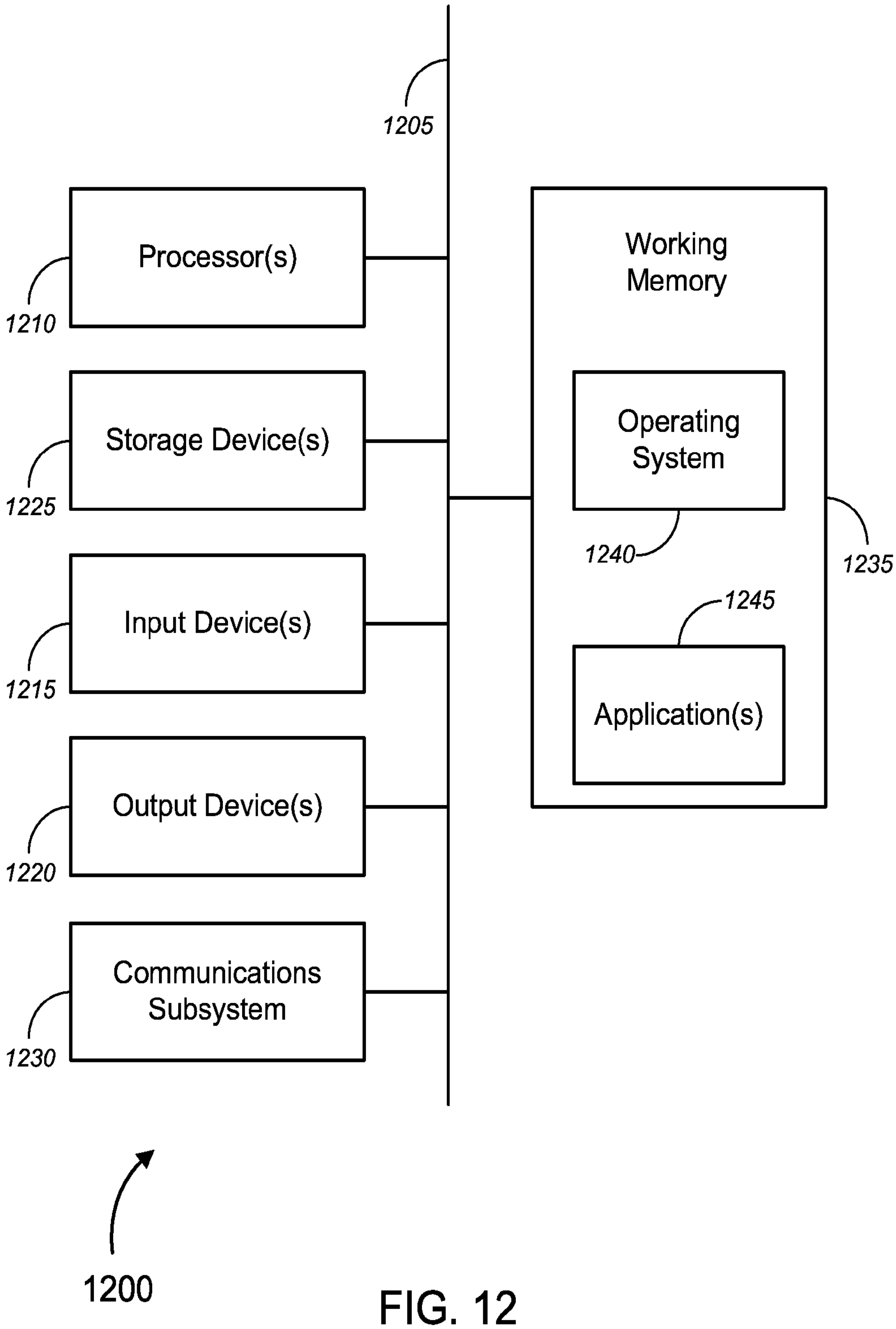

1205
Processor(s)
1210
Storage Device(s)
1225
Input Device(s)
1215
Output Device(s)
1220
Communications Subsystem
1230
Working Memory
Operating System
1240
1245
Application(s)
1235
1200

