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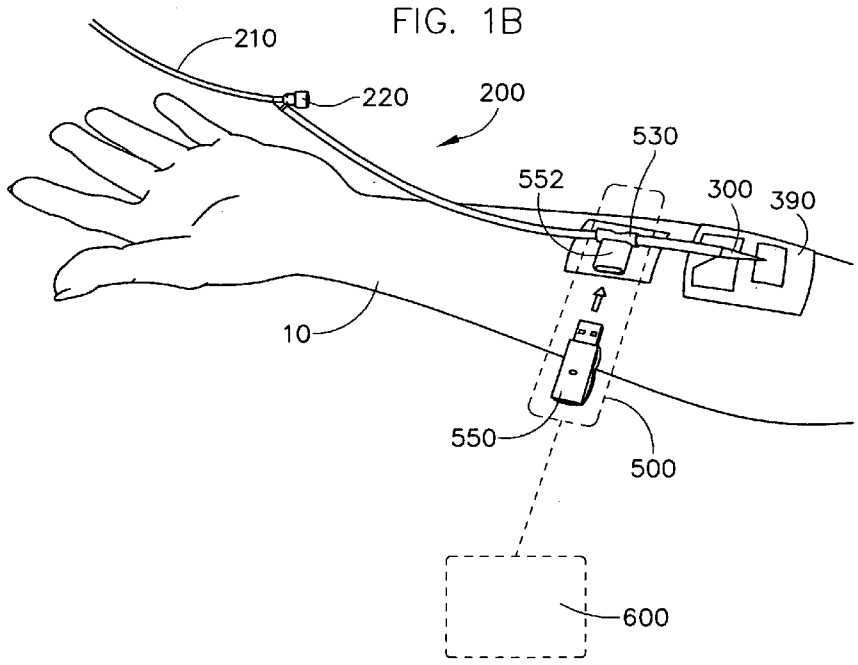
(54) Title: INTRAVENOUS FLUID MONITORING

FIG. 1B



(57) Abstract: Apparatus, systems and methods related to monitoring intravenous fluids during administration to a subject are disclosed. These apparatus, systems and methods provide near real-time monitoring of the identity of one or more components of an intravenous fluid.

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Intravenous Fluid Monitoring

RELATED APPLICATIONS

[0001] The present application is related to certain U.S. provisional applications: Serial No.61/035,339 filed March 10, 2008 by James W. Bennett and Leonid F. Matsiev; Serial No. 61/049,637 filed April 30, 2008 by James W. Bennett and Leonid F. Matsiev; and Serial No. 61/198,523 filed November 6, 2008 by James W. Bennett and Leonid F. Matsiev.

BACKGROUND

[0002] The invention relates to intravenous fluid monitoring apparatus, systems and methods. In particular, the invention relates to intravenous fluid monitoring apparatus and systems comprising sensors for identifying one or more components of an intravenous fluid, and to methods for intravenous delivery of fluid to a subject including sensing of the fluid during administration to the subject.

[0003] Intravenous fluid delivery systems and methods are known in the art. Such systems can generally comprise an intravenous infusion device (e.g, such as a cannula or a catheter) for infusion of fluid into the vasculature system of a subject in need thereof (e.g., a patient), one or more fluid sources for containing an intravenous fluid or a component thereof, and an fluid line assembly providing fluid communication between the one or more fluid sources and the intravenous infusion device. Known systems include multiple arrangements and configurations, including generally for example various systems (e.g., gravity-feed systems; pump systems) for providing a motive force for delivery of the fluid from the source to the subject, as well as various further components typically integrated into the fluid line assembly such as conduits, fittings (e.g., Luer Lock™ fittings), backflow blocks, valves, and injection ports.

[0004] Some intravenous fluid delivery systems known in the art also include one or more sensors, such as flow sensors (to measure a precise amount of a fluid being delivered), pressure sensors (e.g., to detect fluid line blockage) and/or ultrasonic sensors (e.g., to detect air-bubbles). See, for example, U.S. Patent Application No. US 2003/0159741 to Sparks.

[0005] Notwithstanding the various advances known in the art in connection with intravenous fluid delivery, there remains a need in the art for improvements, especially improvements which enhance the accuracy and/or reliability of treatments involving intravenous fluid delivery to patients, and correspondingly which enhance patient safety. In particular, there remains a need for improvements in sensing, monitoring and recording the identity of fluid

compositions (e.g, component identity, component concentration, component dose (e.g, current, projected) etc.) being delivered to patients in the course of treatment.

SUMMARY OF INVENTION

[0006] The present inventions provide apparatus, systems and methods related to intravenous fluid administration. The apparatus, systems and methods of the invention are more specifically related to monitoring of intravenous fluids during administration to a subject. As described herein and in further detail below, the various inventions offer intravenous fluid monitoring approaches which are significantly advantaged over known systems, including for example by providing near real-time monitoring of the identity of one or more components of an intravenous fluid (e.g., the presence or absence of a component, the composition of a component, the concentration of a component, the time (absolute time or relative time versus other components) of infusion of a component, the onset of component infusion (i.e., delivery through an infusion device); the completion of component infusion, the component dosing level (e.g, cumulative dosing level – current or projected), etc.). Such near real-time monitoring of intravenous fluids reduces the potential for errors associated with intravenous administration, and especially intravenous drug administration. Hence, the apparatus, systems and methods of the invention provide substantial advances in patient safety. Such advances in safety can translate to a more meaningful patient treatment experience, and to enhanced operational efficiencies and reduced expenses for hospitals and other entities which administer fluids intravenously. Such inventions can applied, and such advantages can be realized in a number of various settings and applications in which intravenous fluids are administered, including for example, without limitation, at hospitals, clinics, surgical centers, homes (e.g., home hospice), nursing homes, assisted living environments, etc.

[0007] Generally, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject. Preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more active pharmaceutical agents within an intravenous fluid during administration of the fluid to a subject. Such active pharmaceutical agents can include, for example, an anticoagulant (e.g., heparin), a metabolically-active hormone (e.g, insulin), an anesthetic (e.g., propofol), and/or an analgesic (e.g., morphine), among others. Additionally or alternatively, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more other components of an intravenous fluid, preferably components used for hydration and ion metastasis of subjects.

Such components can preferably include, for example one or more components selected from potassium chloride, sodium chloride, Ringer's lactate, and dextrose, in each case in molecular or ionic (e.g, dissociated) form (e.g, sodium ion, potassium ion, chloride ion, calcium ion, lactate ion, and dextrose).

[0008] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject using a multi-parametric approach. In such approach, multiple parameters (e.g, multiple fluid properties such as without limitation refractive index, electrochemical potential, impedance, admittance, conductivity, etc.) can be sensed, and the combination of parameters can be correlated to obtain resolution of components within the fluid. Hence, an intravenous fluid can be sensed – for example with multiple sensors (or with a sensor having multiple sensor elements) and/or with multiplexing of a sensor element to obtain independent sensing measurements – to generate a multi-parametric profile characteristic of component identity within the fluid. A multi-parametric profile can be correlated to determine an identity of one or more components of the fluid. Such multi-parametric approaches advantageously provide for improved resolution of components; therefore such approaches allow for improved ability to distinguish between different fluid compositions, including for example the presence or absence of particular active pharmaceuticals, and/or various concentrations of a particular active pharmaceutical or other component. Multi-parametric approaches as described herein are preferred, an can be generally used with any aspects, embodiments and approaches described herein; however, many aspects, embodiments and approaches of the invention do not require multi-parametric approaches and can be effected independently thereof.

[0009] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject using one or more sensors. The one or more sensors are preferably selected to include at least one sensor other than a flow sensor, and/or in some embodiments also preferably other than a pressure sensor, and/or in some embodiments also preferably other than an ultrasonic sensor. Generally for example, preferred sensors effective with the apparatus, systems and methods of the invention can include, without limitation, one or more sensors selected from an impedance sensor (e.g, an AC impedance spectroscopy sensor), an electrochemical sensor (e.g., an electrochemical potential sensor), a thermal sensor (e.g., a thermal anemometer sensor), an optical sensor (e.g., a refractometer sensor, a

transmission sensor, an absorbance sensor, a spectrometer (including a colorimeter) or, a turbidity sensor), a rheological sensor (e.g.,a viscometer), an electrical property sensor (e.g., a capacitor sensor, a pH sensor, a conductivity sensor, and an inductive sensor), and a fluid-displacing and/or fluid-shearing (e.g, resonator) sensor. In various preferred embodiments, the sensors can be one or more sensors selected from an impedance sensor (e.g, an AC impedance spectroscopy sensor) and an optical sensor (e.g., a refractometry sensor, a transmission sensor, an absorbance sensor, a spectrometer (including a colorimeter) or, a turbidity sensor). In certain preferred embodiments, the apparatus, systems and methods of the invention comprise or use at least two or more sensors or an integrated assembly comprising two or more sensors (e.g., an integrated assembly comprising two or more sensor elements, each sensor element comprising one or more sensing surfaces), and preferably such two or more sensors being of different types and/or having different sensor approaches (e.g., impedance sensor, electrical property sensor, optical sensor, etc.). Preferably, such two or more sensors can include an impedance sensor (e.g, an AC impedance spectroscopy sensor), a thermal sensor, and/or an optical sensor (e.g., a refractometry sensor, a transmission sensor, an absorbance sensor, a spectrometer (including a colorimeter) or, a turbidity sensor). Preferably, such two or more sensors can be integrated into a common assembly, such as a common substrate, e.g., as part of a common sensor subunit. For example, the apparatus, systems and methods of the invention comprise an impedance sensor (e.g, an AC impedance spectroscopy sensor) and an optical sensor (e.g., a refractometry sensor), each integral with and/or in a common sensor assembly such as a common substrate, or a common sensor subunit. The various specific sensors and sensing approaches as described herein are preferred, an can be generally used with any aspects, embodiments and approaches described herein; however, many aspects, embodiments and approaches of the invention do not require such certain specific sensors or sensing techniques and can be effected independently thereof.

[00010] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject using a sensor having a sensor element (e.g., with a sensing surface adapted for interaction with and being responsive to the intravenous fluid), where such sensor element (e.g., such sensing surface) is positioned at a location within an intravenous fluid system such that it interacts with the fluid (e.g, such sensing surface contacts the fluid) in relative proximity to the infusion location – the location at which the fluid enters a subject's vasculature system. Advantageously, monitoring of intravenous fluids proximal to the infusion location (e.g, proximal to the distal end of a fluid line assembly of an intravenous fluid

delivery system, and/or proximal to an infusion device of an intravenous fluid delivery system) can effectively reduce the potential for errors associated with intravenous administration. Such proximity is less constrained by physical distance; rather it more generally refers to a location within an intravenous fluid delivery system at which the composition of the intravenous fluid is representative of (if not identical to) that which is delivered to the subject. Hence, such proximity typically refers to a position or location within the intravenous fluid delivery system which is downstream relative to various components of the intravenous fluid delivery system which could change or otherwise effect the fluid identity (e.g., composition, concentration etc), including for example downstream of infusion valves, injection ports, supply line junctions, etc. In various embodiments of various aspects of the invention, therefore, the apparatus, systems and methods of the invention comprise a sensor element (e.g., having a sensor surface) positioned proximal to (e.g, at or near) the distal end of a fluid line assembly, and/or proximal to an infusion device. For example, such a sensor element can include a sensing surface in a cavity of an in-line housing, where the in-line housing optionally has inlet and outlet fittings (e.g., luer locks), and can be integrated into the fluid line assembly upstream of an infusion device. Alternatively, for example, such a sensor element can include a sensing surface in a cavity of a housing defined in infusion device (e.g., catheter, needle, etc.). Further, in some embodiments, in addition to one or more sensors positioned for monitoring of intravenous fluids proximal to the infusion location (e.g, proximal to the distal end of a fluid line assembly and/or proximal to an infusion device), the apparatus, systems and method of the invention can also include an additional sensor positioned upstream of an injection port – facilitating for example a differential measurement approach. The approaches for positioning of the sensor element proximal to the infusion location, as described and as variously exemplified herein are preferred, and can be generally used with any aspects, embodiments and approaches described herein; however, many aspects, embodiments and approaches of the invention do not require such certain specific positioning approaches and can be effected independently thereof.

[00011] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject (e.g., a specific patient, for example at a hospital, clinic, surgical environment, home hospice, nursing home, assisted living environment, etc), where such subject is positively and specifically identified in connection with monitoring and administration of the intravenous fluid. Various embodiments and aspects of the invention can include approaches for correlating the sensor data (i.e., data (e.g., as represented by a signal) originating from the sensor – either raw data or more typically processed data) to a specific

subject (e.g., patient). For example, the sensor (or apparatus or system comprising a sensor) can include an identifier circuit for correlating sensor data to a specific subject. Typically, and preferably, such identifier circuit may be in communication with one or more other circuits, including for example circuits for receiving ,processing, storing, displaying or transmitting data, including data originating from the sensor element, such as a signal processing circuit or a data retrieval circuit. Such integrated patient-identification approaches can further enhance the benefit to patient safety, by reducing the potential for errors associated with intravenous administration, and especially intravenous drug administration. The various subject-identifier approaches as described herein are preferred, an can be generally used with any aspects, embodiments and approaches described herein; however, many aspects, embodiments and approaches of the invention do not require such certain specific subject-identifier approaches and can be effected independently thereof.

[00012] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject with a remote and/or centralized monitoring approach. Although such remote and/or centralized monitoring approaches can be effected for an individual subject (e.g, in a home hospice environment), such approaches are especially advantageous in connection with multi-subject care environments. For example, different sensor data from one subject or from several different subjects (in each case, such sensor data being locally generated and specifically associated with an intravenous fluid being administered to a particular subject) can be acquired and/or monitored at a location which is remote (relative to the patient) – such as a nursing station; preferably such sensor data can be centrally monitored at such remote location. In various aspects and embodiments therefore, sensor data can be generated in a processor local to and in communication with a sensor element (e.g., having a sensing element in contact with the intravenous fluid), preferably for each of two or more subjects, and then such locally-generated sensor data stream(s) can be acquired by a processor remote from the sensor element. Such acquisition can be effected, for example, via wireless (e.g., WiFi, Bluetooth ®, WiMax, IR, RF) or other communication approaches. The remote processor can comprise one or more circuits for receiving, processing, storing, displaying or transmitting the acquired sensor data. The acquired sensor data can be monitored remotely, including for example at a central monitoring location. Preferably for example, the monitoring can be done visually by human interaction with a display and/or can be further enhanced and effected by various automated approaches. In one such automated monitoring approach, a monitoring circuit can comprise a data comparator module for comparing one or

more parameters (e.g, data values) derived from sensor data with one or more parameters (e.g., data values) which are prescribed or proscribed for a particular subject (e.g. patient). Such patient-relevant parameters can be treatment-centric (e.g., applicable to all such patients undergoing a particular treatment), including semi-customized treatment-centric parameters which include a patient-specific data input (e.g., a patient weight, patient age, etc.) to determine a treatment-centric parameter, and/or such patient-relevant parameters can be patient-centric (e.g., wholly customized for a specific patient). Exemplary non-limiting parameters can include dosing levels, dosing timing (onset or completion), dosing frequency, etc. for various and specific active pharmaceutical agents or other components of an intravenous fluid. Patient-relevant parameters can be specific for the intravenous monitoring system effected by the apparatus, systems and methods of the invention, and/or can be common with (e.g., shared with) various other systems, such as infusion pump systems (e.g., "smart pumps"). In one embodiment, such infusion pump includes a control system with a data input module, whereby patient-specific data (e.g, weight) can be used to determine a patient relevant parameter used by both the pump controller (as known in the art) and/or for use by the monitoring circuit, e.g. a comparator module, of the present inventions for comparison to a sensor-data parameter. In some embodiments, the monitoring circuit can share common circuitry with (or have the same or similar functionality and/or software as) a portion of the pump controller circuit. Advantageously, the monitoring approaches of the apparatus, systems and methods of the invention can also include certain notice (e.g., alarm) features – to provide notice to a caregiver that a specific patient's intravenous fluid delivery system is operating incongruous with a prescribed or proscribed treatment, and /or can also include certain corrective action (e.g., system control) features – to make, preferably automated, a corrective action with the intravenous fluid delivery system. For example, upon determining an inconsistency between corresponding sensor-data-derived parameter and prescribed or proscribed patient-relevant parameter, an alarm can sound and /or a control circuit can activate a control element (e.g., an automated infusion valve) to make a change in the intravenous administration regime. Such remote and/or central monitoring approaches can further enhance the benefit to patient safety, by reducing the potential for errors associated with intravenous administration, and especially intravenous drug administration. The various remote and/or central monitoring approaches as described herein are preferred, an can be generally used with any aspects, embodiments and approaches described herein; however, many aspects, embodiments and approaches of the invention do not require such remote and/or central monitoring approaches and can be effected independently thereof.

[00013] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject with a sensor that comprises a processor (e.g, as included within a processor assembly) which is physically separable from, and intermittently interfaceable with (e.g., for a finite, operationally effective period of time) a sensor element (e.g., as included within a housing assembly). The approach of a temporally-limited engagement (interfacement) of the processor and the sensor element allows for regular operation while engaged / interfaced, and allows for physical separation of sensing function and processing function of a sensor (at least for some period of time) after or between operations, with a corresponding separation of physical treatment of the embodiments which effect such function. For example, the sensor element can be physically separated from the processor for a period of time to allow for sterilizing the sensor element (or a sensing surface thereof) or for disposal and replacement of a (pre-)sterilized sensor element (or a sensing surface thereof). Such separation also allows for re-use of the processor – for example, in connection with a second subsequent subject. Significantly, since processors are generally more expensive than sensor elements (or sensing surfaces thereof), the re-use of processors in such a temporally-limited engagement (interfacing) approach provides for efficiency of capital investment, especially in a multi-subject (e.g., hospital, surgical, nursing care, etc.) environment. The various approaches for temporally-limited / intermittent engagement / interfacing of processor and sensor element as described herein are preferred, an can be generally used with any aspects, embodiments and approaches described herein; however, many aspects, embodiments and approaches of the invention do not require such approaches for temporally-limited / intermittent engagement / interfacing of processor and sensor element, and can be effected independently thereof.

[00014] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject with a sensor that comprises (i) an assembly comprising one or more sensor elements, (ii) a signal-conditioning processor, including one or more circuits adapted for conditioning (e.g, amplifying) a signal, and (iii) a signal-identification processor, including one or more circuits adapted for identifying or determining a signal representative of the identity of one or more components of an intravenous fluid (e.g. as corresponding to a component within a composition or concentration of a component within a composition). In one such preferred subembodiment, each of the assembly comprising the one or more sensor elements, the signal-conditioning processor, and the signal-identification processor are each

physically separate components. In an alternative of such preferred subembodiment, the assembly comprising the one or more sensor elements is physically separate from an integrated assembly comprising the signal-conditioning processor and the signal-identification processor. In another such preferred subembodiment, an integrated assembly comprises each of the one or more sensor elements, the signal-conditioning processor, and the signal-identification processor. Such various approaches for configuring the sensor elements, the signal-conditioning processor and the signal-identification processor are preferred, an can be generally used with any aspects, embodiments and approaches described herein; however, many aspects, embodiments and approaches of the invention do not require such approaches for configuring these sensor components, and can be effected independently thereof.

[00015] Various further aspects, embodiments and features of the inventions are described herein throughout the specification and drawings; the aforementioned general summary is intended to be an introductory and non-limiting summary of several commercially meaningful approaches included separately and in combination in various inventions. Generally, these various inventions enhance the accuracy and/or reliability of treatments involving intravenous administration, thereby reducing risk of error in connection with such treatments, and improving patient safety. The various inventions also enable improved effectiveness and efficiency of operations and improved efficiency of capital investment, especially in a multi-subject environment. The following more detailed summary, and the subsequent detailed description and examples further describe the inventions.

[00016] In particular, in a first aspect, the invention is directed to apparatus comprising a sensor (or a sensor subassembly) for identifying one or more components of an intravenous fluid. In general, in this first aspect of the invention the apparatus comprises one or more sensor elements having a sensing surface responsive to a fluid (e.g., to a fluid property or a fluid composition). Preferably, the sensing surface of a sensor element is positioned for contact with the intravenous fluid. Alternatively, however, the sensing surface of a sensor element can be positioned for indirect, non-contact sensing of a fluid. Preferably, the sensing surface of a sensor element is positioned for contact with the intravenous fluid during the administration of the fluid to the subject.

[00017] In a first general embodiment of the first aspect of the invention, the invention is directed to an apparatus effective for multi-parametric characterization of one or more fluid components. Preferably, in this first general embodiment, the apparatus comprises two or more sensor elements, each sensor element having a sensing surface positioned for contact with the

fluid. Preferably, in this first general embodiments, the two or more sensor elements can have a surface positioned in one or more cavities of a housing. The housing can be adapted for fluidic interface with a fluid line assembly of an intravenous fluid delivery system. For example, the housing can be adapted for in-line fluid communication with the fluid line assembly. Alternatively, the housing can be defined or included in an intravenous infusion device (e.g., a catheter). The two or more sensor elements can be independent of each other, including for example having physically separate sensing surfaces, and/or for example having sensing surfaces which are independently addressable (e.g., independently activated, independently sampled, including for example simultaneously using differentially resolvable (deconvolutable) approaches or at different times). In preferred subembodiments of this first general embodiment, the apparatus can comprise one or more signal processing circuits for (preferably independently) processing data originating from each of the two or more sensor elements, the processing circuits being configured to generate a multi-parametric profile characteristic of a component of the fluid.

[00018] In a second general embodiment of the first aspect of the invention, the invention is directed to an apparatus effective for deploying sensor elements and sensor processors (e.g., including one or more circuits for activating a sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element) in a capital efficient manner. Preferably, in this second general embodiment, the apparatus comprises one or more sensor elements. The sensor element(s) can have a sensing surface positioned for contact with the fluid. Preferably, in this second general embodiment, the sensing surface can be positioned in one or more cavities of a housing. The housing can be adapted for fluidic interface with a fluid line assembly of an intravenous fluid delivery system. For example, the housing can be adapted for in-line fluid communication with the fluid line assembly. Alternatively, the housing can be defined or included in an intravenous infusion device (e.g., a catheter). In any case, the apparatus in this second embodiment, can further comprise one or more contacts in communication with (e.g, in electrical communication with) the sensing surface of the sensor element(s). Such contacts are preferably accessible, to enable a communication interface with a sensor processor. The sensor processor can be in a processor assembly which contains the one or more circuits (as described herein above). The processor assembly can further comprise one or more contacts in communication with the one or more circuits. Such contacts are preferably accessible, for intermittent communication interface with the contacts of the sensing surfaces. The intermittent interface of this general second embodiment of the first aspect of the invention allows for deployment of a relatively inexpensive housing assembly

comprising the one or more sensor element(s), which housing assembly or sensor elements or sensing surfaces thereof can be sterile or sterilizable for use, and/or which can be disposable after use. Such housing assembly or sensor elements or sensing surfaces can be deployed in practice with a reusable sensor processor (e.g., as a processor assembly), thereby providing for capital efficiency. For example, a sensor processor can be interfaced with a first housing assembly for use by a first subject, and following thereafter, the same sensor processor can be interfaced with a second housing assembly for use by a second subject. Further related methods and aspects are described below.

[00019] In a third general embodiment of the first aspect of the invention, the invention is directed to an apparatus effective for ensuring and enhancing the reliability and/or accuracy of a patient-specific treatment. Preferably, in this third general embodiment the apparatus comprises one or more sensor elements. The sensor element(s) can have a sensing surface positioned for contact with the fluid. Preferably, the sensing surface can be positioned in one or more cavities of a housing, as described above in connection with the second general embodiment of the first aspect of the invention. The apparatus can comprise a sensor processor. The sensor processor can include one or more circuits for activating a sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element. Preferably, the apparatus can comprise one or more of a signal processing circuit and/or a data retrieval circuit. Preferably, the apparatus can further comprise an identifier circuit for correlating sensor data to a specific patient. The identifier circuit is preferably in communication with (e.g., electrical communication with) one or more of a signal processing circuit and/or a data retrieval circuit. The identifier circuit can be used in operation to effectively monitor whether a specific patient is receiving an intravenous fluid consistent with a prescribed or proscribed treatment plan.

[00020] In a fourth general embodiment of the first aspect of the invention, the invention is directed to an apparatus effective for deploying a fluid-component sensor into in intravenous delivery system. Preferably, in this fourth general embodiment of the first aspect of the invention, the apparatus comprises an infusion device for infusion of fluid into the vasculature system of a subject, and one or more sensor elements integral with the infusion device. The sensor element(s) can have a sensing surface positioned for contact with the fluid. Preferably, the sensing surface can be positioned in one or more cavities (e.g., of a housing) defined in the infusion device.

[00021] The first, second, third and fourth general embodiments of the first aspect of the invention can be effected in combination with each other. The first, second, third and fourth general embodiments of the first aspect of the invention can be effected and/or used as well with each general embodiment of the second and third aspects of the invention. Various specific subembodiments of each general embodiments of the first aspect of the invention are also applicable with specific subembodiments of general embodiments of the second and third aspects of the invention.

[00022] In a second aspect, the invention is directed to systems for intravenous delivery of fluids into a subject in need thereof (e.g., a patient). In general, in this second aspect of the invention the system comprises a fluid line assembly and one or more sensor elements. The fluid line assembly can generally include one or more conduits and /or other components. The fluid line assembly can have a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the subject (e.g., a patient). The sensor element(s) can have a sensing surface positioned for contact with the fluid. Preferably, in this first general embodiment of the second aspect of the invention, the sensing surface can be positioned in one or more cavities of a housing. The housing can be adapted for fluidic interface with a fluid line assembly of an intravenous fluid delivery system. For example, the housing can be adapted for in-line fluid communication with the fluid line assembly. Alternatively, the housing can be defined or included in an intravenous infusion device (e.g., a catheter).

[00023] In a first general embodiment of the second aspect of the invention, the invention is directed to a system for intravenous fluid delivery to a patient comprising a fluid line assembly and an apparatus of the first aspect of the invention.

[00024] In a second general embodiment of the second aspect of the invention, the invention is directed to a system for intravenous fluid delivery to a patient comprising a fluid line assembly having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the subject (e.g., a patient). The system further comprises a sensor element having a sensing surface proximate to the second distal end of the fluid line assembly. The sensing surface can be positioned in one or more cavities of a housing. The housing can be adapted for fluidic interface with a fluid line assembly proximate to its distal end. For example, the housing can be adapted for in-line fluid communication with the fluid line assembly proximate to its distal end. Alternatively, the housing can be defined or included in an

intravenous infusion device (e.g., a cannula or a catheter). The system can further comprise one or more injection ports and one or more additional sensor elements for one or more additional sensors, such additional sensor elements being positioned upstream of the injection port – facilitating for example a differential measurement approach.

