Title: A SYSTEM AND METHOD FOR EXTERNAL CONTINUOUS BLOOD CONTENT MEASUREMENT AND INJECTION OF PHARMACEUTICALS

Abstract: A system for continuous measurement of a blood characteristic comprising an arterial venous shunt, at least a portion of which appears externally to a subject, the arterial venous shunt arranged to carry blood of the subject, at least one of a spectral measurer and a contact measurer operable on the blood within the externally appearing portion, a computing device receiving an output of the at least one of a spectral measurement means and a contact measurement means, and an injection device responsive to an output of the computing device, the injection device being operable to inject a pharmaceutical from a pharmaceutical reservoir, wherein the computing device responsive to the output of the at least one of a spectral measurer and a contact measurer is operable to output a signal to the injection device, the injection device being operable to inject a measured amount of pharmaceutical responsive to the signal.
A SYSTEM AND METHOD FOR EXTERNAL CONTINUOUS BLOOD
CONTENT MEASUREMENT AND INJECTION OF PHARMACEUTICALS

BACKGROUND OF THE INVENTION

[0001] The invention relates generally to the field of medical devices for sensing the level of a constituent in blood, and in particular sensing the level of glucose and providing a mechanism for injecting insulin or other pharmaceutical responsive to the sensed level of glucose.

[0002] The accurate measure and control of glucose is critical to health of individuals. In particular, diabetic patients experiencing other maladies, such as patient in an intensive care unit of a hospital, experience increased morbidity rates of 25 - 30 % in the absence of frequent accurate glucose measurement and immediate glucose balancing.

[0003] In recent years many technological advances in the field of glucose measurement have occurred, some of which have more successful than others. One approach has been to use a light source shined into the skin, with an optical detector arranged to detect the reflection from the skin. A spectrographic analysis of the reflected light is indicative of glucose levels in the body, as well as of other components. Unfortunately, the reflection from such an external fed light source is influenced by many factors other than blood glucose levels, including varying skin properties, albumin, cholesterol, and other blood components which results in inaccurate readings. Depending on the selected wavelengths of the light source, water absorption may also be a factor.

[0004] U.S. Patent S/N 5,995,860 issued to Sun et al, entitled "Implantable Sensor and System for Measurement and Control of Blood Constituent Levels" is addressed to an implantable device for detecting at least one blood constituent in mammalian vascular tissue. The device comprises at least one implantable source of radiation and a plurality of discrete narrow band implantable detectors. Disadvantageously, implanting a device requires a surgical procedure, which may preferably be avoided. Additionally, in the event of any change of status in the target tissue to which the implanted source of radiation and the detectors are directed, an additional surgical procedure may be required. Furthermore, the implantable device
may impact the target tissue, and cause unreliable readings, or a thrombosis which may cause a medical risk to the patient.

[0005] U.S. Patent S/N 6,122,536 issued to Sun et al, entitled "Implantable Sensor and System for Measurement and Control of Blood Constituent Levels" is addressed to an implantable device for detecting at least one blood constituent in mammalian vascular tissue. The device comprises at least one implantable source of radiation emitting radiation in at least two selected frequency bands and at least one implantable detector adapted to be located out of direct contact with the blood of the patient. Disadvantageously, implanting a device requires a surgical procedure, which may preferably be avoided. Additionally, in the event of any change of status in the target tissue to which the implanted source of radiation and the detectors are directed, an additional surgical procedure may be required. Furthermore, the implantable device may impact the target tissue, and cause unreliable readings, or a thrombosis which may cause a medical risk to the patient.

[0006] Additionally, the devices taught in the above patent are restricted to radiation dependent testing. Thus, in the event that additional testing of blood characteristics is required, a further invasive technique is required.

[0007] There is thus a long felt need for an improved system providing continuous measurement of blood constituent levels, and in particular glucose easily adapted for use with a patient without requiring invasive surgery. Preferably the system is integrated with a mechanism for immediate injection of at least one pharmaceutical active to balance blood constituents or composition. Preferably, the improved system provides accessibility for additional testing of blood constituents without requiring an invasive procedure.

SUMMARY OF THE INVENTION

[0008] Accordingly, it is a principal object of the present invention to overcome the disadvantages of prior art constituent blood level monitoring systems. This is provided in the present invention by providing a supra-cutaneously appearing arterial shunt, preferably an arterial venal shunt. In one embodiment the arterial shunt is provided by a sub-cutaneous fistula preferably inserted by micro-surgery, the supra-cutaneously appearing arterial shunt being inserted in parallel to a portion of the sub-
cutaneous fistula via a pair of needles. In another embodiment an external supra-
cutaneous shunt is supplied, the external supra-cutaneous shunt being inserted by
micro-surgery and exhibiting automatic shut off valves to prevent bleeding in the case
of a rupture or other failure of the external supra-cutaneous shunt.

Blood passing through the supra-cutaneously appearing arterial shunt is measured by at least one of a plurality of measurements including spectral measurements and contact measurements. In addition, in one embodiment a valve is supplied attached to the supra-cutaneously appearing arterial shunt, the valve being arranged to allow for withdrawing a sample of the blood flow for additional testing.