FIG. 12

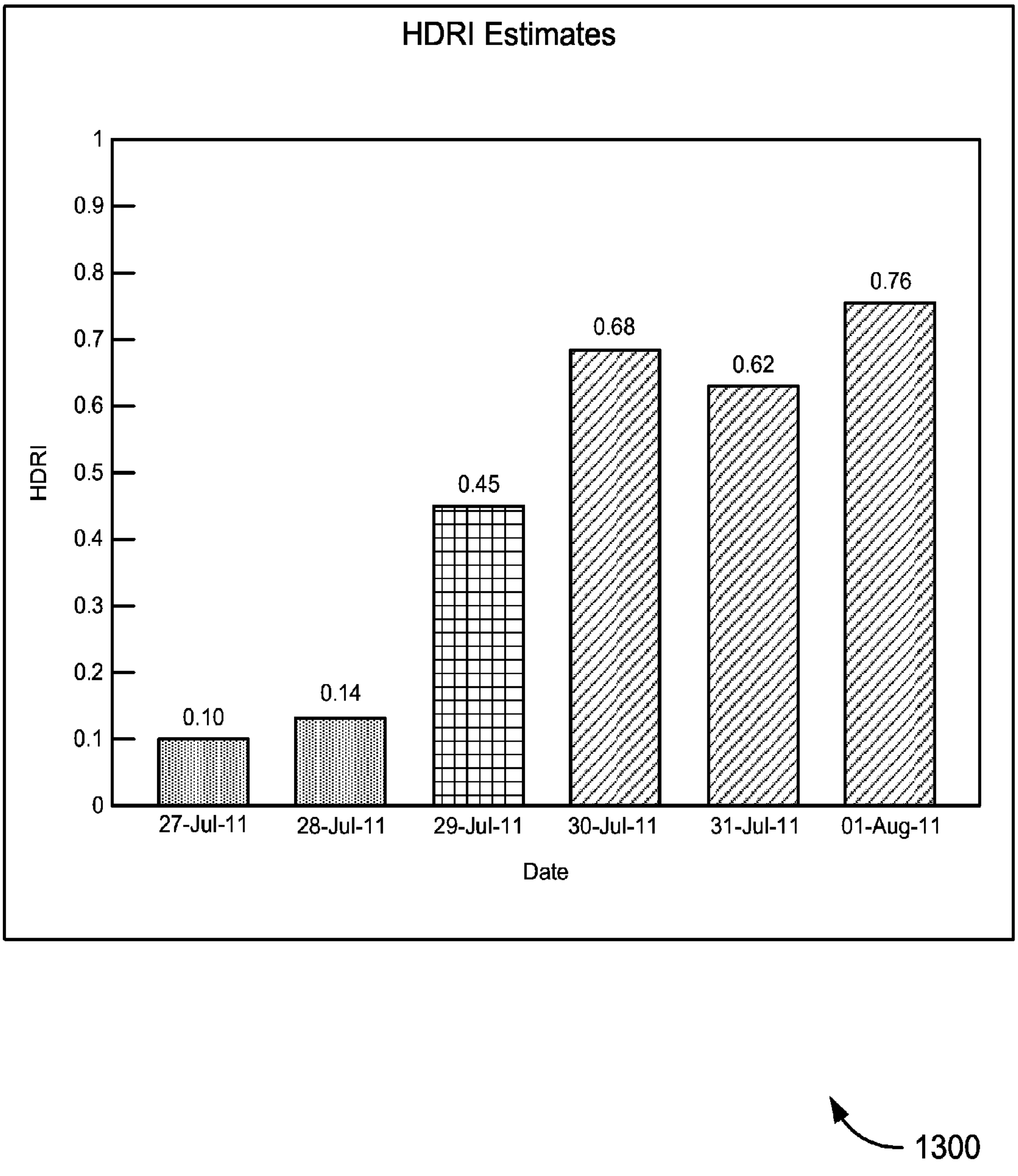

HDRI Estimates
1
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
HDRI
0.10
0.14
0.45
0.68
0.62
0.76
27-Jul-11
28-Jul-11
29-Jul-11
30-Jul-11
31-Jul-11
01-Aug-11
Date
1300

FIG. 13

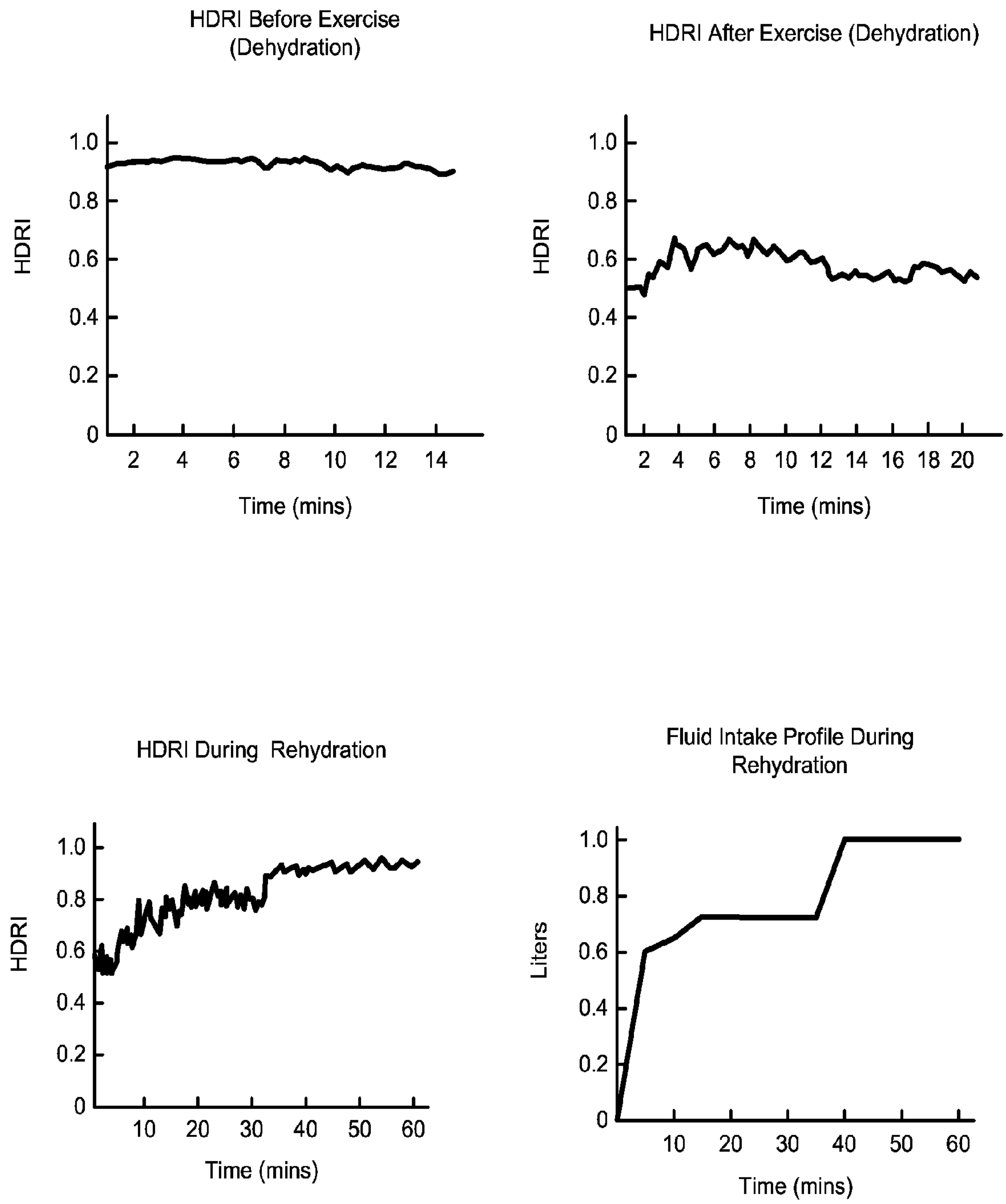

HDRI Before Exercise (Dehydration)
HDRI
1.0
0.8
0.6
0.4
0.2
0
2 4 6 8 10 12 14
Time (mins)
HDRI After Exercise (Dehydration)
HDRI
1.0
0.8
0.6
0.4
0.2
0
2 4 6 8 10 12 14 16 18 20
Time (mins)
HDRI During Rehydration
HDRI
1.0
0.8
0.6
0.4
0.2
0
10 20 30 40 50 60
Time (mins)
Fluid Intake Profile During Rehydration
Liters
1.0
0.8
0.6
0.4
0.2
0
10 20 30 40 50 60
Time (mins)

FIG. 14

HEMODYNAMIC RESERVE MONITOR AND HEMODIALYSIS CONTROL

CROSS-REFERENCE TO RELATED APPLICATIONS

The present disclosure may be related to the following commonly assigned applications/patents:

This non-provisional application claims the benefit, under 35 U.S.C. §119(e), of co-pending provisional U.S. Patent Application No. 61/510,792, filed Jul. 22, 2011 by Grudic et al. and entitled "Cardiovascular Reserve Monitor", and co-pending provisional U.S. Patent Application No. 61/614,426, filed Mar. 22, 2012 by Grudic et al. and entitled "Hemodynamic Reserve Monitor and Hemodialysis Control", both of which are hereby incorporated by reference.

This application is also a continuation-in-part of U.S. patent application Ser. No. 13/041,006 (the "'006 Application"), filed Mar. 4, 2011 by Grudic et al. and entitled "Active Physical Perturbations to Enhance Intelligent Medical Monitoring," which is hereby incorporated by reference, and which claims the benefit, inter alia, of provisional U.S. Patent Application No. 61/310,583, filed Mar. 4, 2010, which is hereby incorporated by reference. The '006 Application is a continuation-in-part of U.S. patent application Ser No. 13/028,140 (the "'140 Application"), filed Feb. 15, 2011 by Grudic et al. and entitled "Statistical, Noninvasive Measurement of Intracranial Pressure," which is hereby incorporated by reference, and which claims the benefit of provisional U.S. Patent Application No. 61/305,110, filed Feb. 16, 2010, by Moulton et al. and titled "A Statistical, Noninvasive Method for Measuring Intracranial Pressure," which is hereby incorporated by reference.