[00025] In a third general embodiment of the second aspect of the invention, the invention is directed to a system for intravenous fluid delivery to a subject which includes a remote processor, effective for example for monitoring sensor data from one or from multiple local sensors (e.g., for remote monitoring of a corresponding multiple subjects). The remote processor can therefore comprise a data acquisition circuit for acquiring sensor data originating from one or more local sensors (e.g, via a corresponding one or more local processors), and a monitoring circuit for monitoring the sensor data. The system can include a local processor comprising one or more circuits for activating a sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element. Preferably, the apparatus can comprise one or more of a signal processing circuit and/or a data retrieval circuit. Preferably, the system can further comprise an identifier circuit for correlating sensor data to a specific patient. The local processor can be proximate to and in communication with one or more sensing surfaces of a sensor element. The sensor element can have a sensing surface positioned to contact the fluid during administration to the subject, as described.

[00026] In a further, fourth general embodiment of the second aspect of the invention, the invention is directed to a system for intravenous fluid delivery to a subject comprising a fluid line assembly and a sensor for identifying one or more active pharmaceutical agents within the fluid. The sensor can comprise a sensor element having a sensing surface positioned for contact with the fluid, and one or more circuits in communication with the sensor element for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element. The sensor is configured to distinguishably detect one or more active pharmaceutical agents. Preferably, the sensor is configured to identify one or more active pharmaceutical agents selected from the group consisting of an anticoagulant (e.g., heparin), a metabolically-active hormone (e.g, insulin), an anesthetic (e.g., propofol), and an analgesic (e.g., morphine).

[00027] In another, fifth general embodiment of the second aspect of the invention, the invention is directed to a system for intravenous fluid delivery to a subject comprising a fluid line assembly and a sensor for identifying one or more components of the fluid. The sensor can comprise a sensor element having a sensing surface positioned for contact with the fluid, and

one or more circuits in communication with the sensor element for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element. The sensor is configured to distinguishably detect one or more components of the fluid. Preferably, the sensor is configured to identify one or more components of the fluid selected from the group consisting of a metal ion, halide ion, organic ion or salts, and a sugar, preferably for example sodium ion, potassium ion, chloride ion, calcium ion, magnesium ion, lactate ion, and dextrose. For example, such ions can be components in fluid compositions comprising potassium chloride, sodium chloride, Ringer's lactate, and dextrose. Preferably, the method comprises sensing the fluid to identify potassium chloride, potassium ion or chloride ion.

[00028] In a sixth general embodiment of the second aspect of the invention, the invention is directed to a system for intravenous fluid delivery to a subject comprising a fluid line assembly and a sensor other than a flow sensor, the sensor comprising a sensor element having a sensing surface positioned for contact with the fluid. The sensor can preferably further comprise one or more circuits in communication with the sensor element for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element.

[00029] The first, second, third, fourth, fifth and sixth general embodiments of the second aspect of the invention can be effected in combination with each other. The first, second, third, fourth, fifth and sixth general embodiments of the second aspect of the invention can be effected and/or used as well with each general embodiment of the first and third aspects of the invention. Various specific subembodiments of each general embodiments of the second aspect of the invention are also applicable with specific subembodiments of general embodiments of the first and third aspects of the invention.

[00030] In a third aspect, the invention is directed to methods for intravenous delivery of fluid to a subject in need thereof (e.g., a patient). In general, such methods comprise administering an intravenous fluid to a subject in need thereof and sensing the fluid, preferably to identify one or more components thereof.

[00031] In a first general embodiment of the third aspect of the invention, the invention is directed to a method for intravenous delivery of fluid to a subject in need thereof. The method comprises administering the fluid to the subject, and sensing the fluid with an apparatus of the first aspect of the invention or with a system of the second aspect of the invention. Preferably, the method further comprises identifying one or more components of the fluid during administration of fluid to the subject.

[00032] In a second general embodiment of the third aspect of the invention, the invention is directed to a method for intravenous delivery of fluid to a subject in need thereof. The method comprises administering the fluid to the subject, sensing the fluid to generate a multi-parameteric profile characteristic of a component of the fluid, and identifying one or more components of the fluid during administration of fluid to the subject based on the multi-parametric profile. In preferred subembodiments, sensing the fluid comprises exposing a sensing surface of a first sensor element to the fluid, exposing a sensing surface of a second sensor element to the fluid, and independently processing data originating from each of the first sensor element and the second sensor element to generate the multi-parametric profile.

[00033] In a third general embodiment of the third aspect of the invention, the invention is directed to a method for intravenous delivery of fluid to a subject in need thereof. The method comprises administering a first fluid to a first subject, exposing a sensing surface of a first sensor element to the first fluid, interfacing (e.g., communicatively engaging) a processor with the first sensor element and identifying one or more components of the first fluid during administration thereof to the first subject. The processor can comprise one or more circuits for activating a sensor element or for receiving, processing, storing, displaying or transmitting data originating from the a sensor element. The method further comprises dis-interfacing (e.g., communicatingly disengaging) the processor from the first sensor element. The method further comprises administering a second fluid to a second subject, exposing a sensing surface of a second sensor element to the second fluid, and interfacing the (same) processor with the second sensor element and identifying one or more components of the second fluid during administration thereof to the second subject. This method preferably, in a subembodiment, can further comprise disposing or sterilizing the sensing surface of each of the first sensor element and the second sensor element after administration of fluid to the respective subject.

[00034] In a fourth general embodiment of the third aspect of the invention, the invention is directed to a method for intravenous delivery of fluid to a subject in need thereof. The method comprises administering the fluid to the subject, sensing the fluid to generate sensor data for identifying one or more components of the fluid during administration of fluid to the subject, and correlating the sensor data to the specific subject. Preferably, this method can further comprise deriving one or more parameters from the sensor data, and comparing the one or more sensor-derived parameters with one or more prescribed or proscribed patient-relevant parameters.

[00035] In a fifth general embodiment of the third aspect of the invention, the invention is directed to a method for intravenous delivery of fluid to a subject in need thereof. The method

comprises administering the fluid to the subject through an intraveneous infusion device, and sensing the fluid with a sensing surface of a sensor element, where the sensing surface is positioned proximate to the intravenous infusion device to identify one or more components of the fluid during administration of fluid to the subject. Preferably in this method, fluid is exposed to a sensing surface of a sensor element, with the sensing surface being positioned within a cavity of a housing adapted for in-line fluid communication of a fluid line assembly. Preferably in this method, such an in-line housing is positioned directionally adjacent to the subject relative to the position of any fluid source supply line or any injection port of the fluid line assembly. Alternatively for this method, fluid is exposed to a sensing surface of a sensor element, and the sensing surface being positioned within a cavity of a housing defined in the intravenous infusion device.

[00036] In a sixth general embodiment of the third aspect of the invention, the invention is directed to a method for intravenous delivery of fluid to a subject in need thereof. The method comprises administering the fluid to the subject, sensing the fluid with a sensor element having a sensing surface exposed to the fluid during administration of fluid to the subject, generating sensor data in a processor local to and in communication with the sensor element, the local processor optionally comprising one or more circuits for activating a sensor element, the local processor comprising one or more circuits for receiving, processing, storing, displaying or transmitting data originating from the sensor element. The method further comprises acquiring the sensor data at a processor remote from the sensor element. The remote processor can comprise one or more circuits for receiving, processing, storing, displaying or transmitting the acquired sensor data. The method further comprises monitoring the acquired sensor data or data derived therefrom.

[00037] In a seventh general embodiment of the third aspect of the invention, the invention is directed to a method for intravenous delivery of fluid to two or more subjects in need thereof. The method comprises administering a first fluid to a first subject, sensing the first fluid with a first sensor element having a sensing surface exposed to the first fluid during administration of fluid to the first subject, and generating sensor data in a first processor local to and in communication with the first sensor element. The method further comprises administering a second fluid to a second subject, sensing the second fluid with a second sensor element having a sensing surface exposed to the second fluid during administration of fluid to the second subject, and generating sensor data in a second processor local to and in communication with the second sensor element. The method can further include acquiring the

sensor data from each of the first local processor and the second local processor at a processor remote from each of the first sensor element and the second sensor element, and monitoring the acquired sensor data from each of the first local processor and the second local processor or monitoring data derived therefrom.

[00038] In an eighth general embodiment of the third aspect of the invention, the invention is directed to a method for intravenous delivery of fluid to two or more subjects in need thereof. The method comprises administering the fluid to the subject, and sensing the fluid to identify one or more active pharmaceutical agents within fluid during administration of fluid to the subject. Preferably, the method of this eighth general embodiment comprises sensing the fluid to identify one or more active pharmaceutical agents selected from the group consisting of: an anticoagulant (e.g, heparin), a metabolically-active hormone (e.g., insulin), an anesthetic (e.g, propofol), and an analgesic (e.g, morphine).

[00039] In a ninth general embodiment of the third aspect of the invention, the invention is directed to a method for intravenous delivery of fluid to two or more subjects in need thereof. The method comprises administering the fluid to the subject, sensing the fluid to identify one or more components within fluid during administration of fluid to the subject, the one or more components being selected from the group consisting of a metal ion, halide ion, organic ion or salts, and a sugar, preferably for example sodium ion, potassium ion, chloride ion, calcium ion, magnesium ion, lactate ion, and dextrose. For example, such ions can be components in fluid compositions comprising potassium chloride, sodium chloride, Ringer's lactate, and dextrose. Preferably, the method comprises sensing the fluid to identify potassium chloride, potassium ion or chloride ion.

[00040] The first, second, third, fourth, fifth, sixth, seventh, eighth and ninth general embodiments of the third aspect of the invention can be effected in combination with each other. The first, second, third, fourth, fifth, sixth, seventh, eighth and ninth general embodiments of the third aspect of the invention can be effected and/or used as well with each general embodiment of the first and second aspects of the invention. Various specific subembodiments of each general embodiments of the third aspect of the invention are also applicable with specific subembodiments of general embodiments of the first and second aspects of the invention.

[00041] Various embodiments of the invention as described above and hereinafter include listings of groups of alternatives (e.g, Markush groups); in each case, any such listing is intended to disclose each such member of the group collectively as well as individually.

[00042] Various features of the invention, including features defining each of the various aspects of the invention, including general and preferred embodiments thereof, can be used in various combinations and permutations with other features of the invention. Features and advantages are described herein, and will be apparent from the Drawings and the following Detailed Description.

BRIEF DESCRIPTION OF DRAWINGS

[00043] **Figure 1(A-C)** illustrate schematic representations of intravenous fluid delivery systems, including a contextual schematic illustration showing general features (Fig. 1A), and more detailed schematic illustrations showing further features thereof (Fig. 1B, Fig. 1C).

[00044] **Figure 2** illustrates a schematic representation of an embodiment of an apparatus comprising a sensor element having a sensing surface integrated into an in-line housing adapted for fluidic interface with a fluid line assembly.

[00045] **Figure 3(A-C)** illustrate schematic representations of an embodiment of an apparatus comprising a sensor element having a sensing surface integrated into an intravenous infusion device (e.g., catheter) adapted for fluid communication with fluid line assembly, including a perspective view (Fig. 3A), side cut-away elevation (Fig. 3B), and detail of the sensor element containing portion thereof (Fig. 3C).

[00046] **Figure 4** illustrates a schematic representation of a multi-parametric approach for identifying one or more components of the intravenous fluid.

[00047] **Figure 5(A-E)** illustrate schematic representations of various circuits associated with sensors of various aspects and embodiments of the inventions, including independently: a block diagram of a specific preferred circuit configuration (Fig. 5A); a high-level schematic diagram showing a sensor element configured in an assembly such as a housing assembly, and various circuits being configured in an assembly such as housing assembly, and/or in a local processor and/or in a remote processor (Fig. 5B); and additional high-level schematic diagrams showing alternative configurations for a system comprising (i) a (one or more) sensor element, (ii) a signal-conditioning processor, including one or more circuits adapted for conditioning (e.g, amplifying) a signal, and (iii) a signal-identification processor, including one or more circuits adapted for identifying or determining a signal representative of the identity of one or more components of an intravenous fluid (e.g. as corresponding to a component within a composition or concentration of a component within a composition) (Fig. 5C through 5E).

[00048] **Figure 6 (A-G)** illustrate schematic representations of various sensors, including an optic fiber refractive index sensor (Fig. 6A), an electrochemical potential sensor (Fig. 6B), and various schematic views of an integrated assembly comprising impedance and refractive index sensor elements (Fig. 6C through Fig. 6G), including a perspective view of the integrated sensor element assembly (Fig. 6C), a top-plan view of a first surface of a first substrate thereof (Fig. 6D), a detail of the sensing surfaces of the impedance sensor elements as shown therein (Fig. 6E), a perspective assembly view of the first substrate and a second substrate, shown with a functional communication port, such as a USB port (Fig. 6F), and a perspective view of the (assembled) integrated assembly of impedance / refractive index sensor elements (Fig. 6G).

[00049] **Figure 7 (A-D)** illustrate various data derived from Example 2, including plots of measurements of admittance, real portion (Fig. 7A), admittance, imaginary portion (Fig. 7B), optical refractive index (Fig. 7C), and a multi-parametric representation of such measurements (Fig. 7D).

[00050] **Figure 8 (A-D)** illustrate various data derived from Example 3, including plots of measurements of admittance, real portion (Fig. 8A), admittance, imaginary portion (Fig. 8B), optical refractive index (Fig. 8C), and a multi-parametric representation of such measurements (Fig. 8D).

[00051] **Figure 9 (A-B)** illustrate various data derived from Example 4, including plots of measurements of out-of-phase current (y-axis) and in-phase current (x-axis) for injections of potassium chloride (KCl) and magnesium sulfate ($MgSO_4$) (Fig 9A), as well as for subsequent injections with water.

[00052] Various aspects of the figures are described in further detail below, in connection with the Detailed Description of the Invention.

DETAILED DESCRIPTION OF INVENTION

[00053] The present inventions provide apparatus, systems and methods related to intravenous fluid administration. The apparatus, systems and methods of the invention are more specifically related to monitoring of intravenous fluids during administration to a subject.

[00054] Generally, as summarized above and described in further detail below, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject. Preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more active pharmaceutical agents within an intravenous fluid during

administration of the fluid to a subject. Other components can also be detected, especially components relevant to hydration and/or ion metastasis (e.g., electrolyte balance) and/or vasculature pressure of patients. The one or more components of an intravenous fluid can preferably be identified during administration of the fluid to a subject using a multi-parametric approach. Many specific sensors known in the art can be used in connection with the various aspects and embodiments of the invention. Preferred sensors include one or more sensors selected from an impedance sensor (e.g, an AC impedance spectroscopy sensor), an electrochemical sensor (e.g., an electrochemical potential sensor), a thermal sensor (e.g., a thermal anemometer sensor), an optical sensor (e.g., a refractometry sensor, a transmission sensor, an absorbance sensor, a spectrometer (including a colorimeter), a turbidity sensor), a rheological sensor (e.g.,a viscometer), an electrical property sensor (e.g., a capacitor sensor, a pH sensor, a conductivity sensor, and an inductive sensor), and a fluid-displacing or fluid-shearing (e.g, resonator) sensor. Preferably, a system comprises two or more sensors, for example an integrated assembly comprising two or more sensor elements, each comprising one or more sensing surfaces (e.g, an impedance sensor and an optical (e.g, refractive index) sensor). Preferably, a sensor having a sensor element (e.g., with a sensing surface adapted for interaction with and being responsive to the intravenous fluid) is positioned such that the sensor element (e.g., the sensing surface) within an intravenous fluid system such that it interacts with the fluid (e.g, such sensing surface contacts the fluid) in relative proximity to the infusion location – the location at which the fluid enters a subject's vasculature system, e.g., proximal to the distal end of the fluid line assembly or proximal to the intravenous infusion device. Preferably, the apparatus, systems and method of the invention provide for the subject being positively and specifically identified in connection with monitoring and administration of the intravenous fluid; hence, for example, the sensor (or apparatus or system comprising a sensor) can include an identifier circuit for correlating sensor data to a specific subject. Preferably, the systems are effected with a remote and/or centralized monitoring approach. For example, different sensor data from one subject or from several different subjects (in each case, such sensor data being locally generated and specifically associated with an intravenous fluid being administered to a particular subject) can be acquired and/or monitored at a location which is remote (relative to the patient) – such as a nursing station; preferably such sensor data can be centrally monitored at such remote location. For example and without limitation, monitoring can be visual by human interaction with a display and/or can be further enhanced and effected by various automated approaches, including automated approaches involving notice to caregivers (alarms, emails, text message) and/or specific corrective or subsequently prescribed

actions within the system. In preferred embodiments of various aspects of the invention, the sensor can comprise a processor which is physically separable from, and conversely, intermittently interfaceable with a sensor element Such temporally-limited engagement (interfacement) of processor and sensor element allows for an operational period (while engaged / interfaced) and a non-operational period (with physical separation of sensor element from the processor). The non-operational period can allow for sterilizing the sensor element (or a sensing surface thereof) or for disposal and replacement of a (pre-)sterilized sensor element (or a sensing surface thereof). The processor can be re-used, for example, in connection with a second subject, either in the same location (a later subject) or in a different location (e.g., multiplexing the same processor over various subjects). In preferred embodiments of various aspects of the invention, the sensor can comprise: an assembly comprising one or more sensor elements; a signal-conditioning processor, including one or more circuits adapted for conditioning (e.g, amplifying) a signal; and a signal-identification processor, including one or more circuits adapted for identifying or determining a signal representative of the identity of one or more components of an intravenous fluid. The various aforementioned attributes and features of the inventions can be used in each of the various possible combinations and permutations with each other, as applicable.

[00055] As described herein and in further detail below, the various inventions offer intravenous fluid monitoring approaches which are significantly advantaged over known systems, including for example by providing near real-time monitoring of the identity of one or more components of an intravenous fluid (e.g., the presence or absence of a component, the composition of a component, the concentration of a component, the time of infusion (absolute time or relative time versus other components), the onset of component delivery; the completion of component infusion, the cumulative dosing level (e.g., current or projected) of a component being delivered, etc.). Such near real-time monitoring of intravenous fluids reduces the potential for errors associated with intravenous administration, and especially intravenous drug administration. Hence, the apparatus, systems and methods of the invention provide substantial advances in patient safety. Such advances in safety can translate to a more meaningful patient treatment experience, and to enhanced operational efficiencies and reduced expenses for hospitals and other entities which administer fluids intravenously. Such inventions can applied, and such advantages can be realized in a number of various settings and applications in which intravenous fluids are administered, including for example, without limitation, at hospitals, clinics, surgical centers, homes (e.g., home hospice), nursing homes, assisted living environments, etc.

Intravenous Fluid Delivery Systems

[00056] Generally, an intravenous fluid delivery system of the invention can include various systems known in the art or later developed which provide for delivery of fluids to the vasculature system of a subject in need thereof. Generally, such systems can be intermittent or continuous (e.g., including intravenous drip systems). With reference to **Figures 1A through 1C**, in operation intravenous fluid delivery systems generally comprise an intravenous fluid source 100 in fluid communication with an intravenous infusion device 300 through a fluid line assembly 200. The intravenous infusion device 300 is adapted for infusion of fluid into the vasculature system (e.g., a vein) of a subject 10. With further reference to Figure 2 and Figures 3A through 3C, the intravenous fluid delivery systems of the invention can comprise a sensor 500 comprising one or more sensor elements 502 having a sensing surface 504. The sensing surface 504 can be in communication (e.g., electrical communication via electrical connector 506) to one or more contacts 508).

[00057] Various intravenous fluid delivery system configurations can be employed, and various such intravenous infusion devices can be employed. For example, the intravenous fluid delivery system can be configured for peripheral intravenous infusion, for central intravenous infusion, or for peripherally-inserted central intravenous infusion. The system can be adapted for various infusion profiles and approaches; for example, infusion can be rapid, can be drip, can be continuous or can be intermittent.

[00058] Various suitable intravenous infusion device can be used in connection with the invention. Preferably, as shown in the **Figures 1A through 1C**, such intravenous infusion devices 300 can be integrated with or in fluid communication with a fluid line assembly 200 and/or a fluid source 100. Generally, and with reference to **Figures 3A through 3C**, such an intravenous infusion device 300 (e.g, a catheter) can comprise a first end 310 adapted for fluid communication with a fluid line assembly, a second distal end 320 adapted for insertion through the skin into the vasculature system of the subject, preferably through a peripheral vein, and a housing 330 (e.g, a catheter hub), providing excorporal structural support and having a cavity 340 providing fluid communication between the first end 310 and the second distal end 320 of the infusion device. The intravenous infusion device 300 can also include a support element 390 (e.g, such as adhesive wings) for supporting the device 300 during administration of fluid to a subject. Other intravenous infusion devices can also be used in connection with aspects and embodiments of the inventions. Such devices can include for example an integrated fluid source - for example, a needle-type infusion device (e.g, comprising a syringe a needle in fluid

communication with the syringe). Such devices can also include ported cannulae having an injection port on a first end and a second distal end adapted for insertion through the skin into the vasculature system of the subject. The intravenous infusion device can also include an implantable infusion device such as an implantable port. The port can be, for example, a central venous line comprising a cavity covered with a pliable sealant as a cavity cover (e.g, silicone rubber) and adapted for being implanted under the skin. A fluid can be administered through such implantable port intermittently by placing a small needle or catheter through the skin, piercing the silicone, and administering the fluid into the cavity. The cavity cover can reseal after withdrawal of the needle or catheter.

[00059] Other system components can include, for example in a typical intravenous fluid delivery system, one or more sterile containers (glass bottle, plastic bottle or plastic bag) adapted for containing (or pre-filled to contain) fluids, typically configured with an attached drip chamber. The system can comprise a fluid line assembly comprising one or more conduit sections (e.g, each conduit for example comprising a long sterile tube), optionally configured with a clamp to regulate or stop the flow, various connectors, one or more infusion pumps, adapted for providing control over the flow rate and total amount of fluid delivered.

Pharmaceutical Agents, Other Components and Preferred Sensors

[00060] Generally, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject. The intravenous fluid is not narrowly critical and can be of various types, including generally for example crystalloid solutions and colloid solutions. Crystalloid solutions can comprise aqueous solutions of mineral salts or other water-soluble molecules, including active pharmaceutical agents. Colloids can comprise larger semi-soluble or insoluble molecules, including active pharmaceutical agents. Generally, the intravenous fluids are sterile fluids.

[00061] Preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more active pharmaceutical agents within an intravenous fluid during administration of the fluid to a subject. Such active pharmaceutical agents can include, for example, an anticoagulant (e.g., heparin), a metabolically-active hormone (e.g, insulin), an anesthetic (e.g., propofol), and/or an analgesic (e.g., morphine), among others. Various one or more sensors are configured for sensing a property of a fluid which can be correlated to identify an active pharmaceutical agent component of the fluid. For example, the sensor can comprise one or more sensor elements having a sensing surface positioned for contact with the fluid, and

one or more circuits in communication with the sensor element for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element. The sensor can be configured to distinguishably detect one or more active pharmaceutical agents. Preferably, the sensor is configured to identify one or more active pharmaceutical agents selected from the group consisting of an anticoagulant (e.g., heparin), a metabolically-active hormone (e.g, insulin), an anesthetic (e.g., propofol), and an analgesic (e.g., morphine).

[00062] Additionally or alternatively, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more other components of an intravenous fluid, preferably components used for hydration and ion metastasis of subjects. Such components can preferably include, for example one or more components selected from potassium chloride, sodium chloride, Ringer's lactate, and dextrose, in each case in molecular or ionic (e.g, dissociated) form (e.g, sodium ion, potassium ion, chloride ion, calcium ion, lactate ion, and dextrose). The sensor can comprise a sensor element having a sensing surface positioned for contact with the fluid, and one or more circuits in communication with the sensor element for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element. The sensor can be configured to distinguishably detect one or more components of the fluid. Preferably, the sensor is configured to identify one or more components of the fluid selected from the group consisting of a metal ion, halide ion, organic ion or salts, and a sugar, preferably for example sodium ion, potassium ion, chloride ion, calcium ion, magnesium ion, lactate ion, and dextrose. For example, such ions can be components in fluid compositions comprising potassium chloride, sodium chloride, Ringer's lactate, and dextrose. Preferably, the method comprises sensing the fluid to identify potassium chloride, potassium ion or chloride ion.

[00063] Typical intravenous fluids can comprise normal saline, preferably for example a solution of sodium chloride at 0.9% concentration, which is close to the concentration in the blood (isotonic). The intravenous fluid can comprise Ringer's lactate or Ringer's acetate, another isotonic solution. In some instances, the intravenous fluid can comprise a sugar such as dextrose, for example a solution of 5% dextrose in water, sometimes referred to as D5W. The selection of a particular carrier fluid may also depend on the chemical properties of the active pharmaceutical agents being administered.

[00064] Table I shows compositions of common intravenous fluids used in connection with intravenous fluid delivery systems.

Table I: Composition of Intravenous Fliud Solutions

Solution	Other Name	[Na^+] (mmol/L)	[Cl^-] (mmol/L)	[Glucose] (mmol/L)	[Glucose] (mg/dl)
D5W	5% Dextrose	0	0	278	5000
2/3D & 1/3S	3.3% Dextrose / 0.3% saline	51	51	185	3333
Half-normal saline	0.45% NaCl	77	77	0	0
Normal saline	0.9% NaCl	154	154	0	0
Ringer's lactate	Lactated Ringer	130	109	0	0

Ringer's lactate also typically can have , for example and without limitation 28 mmol/L lactate, 4 mmol/L K+ and 3 mmol/L Ca2+.

[00065] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject using one or more sensors. The one or more sensors are preferably selected to include at least one sensor other than a flow sensor, and/or in some embodiments also preferably other than a pressure sensor, and/or in some embodiments also preferably other than an ultrasonic sensor. Generally for example, preferred sensors effective with the apparatus, systems and methods of the invention can include, without limitation, one or more sensors selected from an impedance sensor (e.g, an AC impedance spectroscopy sensor), an electrochemical sensor (e.g., an electrochemical potential sensor), a thermal sensor (e.g., a thermal anemometer sensor), an optical sensor (e.g., a refractometry sensor, a transmission sensor, an absorbance sensor, a spectrometer (including a colorimeter)r, a turbidity sensor), a rheological sensor (e.g.,a viscometer), an electrical property sensor (e.g., a capacitor sensor, a pH sensor, a conductivity sensor, and an inductive sensor), and a fluid-displacing (e.g, resonator) sensor. The various specific sensors and sensing approaches as described herein are preferred, an can be generally used with any aspects, embodiments and approaches described herein; however, many aspects, embodiments and approaches of the

invention do not require such certain specific sensors or sensing techniques and can be effected independently thereof.

[00066] Generally, the sensor can be adapted for identifying an anticoagulant, preferably heparin. Preferably the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and ultraviolet absorption, and for identifying an anticoagulant, preferably heparin, based on the one or more determined properties.

[00067] Generally, the sensor can be adapted for identifying a metabolically-active hormone, preferably insulin. Preferably, the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and visible absorption (color), and for identifying a metabolically-active hormone, preferably insulin, based on the one or more determined properties.

[00068] Generally, the sensor can be adapted for identifying an anesthetic, preferably propofol. Preferably, the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and visible absorption (color), and for identifying an anesthetic, preferably propofol, based on the one or more determined properties.