Preferably, the sample is tested in combination with an externally supplied reagent.

The invention also provides at least one pharmaceutical reservoir and an injection device. In an exemplary embodiment the reservoir takes the form of a cartridge or cassette. A computing device, responsive to the measurements, calculates an appropriate amount of pharmaceutical and operates the injection device to inject the appropriate amount of pharmaceutical.

The invention provides for an ambulatory version, having reduced functionality, and a hospital based version having additional functionality.

Additional features and advantages of the invention will become apparent from the following drawings and description.

BRIEF DESCRIPTION OF THE DRAWINGS

For a better understanding of the invention and to show how the same may be carried into effect, reference will now be made, purely by way of example, to the accompanying drawings in which like numerals designate corresponding elements or sections throughout.

With specific reference now to the drawings in detail, it is stressed that the particulars shown are by way of example and for purposes of illustrative discussion of the preferred embodiments of the present invention only, and are presented in the cause of providing what is believed to be the most useful and readily understood description of the principles and conceptual aspects of the invention. In this regard, no attempt is made to show structural details of the invention in more detail than is necessary for a fundamental understanding of the invention, the description taken with the drawings making apparent to those skilled in the art how
the several forms of the invention may be embodied in practice. In the accompanying drawings:

[0015] Fig. 1 illustrates a high level block diagram of an embodiment of a blood characteristic measuring and pharmaceutical injection system according to the principle of the invention;

[0016] Fig. 2 illustrates a high level block diagram of a test cell exhibiting both spectral and contact measurement of a blood flow according to the principle of the invention;

[0017] Fig. 3a illustrates a first example of a spectral response curve of a blood sample without added glucose contrasted with the spectral response curve of the blood sample with added glucose;

[0018] Fig. 3b illustrates a second example of a spectral response curve of a blood sample without added glucose contrasted with the spectral response curve of the blood sample with added glucose;

[0019] Fig. 4 illustrates a subject exhibiting an installed fistula to which the apparatus according to the principle of the invention is secured;

[0020] Fig. 5 illustrates a high level block diagram of an embodiment of a blood characteristic measuring and pharmaceutical injection system comprising a peristaltic pump according to the principle of the invention; and

[0021] Fig. 6a illustrates a high level block diagram of an embodiment of a test cell and measurement tube arrangement according to the principle of the invention;

[0022] Fig. 6b illustrates a high level block depiction of a test cell suitable for use with the arrangement of Fig. 6a;

[0023] Fig. 7 illustrates a high level block diagram of an embodiment of a blood characteristic measuring and pharmaceutical injection system having reduced functionality according to the principle of the invention; and

[0024] Fig. 8 illustrates a high level block diagram of an embodiment of the invention suitable for use without a sub-cutaneous fistula.
DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0025] The present embodiments enable a system for measuring at least one blood characteristic and injecting a pharmaceutical responsive to the measuring by providing a supra-cutaneously appearing arterial shunt. In one embodiment the supra-cutaneously appearing arterial shunt is connected by a pair of needles to appear in parallel to a sub-cutaneous arterial venal fistula, also known as an A-V fistula. In another embodiment the supra-cutaneously appearing arterial shunt is attached to the subject via automatic shut off valves to prevent excess bleeding in the case of failure of the supra-cutaneously appearing arterial shunt. Blood passing through the supra-cutaneously appearing arterial shunt is measured by one of a plurality of measurements including spectral measurements and contact measurements. In addition, in one embodiment a valve is supplied attached to the shunt, the valve being arranged to allow for withdrawing a sample of the blood flow for additional testing. Preferably, the sample is tested in combination with an externally supplied reagent.

[0026] The invention also provides at least one pharmaceutical reservoir and an injection device. In an exemplary embodiment the reservoir takes the form of a cartridge or cassette. A computing device, responsive to the measurements, calculates an appropriate amount of pharmaceutical and operates the injection device to inject the appropriate amount of pharmaceutical. Preferably the pharmaceutical is injected into arterial venal shunt.

[0027] The invention provides for an ambulatory version, having reduced functionality, and a hospital based version having additional functionality.

[0028] Before explaining at least one embodiment of the invention in detail, it is to be understood that the invention is not limited in its application to the details of construction and the arrangement of the components set forth in the following description or illustrated in the drawings. The invention is applicable to other embodiments or of being practiced or carried out in various ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

[0029] Fig. 1 illustrates a high level block diagram of an embodiment of a blood characteristic measuring and pharmaceutical injection system according to the principle of the invention. The system of Fig. 1 comprises: a computing device 10; a user input 11; an alarm and alert block 12; a hospital network connection 15; a
connection to other devices 16; a valve 20; a strip test 21; a test cell 30 comprising at
least one illuminator 31, at least one receiver 32 and optionally other measuring
means 33; the artery side 40 of a sub-cutaneous fistula, a needle 45; the venal side 50
of the sub-cutaneous fistula 400; a needle 60; a connector 70; at least one
pharmaceutical reservoir 80; at least one injection device 81; a measurement tube 90;
a connector 91; and a blood pressure transducer 92.