The '140 Application is a continuation in part of International Application No. PCT/US2009/062119, filed Oct. 26, 2009 by Grudic et al. and entitled "Long Term Active Learning from Large Continually Changing Data Sets" (the "'119 Application"), which is hereby incorporated by reference, and which claims the benefit, under 35 U.S.C. §119(e), of provisional U.S. Patent Application No. 61/252,978 filed Oct. 19, 2009, U.S. Patent Application Nos. 61/166,499, 61/166,486, and 61/166,472, filed Apr. 3, 2009, and U.S. Patent Application No. 61/109,490, filed Oct. 29, 2008, each of which is hereby incorporated by reference.

The respective disclosures of these applications/patents (collectively, the "Related Applications") are incorporated herein by reference in their entirety for all purposes.

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

This invention was made with government support under grant number 0535269 awarded by the National Science Foundation; grant number FA8650-07-C-7702 awarded by the Air Force Research Laboratory; and grant numbers W81XWH-09-C-1060 and W81XWH-09-1-0750 awarded by Army Medical Research Material and Command. The government has certain rights in the invention.

COPYRIGHT STATEMENT

FIELD

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 a patient's cardiac reserve.

BACKGROUND

Hemorrhagic shock induced by traumatic injury is a leading cause of mortality. The first hour following injury has been termed the "golden hour," because there is a short interval of time during which recognition and proper management of a patient with significant, ongoing bleeding can make the difference between life and death. Significant bleeding is not always clinically evident. Many severely injured patients have intracavitary bleeding, which means that bleeding from a major organ or vessel is contained within the thorax or abdomen. There is no external evidence of bleeding and as a result, suspicion and clinical signs of bleeding must be sought by the practitioner. In the field, where imaging and laboratory tests are generally not available, a change in vital signs over time may be the only indication that a patient is bleeding. Thus, during the "golden hour" one must learn to recognize the signs and symptoms of acute blood loss, then initiate fluid resuscitation and frequently estimate the patient's fluid needs in an ongoing fashion.

The problem is that humans are unable to recognize subtle, beat-to-beat vital sign changes that are indicative of bleeding. More importantly, humans are unable to detect subtle vital sign changes that lead to and are characteristic of impending hemodynamic decompensation or cardiovascular collapse, which is heralded by hypotension with bradycardia.

Thus, there is a need for tools and techniques to enable a practitioner to recognize as quickly as possible a probability that a patient is bleeding or has experienced intravascular volume loss (e.g., due to hemodialysis or dehydration) and/or to estimate a patient's current hemodynamic reserve, track the patient's hemodynamic reserve over time, and/or predict a patient's hemodynamic reserve in the future. The term "hemodynamic reserve" is a hemodynamic parameter indicative of the proportion of fluid in the vascular system between normovolemia (full reserve) and the onset of hemodynamic decompensation (no reserve). The latter is typically heralded by hypotension with bradycardia.

BRIEF SUMMARY

A set of embodiments provides tools and techniques for estimating a probability that a patient is bleeding or has experienced intravascular volume loss (e.g., due to hemodialysis, or dehydration) and/or to estimate a patient's current hemodynamic reserve, track the patient's hemodynamic reserve over time, and/or predict a patient's hemodynamic reserve in the future. Some such tools can also control the operation of therapeutic machines, such as hemodialysis machines, intravenous fluid pumps, medication delivery systems, and/or ventilators, based on the predicted hemodynamic reserve. Some embodiments can also estimate and/or predict a patient's state of dehydration.

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).

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.

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.

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 infrared spectrometer, a ventilator, an accelerometer, an electrooculogram, a transcutaneous glucometer, an electrolyte sensor, and/or an electronic stethoscope.

BRIEF DESCRIPTION OF THE DRAWINGS

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.

FIG. **1** is a schematic diagram illustrating a system for estimating hemodynamic reserve, in accordance with various embodiments.

FIG. **2** is a process flow diagram illustrating a method estimating a patient's hemodynamic reserve and/or dehydration state, in accordance with various embodiments.

FIG. **3** illustrates a technique for estimating and/or predicting a patient's hemodynamic reserve index, in accordance with various embodiments.

FIGS. **4-10** are exemplary screen captures illustrating display features of a hemodynamic reserve monitor, in accordance with various techniques.

FIG. **11** is a process flow diagram illustrating a method of generating a model of a physiological state, in accordance with various embodiments.

FIG. **12** is a generalized schematic diagram illustrating a computer system, in accordance with various embodiments.

FIG. **13** illustrates measured CRI values for a dengue fever patient in a clinical setting.

FIG. **14** illustrates measured HDRI values for a test subject undergoing dehydration and rehydration.

DETAILED DESCRIPTION OF CERTAIN EMBODIMENTS

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.

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.

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.

Overview

A set of embodiments provides tools and techniques for estimating a probability that a patient is bleeding (e.g., internally) and/or to estimate a patient's current hemodynamic reserve, track the patient's hemodynamic reserve over time, and/or predict a patient's hemodynamic reserve in the future. Some such tools can also control the operation of therapeutic machines, such as intravenous fluid pumps, medication delivery systems, hemodialysis machines, and ventilators, based on the predicted hemodynamic reserve.

Some embodiments can also estimate and/or predict a patient's state of dehydration.

A hemodynamic reserve monitor in accordance with some embodiments, (described herein as a device and/or a system), along with the methods such a monitor can perform, and the software can employ, constitutes a technology that is able to estimate the hemodynamic 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 hemodynamic reserve by tracking a hemodynamic reserve index (also referred to herein and in the Related Applications as "HDRI," and, equivalently, as a cardiovascular reserve index or "CRI"), to appropriately and effectively guide fluid resuscitation and ongoing patient care.

The Hemodynamic Reserve Index (HDRI) is a hemodynamic parameter that is indicative of the individual-specific proportion of intravascular fluid reserve remaining before the onset of hemodynamic decompensation. HDRI 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.

The mathematical formula of HDRI, at some time "t" is given by the following equation:

$$HDRI(t) = 1 - \frac{BLV(t)}{BLV_{HDD}} \quad \text{(Eq. 1)}$$

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 λ with intravascular volume loss:

$$BLV = \lambda \cdot LBNP \quad \text{(Eq. 2)}$$

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

$$HDRI = 1 - \frac{BLV(t)}{BLV_{HDD}} \approx 1 - \frac{\lambda \cdot LBNP(t)}{\lambda \cdot LBNP_{HDD}} = 1 - \frac{LBNP(t)}{LBNP_{HDD}} \quad \text{(Eq. 3)}$$

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.