[00069] Generally, the sensor can be adapted for identifying an analgesic, preferably morphine. The invention of claim 80 wherein the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and ultraviolet absorption, and for identifying an analgesic, preferably morphine, based on the one or more determined properties.

[00070] Generally, the sensor can be adapted for identifying one or more components selected from the group consisting of a metal ion, a halide ion, an organic ion or salt, and a sugar.

[00071] Generally, the sensor can be adapted for identifying potassium chloride, potassium ion or chloride ion. Preferably, the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and ultraviolet absorption, and for identifying potassium chloride, potassium ion or chloride ion based on the one or more determined properties.

[00072] Generally, in each of the above preferred embodiments, the sensor can be adapted for determining two or more properties of the fluid, and for identifying the one or more active pharmaceutical agents based on the two or more determined properties.

[00073] Preferred sensors and fluid properties for sensing various active pharmaceutical agents (e.g. drug formulations) and other components are shown in Table 2.

Table 2: Preferred Fluid Properties and Sensors for Various Fluid Components

Fluid Property	Sensor Approach	Example Reference
Complex conductivity or admittance	AC impedance spectroscopy	(1)
Ionic properties	Electrochemical potential	(2)
Thermal properties	Pulsed thermal anemometry,	(3)
Index of refraction	Refractometer, fiber optic refractometer	(4)
Optical absorption	Optical absorption spectrometry	(5)
Color	Spectrometer, colorimeter	(6)
Viscosity	Viscometer, resonator	(7)
Density	Viscometer, resonator	(8)
Dielectric constant	Capacitor, resonator	(9)
Turbidity	Turbidity sensor	(10)
Permeability	Chemical sensors with selective membranes	(11)
Ph	Ph meter, MEMS Ph sensor, chemical color change sensor, litmus (e.g., paper)	(12)
Conductivity	DC and or AC conductance	(13)
Air bubbles	Optical	(14)
Surface plasmon effects	Surface Plasmon sensor	(15)
Thermal lensing	Optical detection of refractive index change	(16)
Sono-luminescence spectroscopy	Colorimetric and spectral detection of species	(17)
Flow rate	Thermal anemometer, Doppler flow meter	(18)

[00074] Generally, such sensor approaches and fluid-property measurements as shown in Table 2 can be effective for identification of one or more active pharmaceutical agents, or an intravenous solution component (e.g., saline, potassium chloride, dextrose, etc), in each case within an intravenous fluid during administration of the fluid to a subject. Chemical sensors with selective membranes can differentiate fluid permeability and be useful for example for identifying specific compounds selectively (e.g, based on selection of a particular membrane). Optical detection of air bubbles, can be effective for example for preventing an air embolism, and additionally or alternatively, for detecting flow system failures (and thereby helping to maintain flow). Measurement of flow rate by thermal anemometer and/or by Doppler flow meter can be effective, for example, for detecting blockages, controlling flow rate, determining dosing and detecting flow system failures (and thereby helping to maintain flow).

[00075] Without limitation, and without being bound by theory not expressly recited in the claims, the following references are representative examples of the sensor approach and/or the fluid property measurement as shown in Table 2:

(1) Impedance based flow sensors Green, N. G., Tao, S., Holmes, D. and Morgan, H. (2005) Impedance based flow sensors. In: Microtechnologies for the New Millennium 2005 SPIE, 9-11th May 2005.

(2) http://www.resonancepub.com/electrochem.htm

(3) A pulsed-wire technique for velocity and temperature measurements in natural convection flows; Journal Experiments in Fluids; Publisher: Springer Berlin / Heidelberg; ISSN 0723-4864 (Print) 1432-1114 (Online) Issue Volume 18, Numbers 1-2 / December, 1994

(4) Refractive Index Measurement and its Applications; Shyam Singh 2002 Phys. Scr. 65 167-180 doi: 10.1238/Physica.Regular.065a00167

(5) http://www.doas-bremen.de/paper/spec_euro_06_richter.pdf

(6)http://www.optek.com/Application_Note/General/English/7/Inline_Process_Color_Measurement.asp

(7) http://www.coleparmer.com/techinfo/techinfo.asp?htmlfile=why-meas-viscosity.htm&ID=933

(8) Simultaneous Measurements at U-tube Density Sensors in Fundamental and Harmonic Oscillation; Krasser, E.; Senn, H.; EUROCON, 2007. The International Conference on "Computer as a Tool"; Volume , Issue , 9-12 Sept. 2007 Page(s):551 – 555

(9) www.tmworld.com/contents/pdf/tmw03_05D1_jr.doc

(10) http://www.omega.fr/techref/ph-6.html

(11) A new method for the determination of membrane permeability by spatially resolved concentration measurements; Bernd Schirmer et al 2004 Meas. Sci. Technol. 15 195-202 doi: 10.1088/0957-0233/15/1/027

(12) http://www.sensorland.com/HowPage037.html

(13) Sensor for measuring surface fluid conductivity in vivo; Fouke, J.M.; Wolin, A.D.; Saunders, K.G.; Neuman, M.R.; McFadden, E.R., Jr. Biomedical Engineering, IEEE Transactions Volume 35, Issue 10, Oct. 1988 Page(s):877 – 881

(14)http://www.us.endress.com/eh/sc/america/us/en/home.nsf/imgref/D7A94F680B2EA516C12573A8007833A6/$FILE/TI921C-OUSAF13.pdf

(15) Surface Plasmon Resonance Based Sensors; Springer Series on Chemical Sensors and Biosensors , Vol. 4 Homola, Jirí (Ed.) 2006, XII, 251 p. 134 illus. Hardcover ISBN: 978-3-540-33918-2

(16) Flowing thermal lens micro-flow velocimeter; Yoshikuni Kikutania, b, Kazuma Mawataria, b, Kenji Katayamaa, b, Manabu Tokeshia, b, c, Takashi Fukuzawac, d, Mitsuo Kitaokab and Takehiko Kitamor; Sensors and Actuators B; Chemical; Volume 133, Issue 1, 28 July 2008, Pages 91-96

(17) Malcolm J. Crocker, Handbook of Acoustics, Ch. 4, 1998

(18) A thermoelectric sensor for fluid flow measurement. principles, calibration and solution for self temperature compensation; H. Stachowiaka, S. Lassuea, A. Dubernarda and E. Gaviotb; Flow Measurement and Instrumentation; Volume 9, Issue 3, September 1998, Pages 135-141.

[00076] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject using a sensor having a sensor element (e.g., with a sensing surface adapted for interaction with and being responsive to the intravenous fluid), where such sensor element (e.g., such sensing surface) is positioned at a location within an intravenous fluid system such that it interacts with the fluid (e.g, such sensing surface contacts the fluid) in relative proximity to the infusion location – the location at which the fluid enters a subject's vasculature system.

[00077] In various embodiments of various aspects of the invention, therefore, the apparatus, systems and methods of the invention comprise a sensor element (e.g., having a sensor surface) positioned proximal to (e.g, at or near) the distal end of a fluid line assembly, and/or proximal to an infusion device. For example, with reference to **Figures 1A through 1C** and to **Figure 2**, such a sensor 500 can comprise a sensor element 502 which can include a sensing surface 504 in a cavity 540 of an in-line housing 530, where the in-line housing optionally has inlet 510 and outlet 520, each configured with fittings 212 (e.g., Luer Locks), and

can be integrated into the fluid line assembly upstream of an infusion device 300. Alternatively, for example, and with reference to **Figure 3A through 3C**, such a sensor element 502 can include a sensing surface 504 in a cavity of a housing (hub 330) defined in infusion device 300 (e.g., catheter, needle, etc.). Preferably, with further reference to **Figures 3A through 3C**, the sensor element can be integrated into an intravenous infusion device such as a catheter. In exemplary embodiments, for example, the infusion device can have a first end adapted for fluid communication with a fluid line assembly, a second distal end adapted for insertion through the skin into the vasculature system of the subject, preferably through a peripheral vein, and a housing (e.g., the hub of a catheter) providing excorporal structural support and having a cavity providing fluid communication between the first end and the second distal end of the intravenous infusion device. For example, such housing can be integral with the hub of a catheter. One or more sensor elements can each have a sensing surface positioned within the cavity for contact with the fluid.

[00078] Optionally, in some embodiments, the apparatus, systems and methods of the invention can comprise one or more first sensor elements positioned proximal to the distal end of a fluid line assembly, and/or proximal to an infusion device, at least one injection port (including for example fluid line from an intravenous pump subsystem) upstream of such first sensor elements, and one or more additional second sensor elements positioned upstream of such injection port – facilitating for example a differential measurement approach. Significantly, such second sensor element(s) can be configured to detect a baseline intravenous fluid (e.g, saline or Ringer's lactate), thereby providing a basis to compensate measurements made with the first sensor element(s) for the baseline signal, as well as for any background signal noises associated with the baseline fluid. Such a configuration can improve overall sensor sensitivity, and can thereby enable measurement and identification of components in more complex intravenous compositions. The second upstream sensors can be positioned in the intravenous fluid source container or proximal thereto, for example in a fluid line proximal to an intravenous fluid source container.

[00079] Generally, the sensors of the invention can be used in combination with one or more additional sensors, including without limitation sensors such as thermal (e.g, temperature) sensors and/or flow sensors. For examples, a thermal (e.g., temperature) sensor can include a resistance temperature detector (RTD) configured as known in the art. For example, flow sensors can include a set of two or more physically separated sensor elements, which can determine flow based on detection of a specific component at each sensor element over a

measured period of time. Other known approaches for flow sensor(s) can also be effected. For example, flow sensors based on Doppler flow measurement, thermo-annemometer measurement, electro anemometer measurement and/or acoustic anemometer measurement can be effected in combination with sensors of the invention.

[00080] Generally, the one or more sensor elements can be activated using an activation circuit. The activation signal is not narrowly critical, and can comprise for example a sinusoidal or non-sinusoidal (e.g., square wave) activation signal (e.g., a voltage or current). In each case, the activation signal provided to the sensor element(s) can have a varying amplitude, a varying frequency and/or can be a pulsed signal. Non-steady or modulated wave forms, such as amplitude modulated (AM) or frequency modulated (FM) or pulse modulated (PM), or a combination of any of the foregoing can be employed. In some embodiments, the activation signal can include an alternating current (AC) signal, and can optionally further include a direct current (DC) bias signal. Such a DC bias signal can be varied during measurement of a fluid property or condition. In some embodiments, multiple frequencies can be applied and detected, serially or in some cases, simultaneously applied and detected. In some embodiments, one or more sensor elements can be activated with a broad-band "white noise" excitation signal having a wide range of continuous frequencies.. Such an approach allows for detection of differences from such continuous frequencies. Other activation / excitation approaches are known in the art.

[00081] Generally, one or more sensor elements activated with an activation signal in the presence of a intravenous fluid can generate a response signal which is dependent upon or influenced by the composition of such intravenous fluid. The response signal can be conditioned (e.g, amplified, biased, etc.) for example in a (local or remote) signal conditioning processor (e.g, comprising one or more signal processing circuits), and can be optionally transmitted to a (remote or local) signal identification processor. Calibration signals can be developed and provided corresponding to known pharmaceuticals or other fluid components, or to a baseline intravenous fluid (e.g, saline or Ringers' lactate) to aid in identification of a component of an intravenous fluid. One or more identifier circuits can be effected to correlate a measured signal to a specific patient or a specific device. One or more monitoring circuits can be effected to provide for communication to a human through a user interface, and/or for comparative monitoring (e.g, against a selected setpoint). Other circuits and processors can be used, as described in further detail throughout this specification and/or as otherwise known in the art.

Multi-Parametric Approaches

[00082] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject using a multi-parametric approach. In such approach, multiple parameters (e.g, multiple fluid properties such as without limitation refractive index, electrochemical potential, impedance, admittance, conductivity, etc.) can be sensed, and the combination of parameters can be correlated to obtain resolution of components within the fluid. Hence, an intravenous fluid can be sensed – for example with multiple sensors (or with a sensor having multiple sensor elements) and/or with multiplexing of a sensor element to obtain independent sensing measurements – to generate a multi-parametric profile characteristic of component identity within the fluid. A multi-parametric profile can be correlated to determine an identity of one or more components of the fluid. Such multi-parametric approaches advantageously provide for improved resolution of components; therefore such approaches allow for improved ability to distinguish between different fluid compositions, including for example the presence or absence of particular active pharmaceuticals, and/or various concentrations of a particular active pharmaceutical or other component.

[00083] With further reference to **Figure 4**, for example, a sensor can comprise two or more sensor elements 502, each having a surface positioned within a cavity (e.g, 540, 340) of a housing (e.g., 530, 330) for contact with the fluid. The housing can be adapted for fluidic interface with a fluid line assembly of a system for intravenous delivery of fluid into a patient, or can be defined in an intravenous infusion device. As shown in **Figure 4**, each of the sensor elements can be passively monitored, and/or can be activated using an activating circuit, and the response of each of the sensor elements can be acquired and processed in a processor circuit. The various responses can be correlated to identify a characteristic profile of the one or more components in the fluid. See for example, Examples 2, 3 and 4.

[00084] Generally therefore, and with further reference to **Figure 4**, in preferred embodiments the apparatus, systems and methods of the invention comprise or use at least two or more sensors or an integrated assembly comprising two or more sensors (e.g., an integrated assembly comprising two or more sensor elements, each sensor element comprising one or more sensing surfaces). Preferably, such two or more sensors are of different types and/or having different sensor approaches (e.g., impedance sensor, thermal sensor, electrical property sensor, optical sensor, etc.) thereby enabling for orthogonal fluid property measurements. As a non-limiting example, such two or more sensors can include two or more of an impedance

sensor (e.g, an AC impedance spectroscopy sensor), a thermal sensor, and/or an optical sensor (e.g., a refractometry sensor, a transmission sensor, an absorbance sensor, a spectrometer (including a colorimeter) or, a turbidity sensor). Preferably, such two or more sensors can be integrated into a common assembly, such as a common substrate, e.g., as part of a common sensor subunit, as discussed below in connection with Fig. 6C through Fig. 6G. As a non-limiting example, two or more of an impedance (e.g., AC impedance) sensor, a thermal (e.g, an resistance thermal detector) sensor, and an optical (e.g, refractive index) sensor can be employed in combination.

[00085] In a preferred embodiment, at least one sensor is an electrical properties sensor such as an impedance sensor. Independent electrical property (e.g., impedance) measurements can be derived, for example, from a set of two or more sensor elements having sensing surfaces defined by electrodes consisting essentially of different metal materials. Preferred metals include noble metals and other chemically inert transition metals, such as without limitation, Au, Pt, Pd, Ag, W, Ti, Ni, Sn, Co and others. Electrical property measurements such as impedance measurements can preferably be effected using different pair combinations of three or more sensor elements. For example, for a sensor comprising sensor elements A, B and C, three pairs of sensor elements can be used: an A-B pair, an A-C pair, and a B-C pair, with each of such pairs defining an independent impedance measurement channel. As another example, for a sensor comprising five sensor elements A, B, C, D and E, such five sensor elements can be paired to define ten independent impedance measurement channels: A-B, A-C, A-D, A-E, B-C, B-D, B-E, C-D, C-E, and D-E. Such impedance sensor elements can be activated using alternating current (AC), allowing for determination of both real and imaginary (complex) impedance response for each pair of sensor elements. Hence, three sensor elements can provide for six independent measurement channels at each applied AC frequency for determining the identity of a component of the intravenous fluid. Generally, the number of discrete independent impedance sensor elements can range from 2 to 100, from 2 to 50, from 2 to 20 or from 2 to 10. Pairs of sensor elements can be activated using multiple (different) frequencies. If five frequencies are used for activating an impedance sensor comprising three sensor elements, for example, then the impedance sensor effectively provides for thirty independent measurement channels for determining the identity of a component of the intravenous fluid (three sensor elements -> three channels x real and imaginary components → two channels = six channels per frequency x five frequencies → thirty channels). Generally, the number of discrete independent frequencies can range from 1 to 100, preferably from 2 to 100, from 2 to 50, from 2 to 20, from 2 to 10 or from 2 to five or from 2 to 3. Similarly, pairs of sensor

elements can be activated at multiple (different) amplitudes, with a similar multiplier effect on multi-modal measurements. Generally, the number of discrete independent amplitudes can range from 1 to 100, preferably from 2 to 100, from 2 to 50, from 2 to 20, from 2 to 10 or from 2 to five or from 2 to 3. Further variations, such as use of different input signals – sinusoidal, step-wave, pulse, etc. – can provided for additional independent channels in a multiparametric context.

[00086] Analogous multiplexing can be effected with other sensors types (e.g., optical, electrochemical potential, etc.).

[00087] Processing of the signal acquired from each of a plurality of sensors can be effected in a signal identification processor. Such processor can comprise signal conditioning circuits for conditioning one or more signals (e.g., for amplifying, biasing) prior to or during further processing. Such processor can employ software or firmware or can include an application specific integrated circuit (ASIC) effective for and/or adapted to recognize and distinguish between signals correlating to components of an intravenous fluid. Such software can comprise pattern recognition algorithms known in the art. In one relatively simple algorithm, for example, sensor signals can be processed to recognize the identity of component substances by measuring produced deviations – e.g., in various directions by supplying the values for the expected angles. See for example, Example 4. *See* also for example, J. Ross Macdonald, Impedance Spectroscopy Theory, Experiment, and Applications (2005).

[00088] For example, in embodiments where a set of two or more sensor elements having sensing surfaces defined by metal electrodes are exposed to a fluid, and activated by energizing with an AC voltage or current, the resulting complex current or voltage can be. measured. When the activating signal is sufficiently small, the system can respond linearly, and may be modeled in terms of complex AC impedance or admittance, e.g. having real (x) and imaginary (y) response components. The measured values of x and y as well as their relative magnitude change predominantly with the electrical properties of the fluid flow and fluid-electrode interface, both of which are heavily affected by the composition of the flow. The change in these values can be correlated to the nature of the fluid material and can be used to identify the particular component of the intravenous fluid. As demonstrated in Example 4, for example, highly diluted components injected into saline flow can be identified by such sensors. Generally, a deviation distance from a data point corresponding to pure saline or Ringer's lactate depends on both concentration and molecular or ionic composition of the component, while deviation direction from such data point depends predominantly on the molecular or ionic

composition of the component. For higher concentrations of the component, both magnitude and direction of the deviation become concentration-dependent in unique and distinguishable manner which is specific to and dependent upon the particular component added to the saline. Hence, such deviation dependencies enable identification of components having different compositions or concentrations. For example, pattern recognition algorithms can be adapted to recognize substances that are components of an intravenous fluid. A data signal from sensors can result in deviations from baseline data corresponding to the background composition of the intravenous fluid (e.g, saline or Ringer's lactate), including deviations in magnitudes and/or deviations in directions, the angles for each of which can be determined as described above and exemplified in Example 4. In subsequent operation, such software can compare measured angles determined from detected data with the values for expected angles corresponding to certain substances, thereby identifying the substances. Such pattern recognition algorithms can be advantageously applied to the differentiation and recognition of data generated by the sensors in multi-dimensional space. Additionally, software can be used to determine the cumulative dosing of a component of a fluid, as well as a projected dosing over a certain upcoming period of time. For example and without limitation, once a component is identified, a current cumulative dosing level can be measured by integrating the signal corresponding to that component over time during the period defined from when the signal exceeded a detection threshold to the current time (*e.g.,* taking into account the sensor sensitivity to identified substance and the volumetric flow). Projected dosing levels can extrapolate the component composition and extend the time period for a defined period.

[00089] Adaptations on such algorithms are known in the art. Moreover, more elaborate pattern recognition algorithms can be applied to the differentiation and recognition of curves generated by the multiparametric sensor system in multi-dimensional space. *See,* for example, Sing-Tze Bow, Pattern Recognition and Image Preprocessing (2002); M.S. Nixon, A.S. Aguado, Feature Extraction and Image Processing (2002); and D. Maltoni, D. Maio, A.K. Jain, S. Prabhakar, Handbook of Fingerprint Recognition, 2002. Examples of other pattern recognition software include without limitation artificial neural network and fuzzy logic algorithms.

Preferred Circuit Configurations/ Monitoring Approaches

[00090] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject (e.g., a specific patient, for example at a hospital, clinic, surgical environment, home hospice, nursing home, assisted living environment, etc), where

such subject is positively and specifically identified in connection with monitoring and administration of the intravenous fluid. Various embodiments and aspects of the invention can include approaches for correlating the sensor data (i.e., data (e.g., as represented by a signal) originating from the sensor – either raw data or more typically processed data) to a specific subject (e.g., patient). For example, the sensor (or apparatus or system comprising a sensor) can include an identifier circuit for correlating sensor data to a specific subject. Typically, and preferably, such identifier circuit may be in communication with one or more other circuits, including for example circuits for receiving ,processing, storing, displaying or transmitting data, including data originating from the sensor element, such as a signal processing circuit or a data retrieval circuit. Such integrated patient-identification approaches can further enhance the benefit to patient safety, by reducing the potential for errors associated with intravenous administration, and especially intravenous drug administration.

[00091] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject with a remote and/or centralized monitoring approach. Although such remote and/or centralized monitoring approaches can be effected for an individual subject (e.g, in a home hospice environment), such approaches are especially advantageous in connection with multi-subject care environments. For example, different sensor data from one subject or from several different subjects (in each case, such sensor data being locally generated and specifically associated with an intravenous fluid being administered to a particular subject) can be acquired and/or monitored at a location which is remote (relative to the patient) – such as a nursing station; preferably such sensor data can be centrally monitored at such remote location. In various aspects and embodiments therefore, and with reference to **Figures 1B and 1C, Figure 2,** and **Figures 3A through 3C,** for example sensor data, can be generated in a processor 550 local to and in communication with a sensor element 502 (e.g., having a sensing surface in contact with the intravenous fluid), preferably for each of two or more subjects, and then such locally-generated sensor data stream(s) can be acquired by a processor 600 remote from the sensor element 502. Such acquisition can be effected, for example, via wireless (e.g., Bluetooth ®) or other communication approaches. The local processor 550 can be in communication with the sensor element 502, and particularly with a sensing surface 504 thereof, for example through one or more releasable contacts 508 and one or more electrical connections 506. The local processor 550 can be permanently integrated or intermittently integrated (temporally limited engagement) with the sensing element 502 as described below.

[00092] The remote processor 600 can comprise one or more circuits for receiving, processing, storing, displaying or transmitting the acquired sensor data. The acquired sensor data can be monitored remotely, including for example at a central monitoring location. Preferably for example, the monitoring can be done visually by human interaction with a display and/or can be further enhanced and effected by various automated approaches. In one such automated monitoring approach, a monitoring circuit can comprise a data comparator module for comparing one or more parameters (e.g, data values) derived from sensor data with one or more parameters (e.g., data values) which are prescribed or proscribed for a particular subject (e.g. patient). Such patient-relevant parameters can be treatment-centric (e.g., applicable to all such patients undergoing a particular treatment), including semi-customized treatment-centric parameters which include a patient-specific data input (e.g., a patient weight, patient age, etc.) to determine a treatment-centric parameter, and/or such patient-relevant parameters can be patient-centric (e.g., wholly customized for a specific patient). Exemplary non-limiting parameters can include dosing levels, dosing timing (onset or completion), dosing frequency, etc. for various and specific active pharmaceutical agents or other components of an intravenous fluid. Patient-relevant parameters can be specific for the intravenous monitoring system effected by the apparatus, systems and methods of the invention, and/or can be common with (e.g., shared with) various other systems, such as infusion pump systems (e.g., "smart pumps"). Advantageously, the monitoring approaches of the apparatus, systems and methods of the invention can also include certain notice (e.g., alarm) features – to provide notice to a caregiver that a specific patient's intravenous fluid delivery system is operating incongruous with a prescribed or proscribed treatment, and /or can also include certain corrective action (e.g., system control) features – to make, preferably automated, a corrective action with the intravenous fluid delivery system. For example, upon determining an inconsistency between corresponding sensor-data-derived parameter and prescribed or proscribed patient-relevant parameter, an alarm can sound and /or a control circuit can activate a control element (e.g., an automated infusion valve) to make a change in the intravenous administration regime. Such remote and/or central monitoring approaches can further enhance the benefit to patient safety, by reducing the potential for errors associated with intravenous administration, and especially intravenous drug administration.

[00093] Generally, and preferably, the apparatus, systems and methods of the invention are directed to or effective for identifying one or more components of an intravenous fluid during administration of the fluid to a subject with a sensor that comprises a processor (e.g, as included within a processor assembly) which is physically separable from, and intermittently

interfaceable with (e.g., for a finite, operationally effective period of time) a sensor element (e.g., as included within a housing assembly). The approach of a temporally-limited engagement (interfacement) of the processor and the sensor element allows for regular operation while engaged / interfaced, and allows for physical separation of sensing function and processing function of a sensor (at least for some period of time) after or between operations, with a corresponding separation of physical treatment of the embodiments which effect such function. For example, and with reference to **Figure 1B, Figure 2,** and **Figure 3A through 3C,** the sensor element 502 can be physically separated from the processor 550 for a period of time to allow for sterilizing the sensor element 502 (or a sensing surface 504 thereof) or for disposal and replacement of a (pre-)sterilized sensor element 502 (or a sensing surface 504 thereof). Such separation also allows for re-use of the processor 550 – for example, in connection with a second subsequent subject. The processor 550 can be engaged for example through a processor guide 552. Significantly, since processors 550 are generally more expensive than sensor elements 502 (or sensing surfaces 504 thereof), the re-use of processors 550 in such a temporally-limited engagement (interfacing) approach provides for efficiency of capital investment, especially in a multi-subject (e.g., hospital, surgical, nursing care, etc.) environment.

[00094] In any of the aforementioned approaches and in any of the aspects and embodiments of the invention, the monitoring system can include a logging circuit for recording (e.g., storing) sensor data over time. The logging circuit can be in accessible communication with a display circuit for intermittent (temporally-limited) display of sensor data or of a patient-relevant parameter derived from sensor data. In operation, for example, the logging circuit can record sensor data without displaying such data (or a patient-relevant parameter derived therefrom) unless and until specifically requested (e.g, by a caregiver based on that caregiver's discretion, and/or by another circuit, such as by the comparator module of the monitoring circuit when there is an incongruity between a sensor data parameter and a prescribed or proscribed patient-relevant parameter) to be displayed. Display, such as automated display during an abnormal operational event can help a caregiver understand a situation more quickly and thereby reduce the risk of a compounded error and improve the corrective treatment regime. Additionally or alternatively, such display can be effected *ex-post facto* to reconstruct facts regarding the patient experience based on logged sensor data.