[0030] Needle 45 is inserted to receive a blood flow from the artery side 40 of
a sub-cutaneous fistula of the subject and bring the blood flow externally of the
subject. Connector 91 is connected to needle 45 and is arranged to bring the blood
flow to measurement tube 90 and to blood pressure transducer 92. Measurement tube
90 is arranged to traverse test cell 30. Valve 20 is arranged to controllably withdraw a
blood sample from the blood flow and place the withdrawn sample on test strip 21.
Connector 70 is arranged to return blood withdrawn by needle 45 from artery side 40
to vein side 50 via needle 60. At least one injection device 81 is arranged to inject a
pharmaceutical from a respective pharmaceutical reservoir 80 and inject the
pharmaceutical into vein side 50 of the subject via connector 70. Injection device 81
is connected to be responsive to an output of computing device 10. Pharmaceutical
reservoir 80 may be in the form of a cartridge or cassette.

[0031] Illuminator 31, which comprises at least one illuminating device,
preferably one or more LEDs, and even further preferably one or more LEDs operable
in at least part of the infrared band, is arranged to illuminate blood flow through
measurement tube 90. Receiver 32, which comprises one or more receiving elements
sensitive to at least some of the wavelengths emitted by illuminator 31, is arranged to
receive a reflection of the illumination of illuminator 31. Contact measuring means
33 is arranged to measure an electrical characteristic of the blood flow through
measurement tube 90 by direct contact with the blood flow. Computing device 10 is
arranged to communicate via hospital network connection, control the operation of
test cell 30, receive the output of test cell 30, receive the output of blood pressure
transducer 92, and output a signal to control the operation of injection device 81.
Computing device 10 is further arranged to receive instructions via user input 11 and
to output an alarm via alarm and alert block 12. Optionally, computing device 10 is in
communication with pharmaceutical reservoir 80 to ascertain a fill level, and
optionally to report a low fill level via one of hospital network connection 15 and alarm and alert block 12.

[0032] In operation, blood flows through measurement tube 90, secured within test cell 30. Measurement tube 90 may be any translucent or transparent tube, preferably heparin coated or heparin-bounded to prevent coagulation. In one embodiment, test cell 30 is arranged to surround measurement tube 90, and in another embodiment test cell 30 is arranged with an indentation along one side to receive and secure measurement tube 90. In yet another embodiment test cell 30 comprises a measurement tube 90 having measurement means in a manner that will be explained further hereinto below. Computing device 10, which in an exemplary embodiment comprises a microprocessor, personal computer or workstation, operates test cell 30 to measure at least one blood characteristic. In one embodiment, test cell 30 illuminates blood flowing through measurement tube 90 with an infrared light via the operation of illuminator 31, and receives a reflection of the illumination at receiver 32. Optional other measuring means 33 is operable to optionally measure one of temperature of the blood flow or electrical characteristics of the blood flow. Computing device 10 receives an indication of the output of receiver 31 and optional measuring means 33. Optional measuring means 33 may comprises a temperature measurement sensor and a resistance measurement sensor. Computing device 10 further receives inputs from hospital network connection 15 and from connection to other devices 16. In one embodiment, patient record information is input via hospital network connection 15, and other measuring devices including atmospheric information, or other patient measurement information is input via connection to other devices 16.

[0033] Computing device 10 further receives an output of blood pressure transducer 92, and instructions from user input 11. Computing device 10, responsive to the input received from test cell 30, blood pressure transducer 92 and user input 11, preferably computes an indication of at least one blood characteristic. In the event of the at least one blood characteristic, such as a glucose level, is outside of predetermined parameters, computing device 10 alerts a user via alarm and alert block 12. Computing device 10, further operates injection device 81 to inject at least one pharmaceutical responsive to the computing at least one blood characteristic to control the level of the characteristic within the subject. It is to be understood that computing
device 10 may operate injection device to control the level of the characteristic within
the subject without alerting a user via alarm and alert block 12.

[0034] The apparatus of Fig. 1 has been described as utilizing needle 45 and
needle 60 to connect to a sub-cutaneous fistula, however this is not meant to be
limiting in any way, and may be replaced by a surgically implanted connection to an
artery and a vein, preferably with automatic shut off valves to prevent bleeding in case
of a failure of any of connector 91, measurement tube 90 and connector 70 without
exceeding the scope of the invention. Such an embodiment is further described below
in relation to Fig. 8.

[0035] Fig. 2 illustrates a high level block diagram of a test cell exhibiting
both spectral and contact measurement of a blood flow according to the principle of
the invention comprising an impedance pulse generator 100; an amplifier 101; an
LED current generator 102; an amplifier 103; an LED 112; a first electrode 110; a
second electrode 111; an inlet 120; an outlet 121; a receiver 113; a measurement tube
90; a valve control 130; a valve 131; an inlet for reagents 132; a cleaning valve 140; a
measuring plate 150 comprising a first electrode 141 and a second electrode 141; a
generator 151; and an amplifier 152. LED 112 may comprise one or more LEDs, receiver 113 comprises one or more receivers sensitive to the output of LED 112, and
amplifier 103 may comprise one or more amplifiers.