A measure of HDRI is 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 HDRI can also herald other conditions, including without limitation general fatigue, overheating and certain types of illnesses. Accordingly, the tools and techniques for estimating and/or predicting HDRI can have a variety of applications in a clinical setting, including without limitation diagnosing such conditions.

In various embodiments, a hemodynamic reserve monitor can include, but is not limited to, some or all of the following functionality, as described in further detail herein:

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

B. Estimating, predicting and/or displaying a patient's hemodynamic 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 hemodynamic reserve as an index with a normative value at euvolemia (for example, HDRI=1), representing a state in which the patient is normovolemic; a minimum value (for example, HDRI=0) which implies no circulatory reserve and that the patient is experiencing CV collapse; and/or an excess value (for example, HDRI>1) representing a state in which the patient is hypervolemic; the patient's normalized hemodynamic 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.

In various embodiments, HDRI 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 may use all sensor information gathered during that time to refine and improve HDRI estimates); (iii) based on either establishing a baseline estimate of HDRI when the patient is normovolemic (no volume loss has occurred); and/or (iv) based on NO baselines estimates when patient is normovolemic.

Certain embodiments can also recommend treatment options, based on the analysis of the patient's condition (including the probability of bleeding, state of dehydration, and/or the patient's estimated and/or predicted HDRI). Treatment options can include, without limitation, such things as optimizing hemodynamics, ventilator adjustments, IV fluid adjustments, transfusion of blood or blood products, infusion of volume expanders, medication changes, changes in patient position and surgical therapy.

As a specific 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 HDRI. 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.

As 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 HDRI (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.

Exemplary Systems and Methods

FIG. **1** 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.

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.

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 HDRI 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), a heating/cooling blanket, and/or the like.

FIGS. **2**, **3** and **11** illustrate methods and screen displays in accordance with various embodiments. While the methods of FIGS. **2**, **3** and **11** 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. **2**, **3** and **11** 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. **2**, **3** and **11** can be implemented by (and, in some cases, are described below with respect to) the computer system **100** of FIG. **1** (or components thereof), these methods may also be implemented using any suitable hardware implementation. Similarly, while the computer system **100** of FIG. **1** (and/or components thereof) can operate according to the methods illustrated by FIGS. **2**, **3** and **11** (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 predict and/or estimate a patient's hemodynamic reserve (in real-time, after every heartbeat, or as the information is needed) and/or dehydration state. 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**). Such a model can be generated using a number of different techniques.

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; 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. The one or more physiological states can include, without limitation, a state of hypervolemia, a state of euvolemia, and/or a state of cardiovascular collapse (or near-cardiovascular collapse). In fact, there are a variety of techniques for generating a model in accordance with different embodiments. One exemplary technique for generating a model of a generic physiological state is described below with respect to FIG. **11**, below. Any suitable technique or model may be employed in accordance with various embodiments, however.

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, 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 HDRI. Hence, LBNP studies form a framework (methodology) for the development of the hemodynamic parameter referred to herein as HDRI 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 an HDRI model in different embodiments.

Another example of a model that can be generated by various embodiments is a probability of bleeding model. In such a case, data can be collected from a number of test subjects before, during, and after bleeding (which can be measured directly in the test procedure). This data can then be used (e.g., using the techniques described below with respect to FIG. **11**) to derive a model that can be used to assess the probability that a patient is bleeding.

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. For example, if cardiovascular collapse is a concern, the patient's blood pressure and/or other parameters might be monitored. 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, blood pressure waveform data, plethysmograph waveform data, photoplethysmograph ("PPG") waveform data (such as that generated by a pulse oximeter), and/or the like

The method **200** might further comprise analyzing, with a computer system, the physiological data (block **215**). In some cases, the physiological data is analyzed against a pre-existing model (which, in turn, can be updated based on the analysis, as described in further detail below and in the Related Applications). Based on this analysis, the method **200**, in an exemplary embodiment, includes estimating, with the computer system, a hemodynamic reserve of the patient, based on analysis of the physiological data (block **220**). In some cases, the method might further comprise predicting, with the computer system, the hemodynamic reserve of the patient at one or more time points in the future, based on analysis of the physiological data (block **225**). 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 hemodynamic reserve of the patient can be based on several factors. Merely by way of example, in some cases, the estimated/predicted hemodynamic 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 hemodynamic reserve can be based on a baseline estimate of the patient's hemodynamic reserve established when the patient is euvolemic. In still other cases, the estimate and/or prediction might not be based on a baseline estimate of the patient's hemodynamic reserve established when the patient is euvolemic.

Merely by way of example, FIG. **3** illustrates one technique **300** for deriving an estimate of HDRI in accordance with some embodiments. 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 noninvasive blood pressure waveforms) for a specified period, such as 32 heartbeats (block **305**). That sample is compared with a plurality of waveforms of reference data corresponding to different HDRI values (block **310**). (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 an HDRI of 1 (block **310***a*), an HDRI of 0.5 (block **310***b*), and an HDRI of 0 (block **310***c*), 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 **315**). These similarity coefficients can be normalized (if appropriate) (block **320**), and the normalized coefficients can be summed (block **325**) to produce an estimated value of the patient's HDRI.

Returning to FIG. **2**, the method **200** can comprise estimating and/or predicting a patient's dehydration state (block **230**). 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 hemodynamic reserve and level of dehydration can be modeled. Accordingly, in some embodiments, estimating a dehydration state of the patient might comprise estimating the hemodynamic reserve (e.g., HDRI) of the patient, and then, based on that estimate and the known relationship, estimating the dehydration state. Similarly, a predicted value of hemodynamic 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 HDRI to model dehydration state.

The method **200** might further comprise normalizing the results of the analysis (block **235**), such as the hemodynamic reserve, dehydration state, and/or probability of bleeding, to name a few examples. Merely by way of example, the estimated/predicted hemodynamic reserve of the patient can be normalized relative to a normative normal blood volume value corresponding to euvolemia, 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 HDRI and other estimated parameters.

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 hemodynamic reserve of the patient, that estimate might be normalized relative to a normative normal blood volume value corresponding to euvolemia 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 euvolemia and cardiovascular collapse. Similar normalizing procedures can be implemented for other estimated data (such as probability of bleeding, dehydration, and/or the like).

The method **200** might further comprise displaying data with a display device (block **240**). Such data might include an estimate and/or prediction of the hemodynamic 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 hemodynamic reserve of the patient might comprise displaying the normalized estimate of the hemodynamic reserve of the patient. Alternatively and/or additionally, displaying the normalized estimate of the hemodynamic 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 hemodynamic reserve (e.g., relative to the normalized excess blood volume value, the normalized normal blood volume value, the normalized minimum blood volume value).

To illustrate, FIGS. **4-10** illustrate exemplary screen captures from a display device of a hemodynamic reserve monitor, showing various features that can be provided by one or more embodiments.