[00095] Various preferred schema for circuit configuration and operation are shown in **Figures 5A and 5B**. With reference to **Figure 5B** illustrated is a high-level schematic diagram showing various circuits and one arrangement for their interrelationship with local processor and

remote processor, and/or with housing assembly and processor assembly. **Figure 5A** illustrates a block diagram of a specific preferred circuit configuration for a reader unit comprising a microcontroller. The circuits of such reader unit can include, for example, one or more of any of an activation circuit, a data retrieval circuit, a signal processing circuit, an identifier circuit, a data acquisition circuit, and/or a monitoring circuit. Preferably, one or more of any such circuits can be adapted into a signal conditioning processor and/or a signal identification processor. Such circuits can be included, for example, in a processor assembly for intermittently interfacing / temporally-limited engagement with a sensor element. Alternatively, some of such circuits could be in a housing assembly – see for example **Figure 5B**. Preferably, with reference again to Figure 5A, the reader unit can be programmed when a patient is admitted for treatment. The reader unit can receive and store the identification information about the patient either through RF interface or through I/O interface from the admitting database information, for example in an identifier circuit. The reader unit can be physically co-located adjacent to or attached to the patients, for example as as a bracelet, or adhesively attached to a patient's skin. Once the identification information is received, and the processor assembly is interfaced with a housing assembly (described herein), the reader unit can commence broadcasting identifier information, for example wirelessly via RF interface such as WiFi or Bluetooth ® interface, continuously or periodically. Alternatively the unit can be connected via direct connection (e.g, electrical wire or optical cable) to a bedside monitoring system, which can itself send patient identification information through I/O interface. Along with patient identification information the unit can also send information regarding the status of the interface between the processor assembly and the housing assembly (e.g., whether engaged (operable) or disengaged (non-operable). Once a patient has received an intravenous line , and when the unit is engaged for operation, through the interface to the sensing unit – the reader can verify the connection, energize or activate the sensors, and sense and transmit data from the sensor element, and preferably from a local processor to a remote processor included within a monitoring unit, for example via any suitable communication approach such as hospital radio frequency port; alternatively the monitoring can be local, such as via bedside monitoring equipment.

[00096] Additional preferred schema for an integrated sensor and circuit configuration are shown in **Figures 5C through 5E**. Generally, such configuration can include a sensor that comprises (i) an assembly comprising one or more sensor elements 502, (ii) a signal-conditioning processor (e.g., optionally included within a local processor 550 (which can, optionally, be physically separable from and/or be intermittently interfaceable with the sensor element 502) or included within a remote processor 600), and (iii) a signal-identification

processor, including one or more circuits adapted for identifying or determining a signal representative of the identity of one or more components of an intravenous fluid (e.g., optionally included within a local processor 550 (which can, optionally, be physically separable from and/or be intermittently interfaceable with the sensor element 502) or included within a remote processor 600). With reference to **Figure 5C** for example, in one such preferred subembodiment, each of the assembly comprising the one or more sensor elements 502, the signal-conditioning processor (550 or 600), and the signal-identification processor (550 or 600) are each physically separate components. In an alternative of such preferred subembodiment, represented schematically in **Figure 5D**, the assembly comprising the one or more sensor elements 502 is physically separate from an integrated assembly comprising the signal-conditioning processor (550 or 600) and the signal-identification processor (550 or 600). In another subembodiment shown in **Figure 5E**, each of the one or more sensor elements 502, the signal-conditioning processor (550 or 600), and the signal-identification processor (550 or 600) are integrated into a common (integrated) assembly. Such various approaches for configuring the sensor elements, the signal-conditioning processor and the signal-identification processor are preferred, an can be generally used with any aspects, embodiments and approaches described herein.

[00097] **Figure 6 (A, B)** illustrate schematic representations of various sensors, including an optic fiber refractive index sensor (Fig. 6A) and an electrical property sensor (e,g., which can be configured and employed, for example, as an impedance sensor or for example, as an electrochemical potential sensor) (Fig. 6B). Such sensors and others described herein are known in the art. Briefly, with reference to **Figure 6A**, an optical sensor can comprise a fiber optic, such as a flexible fiber optic formed in a U-shape, and having an optical entrance 501, a sensor element 502 defined by the curved region of fiber optic exposed to the intravenous fluid, and an optical exit 503 into a detector. In operation, a light can be admitted to the fiber optic, guided to the sensor element 502 and exposed to an intravenous fluid in communication with the sensor element 502. Variations in intensity of the light coupled from the entrance to exit are proportional to the refractive index of the fluid. The index of refraction can be fluid-composition variable, thereby providing a parameter for determining the identity of the fluid composition. *See,* for example, Examples 1, 2 and 3. Referring further to **Figure 6B,** an electrical property sensor (e.g, impedance sensor, electrochemical potential sensor, etc.) can comprise a plurality of sensor elements 502a, 502b, 502c. For example, each of the sensor elements can comprise a sensing surface consisting of a material such as a metal, with the sensing surface of each such sensor element being the same material, or in some embodiments a different material,

such as a different metal. Preferably, metal materials are chemically inert within the fluid environment. Preferred metals include noble metals and other chemically inert transition metals, such as without limitation, Au, Pt, Pd, Ag, W, Ti, Ni, Sn, Co and others. Each of the sensor elements 502a, 502b, 502c are in electrical communication with dedicated corresponding contacts 508a, 508b, 508c, respectively, for example, through dedicated corresponding electrical connectors 506a, 506b, 506c. The sensor elements 502, contacts 508 and electrical connectors 506 can be formed or supported on a common substrate, such as common microfabrication substrate. In operation, the electrical property (e.g, impedance or electrochemical potential) associated with each of the sensor elements 502a, 502b, 502c can be measured independently and simultaneously, proving for three independent real-time channels for multiparametric characterization of a component within an intravenous fluid.

[00098] A preferred sensor embodiment can comprise an integrated assembly comprising two or more sensor elements, such as impedance sensor elements, thermal sensor elements and/or refractive index sensor elements. With reference to **Figure 6C through Figure 6G**, for example, an integrated sensor assembly can comprise one or more substrates, such as a first sensor element substrate 520 and comprising two or more sensor elements. The first sensor element substrate 520 can have a first (top as shown) surface 521 and a second (bottom as shown) surface 522. As depicted, and with specific reference to Fig. 6C, Fig. 6D and Fig. 6E (showing detail of tip portion of the sensor element substrate of Fig. 6D) for example, the first substrate can comprise impedance sensor elements 502b, 502c, 502d, and also thermal sensor elements 502a, 502e. The impedance sensor elements 502b, 502c, 502d, and the thermal sensor elements 502a, 502e, can each comprise a sensing surface defined by a metal electrode. The metal electrode preferably consists essentially of a chemically inert, conductive material. Metals or metal compositions comprising noble metals and other transition metals are preferred. Examples include Au, Pt, Pd, Ag, W, Ti, Ni, Sn, Co and others. Preferably, the impedance sensor elements 502b, 502c, 502d each comprise a sensing surface defined by different types of metals (e.g., where 502b, 502c, 502d have a sensing surface defined by electrodes consisting essentially of Au, Pt, Pd, respectively). The thermal sensor elements 502a, 502e can each comprise a sensing surface defined by the same type of metal (e.g., Au). Electrical connectors 506b, 506c, 506d provide a conductive path (for signal communication) between impedance sensor elements 502b, 502c, 502d and corresponding contacts 508b, 508c, 508d, respectively. Similarly, electrical connectors 506a, 506e, provide a conductive path (for signal communication) between thermal sensor elements 502a, 502e, and corresponding contacts 508a, 508e, respectively. As depicted, and with specific reference to

Fig. 6C, the first substrate 520 can also comprise a refractive index sensor element 502' integrally configured within the body of the first substrate 520. As shown for example, such refractive index sensor element can comprise an optically transparent region of the substrate 520 defining a wave guide 524, 525, 526, and further defined by a region 528 of the substrate which is optically less transparent or substantially non-transparent. With specific reference to Fig. 6F and 6G, the integrated sensor assembly can further comprise a second capping substrate 530 having a first (top as shown) surface 531 and a second (bottom as shown) surface 532. The second capping substrate 530 can be adapted with an aperture situated over and providing for fluid access to sensor elements 502a, 502b, 502c, 502d, 502e, and being further adapted with apertures situated over and providing electrical access to each of the contacts 508a, 508b, 508c, 508d, 508e. In the configured sensor assembly, the first (top) surface 521 of the first sensor element substrate 520 can be capped / sealed by integral contact with the second (bottom) surface 532 of the second capping substrate 530. Fabrication of such integrated subassembly can be facilitated by alignment pads 535 on the first surface 521 of the first substrate 520 and spatially corresponding apertures in the second capping substrate 530. As shown in Fig. 6F and Fig. 6G, the integrated sensor assembly can further comprise a functional communication port 536, such as a USB port, providing independent electrical communication with each of the contacts 508a, 508b, 508c, 508d, 508e.

[00099] In operation, with reference to **Figure 6C and 6G**, an intravenous fluid being measured can be in fluid communication with the curved tip portion of the integrated sensor assembly. The impedance sensor elements 502b, 502c, 502d can be activated using an activation circuit in electrical communication with these sensor elements through communication port 536, contacts 508b, 508c, 508d and electrical connectors 506b, 506c, 506d, respectively. A responsive signal can be received from each of these sensor elements by a data retrieval circuit in electrical communication therewith through the same independent communication paths. Three independent channels can be configured for impedance measurements – using different pairs of impedance sensor elements in combination – namely: (i) 506b-506c; (ii) 506c-506d; and (iii) 506b-506d. Each of such pairs of sensor elements can be activated using alternating current (AC), allowing for determination of both real and imaginary (complex) impedance response for each pair of sensor elements. In this configuration therefore, the impedance sensor can effectively provide for six independent measurement channels at each applied AC frequency for determining the identity of a component of the intravenous fluid. These pairs of sensor elements can be activated using multiple frequencies. If five frequencies are used for impedance sensor element activation, for example, then the impedance sensor

effectively provides for thirty independent measurement channels for determining the identity of a component of the intravenous fluid. The thermal sensor elements 502a, 502e can be variously configured, for example for measuring temperature and or flow (e.g., as a thermal flow anemometer). In one embodiment for example, thermal sensor elements 502a, 502e are configured as a resistance temperature detector (RTD), and can be activated using an activation circuit in electrical communication with these sensor elements through communication port 536, contacts 508a, 508e and electrical connectors 506a, 506e, respectively. A responsive signal can be received from each of these sensor elements by a data retrieval circuit in electrical communication therewith through the same independent communication paths. The refractive index sensor can be used simultaneously and in combination with the impedance sensor elements 502b, 502c, 502d, and the thermal sensor elements 502a, 502e. With reference to Fig. 6C, for example, incident light (e.g, from an infrared light emitting diode (LED) source) can be admitted through an inlet end into a first section 524 of the wave guide, and allowed to interact with the intravenous fluid in a second section 525 of the wave guide which defines the refractive index sensor element 502'. The efficiency of light coupled through the waveguide is affected by refractive index of a fluid into which the waveguide is immersed; the resulting signal is proportional to the fluid refractive index. Light can be retrieved through a third section 526 of the wave guide at an outlet end of the wave guide into a photo-sensitive detector (for example into an infrared phototransistor) configured for detecting the output light. A multimeter (e.g., a Keithley Model 2100 Multimeter) can measure voltage output of the photo-sensitive detector, and such output signal can be communicated to a data retrieval circuit. Generally, each of the signals received from the impedance sensor elements, thermal sensor elements, or refractive index sensor element can be independently conditioned (e.g., amplified, biased, etc.) in signal processing circuit within a (e.g., local or remote) signal conditioning processor, and can processed in a signal identification processor (e.g., local or remote), for example using multiparametric analysis, to identify a component of the intravenous fluid. The identified component can be correlated to a specific patient through use of an identifier circuit, as described above.

EXAMPLES

Example 1: General methods for identifying a components typical of an intravenous fluid.

[000100] In this example, materials were obtained from Sigma Aldrich and dissolved or diluted with 0.9% saline to reach the desired concentrations. Solutions of insulin, heparin and potassium chloride were prepared at concentrations comparable to typical bolus doses used in

medical settings. All experiments were carried out using prepared solutions contained in 20 ml glass vials. Samples were measured by dipping admittance and optical sensor probes into each vial such that the active area of each probe was fully submerged in the solution to be tested. The response of each sensor to air and tap water were also measured.

[000101] The admittance signal is measured using a probe constructed with noble metal pads embedded in a polymer substrate. All measurements were performed at a frequency of 100 kHz. An Agilent Model 4395A network analyzer was utilized for measuring the admittance probe.

[000102] The optical sensor is constructed from a section of optic fiber with an infrared LED fed into one end and an infrared phototransistor detecting the output at the opposite end. The fiber jacket is removed along a section of its length and this section is bent into a curve. In this configuration, the efficiency of light coupled through the fiber is affected by refractive index of a fluid into which it is immersed and the resulting signal is inversely proportional to the fluid refractive index. A Keithley Model 2100 Multimeter was used to measure the voltage output of the optical sensor phototransistor detector and all data is recorded using a PC.

Example 2: Identification of various active pharmaceutical agents and other components typical in an intravenous fluid.

[000103] The sensor configuration and method described in Example 1 was used to identify components typically included in intravenous fluids, including pharmaceutical agents and other components. Specficially, the methods were applied to identify potassium chloride (KCl), sodium chloride (saline) (NaCl), heparin, water, insulin and air using admittance and refractive index sensors.

[000104] The results are summarized in Table 3, and shown graphically in **Figures 7(A-C)** for measurements of admittance, real portion **(Fig. 7A)**, admittance, imaginary portion **(Fig. 7B),** optical refractive index **(Fig. 7C).**

[000105] A multi-parametric representation of such measurements is shown in **Figure 7D**. As observed from these results, the multi-parametric analysis and data provide improved resolution of the various components of the intravenous fluid, and therefore allow for a more robust approach for distinguishable measurement thereof. The multi-parametric profile can be characteristic of the fluid component.

Table 3: Sensor Responses for Various Components

Material	Admittance	Admittance*	Optical Signal
KCL	64.310	55.094	2.084
Saline	25.368	12.800	2.168
Heparin	14.200	3.775	2.144
Water	0.481	0.129	2.171
Insulin	5.857	1.339	2.166
Air	0.010	0.141	2.210

Note 1: The optical signal is inversely proportional to refractive index.
Note 2: Admittance denotes the real admittance.
Note 3: Admittance* denotes the imaginary (complex) admittance.

Example 3: Identification of component typical of intravenous fluid in dilution series.

[000106] A set of dilution series experiments were conducted, in which concentrated samples of heparain, insulin and potassium chloride were each diluted by half concentration a total of three times to give concentrations of 1, ½, ¼, and 1/8 of a typical bolus dose and each one measured using the admittance and optical sensors described in Example 1 according to the approach described in Example 1.

[000107] The data for each dilution series of heparin, insulin and potassium chloride are shown in Tables 4A, 4B and 4C, respectively. Concentration is relative dilution. Admitt. = Admittance (real portion). Admitt.* = Admittance (imaginary portion).

[000108] These results are also shown graphically in **Figures 8(A-C)** for measurements of admittance, real portion **(Fig. 8A)**, admittance, imaginary portion **(Fig. 8B),** optical refractive index **(Fig. 8C).** A multi-parametric representation of such measurements is shown in **Figure 8D;** the multi-parametric analysis and data demonstrate resolution of these various components at different concentrations.

Example 4: Identification of intravenous fluid components with multi-channel impedance sensor.

[000109] A set of experiments were conducted using a multi-channel impedance sensor comprising two sensor elements. The two sensor elements each comprised a sensing surface defined by circular gold electrodes, 0.32mm diameter, situated coplanar and at a distance of 0.75mm from each other on a wall of a non-conductive flow path. An intravenous fluid consisting of 0.9% saline was provided in an infusion bag set on hanger. A fluid line assembly comprising an intravenous dripper was inserted, and flow from the infusion bag was initiated at a typical infusion rate (~120 cc/hr). The fluid line assembly comprised an injection port. The aforementioned gold electrode sensor elements were provided downstream from the injection port.

[000110] In this example, the sensor was used to measure the real and imaginary impedance of saline (0.90) flowing through the fluid line assembly at steady state. A bolus (1ml) of saline-diluted potassium chloride (10 mg/ml) was injected into the flowing saline, and detected by the sensor. Independently and subsequently, a bolus (1ml) of saline-diluted magnesium sulfate (40 mg/ml) was injected into the flowing saline and detected by the sensor. Independently and subsequently, a bolus of approximately 1ml of plain deionized water was injected into the flowing saline, and detected by the sensor.

[000111] In each case, both in-phase and out-of-phase components of the current through the sensor were continuously recorded and plotted by the system. The real, in-phase component of the current was plotted along the X-axis and the imaginary, out-of-phase of the current was plotted along the Y-axis of the chart. Briefly, a 100KHz AC voltage of 8mV amplitude was applied across the electrodes in series with a 50 Ohm resistor, and the voltage drop across the resistor was measured using a Stanford Research Model SR830 lock-in amplifier. A microprocessor (a personal computer) was connected to the lock-in amplifier via RS232 interface with software recording the complex voltage read by the lock-in amplifier at a data sampling rate of approximately twice per second. The data was plotted with the real part of the measured voltage value along X-axis and the imaginary part – along Y-axis. In our experiments, an average x_0+iy_0 and standard deviation σ were determined, accounting for naturally occurring noise. A measured voltage value $x+iy$ deviating from the average value by $|\Delta x+i\Delta y| > 6\sigma$ in any direction on the XY chart is a statistically significant indication of a change in the fluid. In this case, $arg(\Delta x+i\Delta y)$ defines the angular direction of the deviation vector. Two deviations $\Delta x_1+i\Delta y_1$ and $\Delta x_2+i\Delta y_2$ are statistically distinguishable if $|\Delta x_1+i\Delta y_1| > 6\sigma$ and $|\Delta x_2+i\Delta y_2| > 6\sigma$ and $|\Delta x_1 - \Delta x_2 + i(\Delta y_1 - \Delta y_2)| > 6\sigma$. The latter inequality defines the relationship between the magnitude of the deviations and the angle between them for the deviations to be distinguishable from each other.

[000112] The values determined from the sensor in flowing saline resulted in substantially overlapping data points, as shown on the plot included as Figure 9A.

[000113] The bolus of saline-diluted potassium chloride (KCl) injected into the saline flow through the injection port was detected by the sensor, resulting in a 2-dimensional characteristic signature for the KCl component. (*See* Fig. 9A). Multiple injections of potassium chloride (KCl) resulted in distinct substantially overlapping curves, as shown. Without being bound by theory not expressly recited in the claims, following injection of the saline-diluted potassium chloride into the flow as a bolus dose, the leading "front" edge of the flow profile for the bolus reaches

the vicinity of the electrodes, and the complex current deviates from its average value in pure saline and returns back when trailing "back" edge of the flow profile for the bolus passes the vicinity of the electrodes, thereby producing the characteristic signature. One can observe that the leading edge of the potassium chloride injection produces deviation from the data point representing the saline and that such deviation is nearly linear and at a distance far greater than the 6σ threshold of detection, thereby allowing for accurate determination of the direction of the deviation vector. For example, one can effect a linear regression of the measurement points from the 6σ threshold of detection to the distance where residuals start exceeding 6σ. For further results, one can also calculate an angle between X-axis and the directional vector of the deviation based on regression coefficients, which angle was found to be about 74.4° for potassium chloride under the conditions of this experiment.

[000114] The bolus of saline-diluted magnesium sulfate (MgSO4) injected into the saline flow through the injection port was also detected by the sensor, resulting in a 2-dimensional characteristic signature of the MgSO4 component – which was readily distinguishable from the signature for the KCl component. (See Fig. 9A) Multiple injections of magnesium sulfate (MgSO4) resulted in distinct substantially overlapping curves, as shown. Without being bound by theory not expressly recited in the claims, the saline-diluted magnesium sulfate results in a unique characteristic signature which was differentiated from the data resulting from the potassium chloride. As seen in Fig. 9A, the deviation from the saline point is relatively more vertical and of a relatively smaller magnitude as compared to the deviation of potassium chloride. The angle of the initial deviation, calculated as explained above, was found to be 85.6° for the magnesium sulfate under the conditions of this experiment.

[000115] The bolus of deionized water injected into the saline flow through the injection port was likewise detected by the sensor, resulting in a 2-dimensional characteristic signature of the H_2O component – which was readily distinguishable from both the signature for the KCl component and the signature of the MgSO4 component, deviating in nearly the opposite direction therefrom. (See Fig. 9B) The angle of initial deviation for the water component as detected by the sensor was -118.2°.

[000116] In each case, the statistical uncertainty for the determined angles was estimated from the residuals of the linear regression used to calculate coefficients determining the angles, and for all three substances – potassium chloride, magnesium sulfide and water – was found to be ±0.62°.

[000117] These data demonstrate that highly diluted components injected into saline flow can be identified. Generally, deviation distance from a data point corresponding to pure saline depends on both concentration and molecular or ionic composition of the component, while deviation direction from such data point depends predominantly on the molecular or ionic composition of the component. For higher concentrations of the component, both magnitude and direction of the deviation become concentration-dependent in unique and distinguishable manner which is specific to and dependent upon the particular component added to the saline. Hence, such deviation dependencies enable identification of components having different compositions or concentrations.

[000118] Software can be used to identify potassium chloride, magnesium sulfide and water components within an intravenous saline fluid, based on the results of the aforedescribed experimental data. In one approach, for example, pattern recognition software can continuously observe voltage data derived from the sensor and check whether the value exceeds the 6σ threshold. Once the threshold is exceeded, the software can indicate that a different substance is likely present in the flow and can start a linear regression on the consecutively measured points, checking whether residuals exceed the 6σ threshold. The algorithm may, at that point, conclude that the linear section of the deviation curve was over, and may calculate a directional vector for the data set being reduced. The directional vector can be compared to vector values previously determined for specific components (e.g, pharmaceuticals) of interest. More specifically, for example, such analysis can be effected in terms of angles. For example, when the detected deviation corresponds to an angle of 74.4±0.62° - the software can identify the injected bolus as likely being potassium chloride. Similarly, for example, if the detected deviation corresponds to an angle of 85.6±0.62° or an angle of -118.2±0.62°, the software can identify injected substance as magnesium sulfate or deionized water, respectively. If the detected deviation angle does not correspond to angle for any known substances under the conditions of measurement, then the algorithm can report a detected unknown substance. Once a component is identified, a current cumulative dosing level can be measured by integrating either x or y or $|\Delta x + i\Delta y|$ over time during the period defined from when the signal exceeded the detection threshold to the current time (*e.g.*, taking into account the sensor sensitivity to identified substance and the volumetric flow).

[000119] Such pattern recognition algorithm can also be adapted to recognize other substances that are components of an intravenous fluid. Such substances will produce deviations in various directions, the angles for each of which can be determined as described

above. In subsequent operation, such software can compare measured angles determined from detected data with the values for expected angles corresponding to certain substances, thereby identifying the substances. More elaborate pattern recognition algorithms can also be applied to the differentiation and recognition of data generated by the sensors in multi-dimensional space, as described in the specification.

[000120] The various examples described herein are representative of, and not to be considered limiting of the inventions disclosed and claimed herein.

* * * *

[No further entries this page. Tables 4A, 4B and 4C follow on the next page.]

Table 4A: Heparin Dilution Series

Heparin			
Relative Conc.	**Optic**	**Admitt.**	**Admitt.***
1.000	2.1284	33.68978	14.12309
0.504	2.1390	29.85923	13.55784
0.248	2.1455	29.57476	13.1181
0.124	2.1432	26.91454	13.59039
0.000	2.1434	23.98381	10.90867

Table 4B: Insulin Dilution Series

Insulin			
Relative Conc.	**Optic**	**Admitt.**	**Admitt.***
1.000	2.1313	6.59935	1.33295
0.503	2.1402	10.9246	3.14695
0.240	2.1424	17.6113	7.30539
0.126	2.1434	21.2221	10.3648
0.000	2.1434	23.9838	10.9087

Table 4C, Potassium Chloride Dilution Series

KCL			
Relative Conc	**Optic**	**Admitt**	**Admitt.***
1.000	2.0889	66.51804	57.43262
0.496	2.1258	54.16412	39.15326
0.221	2.1360	42.24291	27.72464
0.123	2.1420	36.42675	20.27508
0.000	2.1434	23.98381	10.90867

We claim:

1. An apparatus comprising a sensor for identifying one or more components of an intravenous fluid, the apparatus comprising

a housing adapted for fluidic interface with a fluid line assembly of a system for intravenous delivery of fluid into a patient, the housing comprising a cavity in fluid communication with the fluid, and

two or more sensor elements, each sensor element having a sensing surface positioned within the cavity for contact with the fluid.

2. A apparatus comprising a sensor for identifying one or more components of an intravenous fluid, the apparatus comprising

a housing assembly comprising

a housing adapted for fluidic interface with a fluid line assembly of a system for intravenous delivery of fluid into a patient, the housing comprising a cavity in fluid communication with the fluid,

a sensor element having a sensing surface positioned within the cavity for contact with the fluid, and

one or more accessible contacts in communication with the sensor element, and

a processor assembly adapted for intermittent interface with the housing assembly, comprising

one or more circuits for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element, and

one or more contacts in communication with the one or more circuits, and adapted for intermittent interface with the one or more accessible contacts of the housing assembly.

3. A apparatus comprising a sensor for identifying one or more components of an intravenous fluid, the apparatus comprising

a sensor element having a sensing surface positioned for contact with the fluid,

a signal processing circuit for processing data originating from the sensor element, the signal processing circuit being in communication with the sensing element directly or indirectly, including through a data retrieval circuit,

a data retrieval circuit for receiving, storing, displaying or transmitting data originating from the sensor element, the data retrieval circuit being in communication with the sensing element directly or indirectly, including through a signal processing circuit, and

an identifier circuit for correlating sensor data to a specific patient, the identifier circuit being in communication with the signal processing circuit or the data retrieval circuit.

4. The apparatus of claim 3 further comprising a housing adapted for fluidic interface with a fluid line assembly of a system for intravenous delivery of fluid into a patient, the housing comprising a cavity in fluid communication with the fluid, the sensing surface of the sensor element being positioned within the cavity for contact with the fluid.

5. The apparatus of any of claims 1 through 4 wherein the housing is adapted for in-line fluid communication with the fluid line assembly.

6. The apparatus of any of claims 1 through 4 wherein the housing is defined in an intravenous infusion device.

7. An apparatus comprising a sensor for identifying one or more components of an intravenous fluid, the apparatus comprising

an intravenous infusion device for infusion of fluid into the vascular system of a patient, the infusion device comprising a cavity in fluid communication with the fluid, and

a sensor element having a sensing surface positioned within the cavity for contact with the fluid.

8. The apparatus of any of claims 6 or 7 wherein the intravenous infusion device is a catheter.

9. The apparatus of claim 8 wherein the catheter comprises

a first end adapted for fluid communication with a fluid line assembly,

a second distal end adapted for insertion into the vascular system of the patient, and

a housing comprising a cavity in fluid communication with the fluid line assembly, and

a sensor element having a sensing surface positioned within the cavity for contact with the fluid.

10. The apparatus of any of claims 6 or 7 wherein the intravenous infusion device is an implantable intravenous infusion device.