[0036] Impedance pulse generator 100 is in communication with first
electrode 110, second electrode 111 and amplifier 101. LED current generator 102 is
in communication with LED 112 and receiver 113 is in communication with amplifier
103. Blood flow through measurement tube 90 arrives from inlet 120 and departs via
outlet 121. First electrode 110 and second electrode 111 are in contact with the blood
flow through measurement tube 90, and LED 112 and receiver 113 are arranged to
respectively illuminate the blood flow and receive a reflection of the illumination.
Amplifier 103 is arranged to amplify a signal from receiver 113 and transmit the
amplified signal to computing device 10 of Fig. 1.

[0037] Valve control 130 is arranged to control the operation of valve 131,
and valve 31 is arranged to remove a blood sample from the blood flow of
measurement tube 90. Measuring plate 150 is arranged to receive the blood sample
removed via the operation of valve 31, and valve 132 is arranged to a How for the
addition of at least one reagent to the blood sample received on measuring plate 150.
Electrodes 141 and 142 are arranged to receive an electrical signal from generator 151 and to pass the electrical signal through the blood sample on measuring plate 150. Amplifier 152 is arranged to receive the electrical signal passed via electrodes 141 and 142 through the blood sample on measuring plate 150, and preferably to further receive an electrical signal from generator 151, preferably as a comparison signal. Amplifier 152 is further arranged to amplify a signal responsive to the received electrical signal that has passed through the blood sample, and transmit the amplified signal to computing device 10 of Fig. 1.

[0038] In operation, current generator 102 generates an electrical signal to operate LED 112, which preferably is operable in the infrared band, and receiver 113 is operable to receive a portion of the reflection of the illumination from LED 112 through the blood flow through measurement tube 90. Amplifier 103 is operable to amplify the output of receiver 113 and transmit it to computing device 10. Preferably, generator 102, LED 112, receiver 113, and amplifier 103 cooperate to be operable as a spectrometer, outputting an indication of amplitude for each of a plurality of spectral wavelengths. The combination of current generator 102, LED 112, receiver 113 and amplifier 103 thus outputs a spectral measurement of a characteristic of the blood flow through measurement tube 90.

[0039] Pulse generator 100 is operable to generate an electrical test pulse for connection to electrodes 110 and 111, which function to measure at least one electrical characteristic of the blood flow through measurement tube 90. Amplifier 101 is operable to amplify the measured electrical characteristic, and preferably to compare the measured electrical characteristic with the pulse generated by pulse generator 100. Amplifier 101 is further operable to transmit an output responsive to the measured electrical characteristic to computing device 10 of Fig. 1. Electrodes 110 and 111 are preferably in contact with the blood flow, and thus represent a contact measurement of the blood flow.

[0040] Valve 131 is operable, under control of valve control 130, to allow for the withdrawal of a blood sample from the blood flowing through measurement tube 90, and deposit the withdrawn sample onto measuring plate 150. Valve 132 allows for the addition of at least one reagent to aid in measuring a pre-determined characteristic of the withdrawn sample. Generator 151 is operable to generate an electrical test pulse for connection to electrodes 141 and 142, which function to
measure at least one electrical characteristic of the blood sample deposited on measuring plate 150. Amplifier 152 is operable to amplify the measured electrical characteristic, and preferably to compare the measured electrical characteristic with the electrical output of generator 151. Amplifier 152 is further operable to transmit an output responsive to the measured electrical characteristic of the blood sample after interaction with the reagent to computing device 10 of Fig. 1.

[0041] Fig. 3a illustrates a first example of a spectral response curve of a first blood sample without added glucose contrasted with the spectral response curve of the first blood sample with added glucose in which the x-axis represents wavelength and the y-axis represents transmission along an arbitrary scale. Curve 200 represents the spectral curve in the infra-red band from 750 nm to 1800 nm of a first sample plasma, and curve 220 represent the spectral curve of the first sample plasma having an addition of 150 mg/deciliter glucose. The additional glucose increases the transmission throughout the band, and is most marked around the 1000 nm range. Thus, computing device 10 can calculate the amount of glucose in the blood flowing through measurement tube 90 from the spectral output of amplifier 103.

[0042] Fig. 3b illustrates a first example of a spectral response curve of a second blood sample without added glucose contrasted with the spectral response curve of the second blood sample with added glucose in which the x-axis represents wavelength and the y-axis represents transmission along an arbitrary scale. Curve 240 represents the spectral curve in the infra-red band from 750 nm to 1800 nm of the second sample plasma, and curve 260 represent the spectral curve of the second sample plasma having an addition of 100 mg/deciliter. The additional glucose increases the transmission throughout the band, and is most marked around the 1000 nm range. Thus, computing device 10 can calculate the amount of glucose in the blood flowing through measurement tube 90 from the spectral output of amplifier 103.

[0043] A comparison of Fig. 3a and 3b is instructive to realize that the spectral curve for each blood sample is different, however the peak increases with increasing glucose. Thus, with proper calibration, changes in glucose levels are detected by spectral measurement and comparison with a calibration sample.