FIG. **4** illustrates a display **400** from a prototype device that is designed to give medical personnel the ability to quickly assess how much blood a patient has lost (solid lines **405**, which might correspond to red lines on a color display). More importantly, the monitor provides real-time information on the rate of bleeding and the patient's predicted level for CV collapse (dashed lines **410**, which might correspond to blue lines on a color display). If the red **405** and blue **410** waveforms continue to converge, bleeding is ongoing. If the red waveform **405** flattens, IV fluid therapy is keeping up with blood loss. If the red **405** and blue **410** waveforms are diverging, then the provider knows, in real-time, that IV fluid resuscitation efforts are effective. Hemodynamic reserve is here measured as the distance between the red **405** and blue line **410**, with CV collapse occurring when the two lines meet.

FIG. **5** shows an implementation of an "Absolute Hemodynamic Reserve Index (HDRI)" monitor screen display **500** and results on data gathered from a subject at the USAISR in the LBNP studies described herein (and in further detail in the Related Applications). The solid line **505** (which might be light green in a color display) shows the estimated Absolute HDRI and the dashed line **510** (which might be red in a color display) the actual, measured HDRI. The Y-axis is an absolute measure of HDRI, with each patient starting with a different amount of fluid reserve.

In contrast, FIG. **6** shows an implementation of a "Proportional Hemodynamic reserve Index (HDRI)" monitor and results on the data gathered from the same subject. The solid line **605** (which might be light green in a color display) shows the estimated Normalized HDRI and the dashed line **610** (which might be red in a color display) the actual, measured HDRI. The Y-axis is a proportional measure of HDRI, with a value of 1 indicating that the patient has full volume of fluid and is not bleeding, and 0 indicating that the patient is in CV collapse. HDRI values in between 0 and 1 show a continuum of fluid reserve as the patient loses fluid volume.

It should be noted that the "actual" HDRI values illustrated on FIGS. **5** and **6**, as well as the "actual" probability of bleeding on FIG. **10**, correspond to LBNP levels applied to the text subject during the trials described above and in the Related Applications. This actual HDRI can be calculated after an LBNP experiment is completed using Eq. 2, above. Moreover, in a typical clinical setting, the screen displays of FIGS. **5**, **6**, and **10** typically would not include a tracing for an "actual" value, since the actual value is unknown—as noted above, it may not be feasible to measure these parameters directly, so many embodiments would only include the tracings of the estimated values. The tracings of actual values are included herein to illustrate the degree of correspondence between the estimates provided by various embodiments and the actual values of the estimated parameters.

FIG. **7** illustrates an exemplary display **700** of a HDRI monitor implementation where a normalized HDRI of "1" implies circulatory volume is normal, and "0" implies no circulatory reserve and the patient is experiencing CV collapse. Values in between "0" and "1" imply a continuum of reserve.

FIG. **8**A illustrates four screen captures **800** of a display of a HDRI monitor implementation that displays HDRI as a "fuel gauge" type bar graph for a person undergoing central volume blood loss during an LBNP study. While FIG. **7** illustrates a trace of HDRI over time, the bar graphs of FIG. **7** provide snapshots of HDRI at the time of each screen capture. (In the illustrated implementation, the bar graphs are continuously and/or periodically updates, such that each bar graph could correspond to a particular position on the X-axis of FIG. **7**.)

A variety of additional features are possible. Merely by way of example FIG. **8**B illustrates similar "fuel gauge" type displays, but the displays **805** of FIG. **8**B 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 HDRI, along with arrows **910** indicating trending in the HDRI values (e.g., rising, declining, or remaining stable).

In some embodiments, such a "fuel gauge" display (or other indicator of HDRI and/or different physiological parameters) can be incorporated in a more comprehensive user interface. Merely by way of example, FIG. **9** illustrates an exemplary display **900** of a monitoring system. The display **900** includes a graphical, color-coded "fuel gauge" type display **905** of the current estimated HDRI (similar to the displays illustrated by FIG. **8**B), along with a historical display **910** of recent HDRI estimates; in this example, each bar on the historical display **910** 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 **900** also includes numerical display **915** of the current HDRI as well as a trend indicator **920** (similar to that indicated above). In particular embodiments, the display **900** 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 **900** includes an indicator **925** of the patient's current heart rate and an indicator **930** of the patient's blood oxygen saturation level (SpO2). Other monitored parameters might be displayed as well, such as an ECG tracing, probability of bleeding estimates, and/or the like.

Returning to FIG. **2**, in some cases, the method **200** might comprise repeating the operations of monitoring physiological data of the patient, analyzing the physiological data, and estimating (and/or predicting) the hemodynamic reserve of the patient, to produce a new estimated (and/or predicted) hemodynamic reserve of the patient. Thus, displaying the estimate (and/or prediction) of the hemodynamic reserve of the patient might comprises updating a display of the estimate of the hemodynamic reserve to show the new estimate (and/or prediction) of the hemodynamic reserve, in order to display a plot of the estimated hemodynamic reserve over time. Hence, the patient's hemodynamic reserve can be repeatedly estimated and/or predicted on any desired interval (e.g., after every heartbeat), on demand, etc.

In further embodiments, the method **200** 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 **245**). 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., 500 cc) 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).

FIG. **10**, for instance, depicts an exemplary screen display **1000** of an HDRI monitor displaying an estimate, over time, of the probability that a patient is bleeding. A probability close to "1" indicates that bleeding is or has occurred, while a probability near "0" indicates that bleeding is unlikely. In this example, the dashed line shows the estimated probability that the patient is bleeding, while the solid line shows an actual probability (which may be omitted in a clinical setting, since the actual probability (which is binary) may be difficult to ascertain clinically.

In some cases, the probability that the patient is bleeding can be used to adjust the patient's estimated HDRI. Specifically, give a probability of bleeding expressed as Pr_Bleed at a time t, the adjusted value of HDRI can be expressed as:

$$\mathrm{HDRI}_{Adjusted}(t)=1-((1-\mathrm{HDRI}(t))\times Pr\_\mathrm{Bleed}(t)) \qquad \text{(Eq. 4)}$$

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

The method **200** 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 **255**). 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.

In a specific example, the method might comprise controlling operation of hemodialysis equipment (block **260**), based at least in part on the estimate of the patient's hemodynamic 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 HDRI 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.

In some embodiments, the method **200** might include assessing the tolerance of an individual to blood loss, general volume loss, and/or dehydration (block **265**). For example, such embodiments might include estimating a patient's HDRI 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 HDRI 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 an HDRI 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.

FIG. **11** illustrates a method of employing such a self-learning predictive model (or machine learning) method **1100**, according to some embodiments. In particular, the method **1100** 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 **1100** can be used to generate a model for predicting and/or estimating various physiological parameters, such as HDRI, the probability that a patient is bleeding, a patient's dehydration state, and/or the like.

The method **1100** begins at block **1105** by collecting raw data measurements that may be used to derive a set of D data signals $s_1, \ldots, S_D$ as indicated at block **1110** (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 **1105** 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 blood pressure waveform data).

A set of K current or future outcomes $\vec{o}=(o_1, \ldots, o_K)$ is hypothesized at block **1115** (the outcomes o being, in this case, past and/or future physiological states, such as HDRI, dehydration state, probability of bleeding, etc.). The method autonomously generates a predictive model M that relates the derived data signals $\vec{s}$ with the outcomes $\vec{o}$. As used herein, "autonomous," means "without human intervention."