11. The apparatus of claim 10 wherein the implantable infusion device comprises an implantable body, the body comprising

a receiving port adapted for fluid communication with a fluid line assembly,

a delivery port for delivering fluid to the vascular system of the patient,

a housing comprising a cavity in fluid communication with the receiving port, and

a sensor element having a sensing surface positioned within the cavity for contact with the fluid.

12. The apparatus of any of claims 1, or 5 through 11 further comprising one or more circuits for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element.

13. The apparatus of any of claims 1, 2 or 5 through 12 further comprising a signal processing circuit for processing data originating from the sensor element, the signal processing circuit being in communication with the sensing element directly or indirectly, including through a data retrieval circuit.

14. The apparatus of any of claims 1, 2 or 5 through 13 further comprising a data retrieval circuit for receiving, storing, displaying or transmitting data originating from the sensor element, the data retrieval circuit being in communication with the sensing element directly or indirectly, including through a signal processing circuit.

15. The apparatus of any of claims 1 through 14 further comprising an activation circuit for activating the sensor element, the activation circuit being in communication with the sensing element directly or indirectly.

16. A system for intravenous delivery of fluid into a patient, the system comprising

a fluid line assembly including one or more conduits and having a first end adapted for fluid communication with a fluid source and a second end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient, and

an apparatus any of claims 1 through 15.

17. A system for intravenous delivery of fluid into a patient, the system comprising

a fluid line assembly including one or more conduits and having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient, and

a housing comprising a cavity in fluid communication with and proximate to the second distal end of the fluid line assembly, and

a sensor element having a sensing surface positioned within the cavity for contact with the fluid.

18. The system of claim 17 wherein the housing is adapted for in-line fluid communication with the fluid line assembly.

19. The system of claim 17 wherein the housing is defined in an intravenous infusion device.

20. The system of any of claims 17 through 19 further comprising one or more circuits for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element.

21. The system of any of claims 17 through 19 further comprising a signal processing circuit for processing data originating from the sensor element, the signal processing circuit being in communication with the sensing element directly or indirectly, including through a data retrieval circuit.

22. The system of any of claims 17 through 19 further comprising a data retrieval circuit for receiving, storing, displaying or transmitting data originating from the sensor element, the data retrieval circuit being in communication with the sensing element directly or indirectly, including through a signal processing circuit.

23. The system of any of claims 17 through 19 further comprising an activation circuit for activating the sensor element, the activation circuit being in communication with the sensing element directly or indirectly.

24. A system for intravenous delivery of fluid into a patient, the system comprising

a fluid line assembly including one or more conduits and having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient, and

a sensor comprising

a sensor element having a sensing surface positioned for contact with the fluid,

a local processor comprising

a signal processing circuit for processing data originating from the sensor element, the signal processing circuit being proximate to and in communication with the sensing element directly or indirectly, including through a data retrieval circuit, and

a data retrieval circuit for receiving, storing, displaying or transmitting data, the data retrieval circuit being proximate to and in communication with the sensing element directly or indirectly, including through a signal processing circuit, and

a remote processor comprising

a data acquisition circuit for acquiring sensor data from the local processor, and

a monitoring circuit for monitoring the sensor data.

25. The system of claim 24 wherein the local processor further comprises an activation circuit for activating the sensor element, the activation circuit being in communication with the sensing element directly or indirectly.

26. The apparatus of any of claims 2 through 15 comprising two or more sensor elements, each sensor element having a sensing surface positioned for contact with the fluid.

27. The system of any of claims 16 through 25 further comprising two or more sensor elements, each sensor element having a sensing surface positioned for contact with the fluid.

28. The invention of any of claims 1, 26 or 27 wherein the two or more sensor elements are independent sensor elements.

29. The invention of claim 28 wherein each of the two or more sensor elements has a physically separate sensing surface.

30. The invention of any of claims 28 or 29 wherein each of the two or more sensor elements has a separately addressable sensing surfaces.

31. The invention of any of claims 1, or 26 through 30 comprising one or more signal processing circuits for independently processing data originating from each of the two or more sensor elements to generate a multi-parametric profile characteristic of a component of the fluid.

32. The apparatus of any of claims 1, 3 through 15, 26, or 28 through 31 comprising

a housing assembly comprising a housing adapted for fluidic interface with a fluid line assembly of a system for intravenous delivery of fluid into a patient, the housing comprising a cavity in fluid communication with the fluid, the sensor element having a sensing surface positioned within the cavity for contact with the fluid, and one or more accessible contacts in communication with the sensor element, and

a processor assembly adapted for intermittent interface with the housing assembly, comprising one or more circuits for activating the sensor element or for receiving,

processing, storing, displaying or transmitting data originating from the sensor element, and one or more contacts in communication with the one or more circuits, the one or more contacts being adapted for intermittent interface with the one or more accessible contacts of the housing assembly.

33. The system of any of claims 16 through 25, or 27 through 31 further comprising

a housing assembly comprising a housing adapted for fluidic interface with a fluid line assembly of a system for intravenous delivery of fluid into a patient, the housing comprising a cavity in fluid communication with the fluid, the sensor element having a sensing surface positioned within the cavity for contact with the fluid, and one or more accessible contacts in communication with the sensor element, and

a processor assembly adapted for intermittent interface with the housing assembly, comprising one or more circuits for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element, and one or more contacts in communication with the one or more circuits, the one or more contacts being adapted for intermittent interface with the one or more accessible contacts of the housing assembly.

34. The invention of any of claims 2, 32 or 33 wherein the one or more accessible contacts of the housing assembly are in electrical communication with the sensor element.

35. The invention of any of claims 2, or 32 through 34 wherein the one or more contacts of the processor assembly are in electrical communication with the one or more circuits.

36. The invention of any of claims 2, or 32 through 35 wherein the one or more contacts of the processor assembly are releasably engagable with the one or more accessible contacts of the housing assembly, whereby when engaged, the one or more circuits of the processor assembly are in communication with the sensor element.

37. The invention of any of claims 2 or 32 through 36 wherein the contacts of the housing assembly are accessible on an external surface of the housing.

38. The invention of any of claims 2, or 32 through 36 wherein the contacts of the housing assembly are accessible via leads protruding through an external surface of the housing.

39. The invention of any of claims 2 or 32 through 38 wherein the housing assembly is sterile or sterilizable.

40. The invention of any of claims 2 or 32 through 38 wherein the processor assembly is hand portable.

41. The apparatus of any of claims 1, 2, 5 through 15, 26, 28 through 31, 32, or 34 through 40 further comprising an identifier circuit for correlating sensor data to a specific patient.

42. The system of any of claims 16 through 25, 27 through 31, or 33 through 40 further comprising an identifier circuit for correlating sensor data to a specific patient.

43. The invention of any of claims 3, 4, 41 or 42 wherein the identifier circuit provides location-specific identifying data.

44. The invention of claim 43 wherein the identifier circuit provides location-specific identifying data derived from a readable indicia associated with the location of the patient.

45. The invention of any of claims 3, 4, 41 or 42 wherein the identifier circuit provides patient- specific identifying data.

46. The invention of claim 45 wherein the identifier circuit provides patient-specific identifying data derived from a readable indicia associated with the patient.

47. The invention of any of claims 7 through 16 and 24 through 46, further comprising a housing comprising a cavity in fluid communication with the fluid, wherein the sensing surface of the sensing element is positioned within the cavity for contact with the fluid.

48. The invention of any of claims 1 through 6, 17 through 23, or 47 wherein the housing is adapted for in-line fluid communication with the fluid line assembly.

49. The invention of claims 1 through 6, 17 through 23, or 47 wherein the housing is defined in an intravenous infusion device.

50. The invention of claim 49 wherein the intravenous infusion device is a catheter.

51. The invention of claim 49 wherein the intravenous infusion device is an implantable intravenous infusion device.

52. The invention of any of claims 1 through 6, 17 through 23, or 45 through 51 wherein the housing comprises a hermetically sealed fitting as a fluidic interface with a fluid line assembly.

53. The invention of any of claims 1 through 6, 17 through 23, or 45 through 51 wherein the housing comprises a releasably sealed fitting as a fluidic interface with a fluid line assembly.

54. The apparatus of any of claims 1 through 15, 26, 28 through 31, 32, 34 through 40, 41, 43 through 46, or 47 through 53 comprising

a local processor comprising one or more circuits for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element, and

a remote processor comprising a data acquisition circuit for acquiring sensor data from the local processor, and a monitoring circuit for monitoring the sensor data.

55. The system of any of claims 16 through 23, 27 through 31, 33 through 40, 42 through 46, or 47 through 53 comprising

a local processor comprising one or more circuits for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element, and

a remote processor comprising a data acquisition circuit for acquiring sensor data from the local processor, and a monitoring circuit for monitoring the sensor data.

56. The invention of any of claims 24, 25, 54 or 55 wherein the monitoring circuit comprises a sensor data module for providing, optionally over time, one or more parameters derived from sensor data.

57. The invention of claim 56 wherein the one or more parameters derived from sensor data are selected from:
(a) an onset of infusion of the fluid or of a component thereof,
(b) a presence or absence of one or more components of the fluid,
(c) a composition of one or more components of the fluid,
(d) a concentration of one or more components of the fluid,
(e) an intravenous infusion rate of the fluid or of one or more components of the fluid,
(f) a completion of infusion of the fluid or of a component thereof, and
(g) a dosing level of one or more components of the fluid.

58. The invention of any of claims 24, 25, or 54 through 57 wherein the monitoring circuit comprises a user-defined data module for providing one or more prescribed or proscribed patient-relevant parameters.

59. The invention of claim 58 wherein the one or more prescribed or proscribed patient-relevant parameters are selected from:
(a) a time of onset of infusion of the fluid or of a component thereof,
(b) a presence or absence of one or more components of the fluid,
(c) a composition of one or more components of the fluid,
(d) a concentration of one or more components of the fluid,
(e) an intravenous infusion rate of the fluid or of one or more components of the fluid,
(f) a time of completion of infusion of the fluid or of a component thereof, and
(g) a dosing level of one or more components of the fluid.

60. The invention of any of claims 24, 25, or 54 through 59 wherein the monitoring circuit comprises a data comparator module for comparing one or more parameters derived

from sensor data with one or more prescribed or proscribed patient-relevant parameters, and for generating an output signal based on the comparison thereof.

61. The invention of claim 60 further comprising a notice circuit, preferably an alarm circuit, for notifying a caregiver based on the output signal of the data comparator module of the monitoring circuit.

62. The invention of any of claims 60 or 61 further comprising a control circuit for activating a control element configured for effecting a change based on the output signal of the comparator module of the monitoring circuit.

63. The invention of claim 62 wherein the control element is an infusion valve in fluid communication with a fluid line assembly, wherein the control circuit effects a change in flow through the infusion valve.

64. The invention of claim 63 wherein the infusion valve is controlled with an electronic valve control system comprising a controller, the valve controller including a user-defined data module for providing patient-relevant input data defining or used to derive one or more prescribed or proscribed patient-relevant parameters.

65. The invention of 64 wherein the patient-relevant parameter is derived from patient-relevant input data and a therapy-relevant parameter.

66. The invention of any of the preceding claims comprising a sensor adapted for identifying one or more components of the fluid.

67. The invention of claim 66 wherein the sensor is adapted for identifying the presence or absence of one or more components of the fluid.

68. The invention of any of claims 66 or 67 wherein the sensor is adapted for identifying the composition of one or more components of the fluid.

69. The invention of any of claims 55 through 68 wherein the sensor is adapted for identifying the concentration of one or more components of the fluid.

70. The invention of any of the preceding claims comprising a sensor adapted for identifying one or more active pharmaceutical agents within the fluid.

71. A system for intravenous delivery of fluid into a patient, the system comprising

a fluid line assembly including one or more conduits and having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient, and

a sensor for identifying one or more components of the fluid, the sensor comprising a sensor element having a sensing surface positioned for contact with the fluid, and one or more circuits in communication with the sensor element for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element, the sensor being adapted for identifying one or more active pharmaceutical agents within the fluid.

72. The invention of any of claims 70 or 71 wherein the sensor is adapted for identifying one or more active pharmaceutical agents selected from the group consisting of: an anticoagulant, a metabolically-active hormone, an anesthetic, and an analgesic.

73. The invention of any of claims 70 or 71 wherein the sensor is adapted for identifying one or more active pharmaceutical agents selected from the group consisting of: heparin, insulin, propofol, and morphine.

74. The invention of any of claims 70 or 71 wherein the sensor is adapted for identifying an anticoagulant, preferably heparin.

75. The invention of claim 74 wherein the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and ultraviolet absorption, and for identifying an anticoagulant, preferably heparin, based on the one or more determined properties.

76. The invention of any of claims 70 or 71 wherein the sensor is adapted for identifying a metabolically-active hormone, preferably insulin.

77. The invention of claim 76 wherein the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and visible absorption (color), and for identifying a metabolically-active hormone, preferably insulin, based on the one or more determined properties.

78. The invention of any of claims 70 or 71 wherein the sensor is adapted for identifying an anesthetic, preferably propofol.

79. The invention of claim 78 wherein the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and visible absorption (color), and for identifying an anesthetic, preferably propofol, based on the one or more determined properties.

80. The invention of any of claims 70 or 71 wherein the sensor is adapted for identifying an analgesic, preferably morphine.

81. The invention of claim 80 wherein the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and ultraviolet absorption, and for identifying an analgesic, preferably morphine, based on the one or more determined properties.

82. The invention of any of claims 70 through 81 wherein the sensor is adapted for determining two or more properties of the fluid, and for identifying the one or more active pharmaceutical agents based on the two or more determined properties.

83. The invention of any of claims 70 through 82 wherein the sensor comprises one or more signal processing circuits for independently processing data originating from each of the two or more sensor elements to generate a multi-parametric profile characteristic of the one or more active pharmaceutical agents, preferably of an agent selected from an anticoagulant (preferably heparin), a metabolically-active hormone (preferably insulin), an anesthetic (preferably propofol), and an analgesic (preferably morphine).

84. The invention of any of the preceding claims comprising a sensor adapted for identifying one or more components selected from the group consisting of a metal ion, a halide ion, an organic ion or salt, and a sugar.

85. A system for intravenous delivery of fluid into a patient, the system comprising

a fluid line assembly including one or more conduits and having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient, and

a sensor for identifying one or more components of the fluid, the sensor comprising a sensor element having a sensing surface positioned for contact with the fluid, and one or more circuits in communication with the sensor element for activating the sensor element or for receiving, processing, storing, displaying or transmitting data originating from the sensor element, the sensor being adapted for identifying one or more components selected from the group consisting of a metal ion, a halide ion, an organic ion or salt, and a sugar.

86. The invention of any of claims 84 or 85 wherein the sensor is adapted for identifying (i) one or more components selected from the group consisting of potassium chloride, sodium chloride, Ringer's lactate, and dextrose, or (ii) one or more components selected from the group consisting of a sodium ion, a potassium ion, a chloride ion, a calcium ion, a lactate ion, and dextrose.

87. The invention of any of claims 84 or 85 wherein the sensor is adapted for identifying potassium chloride, potassium ion or chloride ion.

88. The invention of claim 87 wherein the sensor is adapted for determining one or more properties of the fluid selected from electrochemical potential, impedance, refractive index and ultraviolet absorption, and for identifying potassium chloride, potassium ion or chloride ion based on the one or more determined properties.

89. The invention of any of claims 84 through 87 wherein the sensor is adapted for determining two or more properties of the fluid, and for identifying the one or more components of the fluid based on the two or more determined properties; preferably in this embodiment, the sensor comprises one or more signal processing circuits for independently processing data originating from each of the two or more sensor elements to generate a multi-parametric profile characteristic of the one or more components of the fluid, preferably potassium chloride, potassium ion or chloride ion.

90. The invention of any of the preceding claims comprising a sensor other than a flow sensor.

91. A system for intravenous delivery of fluid into a patient, the system comprising

a fluid line assembly including one or more conduits and having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient, and

a sensor other than a flow sensor, the sensor comprising a sensor element having a sensing surface positioned for contact with the fluid.

92. The invention of any of the preceding claims wherein the sensor is adapted for determining one or more properties of the fluid.

93. The invention of any of the preceding claims wherein the sensor is adapted for determining one or more properties of the fluid selected from ionic properties (preferably conductivity, admittance, pH, electrochemical potential), rheological properties (preferably viscosity), density, dielectric constant, electromagnetic absorption properties (preferably optical absorption (including visible color), infrared absorption, ultraviolet absorption), optical properties (preferably refractive index, turbidity, opacity, fluorescence), physical properties (preferably particle size), physiochemical properties (preferably permeability) and thermal properties (preferably thermal diffusivity, boiling point).

94. The invention of any of the preceding claims wherein the sensor is adapted for determining one or more properties of the fluid selected from conductivity, admittance, pH, electrochemical potential, viscosity, density, dielectric constant, optical absorption (including visible color), infrared absorption, ultraviolet absorption, preferably refractive index, turbidity, opacity, fluorescence, particle size, permeability thermal diffusivity, and boiling point.

95. The invention of any of the preceding claims further comprising a pressure sensor or flow sensor.

96. A system for intravenous delivery of fluid into a patient, the system comprising

a fluid line assembly including one or more conduits and having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient, and

a sensor for identifying one or more components of the fluid, the sensor being selected from an AC impedance spectroscopy sensor, an electrochemical potential sensor, a thermal anemometer sensor, a refractometry sensor, a transmission sensor, an absorbance sensor, a spectrometer (including a colorimeter), a viscometer, a capacitor sensor, a resonator sensor, an optical sensor (including a turbidity sensor), a pH sensor, a conductivity sensor, and an inductive sensor.

97. The invention of any of the preceding claims comprising a sensor:

(i) wherein the sensor is selected from a static light scattering sensor, a dynamic light scattering sensor, an inductive sensor, a magnetic sensor, a capacitive sensor, a thermal sensor, a thermal anemometer, an ultrasonic sensor, an optical bubble detector, a resonator sensor, a surface chemistry sensor, a nanowire sensor, a nanostructure sensor, a bacteria sensor, a sensor with a semi-permeable membrane, a sensor with selectively absorbing coating and a boiling point sensor; or

(ii) preferably, the sensor is selected from an impedance sensor (e.g, an AC impedance spectroscopy sensor), an electrochemical sensor (e.g., an electrochemical potential sensor), a thermal sensor (e.g., a thermal anemometer

sensor), an optical sensor (e.g., a refractometry sensor, a transmission sensor, an absorbance sensor, a spectrometer (including a colorimeter)r, a turbidity sensor), a rheological sensor (e.g.,a viscometer), an electrical property sensor (e.g., a capacitor sensor, a pH sensor, a conductivity sensor, and an inductive sensor), and a fluid-displacing or fluid-shearing (e.g, resonator) sensor.

98. A system for intravenous delivery of fluid into a patient, the system comprising

a fluid line assembly including one or more conduits and having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient, and

a sensor for identifying one or more components of the fluid, the sensor comprising

a cavity in fluid communication with and proximate to the second distal end of the fluid line assembly

a sensor element having a sensing surface positioned within the cavity for contact with the fluid,

a local signal processing circuit for processing data originating from the sensor element, the signal processing circuit being proximate to and in communication with the sensing element directly or indirectly, including through a data retrieval circuit,

a local data retrieval circuit for receiving, storing, displaying or transmitting data, the data retrieval circuit being proximate to and in communication with the sensing element directly or indirectly, including through a signal processing circuit, and

an identifier for correlating sensor data to a specific patient and adapted for use by the signal processing circuit or the data retrieval circuit, and

a remote monitoring circuit for acquiring data comprising or derived from an output signal of the sensor and adapted for monitoring the data, preferably for a condition of interest.

99. The invention of any of the preceding claims further comprising

a fluid source in fluid communication with the first end of the fluid line assembly, and

an intravenous infusion device in fluid communication with the second end of the fluid line assembly.

100. The invention of any of the preceding claims wherein the fluid line assembly further includes one or more injection ports for injection of a pharmaceutical or other agent into the fluid within the fluid line assembly.

101. The invention of any of the preceding claims wherein the fluid line assembly further includes a pump in fluid communication with the fluid line assembly.

102. The invention of any of the preceding claims wherein the fluid line assembly further includes one or more of a conduit, a backflow block, a valve, of an injection port assembly.

103. The invention of any of the preceding claims comprising a housing adapted to interface with a fluid line assembly of a system for intravenous delivery of fluid into a patient, the fluid line assembly comprising one or more conduits and having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient.

104. The invention of claim 103 wherein the housing further comprises a first fitting for fluidic interface with the first end of the fluid line assembly, a cavity having an inlet for receiving the fluid and an outlet for discharging the fluid, and a second fitting adapted for fluidic interface with the second end of the fluid line assembly.

105. The invention of any preceding claim further comprising a housing having a cavity in fluid communication with the fluid line assembly, the sensing surface of the sensor element being positioned within the cavity of the sensor.

106. The invention of any of the preceding claims wherein one or more circuits are defined in a microprocessor.

107. The invention of of any of the preceding claims wherein one or more circuits are defined in an application-specific integrated circuit (ASIC).

108. A method for intravenous delivery of fluid to a subject in need thereof, the method comprising

administering the fluid to the subject, and

sensing the fluid with an apparatus or system of any of claims 1 through 107.

109. The method of claim 108 further comprising identifying one or more components of the fluid during administration of fluid to the subject.

110. A method for intravenous delivery of fluid to a subject in need thereof, the method comprising

administering the fluid to the subject, and

sensing the fluid to generate a multi-parameteric profile characteristic of a component of the fluid, and

identifying one or more components of the fluid during administration of fluid to the subject based on the multi-parametric profile.

111. The method of claim 110 wherein sensing the fluid comprises exposing a sensing surface of a first sensor element to the fluid, exposing a sensing surface of a second sensor element to the fluid, and independently processing data originating from each of the first sensor element and the second sensor element to generate the multi-parametric profile.

112. A method for intravenous delivery of fluid to two or more subjects in need thereof, the method comprising

administering a first fluid to a first subject,

exposing a sensing surface of a first sensor element to the first fluid,

interfacing a processor with the first sensor element and identifying one or more components of the first fluid during administration thereof to the first subject, the processor comprising one or more circuits for activating a sensor element or for receiving, processing, storing, displaying or transmitting data originating from the a sensor element,

dis-interfacing the processor from the first sensor element,

administering a second fluid to a second subject, and

exposing a sensing surface of a second sensor element to the second fluid, and

interfacing the (same) processor with the second sensor element and identifying one or more components of the second fluid during administration thereof to the second subject.

113. The method of claim 112 further comprising disposing or sterilizing the sensing surface of each of the first sensor element and the second sensor element after administration of fluid to the respective subject.

114. A method for intravenous delivery of fluid to a subject in need thereof, the method comprising

administering the fluid to the subject,

sensing the fluid to generate sensor data for identifying one or more components of the fluid during administration of fluid to the subject, and

correlating the sensor data to the specific subject.

115. The method of claim 114 further comprising deriving one or more parameters from the sensor data, and comparing the one or more sensor-derived parameters with one or more prescribed or proscribed patient-relevant parameters.

116. A method for intravenous delivery of fluid to a subject in need thereof, the method comprising

administering the fluid to the subject through an intraveneous infusion device, and

sensing the fluid with a sensing surface of a sensor element, the sensing surface being positioned proximate to the intravenous infusion device to identify one or more components of the fluid during administration of fluid to the subject.

117. The method of claim 116 wherein fluid is exposed to a sensing surface of a sensor element, the sensing surface being positioned within a cavity of a housing adapted for in-line fluid communication of a fluid line assembly.

118. The method of claim 117 wherein in-line housing is positioned directionally adjacent to the subject relative to the position of any fluid source supply line or any injection port of the fluid line assembly.

119. The method of claim 116 wherein fluid is exposed to a sensing surface of a sensor element, the sensing surface being positioned within a cavity of a housing defined in the intravenous infusion device.

120. A method for intravenous delivery of fluid to a subject in need thereof, the method comprising

administering the fluid to the subject, and

sensing the fluid with a sensor element having a sensing surface exposed to the fluid during administration of fluid to the subject,

generating sensor data in a processor local to and in communication with the sensor element, the local processor optionally comprising one or more circuits for activating a sensor element, the local processor comprising one or more circuits for receiving, processing, storing, displaying or transmitting data originating from the sensor element,

acquiring the sensor data at a processor remote from the sensor element, the remote processor comprising one or more circuits for receiving, processing, storing, displaying or transmitting the acquired sensor data,

monitoring the acquired sensor data or data derived therefrom.

121. A method for intravenous delivery of fluid to two or more subjects in need thereof, the method comprising

administering a first fluid to a first subject,

sensing the first fluid with a first sensor element having a sensing surface exposed to the first fluid during administration of fluid to the first subject,

generating sensor data in a first processor local to and in communication with the first sensor element,

administering a second fluid to a second subject,

sensing the second fluid with a second sensor element having a sensing surface exposed to the second fluid during administration of fluid to the second subject,

generating sensor data in a second processor local to and in communication with the second sensor element,

acquiring the sensor data from each of the first local processor and the second local processor at a processor remote from each of the first sensor element and the second sensor element,

monitoring the acquired sensor data from each of the first local processor and the second local processor or monitoring data derived therefrom.

122. A method for intravenous delivery of fluid to a subject in need thereof, the method comprising

administering the fluid to the subject, and

sensing the fluid to identify one or more active pharmaceutical agents within fluid during administration of fluid to the subject.

123. The method of claim 122 comprising sensing the fluid to identify one or more active pharmaceutical agents selected from the group consisting of: an anticoagulant, a metabolically-active hormone, an anesthetic, and an analgesic.

124. The method of claim 122 comprising sensing the fluid to identify one or more active pharmaceutical agents selected from the group consisting of: heparin, insulin, propofol, and morphine.

125. A method for intravenous delivery of fluid to a subject in need thereof, the method comprising

administering the fluid to the subject, and

sensing the fluid to identify one or more components within fluid during administration of fluid to the subject, the one or more components being selected from the group consisting of a metal ion, a halide ion, an organic ion or salt, and a sugar.

126. The method of claim 125 comprising sensing the fluid to identify potassium chloride.

127. A system for intravenous delivery of fluid into a patient, the system comprising

a fluid line assembly including one or more conduits and having a first end adapted for fluid communication with a fluid source and a second distal end adapted for fluid communication with an intravenous infusion device for infusion of fluid into the vascular system of the patient,

a pump in fluid communication with the fluid line assembly,

a sensor comprising

a sensor element having a sensing surface positioned for contact with the fluid,

a processor for generating sensor data, the processor comprising

a signal processing circuit for processing data originating from the sensor element, the signal processing circuit being in communication with the sensing element directly or indirectly, including through a data retrieval circuit,

a data retrieval circuit for receiving, storing, displaying or transmitting data, the data retrieval circuit being in communication with the sensing element directly or indirectly, including through a signal processing circuit,

a monitoring circuit for monitoring the sensor data, the monitoring circuit comprising a data comparator module for comparing one or more parameters derived from sensor data with one or more prescribed or proscribed patient-relevant parameters, and for generating an output signal based on the comparison thereof,

a control circuit for controlling the pump based on the output signal of the comparator module of the monitoring circuit.