[0044] Fig. 4 illustrates a subject having an installed sub-cutaneous fistula 400 to which an apparatus 410 according to the principle of the invention is secured. The apparatus comprises: a needle 45 attached to an artery side 40 of sub-cutaneous fistula
400; and a needle 60 attached to a venal side 50 sub-cutaneous fistula 400. In an exemplary embodiment sub-cutaneous fistula 400 is attached by micro-surgery respectively to one of the brachial artery or a branch of the brachial artery, and to one of the cubital vein and the basal vein. The illustrated apparatus 410 is ambulatory, and is secured to the body with a strap or other appurtenance. In one embodiment pharmaceutical reservoir 80 and injection device 81 are collocated with apparatus 410 and in another embodiment are located separately on the user's body. Preferably apparatus 410 communicates with the separately located pharmaceutical reservoir 80 and injection device 81 via a low power RF transmission such as Bluetooth.

Fistula 400 is inserted on a short or long term basis. Such fistulas are well known for use with dialysis patients. Fistula 400 appears sub-cutaneously, and needles 45 and 60 are inserted into sub-cutaneous fistula 400, thus providing an external supra-cutaneously appearing shunt in parallel with a portion of fistula 400. Thus, access to measuring tube of Figs. 1 and is simplified, and replacement, and additional testing can be accomplished without further invasive procedures.

Fig. 5 illustrates a high level block diagram of an embodiment of a blood characteristic measuring and pharmaceutical injection system comprising a peristaltic pump according to the principle of the invention. The system of Fig. 5 comprises: a computing device 10; a user input 11; an alarm and alert block 12; a hospital network connection 15; a connection to other devices 16; a valve 20; a strip test 21; a test cell 30 comprising at least one illuminator 31, at least one receiver 32 and optionally other measuring means 33; the artery side 40 of a sub-cutaneous fistula; a needle 45; the venal side of a 50 of a sub-cutaneous fistula; a needle 60; a connector 70; at least one pharmaceutical reservoir 80; at least one injection device 81; a measurement tube 90; a peristaltic pump 93; a connecting line 94; a connector 91; and a blood pressure transducer 92.

Needle 45 is inserted to receive a blood flow from the artery side 40 of a sub-cutaneous fistula of the subject, such as fistula 400 of Fig. 4, and bring the blood flow externally of the subject. Connector 91 is connected to needle 45 and is arranged to bring the blood flow to measurement tube 90 and to blood pressure transducer 92. Measurement tube 90 is arranged to traverse test cell 30. Valve 20 is arranged to controllably withdraw a blood sample from the blood flow and place the withdrawn sample on test strip 21. Peristaltic pump 93 is arranged to ensure
continuous blood flow through measurement tube 90 irrespective of subject blood pressure. Connecting line 94 is arranged to connect the output of peristaltic pump 93 to connector 70. Connector 70 is arranged to return blood withdrawn by needle 45 from artery side 40 to vein side 50 via needle 60. At least one injection device 81 is arranged to inject a pharmaceutical from a respective pharmaceutical reservoir 80 and inject the pharmaceutical into vein side 50 of the subject via connector 70. Injection device 81 is connected to be responsive to an output of computing device 10. Pharmaceutical reservoir 80 may be in the form of a cartridge or cassette.

[0048] Illuminator 31, which comprises at least one illuminating device, preferably one or more LEDs, and even further preferably one or more LEDs operable in at least part of the infrared band, is arranged to illuminate blood flow through measurement tube 90. Receiver 32, which comprises one or more receiving elements sensitive the band of light output by LED 31, is arranged to receive a reflection of the illumination of LED 31. Contact measuring means 33 is arranged to measure an electrical characteristic of the blood flow through measurement tube 90 by direct contact with the blood flow. Computing device 10 is arranged to communicate via hospital network connection, control the operation of test cell 30, receive the output of test cell 30, receive the output of blood pressure transducer 92, and output a signal to control the operation of injection device 81. Computing device 10 is further arranged to receive instructions via user input 11 and to output an alarm via alarm and alert block 12. Optionally, computing device 10 is in communication with pharmaceutical reservoir 80 to ascertain a fill level, and optionally to report a low fill level via one of hospital network connection 15 and alarm and alert block 12.

[0049] In operation blood, aided by the operation of peristaltic pump 93, flows through measurement tube 90, secured within test cell 30. Measurement tube 90 may be any translucent or transparent tube, preferably heparin coated or heparin-bounded to prevent coagulation. In one embodiment, test cell 30 is arranged to surround measurement tube 90, and in another embodiment test cell 30 is arranged with an indentation along one side to receive and secure measurement tube 90. In yet another embodiment test cell 30 comprises a measurement tube 90 having contact measurement means in a manner that will be explained further hereinto below. Computing device 10, which in an exemplary embodiment comprises a microprocessor, personal computer or workstation, operates test cell 30 to measure at
least one blood characteristic. In one embodiment, test cell 30 illuminates blood flowing through measurement tube 90 with an infrared light via the operation of illuminator 31, and receives a reflection of the illumination at receiver 32. Optional other measuring means 33 is operable to optionally measure one of temperature of the blood flow or electrical characteristics of the blood flow. Computing device 10 receives an indication of the output of receiver 32 and optional measuring means 33. Optional measuring means 33 may comprise at least one of a temperature measurement sensor and a resistance measurement sensor. Computing device 10 further receives inputs from hospital network connection 15 and from connection to other devices 16. In one embodiment, patient record information is input via hospital network connection 15, and other measuring devices including atmospheric information, or other patient measurement information is input via connection to other devices 16.