As indicated at block **1120**, 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 $s_1, \ldots, s_D$ for each outcome o_k, where $k \in \{1, \ldots, K\}$. A probabilistic predictive model $\hat{o}_k=M_k(S_k)$ is learned at block **1125**, where $\hat{o}_k$ 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 $k \in \{1, \ldots, K\}$. The method **1100** can learn the predictive models $\hat{o}_k=M_k(S_k)$ incrementally (block **1130**) from data that contains example values of signals $s_1, \ldots, s_D$, and the corresponding outcomes $o_1, \ldots, o_K$. As the data become available, the method **1100** loops so that the data are added incrementally to the model for the same or different sets of signals S_k, for all $k \in \{1, \ldots, K\}$.

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 $\{(\vec{s}_1, \vec{o}_1), (\vec{s}_2, \vec{o}_2), \ldots\}$, a linear model may be constructed that has the form, for all $k \in \{1, \ldots, K\}$,

$$\hat{o}_k=f_k(a_0+\sum_{i=1}^{d} a_i s_i) \quad \text{(Eq. 5)}$$

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, $\{(\vec{s}_1, \vec{o}_1), (\vec{s}_2, \vec{o}_2), \ldots\}$. 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.

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, as described herein. These functions include, but are not limited to monitoring, estimating and/or predicting a subject's (including without limitation, a patient's) hemodynamic 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.

Hence, FIG. **12** provides a schematic illustration of one embodiment of a computer system **1200** that can perform the methods provided by various other embodiments, as described herein, and/or can function as an HDRI monitor, etc. It should be noted that FIG. **12** 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. **12**, therefore, broadly illustrates how individual system elements may be implemented in a relatively separated or relatively more integrated manner.

The computer system **1200** is shown comprising hardware elements that can be electrically coupled via a bus **1205** (or may otherwise be in communication, as appropriate). The hardware elements may include one or more processors **1210**, 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 **1215**, which can include without limitation a mouse, a keyboard and/or the like; and one or more output devices **1220**, which can include without limitation a display device, a printer and/or the like.

The computer system **1200** may further include (and/or be in communication with) one or more storage devices **1225**, 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.

The computer system **1200** might also include a communications subsystem **1230**, 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 **1230** 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 **1200** will further comprise a working memory **1235**, which can include a RAM or ROM device, as described above.

The computer system **1200** also may comprise software elements, shown as being currently located within the working memory **1235**, including an operating system **1240**, device drivers, executable libraries, and/or other code, such as one or more application programs **1245**, 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.

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) **1225** described above. In some cases, the storage medium might be incorporated within a computer system, such as the system **1200**. 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 **1200** and/or might take the form of source and/or installable code, which, upon compilation and/or installation on the computer system **1200** (e.g., using any of a variety of generally available compilers, installation programs, compression/decompression utilities, etc.) then takes the form of executable code.

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.

As mentioned above, in one aspect, some embodiments may employ a computer system (such as the computer system **1200**) 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 **1200** in response to processor **1210** executing one or more sequences of one or more instructions (which might be incorporated into the operating system **1240** and/or other code, such as an application program **1245**) contained in the working memory **1235**. Such instructions may be read into the working memory **1235** from another computer readable medium, such as one or more of the storage device(s) **1225**. Merely by way of example, execution of the sequences of instructions contained in the working memory **1235** might cause the processor(s) **1210** 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 **1200**, various computer readable media might be involved in providing instructions/code to processor(s) **1210** 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) **1225**. Volatile media includes, without limitation, dynamic memory, such as the working memory **1235**. Transmission media includes, without limitation, coaxial cables, copper wire and fiber optics, including the wires that comprise the bus **1205**, as well as the various components of the communication subsystem **1230** (and/or the media by which the communications subsystem **1230** 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, punch cards, paper tape, any other physical medium with patterns of holes, a RAM, 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) **1210** 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 **1200**. 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.

The communications subsystem **1230** (and/or components thereof) generally will receive the signals, and the bus **1205** then might carry the signals (and/or the data, instructions, etc. carried by the signals) to the working memory **1235**, from which the processor(s) **1205** retrieves and executes the instructions. The instructions received by the working memory **1235** may optionally be stored on a storage device **1225** either before or after execution by the processor(s) **1210**.

Clinical Examples

In one study, data was collected in Thailand on children that have dengue hemorrhagic fever. The patients were periodically monitored with a NEXFIN continuous non-invasive blood pressure monitor for 10 to 15 min periods each day. Using the NEXFIN signals, the HDRI value was calculated during these monitoring periods. FIG. **13** shows a plot **1300** of HDRI data from one subject. The horizontal axis shows the day and vertical axis shows the estimated HDRI value. The HDRI can clearly be seen tracking resuscitation over a period of 6 days, starting when the patient is the sickest (27Jul. 2011) and treatment begins, and ending on 1 Aug. 2011 when the patient has shown significant recovery. This patient received a blood transfusion on 29 Jul. 2011.

In another study, a subject was monitored by a HDRI monitor (including a NONIN OEM III pulse ox sensor) during a dehydration study with the following protocol. The subjected started well hydrated, jogged for 44 minutes, at an ambient temperature of 30 C, and then rehydrated over a 1 hour period. The HDRI profiles for this are shown in FIG. **14**. The subject's weight was recorded before exercise, immediately after exercise and after rehydration. The subject lost 0.7 Kg while exercising and increased 0.9 Kg by consuming 1 of fluids. We assume this 700 g loss represents a 700 ml loss of fluids.

The loss of 700 ml of fluids due to dehydration is clearly observable using HDRI. From the pre-exercise plot **1400** and post-exercise plot **1405**, one can see that the subject's HDRI is reduced from about 0.95 to as low as 0.5 after exercise. Note also that the HDRI levels are stable in the pre-exercise plot **1400** and post-exercise plot **1405**. We can also see the oral rehydration taking effect in the rehydration plot **1400**. After about 35 minute the subject appears fully rehydrated, with an HDRI of about 0.95, similar to the subject's pre-exercise HDRI.

Conclusion

This document discloses novel tools and techniques for estimating hemodynamic 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 system, 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, wherein the physiological data comprises waveform data;

instructions for analyzing the physiological data;

instructions for estimating a hemodynamic reserve index of the patient, based on analysis of the physiological data, by comparing the physiological data to a model constructed using the following formula:

$$HDRI(t) = 1 - \frac{BLV(t)}{BLV_{HDD}}$$

where HDRI(t) is the hemodynamic 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, and wherein the instructions for estimating the hemodynamic reserve index comprise:

instructions for comparing the waveform data with a plurality of sample waveforms, each of the sample waveforms corresponding to a different value of the hemodynamic reserve index, to produce a similarity coefficient expressing a similarity between the waveform data and each of the sample waveforms;

instructions for normalizing the similarity coefficients for each of the sample waveforms; and

instructions for summing the normalized similarity coefficients to produce an estimated hemodynamic reserve index value for the patient; and

instructions for displaying, on a display device, an estimate of the hemodynamic reserve index of the patient.