128. The invention of claim 127 wherein the local processor further comprises an activation circuit for activating the sensor element, the activation circuit being in communication with the sensing element directly or indirectly.

129. The invention of any of claims 126 and 127 further comprising a notice circuit, preferably an alarm circuit, for notifying a caregiver based on the output signal of the data comparator module of the monitoring circuit.

130. The invention of any of claims 126 through 128 wherein the pump is controlled with an electronic control system comprising a controller, the pump controller including a user-defined data module for providing patient-relevant input data defining or used to derive one or more prescribed or proscribed patient-relevant parameters.

131. The invention of 130 wherein the patient-relevant parameter is derived from patient-relevant input data and a therapy-relevant parameter.

132. The invention of any of claims 130 and 131 further comprising one or more circuits for communicating one or more prescribed or proscribed patient-relevant parameters defined by or derived from input data from the user-defined data module of the pump controller to the data comparator module of the monitoring circuit.

FIG. 1A

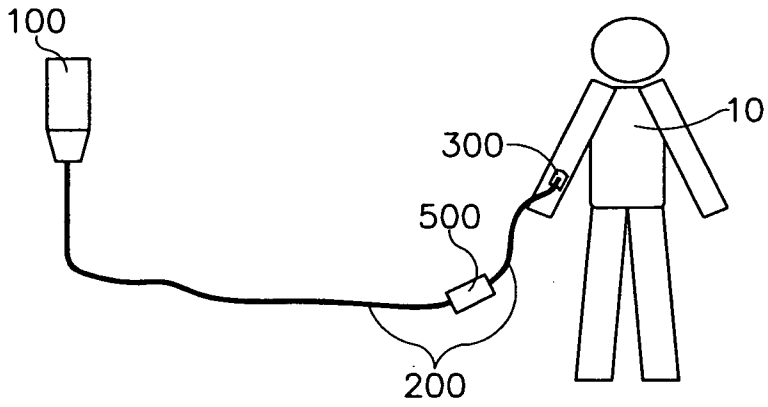


FIG. 1B

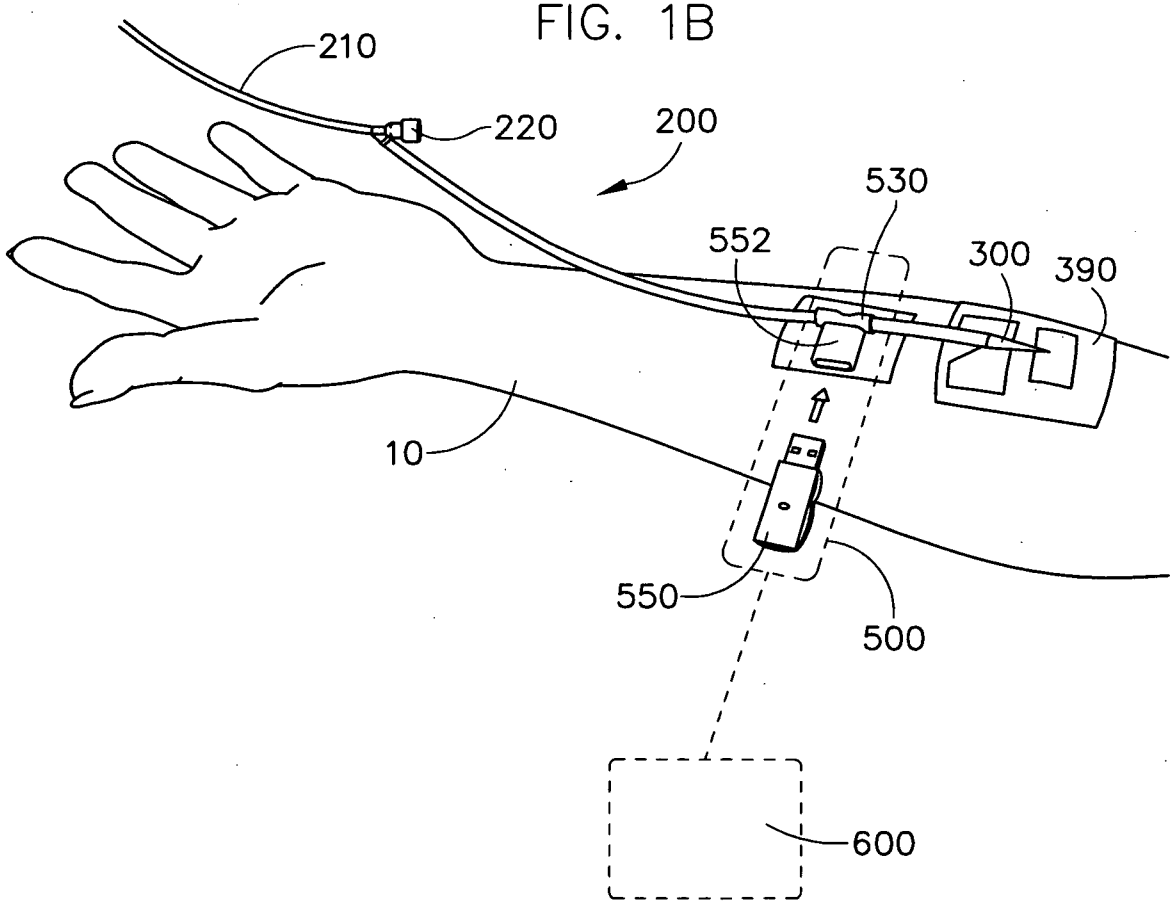
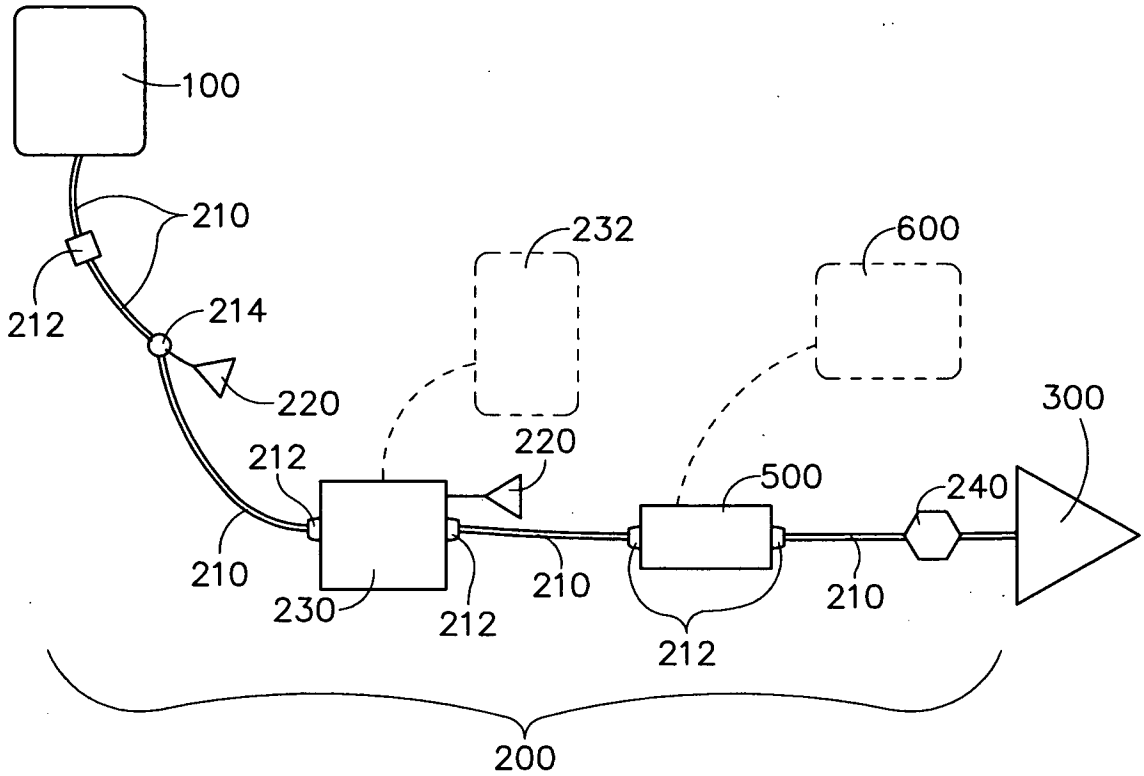


FIG. 1C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200

FIG. 2

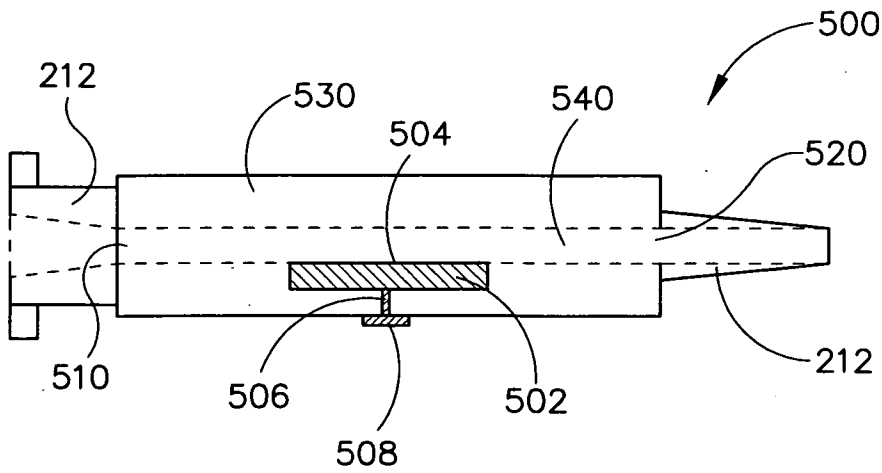
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FIG. 3A

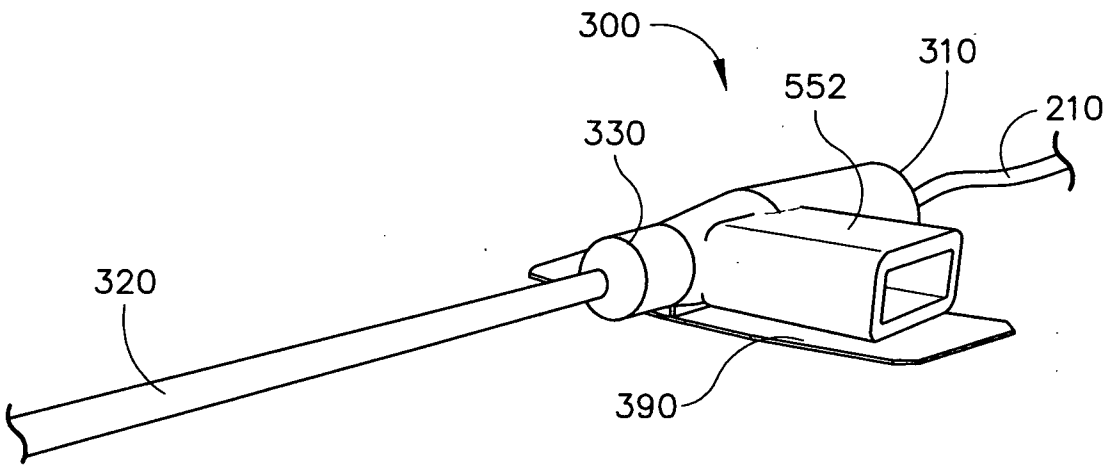
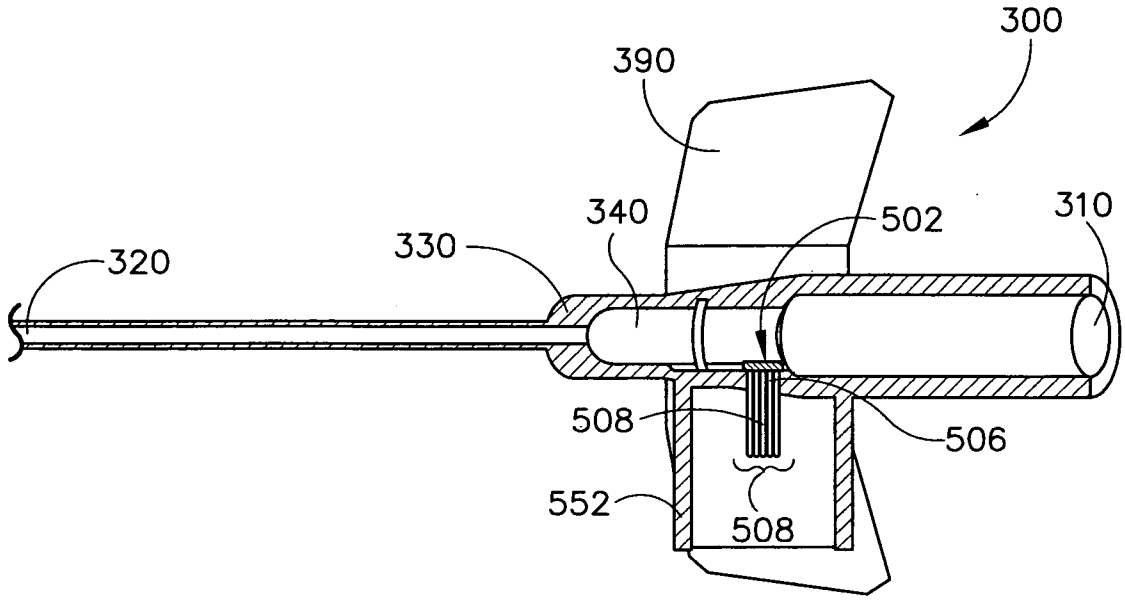


FIG. 3B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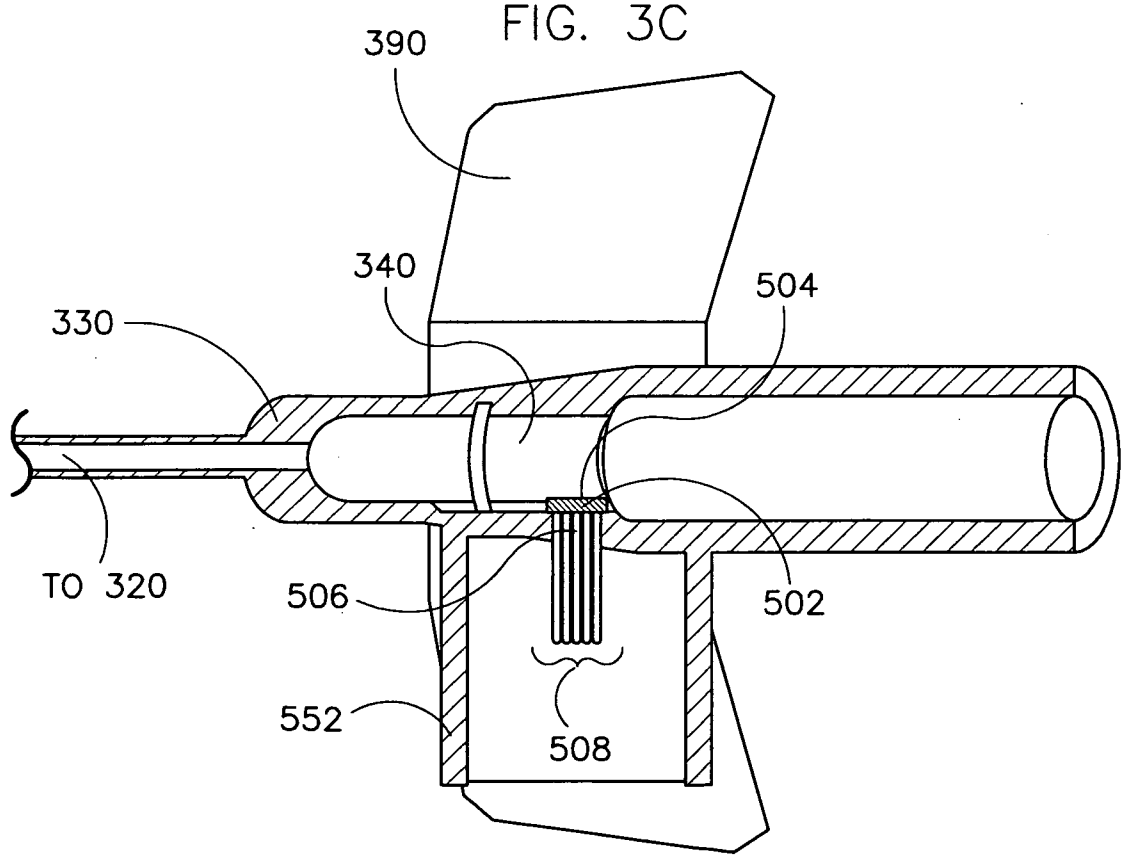
508

FIG. 3C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TO 320
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502
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508

FIG. 4

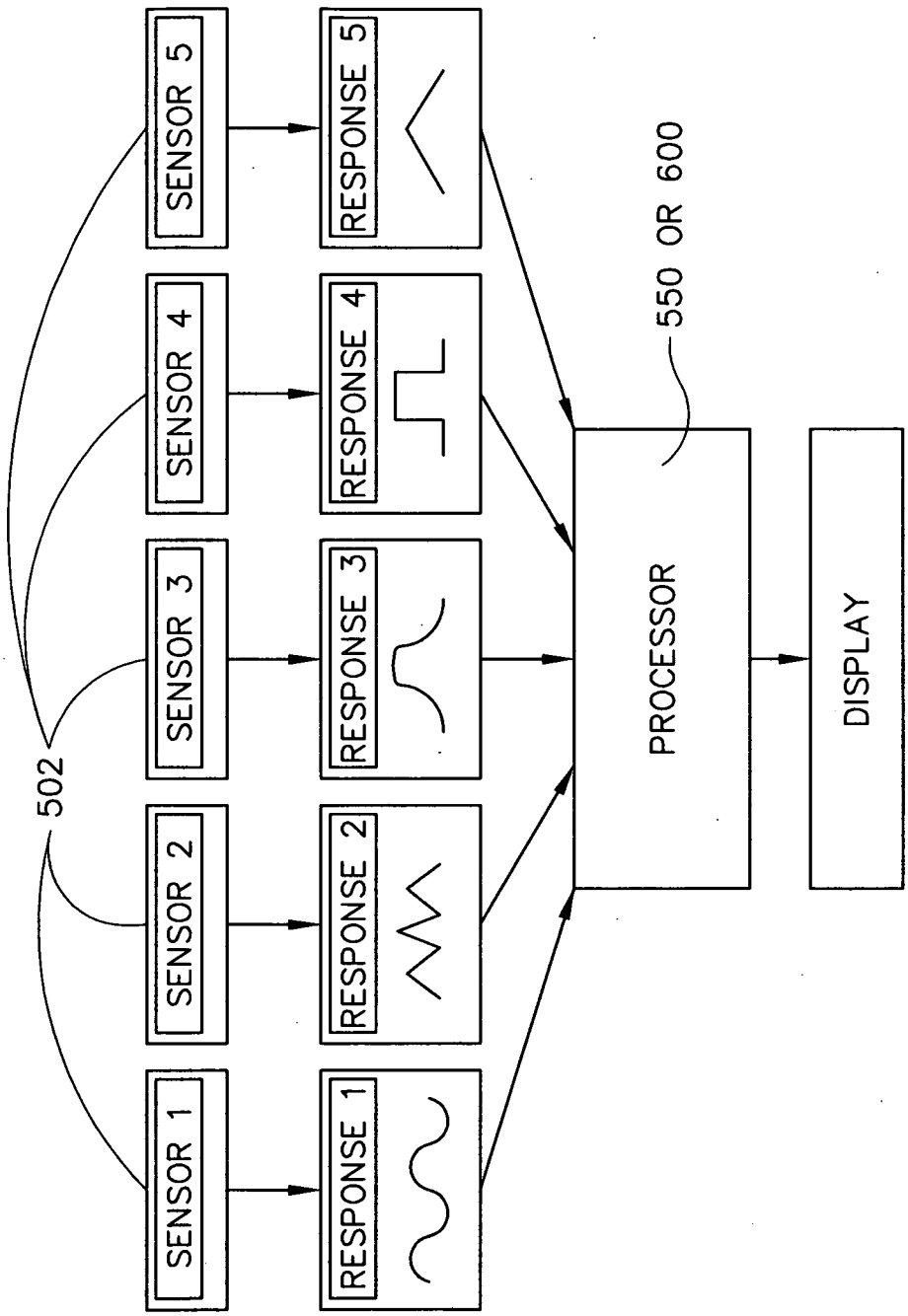

SENSOR 1
SENSOR 2
SENSOR 3
SENSOR 4
SENSOR 5
RESPONSE 1
RESPONSE 2
RESPONSE 3
RESPONSE 4
RESPONSE 5
502
550 OR 600
PROCESSOR
DISPLAY

FIG. 5A

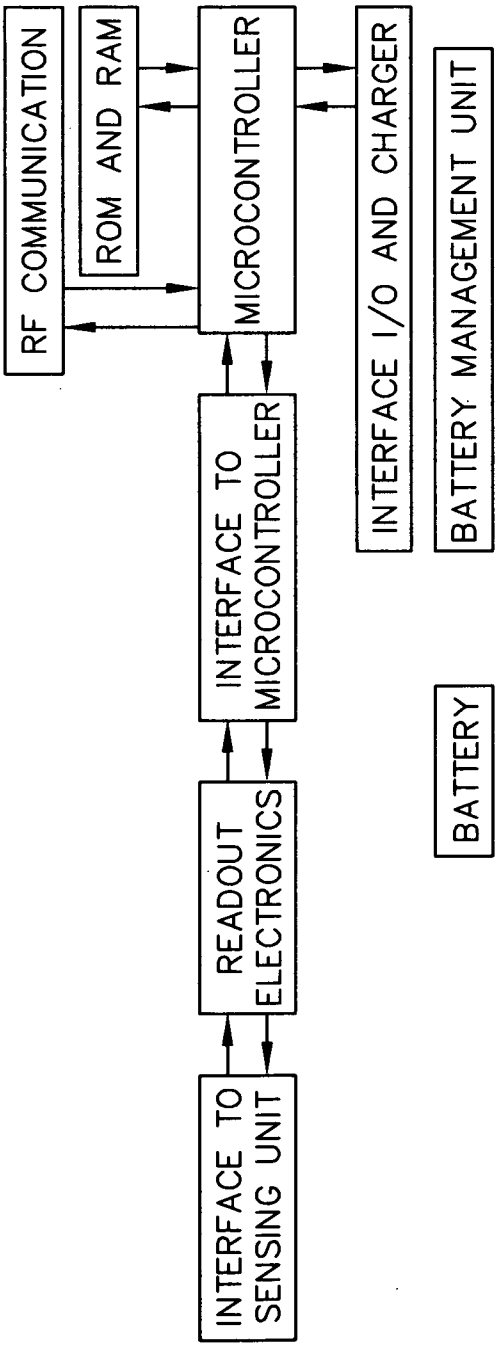

RF COMMUNICATION
ROM AND RAM
MICROCONTROLLER
INTERFACE I/O AND CHARGER
BATTERY MANAGEMENT UNIT
INTERFACE TO MICROCONTROLLER
BATTERY
READOUT ELECTRONICS
INTERFACE TO SENSING UNIT

FIG. 5B

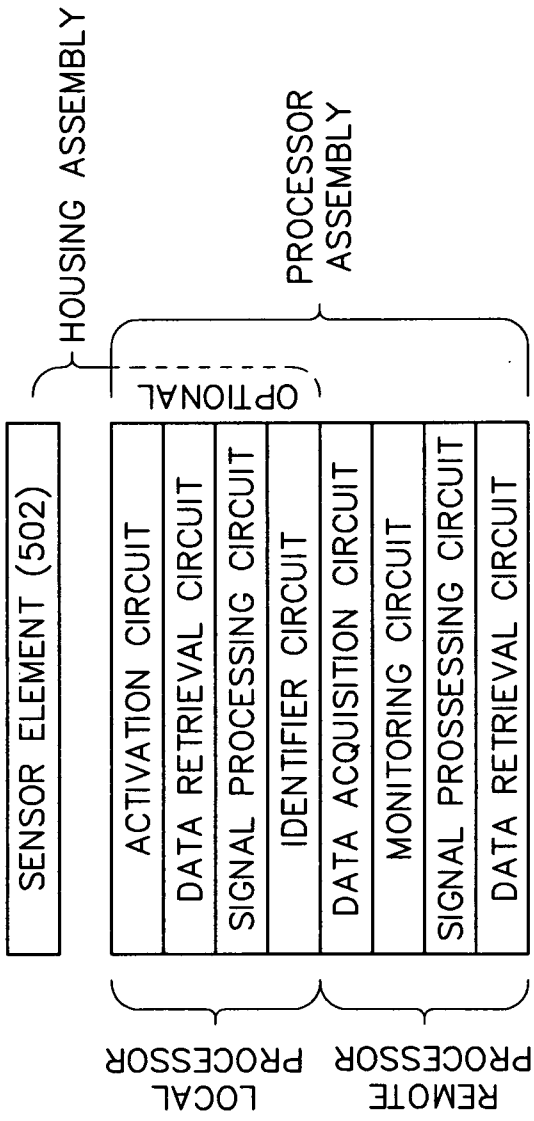

HOUSING ASSEMBLY
PROCESSOR ASSEMBLY
OPTIONAL
SENSOR ELEMENT (502)
ACTIVATION CIRCUIT
DATA RETRIEVAL CIRCUIT
SIGNAL PROCESSING CIRCUIT
IDENTIFIER CIRCUIT
DATA ACQUISITION CIRCUIT
MONITORING CIRCUIT
SIGNAL PROSSESSING CIRCUIT
DATA RETRIEVAL CIRCUIT
LOCAL PROCESSOR
REMOTE PROCESSOR