[0050] Computing device 10 further receives an output of blood pressure transducer 92, and instructions from user input 11. Computing device 10, responsive to the input received from test cell 30, blood pressure transducer 92 and user input 11, preferably computes an indication of at least one blood characteristic. Computing device 10, operates injection device 81 to inject at least one pharmaceutical responsive to the computing at least one blood characteristic to control the level of the characteristic within the subject. In the event of the at least one blood characteristic, such as a glucose level, being outside of safe pre-determined parameters, computing device 10 alerts a user via alarm and alert block 12.

[0051] The apparatus of Fig. 5 has been described as utilizing needle 45 and needle 60 to connect to a sub-cutaneous fistula, however this is not meant to be limiting in any way, and may be replaced by a surgically implanted connection to an artery and a vein, preferably with automatic shut off valves to prevent excess bleeding in case of a failure of any of connector 91, measurement tube 90 and connector 70 without exceeding the scope of the invention. Such an embodiment is further described below in relation to Fig. 8.

[0052] Fig. 6a illustrates a high level block diagram of an embodiment of a test cell and measurement tube arrangement according to the principle of the invention comprising a measurement tube 90; an injection device 81; a test cell 30; an optional blood pressure transducer 92; a T-connection 320; a T-connection 321; and a
plurality of connecting tubes 310. Connecting tubes 310 are arranged to detachably connect to either side of T-connections 320, 321. T connections 320, 321 are arranged to accept the respective terminations of measurement tube 90. Test cell 30 is arranged to removably at least partially enclose measurement tube 90. Injection device 81 is further arranged to connect to T-connection 320. Optional blood pressure transducer 92 is arranged to connect to T-connection 321.

[0053] Fig. 6b illustrates a high level block depiction of test cell 30 suitable for use with the arrangement of Fig. 6a exhibiting a receiving notch 340 according to the principle of the invention. Receiving notch 340 is configured and dimensioned to receive measurement tube 90, and allow for the removal and placement of measurement tube 90.

[0054] Fig. 7 illustrates a high level block diagram of an embodiment of a blood characteristic measuring and pharmaceutical injection system having reduced functionality according to the principle of the invention comprising a computing device 10; an alarm and alert block 12; a test cell 30 comprising at least one illuminator 31, and at least one receiver 32; an artery side 40 of a sub-cutaneous fistula 400, a needle 45; a venal side 50 of sub-cutaneous fistula 400; a needle 60; a connector 70; at least one pharmaceutical reservoir 80; at least one injection device 81; and a measurement tube 90.

[0055] Needle 45 is inserted to receive a blood flow from the artery side 40 of sub-cutaneous fistula 400 of the subject and bring the blood flow externally of the subject. Measurement tube 90 is arranged to receive the blood flow from needle 45. Measurement tube 90 is further arranged to traverse test cell 30. Connector 70 is arranged to return blood withdrawn by needle 45 from artery side 40 to vein side 50 via needle 60. At least one injection device 81 is arranged to inject a pharmaceutical from a respective pharmaceutical reservoir 80 and inject the pharmaceutical into vein side 50 of the subject via connector 70. Injection device 81 is connected to be responsive to an output of computing device 10. Pharmaceutical reservoir 80 may be in the form of a cartridge or cassette.

[0056] Illuminator 31, which comprises at least one illuminating device, preferably one or more LEDs, and even further preferably one or more LEDs operable in at least part of the infrared band, is arranged to illuminate blood flow through measurement tube 90. Receiver 32, which comprises one or more receiving elements
sensitive to at least some of the wavelengths emitted by illuminator 31, are arranged
to receive a reflection of the illumination of illuminator 31. Computing device 10 is
arranged to control the operation of test cell 30, receive the output of test cell 30, and
output a signal to control the operation of injection device 81. Computing device 10
is further arranged to output an alarm via alarm and alert block 12. Optionally,
computing device 10 is in communication with pharmaceutical reservoir 80 to
ascertain a fill level, and optionally to report a low fill level via alarm and alert block
12.

[0057] In operation, blood flows through measurement tube 90, secured within
test cell 30. Measurement tube 90 may be any translucent or transparent tube,
preferably heparin coated or heparin-bounded to prevent coagulation. In one
embodiment, test cell 30 is arranged to surround measurement tube 90, and in another
embodiment test cell 30 is arranged with an indentation along one side to receive and
secure measurement tube 90. Computing device 10, which in an exemplary
embodiment comprises a microprocessor, operates test cell 30 to measure at least one
blood characteristic. In one embodiment, test cell 30 illuminates blood flowing
through measurement tube 90 with an infrared light via the operation of illuminator
31, and receives a reflection of the illumination at receiver 32. Computing device 10
receives an indication of the output of receiver 31 and responsive to the input received
from test cell 30, computes an indication of at least one blood characteristic. In the
event of the at least one blood characteristic, such as a glucose level, is outside of pre-
determined parameters, computing device 10 alerts a user via alarm and alert block
12. Computing device 10, further operates injection device 81 to inject at least one
pharmaceutical responsive to the computing at least one blood characteristic to control
the level of the characteristic within the subject. It is to be understood that computing
device 10 may operate injection device to control the level of the characteristic within
the subject without alerting a user via alarm and alert block 12.