2. A method, comprising:

monitoring, with one or more sensors, physiological data of a patient, wherein the physiological data comprises waveform data;

analyzing, with a computer system, the physiological data;

estimating, with the computer system, a hemodynamic reserve index of the patient, based on analysis of the physiological data, by comparing the physiological data to a model constructed using the following formula:

$$HDRI(t) = 1 - \frac{BLV(t)}{BLV_{HDD}}$$

where HDRI(t) is the hemodynamic 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, and wherein estimating the hemodynamic reserve index comprises:

comparing the waveform data with a plurality of sample waveforms, each of the sample waveforms corresponding to a different value of the hemodynamic 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 hemodynamic reserve index value for the patient; and

displaying, with a display device, an estimate of the hemodynamic reserve index of the patient.

3. The method of claim **2**, further comprising:

estimating a dehydration state of the patient.

4. The method of claim **2**, further comprising:

predicting, with the computer system, the hemodynamic reserve index of the patient at one or more time points in the future, based on analysis of the physiological data; and

displaying, with the display device, a predicted hemodynamic reserve index of the patient at one or more points in the future.

5. The method of claim **2**, wherein the estimate of the hemodynamic reserve index of the patient is based on a fixed time history of monitoring the physiological data of the patient.

6. The method of claim **2**, wherein the estimate of the hemodynamic reserve index of the patient is based on a dynamic time history of monitoring the physiological data of the patient.

7. The method of claim **2**, wherein the estimate of the hemodynamic reserve index of the patient is based on a baseline estimate of the patient's hemodynamic reserve index established when the patient is euvolemic.

8. The method of claim **2**, wherein the estimate of the hemodynamic reserve index of the patient is not based on a baseline estimate of the patient's hemodynamic reserve index established when the patient is euvolemic.

9. The method of claim **2**, further comprising:

normalizing the estimate of the hemodynamic reserve index of the patient relative to a normative normal blood volume value corresponding to euvolemia and a normative minimum blood volume value corresponding to cardiovascular collapse;

wherein displaying the estimate of the hemodynamic reserve index of the patient comprises displaying the normalized estimate of the hemodynamic reserve index of the patient.

10. The method of claim **9**, wherein the normative normal blood volume value corresponding to euvolemia is 1 and the normative minimum blood volume value corresponding to cardiovascular collapse is 0.

11. The method of claim **9**, wherein displaying the normalized estimate of the hemodynamic reserve index of the patient comprises displaying a graphical plot showing the normalized normal blood volume value, the normalized minimum blood volume value, and the normalized estimate of the hemodynamic reserve index relative to the normalized normal blood volume value, the normalized minimum blood volume value.

12. The method of claim **2**, further comprising:

normalizing the estimate of the hemodynamic reserve index of the patient relative to a normative normal blood volume value corresponding to euvolemia, a normative excess blood volume value corresponding to circulatory overload, and a normative minimum blood volume value corresponding to cardiovascular collapse;

wherein displaying the estimate of the hemodynamic reserve index of the patient comprises displaying the normalized estimate of the hemodynamic reserve index of the patient.

13. The method of claim **12**, wherein the normative excess blood volume value corresponding to circulatory overload is 1, the normative normal blood volume value corresponding to euvolemia is 0, and the normative minimum blood volume value corresponding to cardiovascular collapse is −1.

14. The method of claim **12**, wherein the normative excess blood volume value corresponding to circulatory overload is >1, the normative normal blood volume value corresponding to euvolemia is 1, and the normative minimum blood volume value corresponding to cardiovascular collapse is 0.

15. The method of claim **12**, wherein displaying the normalized estimate of the hemodynamic reserve index of the patient comprises 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 hemodynamic reserve index relative to the normalized excess blood volume value, the normalized normal blood volume value, the normalized minimum blood volume value.

16. The method of claim **2**, further comprising:

determining a probability that the patient is bleeding; and

displaying, with the display device, an indication of the probability that the patient is bleeding.

17. The method of claim **2**, further comprising:

determining a probability that the patient is bleeding; and

adjusting the estimate of the hemodynamic reserve index of the patient, based on the probability that the patient is bleeding.

18. The method of claim **2**, further comprising:

selecting, with the computer system, a recommended treatment option for the patient; and

displaying, with the display device, the recommended treatment option.

19. The method of claim **18**, wherein the recommended treatment option is selected from the group consisting of: 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.

20. The method of claim **2**, further comprising:

repeating the operations of monitoring physiological data of the patient, analyzing the physiological data, and estimating the hemodynamic reserve index of the patient, to produce a new estimated hemodynamic reserve index of the patient;

wherein displaying the estimate of the hemodynamic reserve index of the patient comprises updating a display of the estimate of the hemodynamic reserve index to show the new estimate of the hemodynamic reserve index, in order to display a plot of the estimated hemodynamic reserve index over time.

21. The method of claim **2**, 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.

22. The method of claim **2**, wherein the physiological data comprises blood pressure waveform data.

23. The method of claim **2**, wherein the physiological data comprises plethysmograph waveform data.

24. The method of claim **2**, wherein the physiological data comprises photoplethysmograph (PPG) waveform data.

25. The method of claim **2**, further comprising:

estimating a first value of the hemodynamic reserve index when the patient is in a first position;

estimating a second value of the hemodynamic reserve index when the patient is in a second position; and

estimating a sensitivity of the patient to volume loss based on a difference between the first value and the second value.

26. The method of claim **24**, wherein the first position is selected from the group consisting of lying prone and sitting, and wherein the second position is selected from the group consisting of sitting and standing.

27. The method of claim **2**, wherein analyzing the physiological data comprises: analyzing the physiological data against a pre-existing model.

28. The method of claim **27**, further comprising:

generating the pre-existing model.

29. The method of claim **28**, 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 plurality of physiological data sets with the plurality of physiological state measurements of the test subject.

30. The method of claim **29**, wherein the one or more physiological states comprise reduced circulatory system volume.

31. The method of claim **30**, further comprising:

inducing the physiological state of reduced circulatory system volume in the test subject.

32. The method of claim **31**, wherein inducing the physiological state comprises subjecting the test subject to lower body negative pressure ("LBNP").

33. The method of claim **31**, wherein inducing the physiological state comprises subjecting the test subject to dehydration.

34. The method of claim **29**, wherein the one or more physiological states comprise a state of cardiovascular collapse or near-cardiovascular collapse.

35. The method of claim **29**, wherein the one or more physiological states comprise a state of euvolemia.

36. The method of claim **29**, wherein the one or more physiological states comprise a state of hypervolemia.

37. The method of claim **29**, wherein the one or more physiological states comprise a state of dehydration.

38. The method of claim **2**, further comprising:

controlling operation of hemodialysis equipment, based at least in part on the estimate of the hemodynamic reserve index of the patient.