FIG. 5E

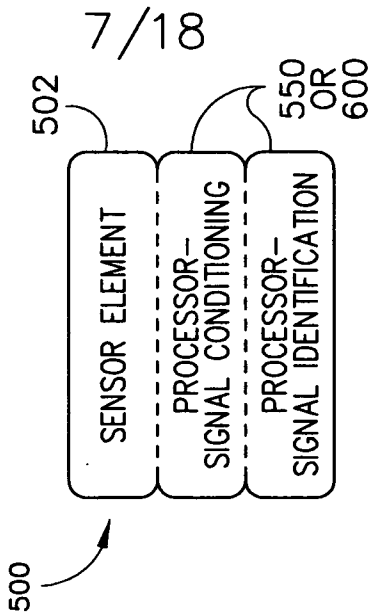


FIG. 5D

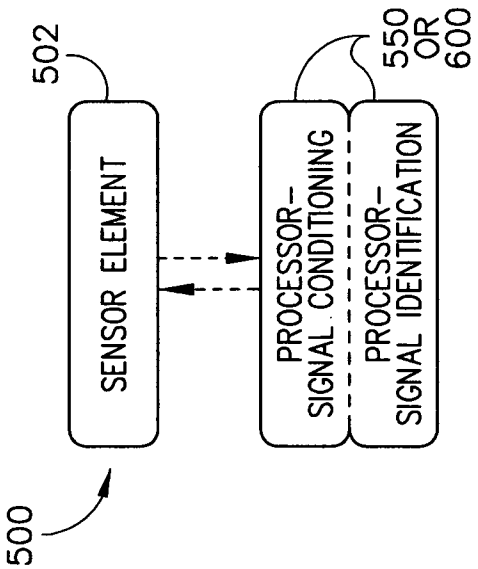


FIG. 5C

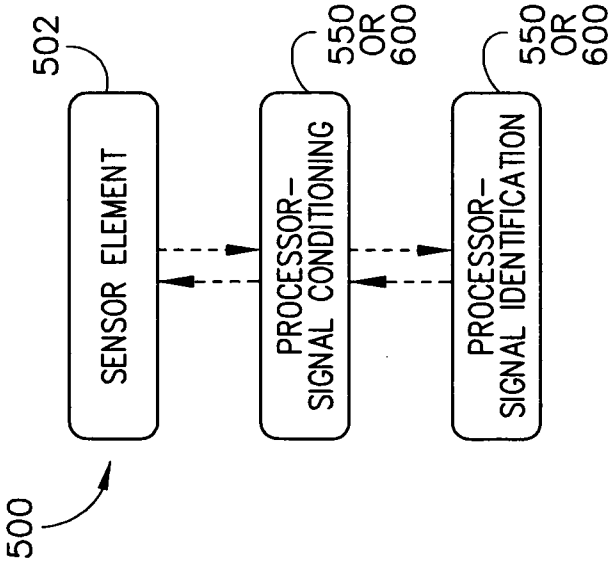
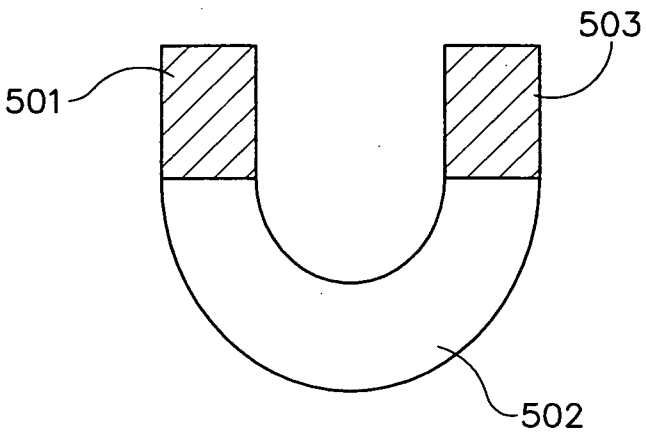


FIG. 6A



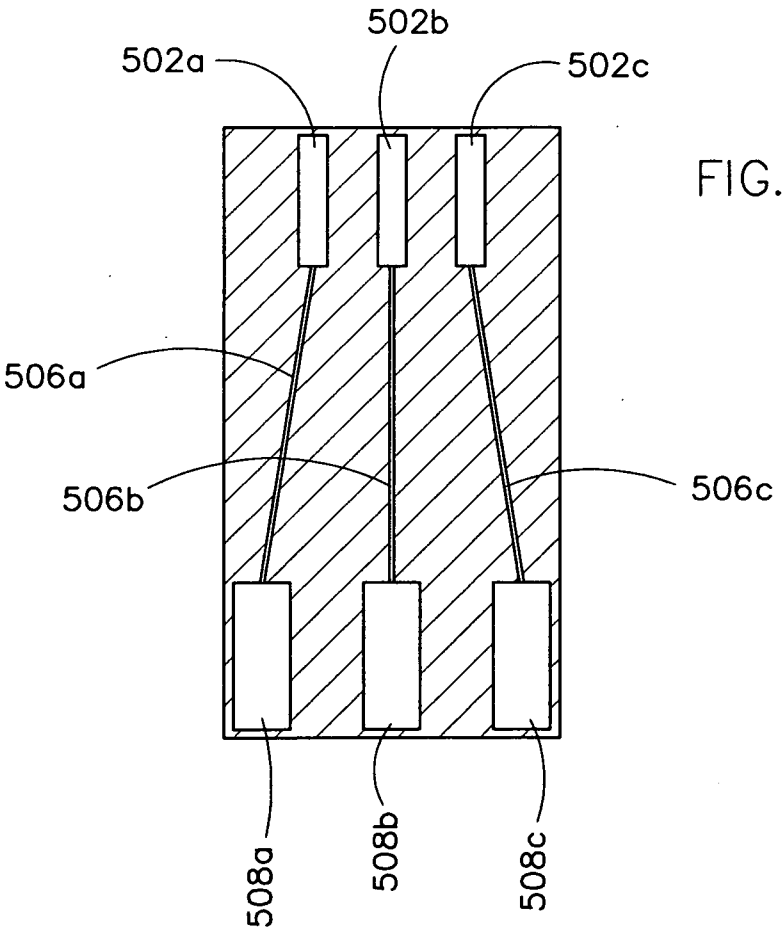


FIG. 6B

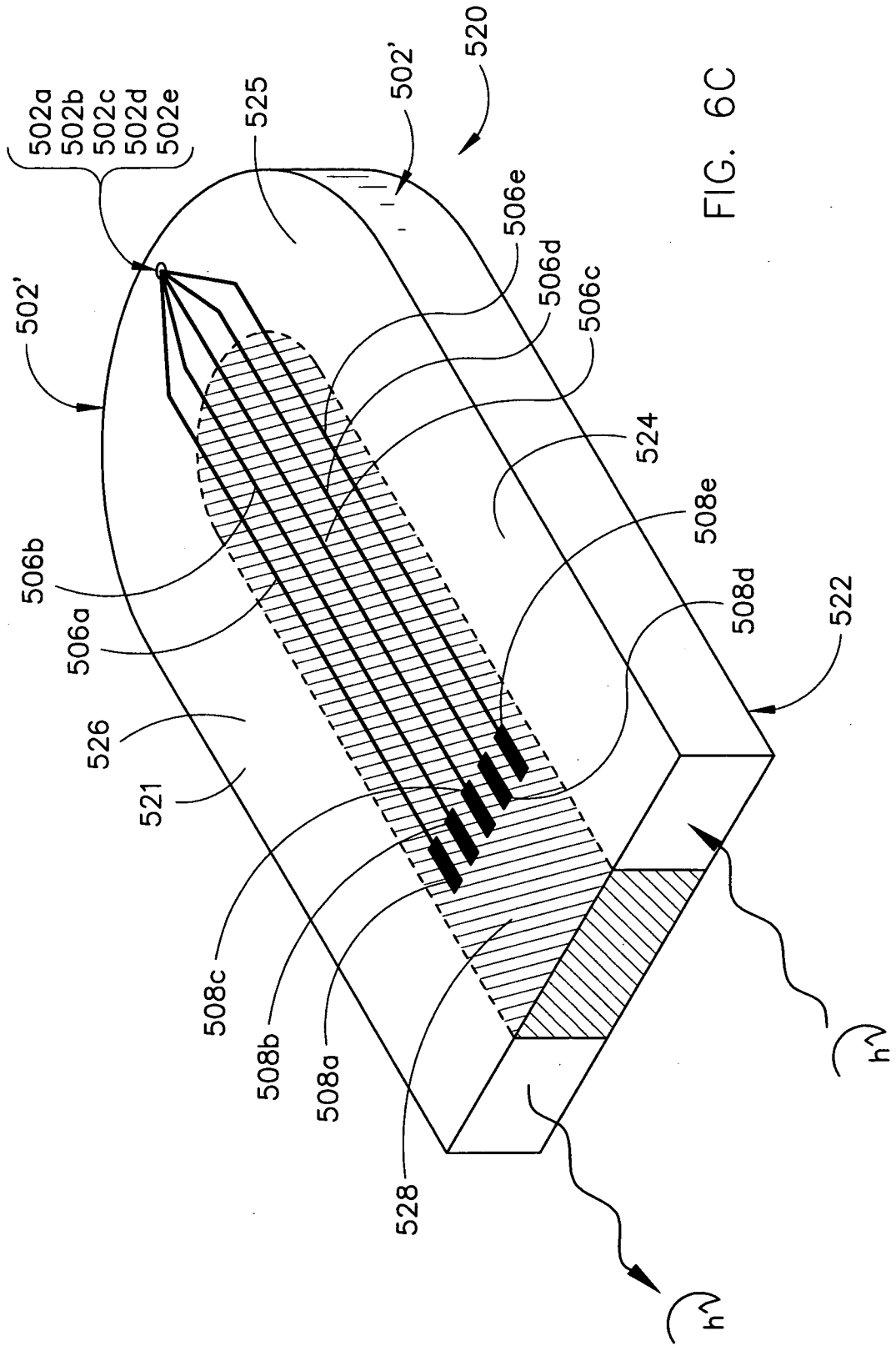
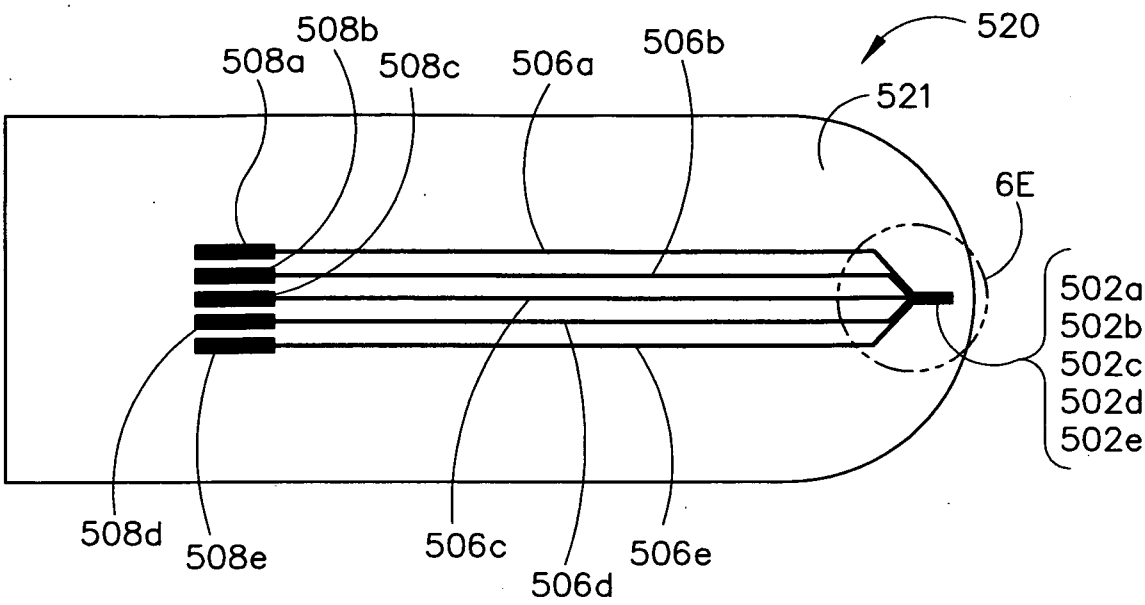

502a
502b
502c
502d
502e
525
502'
520
506e
506d
506c
502'
524
508e
506b
506a
508d
522
526
521
508c
508b
508a
528
h1
h1

FIG. 6C

FIG. 6D


508b
508a
508c
506a
506b
520
521
6E
502a
502b
502c
502d
502e
508d
508e
506c
506d
506e

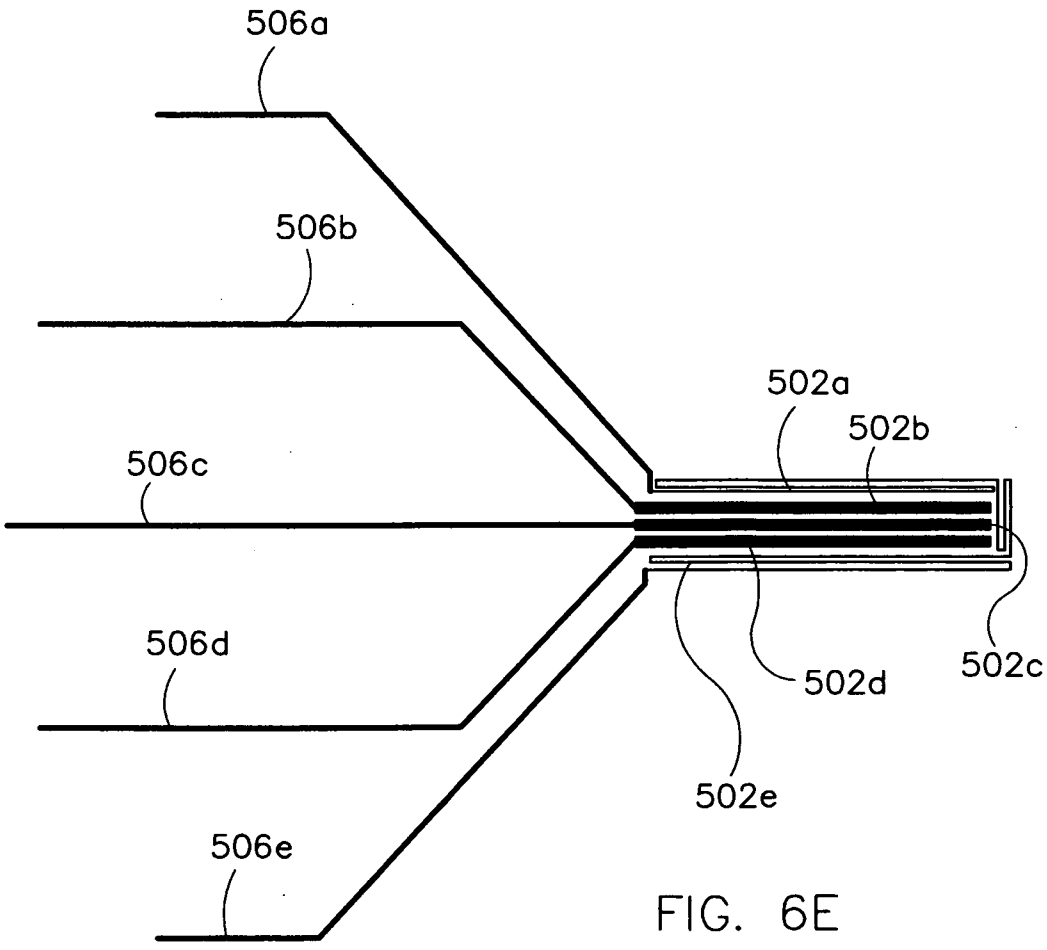

506a
506b
502a
502b
506c
506d
502d
502c
502e
506e

FIG. 6E

FIG. 6F

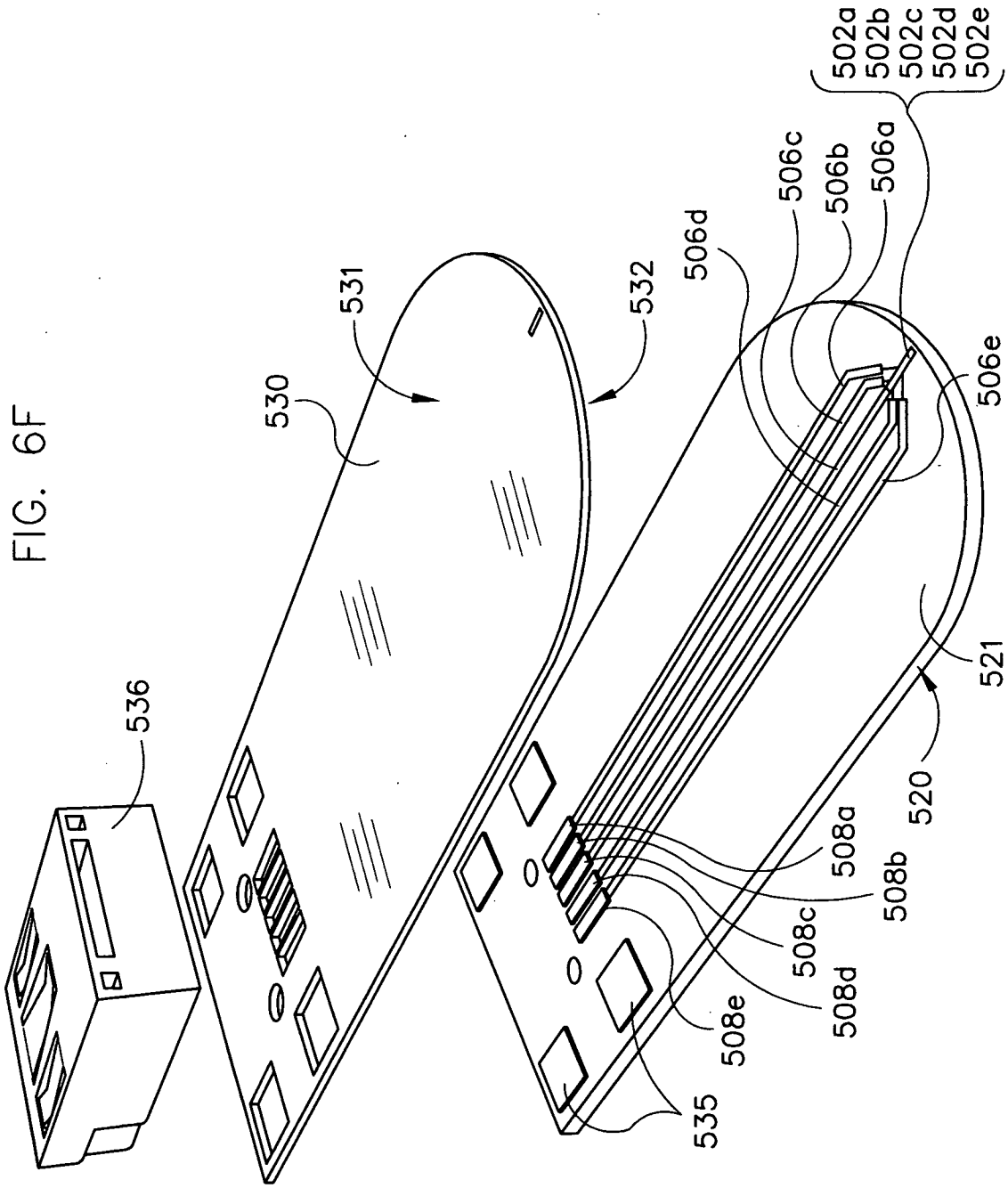

502a
502b
502c
502d
502e
506c
506b
506a
506d
506e
531
532
530
536
521
520
508a
508b
508c
508d
508e
535