[0058] The apparatus of Fig. 7 has been described as utilizing needle 45 and
needle 60 to connect to a sub-cutaneous fistula, however this is not meant to be
limiting in any way, and may be replaced by a surgically implanted connection to an
artery and a vein, preferably with automatic shut off valves to prevent excess bleeding
in case of a failure of any of measurement tube 90 and connector 70 without
exceeding the scope of the invention
Fig. 8 illustrates a high level block diagram of an embodiment of the invention suitable for use without a sub-cutaneous fistula comprising: a connection 800 to an artery; an automatic shut-off valve 840; a measurement tube 90; one way valve 860; and a connection to a vein 870. Automatic shut off valve 840 is arranged to receive a blood flow from connection 800, and to sense the volume of blood flow. In the event that the blood flow exceeds a pre-determined quantity, automatic shut-off valve 840 is operative to shut down thereby stopping the blood flow from connection 800. The pre-determined quantity is selected such as to allow normal blood flow through measurement tube 90, and to shut down automatic shut-off valve 840 in the event of an excess above the normal blood flow.

Measurement tube 90 is arranged to receive the blood flow from automatic shut off valve 840 and return the blood flow via one way valve 860 to connection 870. One way off valve 870 operates to ensure that blood flow is only towards connection 870, and to prevent any reverse blood flow. Thus, in the event of a disconnection or failure of measurement tube 90, one way valve 870 prevents blood loss from connection 870.

Thus the present embodiments enable a system for measuring at least one blood characteristic and injecting a pharmaceutical responsive to the measuring by providing a supra-cutaneously appearing arterial shunt. In one embodiment the supra-cutaneously appearing arterial shunt is connected by a pair of needles to appear in parallel to a sub-cutaneous arterial venal fistula, also known as an A-V fistula. In another embodiment the supra-cutaneously appearing arterial shunt is attached to the subject via automatic shut off valves to prevent excess bleeding in the case of failure of the supra-cutaneously appearing arterial shunt. Blood passing through the supra-cutaneously appearing arterial shunt is measured by one of a plurality of measurements including spectral measurements and contact measurements. In addition, in one embodiment a valve is supplied attached to the shunt, the valve being arranged to allow for withdrawing a sample of the blood flow for additional testing. Preferably, the sample is tested in combination with an externally supplied reagent.

The invention also provides at least one pharmaceutical reservoir and an injection device. In an exemplary embodiment the reservoir takes the form of a cartridge or cassette. A computing device, responsive to the measurements, calculates an appropriate amount of pharmaceutical and operates the injection device to inject
the appropriate amount of pharmaceutical. Preferably the pharmaceutical is injected into arterial venal shunt.

[0063] The invention provides for an ambulatory version, having reduced functionality, and a hospital based version having additional functionality.

[0064] It is appreciated that certain features of the invention, which are, for clarity, described in the context of separate embodiments, may also be provided in combination in a single embodiment. Conversely, various features of the invention which are, for brevity, described in the context of a single embodiment, may also be provided separately or in any suitable sub-combination.

[0065] Unless otherwise defined, all technical and scientific terms used herein have the same meanings as are commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods similar or equivalent to those described herein can be used in the practice or testing of the present invention, suitable methods are described herein.

[0066] All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the patent specification, including definitions, will prevail. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

[0067] It will be appreciated by persons skilled in the art that the present invention is not limited to what has been particularly shown and described hereinabove. Rather the scope of the present invention is defined by the appended claims and includes both combinations and sub-combinations of the various features described hereinabove as well as variations and modifications thereof, which would occur to persons skilled in the art upon reading the foregoing description.
We claim:

1. A system for continuous measurement of at least one blood characteristic, the system comprising:
   - an arterial shunt, at least a portion of which appears supra-cutaneously, said arterial shunt arranged to carry blood of a subject; and
   - at least one of a spectral measurement means and a contact measurement means operable on said blood within said supra-cutaneously appearing portion,
   wherein said at least one of a spectral measurement means and a contact measurement means is operable to measure at least one blood characteristic of the subject.

2. A system according to claim 1, wherein said spectral measurement means comprises an at least one infra-red LED and at least one receiver sensitive to at least one wavelength transmitted by said at least one infra-red LED.

3. A system according to claim 2, further comprising a generator, the output of said generator driving said infra-red LED.

4. A system according to any of claims 1 to 3, wherein said arterial shunt comprises an arterial venal shunt.

5. A system according to any of claims 1 to 4, wherein said arterial shunt is arranged to connect to a sub-cutaneous fistula.