39. The method of claim **38**, wherein controlling operation of the hemodialysis equipment comprises adjusting an ultra-filtration rate of the hemodialysis equipment.

40. The method of claim **29**, 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 $s_1, s_2, \ldots, S_D$ 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 $\hat{o}_k = M_k(S_k)$, where $\hat{o}_k$ 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_k; and

repeating the operation of autonomously learning incrementally from data that contains examples of values of signals $s_1, s_2, \ldots, S_D$ and corresponding outcomes $o_1, o_2, \ldots, o_K$.

41. 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 physiological data from one or more sensors, wherein the physiological data comprises waveform data;

instructions for analyzing the physiological data;

instructions for estimating a hemodynamic reserve index of the patient, based on analysis of the physiological data, by comparing the physiological data to a model constructed using the following formula:

$$HDRI(t) = 1 - \frac{BLV(t)}{BLV_{HDD}}$$

where HDRI(t) is the hemodynamic 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, and wherein the instructions for estimating the hemodynamic reserve index comprise:

instructions for comparing the waveform data with a plurality of sample waveforms, each of the sample waveforms corresponding to a different value of the hemodynamic reserve index, to produce a similarity coefficient expressing a similarity between the waveform data and each of the sample waveforms;

instructions for normalizing the similarity coefficients for each of the sample waveforms; and

instructions for summing the normalized similarity coefficients to produce an estimated hemodynamic reserve index value for the patient; and instructions for displaying, on a display device, an estimate of the hemodynamic reserve index of the patient.

42. A method, comprising:

monitoring, with one or more sensors, physiological data of a patient, wherein the physiological data comprises waveform data;

analyzing, with a computer system, the physiological data;

estimating, with the computer system, a dehydration state of the patient from a hemodynamic reserve index of the patient, based on analysis of the physiological data, by comparing the physiological data to a model constructed using the following formula:

$$HDRI(t) = 1 - \frac{BLV(t)}{BLV_{HDD}}$$

where HDRI(t) is the hemodynamic 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, and wherein estimating the dehydration state comprises:

comparing the waveform data with a plurality of sample waveforms, each of the sample waveforms corresponding to a different value of the hemodynamic 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 hemodynamic reserve index value for the patient; and

displaying, on a display device, an estimate of the dehydration state of the patient.

43. The method of claim **42**, further comprising:

predicting the dehydration state of the patient at one or more future points in time.

44. The method of claim **42**, wherein estimating a dehydration state of the patient comprises:

estimating a hemodynamic reserve index of the patient, based on analysis of the physiological data; and

estimating the dehydration state based on the estimated hemodynamic reserve index of the patient.

45. A method, comprising:

monitoring, with one or more sensors, physiological data of a patient, wherein the physiological data comprises waveform data;

analyzing, with a computer system, the physiological data;

estimating, with the computer system, a hemodynamic reserve index of the patient, based on analysis of the physiological data, by comparing the physiological data to a model constructed using the following formula:

$$HDRI(t) = 1 - \frac{BLV(t)}{BLV_{HDD}}$$

where HDRI(t) is the hemodynamic 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, and wherein estimating the hemodynamic reserve index comprises:

comparing the waveform data with a plurality of sample waveforms, each of the sample waveforms corresponding to a different value of the hemodynamic 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 hemodynamic reserve index value for the patient;

displaying, with a display device, an estimate of the hemodynamic reserve index of the patient; and

controlling operation of hemodialysis equipment based on the estimated hemodynamic reserve index.

46. The method of claim **45**, further comprising:

predicting the hemodynamic reserve index of the patient at one or more future points in time.

47. The method of claim **46**, wherein controlling operation of the hemodialysis equipment further comprises controlling operation of the hemodialysis equipment based on the predicted hemodynamic reserve index of the patient at one or more future points in time.

48. The method of claim **45**, wherein controlling operation of hemodialysis equipment comprises providing, with the computer system, instructions to a human operator of the hemodialysis equipment.

49. A system, comprising:

a hemodialysis machine;

one or more sensors to obtain physiological data from a patient; and

a computer system in communication with the one or more sensors and the hemodialysis machine, 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, wherein the physiological data comprises waveform data;

instructions for analyzing the physiological data;

instructions for estimating a hemodynamic reserve index of the patient, based on analysis of the physiological data, by comparing the physiological data to a model constructed using the following formula:

$$HDRI(t) = 1 - \frac{BLV(t)}{BLV_{HDD}}$$

where HDRI(t) is the hemodynamic 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, and wherein the instructions for estimating the hemodynamic reserve index comprise:

instructions for comparing the waveform data with a plurality of sample waveforms, each of the sample waveforms corresponding to a different value of the hemodynamic reserve index to produce a similarity coefficient expressing a similarity between the waveform data and each of the sample waveforms;

instructions for normalizing the similarity coefficients for each of the sample waveforms; and

instructions for summing the normalized similarity coefficients to produce an estimated hemodynamic reserve index value for the patient; and

instructions for controlling operation of hemodialysis machine based on the estimated hemodynamic reserve index.

50. The system of claim **49**, wherein the computer system is incorporated within the hemodialysis machine.

51. The method of claim **2**, wherein one or more of the sample waveforms are generated by exposing a test subject to a state of hemodynamic decompensation, near hemodynamic decompensation, or a series of states progressing towards hemodynamic decompensation and monitoring physiological data of the test subject.

52. The system of claim **1**, wherein the physiological data comprises waveform data and wherein estimating a hemodynamic reserve index of the patient comprises comparing the waveform data with one or more sample waveforms generated by exposing one or more test subjects to a 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.

53. The method of claim **2**, wherein the physiological data comprises waveform data and wherein estimating a hemodynamic reserve index 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.

54. The method of claim **44**, wherein the physiological data comprises waveform data and wherein estimating a hemodynamic reserve index of the patient comprises comparing the waveform data with one or more sample waveforms generated by exposing one or more test subjects to a 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.

55. The method of claim **45**, wherein the physiological data comprises waveform data and wherein estimating a hemodynamic reserve index of the patient comprises comparing the waveform data with one or more sample waveforms generated by exposing one or more test subjects to a 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.

56. The system of claim **49**, wherein the physiological data comprises waveform data and wherein estimating a hemodynamic reserve index of the patient comprises comparing the waveform data with one or more sample waveforms generated by exposing one or more test subjects to a 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.

57. The method of claim **29**, wherein the one or more physiological states is a plurality of physiological states, the plurality of physiological states comprising:

a state of cardiovascular collapse or near-cardiovascular collapse;

a state of euvolemia;

a state of hypervolemia; and

a state of dehydration.

* * * * *

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摘要(译)

用于估计患者出血或持续血管内容量减少（例如，由于血液透析或脱水）和/或估计患者当前血液动力学储备指数的概率的工具和技术，跟踪患者的血液动力学储备指数随时间的变化，和/或或预测未来患者的血液动力学储备指数。用于估计和/或预测患者脱水状态的工具和技术。用于基于患者的估计和/或预测的血液动力学储备指数来控制血液透析机的工具和技术。