6. A system according to any of claims 1 - 5, further comprising a computing device arranged to receive an indication from said at least one of a spectral measurement means and a contact measurement means.

7. A system according to claim 6, further comprising at least one pharmaceutical reservoir and an injection device, said injection device arranged to receive a signal from with said computing device and being operable responsive to said received signal to inject said at least one pharmaceutical from said reservoir.
8. A system according to claim 7, wherein said computing device is operable responsive to said at least one of a spectral measurement means and a contact measurement means to determine an indicative value of said at least one blood characteristic, and to operate said injection device via said signal responsive to said determined indicative value.

9. A system according to claim 7, wherein said signal is operable under the Bluetooth standard.

10. A system according to claim 7, wherein said pharmaceutical reservoir is constituted of one of a cassette and a cartridge.

11. A system according to any of claims 1 - 10, further comprising a valve in communication with said shunt, said valve being arranged to allow for withdrawing a sample of the blood carried by said shunt for additional testing.

12. A system according to any of claims 1 - 10, further comprising a valve in communication with said shunt and a measuring plate, said valve being arranged to allow for withdrawing a sample of the blood carried by said shunt to said measuring plate.

13. A system according to claim 12, wherein said measuring plate is arranged for use with an externally supplied reagent.

14. A system according to claim 12, wherein said measuring plate is operable to measure an electrical characteristic of said withdrawn blood sample, said electrical characteristic being measurable in concert with an externally applied reagent.

15. A system according to any of claims 1 - 14, further comprising a blood pressure transducer operable to measure a blood pressure responsive to said blood in said shunt.
16. A system according to any of claims 1 - 6, further comprising at least one pharmaceutical reservoir and an injection device.

17. A system according to any of claims 1 - 16, further comprising a peristaltic pump operable to pump said blood flow through said arterial shunt.

18. A system for continuous measurement of at least one blood characteristic, the system comprising:
   an arterial venal shunt, at least a portion of which appears externally to a subject, said arterial venal shunt arranged to carry blood of the subject;
   at least one of a spectral measurer and a contact measurer operable on said blood within said externally appearing portion;
   a computing device receiving an output of said at least one of a spectral measurement means and a contact measurement means; and
   an injection device responsive to an output of said computing device, said injection device being operable to inject a pharmaceutical from a pharmaceutical reservoir,

   wherein said computing device responsive to said output of said at least one of a spectral measurer and a contact measurer is operable to output a signal to said injection device, said injection device being operable to inject a measured amount of pharmaceutical responsive to said signal.

19. A method for continuous measurement of at least one blood characteristic, the method comprising:

   shunting a blood flow of a subject, at least a portion of said shunted blood flow appearing supra-cutaneously; and
   measuring one of a spectral response and a electrical response of said blood flow within said supra-cutaneously appearing portion.

20. A method according to claim 19, wherein said measuring of a spectral measurement comprises illuminating said blood flow with an infra-red LED and receiving a reflection of said illumination.
21. A method according to claim 20, further comprising generating a driving signal for said infra-red LED, said illuminating being responsive to said generating.

22. A method according to claim 19, wherein said shunting comprising shunting a sub-cutaneous fistula.

23. A method according to claim 19, wherein said shunting comprises attaching a measurement tube to receive blood from an artery via a automatic shut off valve and attaching said measurement tube to return blood to a vein via a one way valve.

24. A method according to claim 19, further comprising:
   receiving an indication of said measuring.

25. A method according to claim 24, further comprising:
   computing an indicative value of the at least one blood characteristic responsive to said received indication; and
   injecting at least one pharmaceutical to the subject responsive to said computing.

26. A method according to claim 24, further comprising:
   computing an indicative value of the at least one blood characteristic responsive to said received indication;
   computing an appropriate amount of pharmaceutical to be injected to the subject responsive to said computed indicative value; and
   injecting at least one pharmaceutical to the subject responsive to said computing an appropriate amount.

27. A method according to claim 19, further comprising withdrawing a sample of the blood flow carried by said shunted blood flow for additional testing.

28. A method according to claim 19, further comprising withdrawing a sample of said shunted blood flow carried to a measuring plate.
29. A method according to claim 28, further comprising applying a reagent to said measuring plate and measuring a characteristic of said sample in concert with said applied reagent.

30. A method according to claim 29, wherein said measuring a characteristic of said sample comprises measuring an electrical characteristic of said withdrawn blood sample in concert with said applied reagent.

31. A method according to claim 19, further comprising measuring a blood pressure responsive to said blood flow in said shunt.

32. A method according to claim 19, further comprising pumping said blood through said supra-cutaneously appearing portion.
Fig. 5

- Vein
- Needle
- Connector
- Artery
- Blood pressure transducer
- Microprocessors Device
- User Input
- Hospital Network
- Pump
- Peristaltic Pump
- Alarm & Alert Block
- Test-cell
- Others Measur.
- Drug Reservoir #1
- Drug Reservoir #N
- Injection Device #1
- Injection Device #N
- Receivers
- 10
- 15
- 16
- 20
- 21
- 30
- 40
- 45
- 50
- 60
- 70
- 90
- 91
- 92
- 93
- 94