FIG. 6G

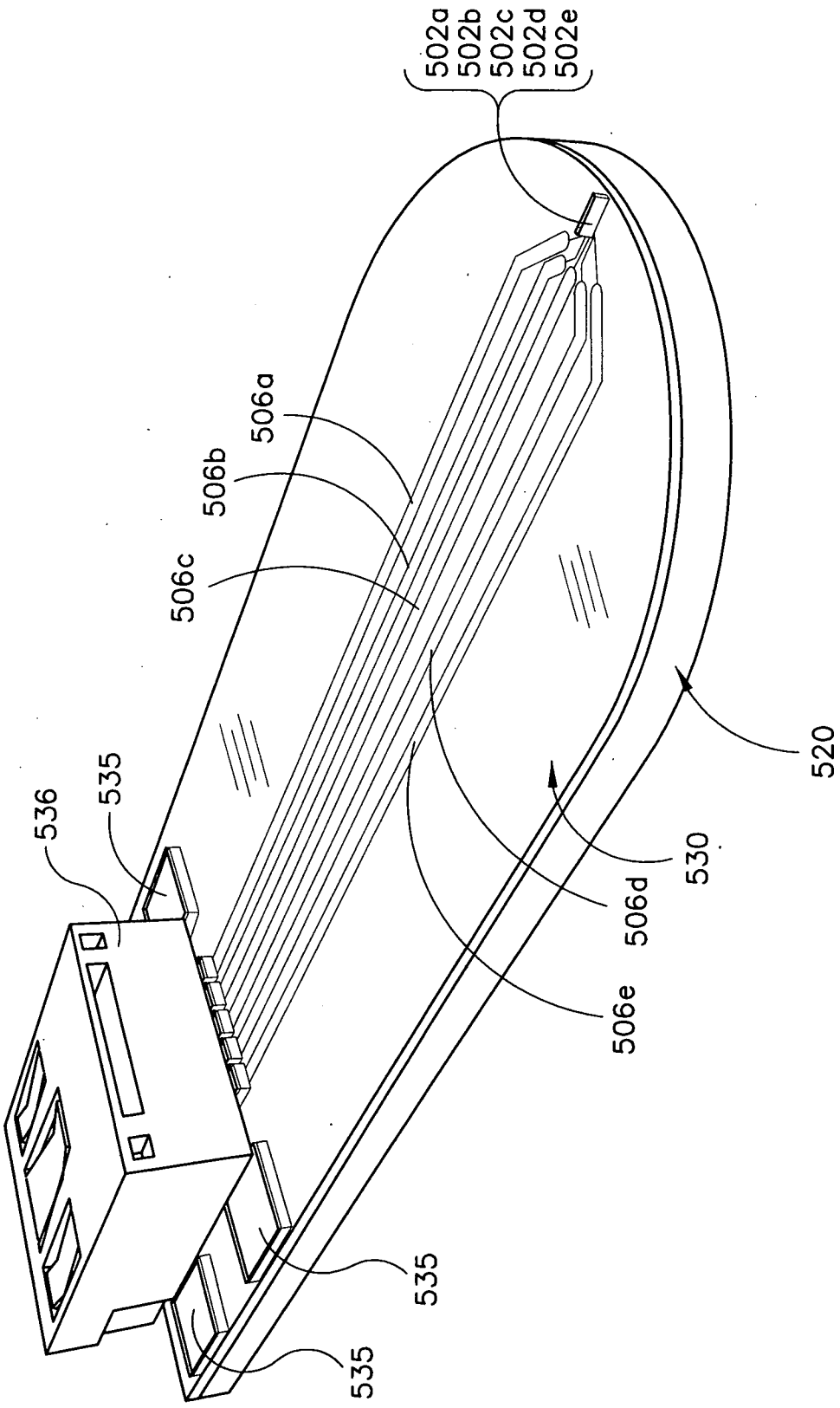

502a
502b
502c
502d
502e
506a
506b
506c
506d
506e
520
530
535
536
535
535

FIG. 7A

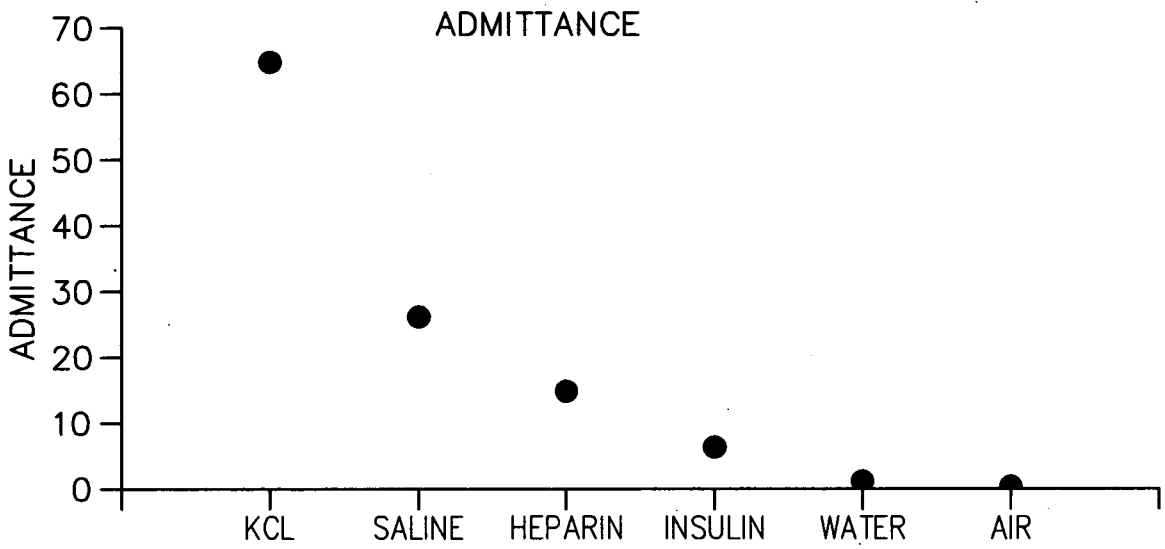

ADMITTANCE
ADMITTANCE
70
60
50
40
30
20
10
0
KCL
SALINE
HEPARIN
INSULIN
WATER
AIR

FIG. 7B

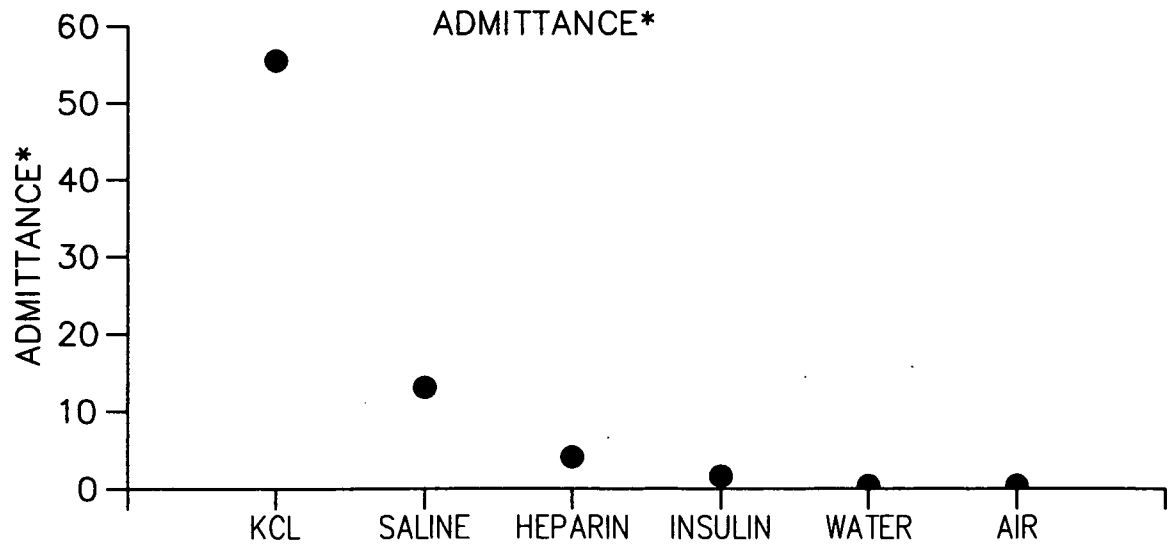

ADMITTANCE*
ADMITTANCE*
60
50
40
30
20
10
0
KCL
SALINE
HEPARIN
INSULIN
WATER
AIR

FIG. 7C

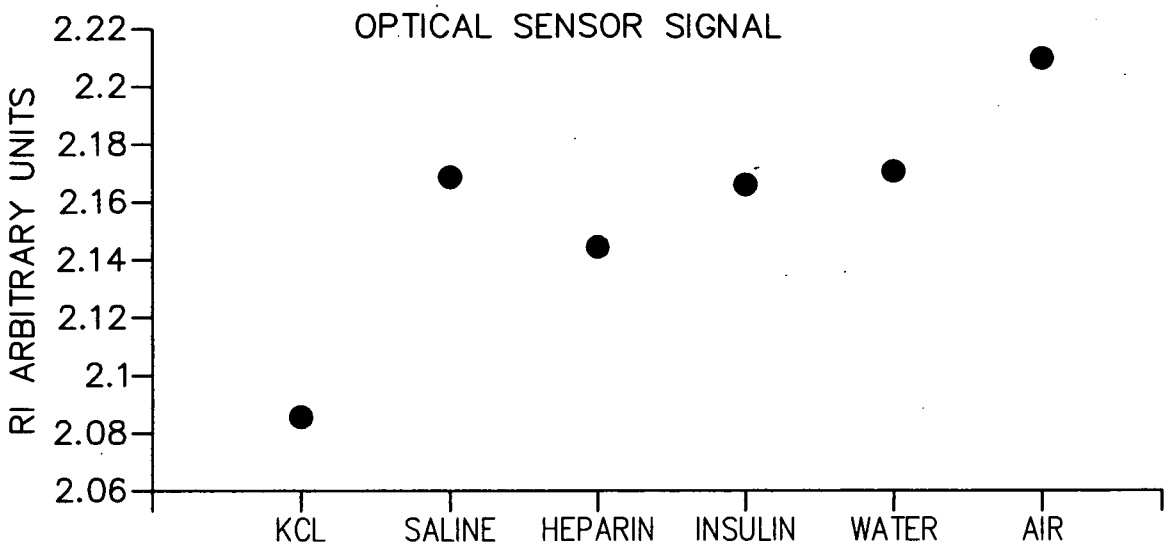

OPTICAL SENSOR SIGNAL
RI ARBITRARY UNITS
2.22
2.2
2.18
2.16
2.14
2.12
2.1
2.08
2.06
KCL
SALINE
HEPARIN
INSULIN
WATER
AIR

FIG. 7D

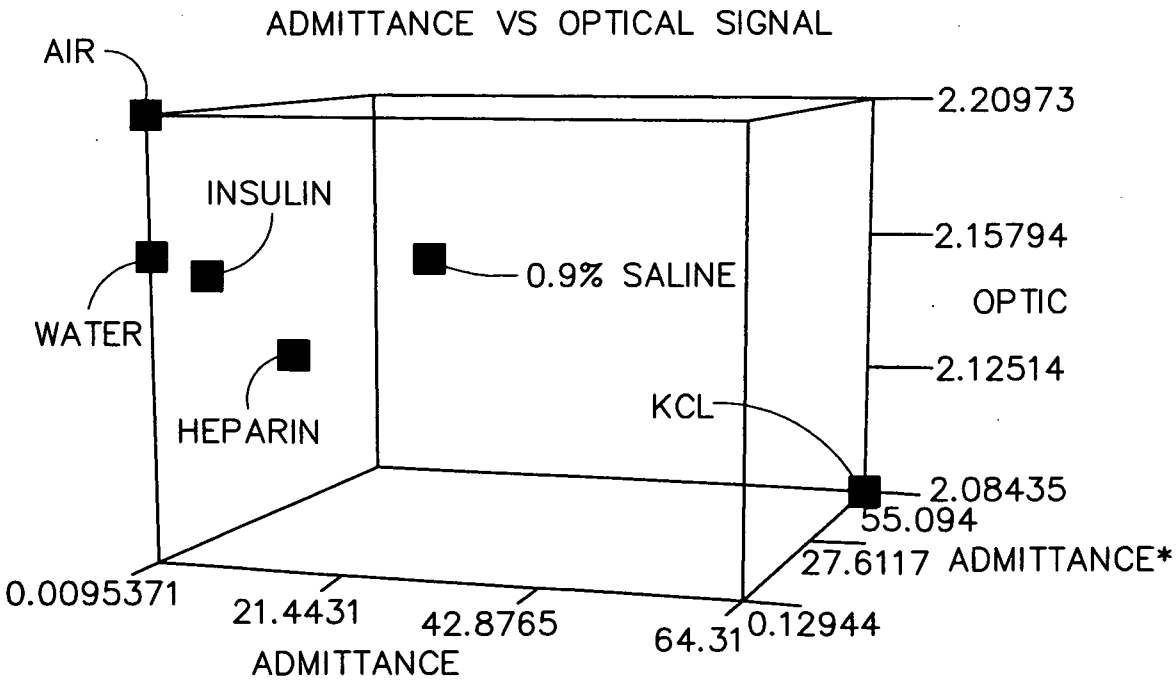

ADMITTANCE VS OPTICAL SIGNAL
AIR
INSULIN
WATER
HEPARIN
0.9% SALINE
KCL
2.20973
2.15794
OPTIC
2.12514
2.08435
55.094
27.6117 ADMITTANCE*
0.12944
64.31
42.8765
21.4431
0.0095371
ADMITTANCE

FIG. 8A

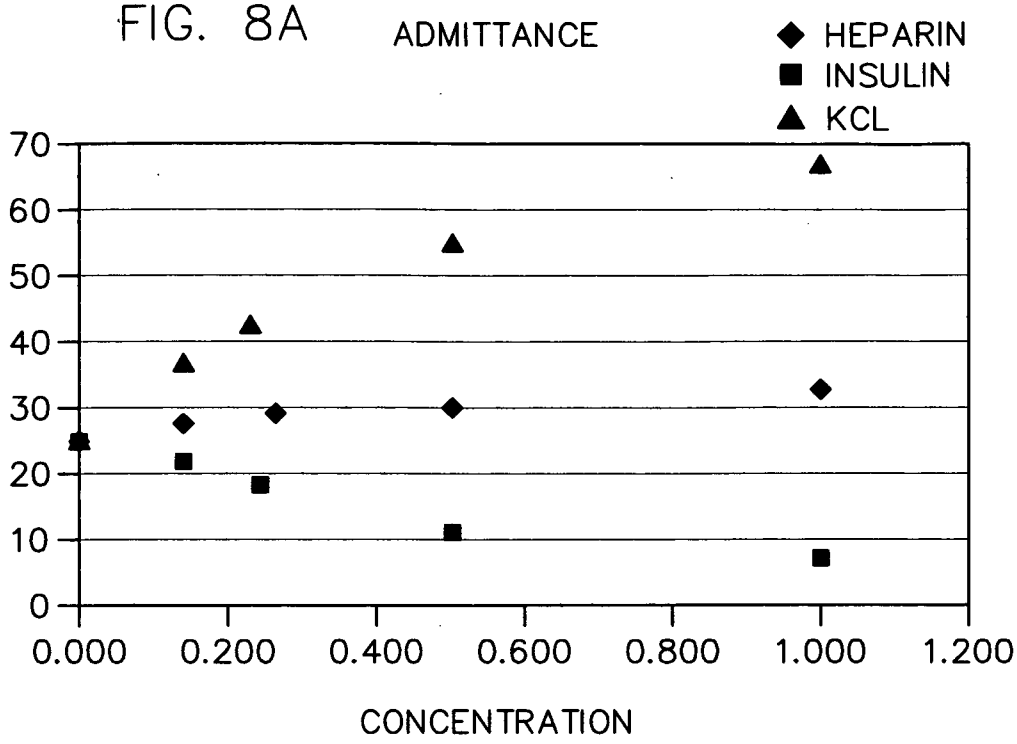

ADMITTANCE
HEPARIN
INSULIN
KCL
70
60
50
40
30
20
10
0
0.000
0.200
0.400
0.600
0.800
1.000
1.200
CONCENTRATION

FIG. 8B

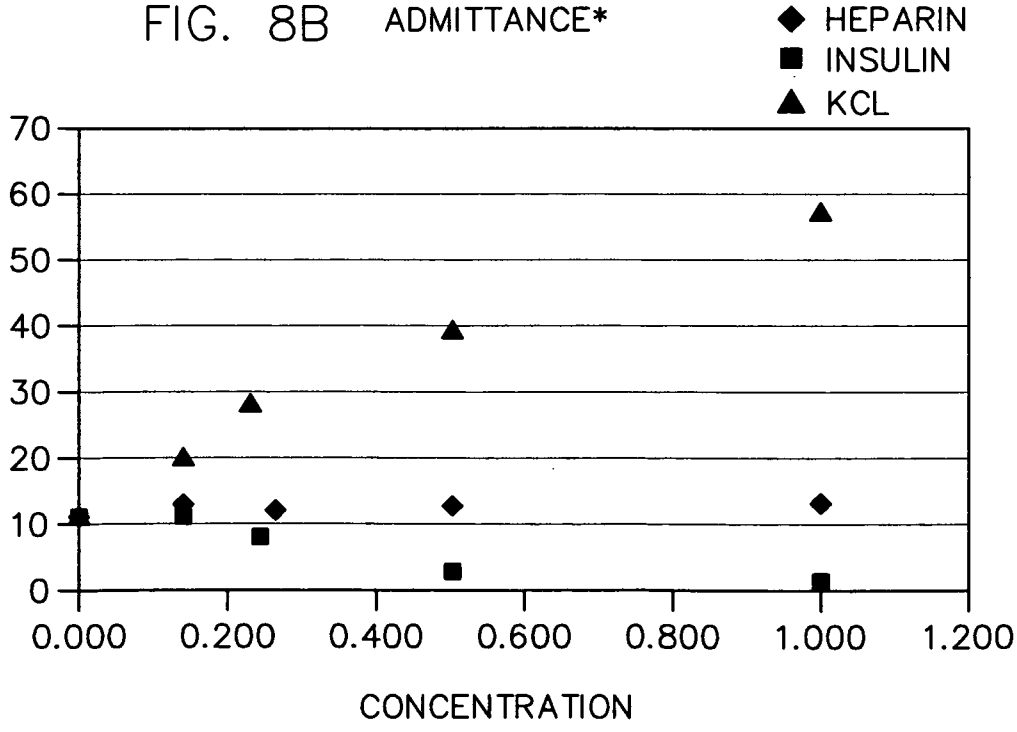

ADMITTANCE*
HEPARIN
INSULIN
KCL
70
60
50
40
30
20
10
0
0.000
0.200
0.400
0.600
0.800
1.000
1.200
CONCENTRATION

FIG. 8C

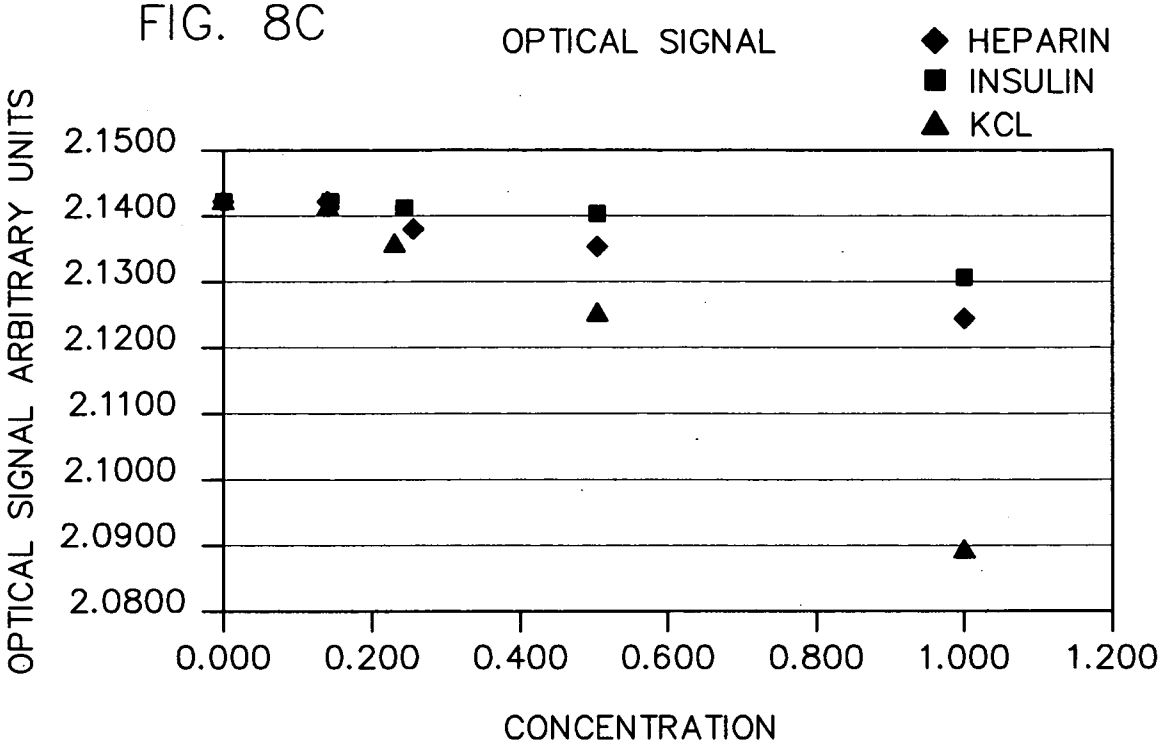

OPTICAL SIGNAL
HEPARIN
INSULIN
KCL
OPTICAL SIGNAL ARBITRARY UNITS
2.1500
2.1400
2.1300
2.1200
2.1100
2.1000
2.0900
2.0800
0.000
0.200
0.400
0.600
0.800
1.000
1.200
CONCENTRATION

FIG. 8D

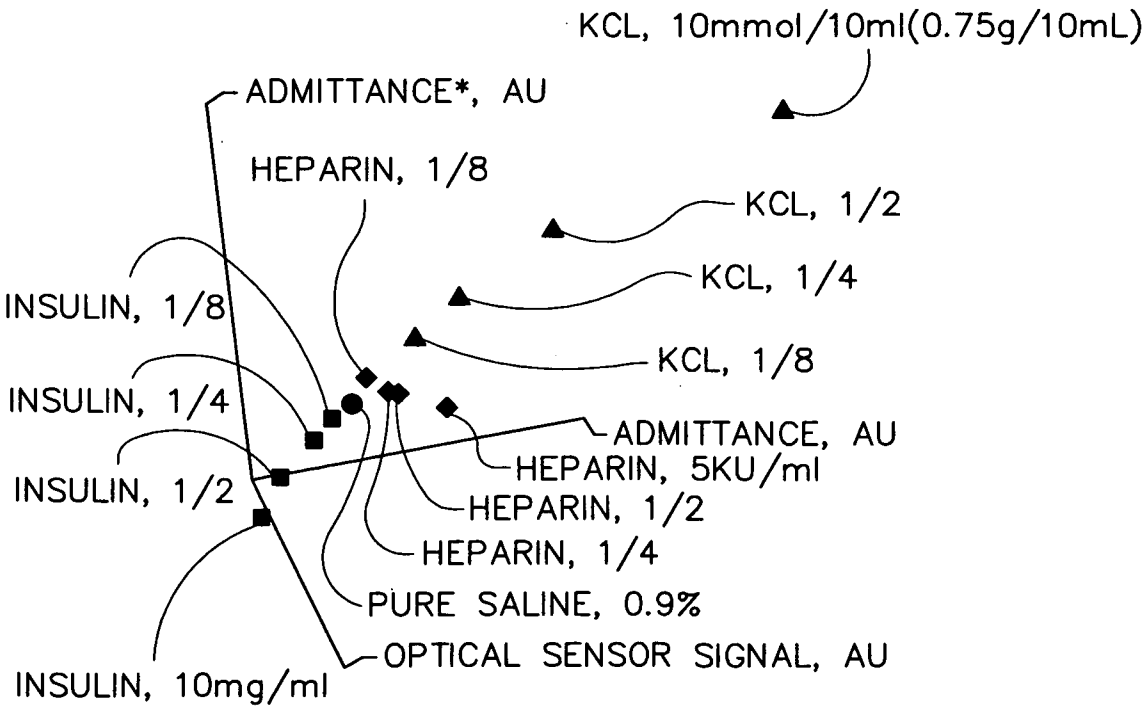

KCL, 10mmol/10ml(0.75g/10mL)
ADMITTANCE*, AU
HEPARIN, 1/8
KCL, 1/2
KCL, 1/4
INSULIN, 1/8
KCL, 1/8
INSULIN, 1/4
ADMITTANCE, AU
HEPARIN, 5KU/ml
INSULIN, 1/2
HEPARIN, 1/2
HEPARIN, 1/4
PURE SALINE, 0.9%
OPTICAL SENSOR SIGNAL, AU
INSULIN, 10mg/ml

FIG. 9A

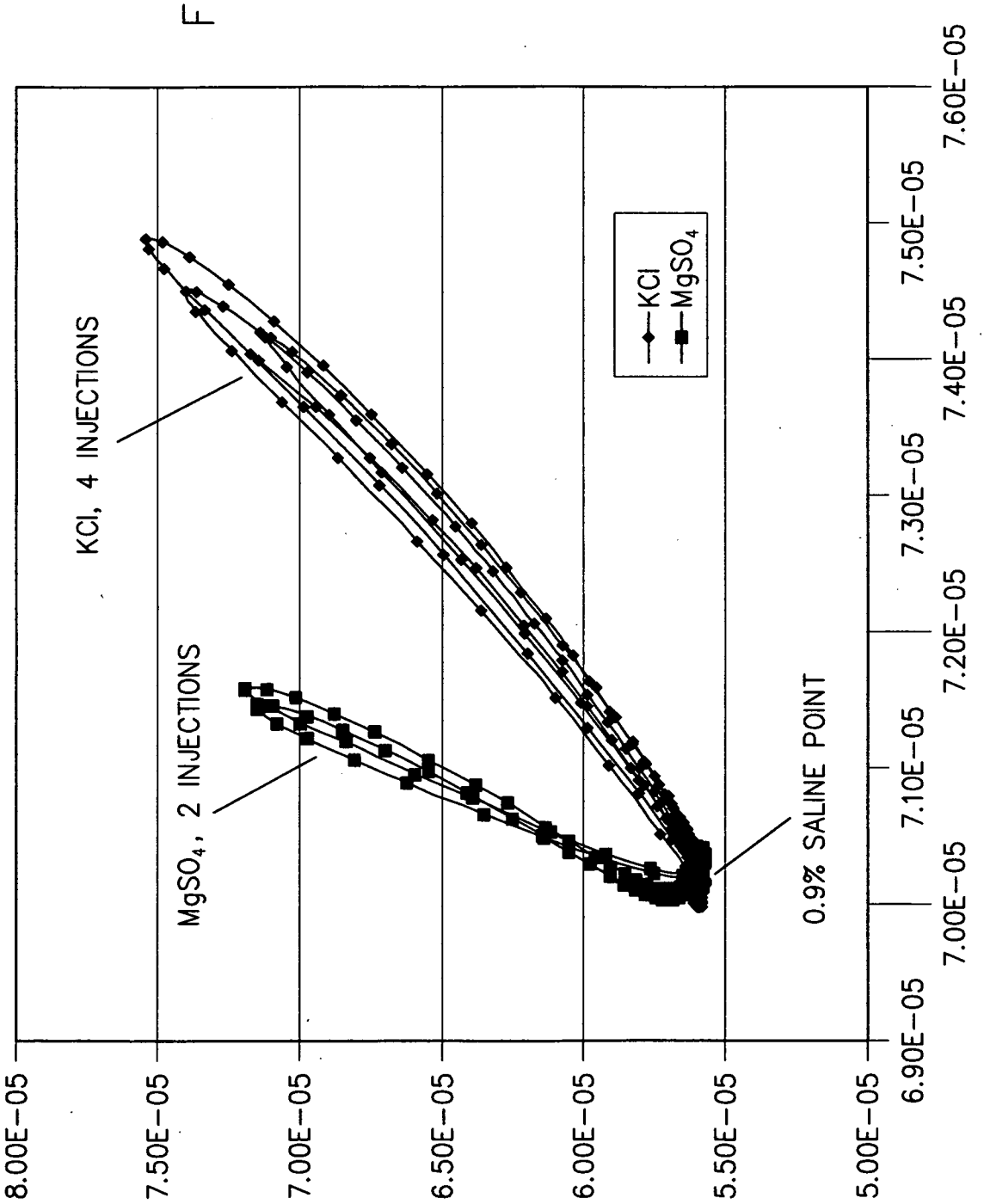
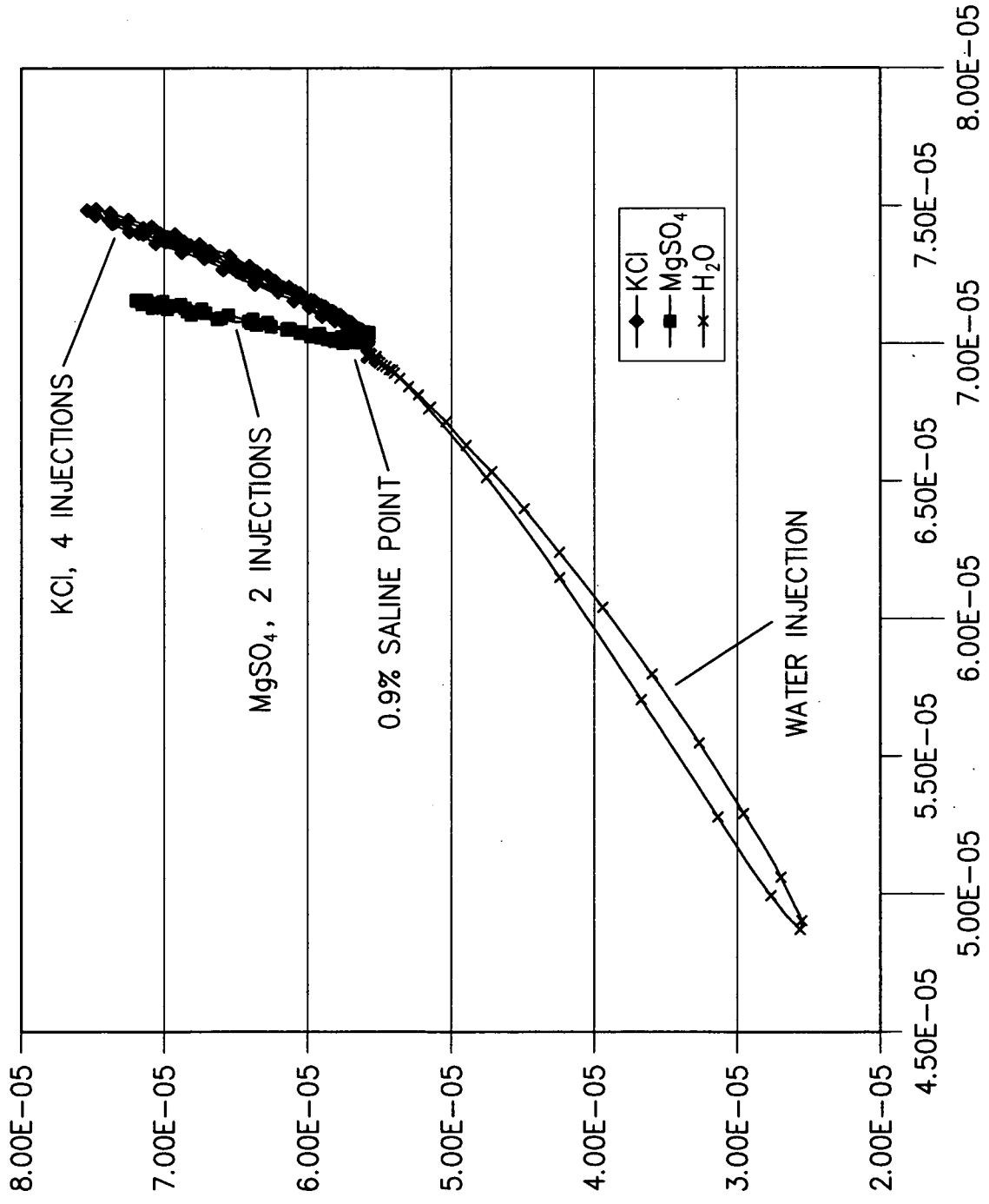

KCl, 4 INJECTIONS
$MgSO_4$, 2 INJECTIONS
0.9% SALINE POINT
KCl
$MgSO_4$
8.00E−05
7.50E−05
7.00E−05
6.50E−05
6.00E−05
5.50E−05
5.00E−05
6.90E−05
7.00E−05
7.10E−05
7.20E−05
7.30E−05
7.40E−05
7.50E−05
7.60E−05

FIG. 9B


KCl, 4 INJECTIONS
$MgSO_4$, 2 INJECTIONS
0.9% SALINE POINT
WATER INJECTION
KCl
$MgSO_4$
H_2O
8.00E−05
7.00E−05
6.00E−05
5.00E−05
4.00E−05
3.00E−05
2.00E−05
4.50E−05
5.00E−05
5.50E−05
6.00E−05
6.50E−05
7.00E−05
7.50E−05
8.00E−05

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/001494

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/142 G06F19/00

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
G06F A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2004/033003 A (ALLGEYER DEAN O [US]) 22 April 2004 (2004-04-22) the whole document -----	1-7, 12-39, 41-43, 45, 47-50, 52-107, 127-129
X	US 2004/171983 A1 (SPARKS DOUGLAS R [US] ET AL) 2 September 2004 (2004-09-02) the whole document -----	17-41, 47-50, 52-56, 60-64, 99-107, 127-132

-/--

[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
25 June 2009	02/07/2009
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Guidoin, M

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2009/001494

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2005/007223 A (JOHN SASHA [CA]) 27 January 2005 (2005-01-27) abstract; figure 1 paragraph [0062] - paragraph [0099] paragraphs [0133], [0144], [0156]	1-107, 127-132
X	US 2003/204330 A1 (ALLGEYER DEAN O [US]) 30 October 2003 (2003-10-30) the whole document	96-107
X	US 2002/183693 A1 (PETERSON THOMAS L [US] ET AL) 5 December 2002 (2002-12-05) the whole document	17-41, 47-50, 52-56, 60-64, 99-107, 127-132
A	EP 1 739 585 A (GEN ELECTRIC [US]) 3 January 2007 (2007-01-03) the whole document	1-107, 127-132
A	US 2007/191700 A1 (SAY JAMES [US] ET AL) 16 August 2007 (2007-08-16) abstract	1-107, 127-132

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2009/001494

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.: 108-126
because they relate to subject matter not required to be searched by this Authority, namely:

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by surgeryRule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

2. [ ] Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this international search reportcovers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.

[ ] The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No
PCT/US2009/001494

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 2004033003 A	22-04-2004	AT 400312 T	15-07-2008
		AU 2003239122 A1	04-05-2004
		EP 1545659 A1	29-06-2005
US 2004171983 A1	02-09-2004	NONE	
WO 2005007223 A	27-01-2005	US 2006204532 A1	14-09-2006
		US 2005277912 A1	15-12-2005
US 2003204330 A1	30-10-2003	NONE	
US 2002183693 A1	05-12-2002	US 2008132844 A1	05-06-2008
		US 2008065016 A1	13-03-2008
		US 2008065007 A1	13-03-2008
EP 1739585 A	03-01-2007	CN 1971271 A	30-05-2007
		US 2006287884 A1	21-12-2006
US 2007191700 A1	16-08-2007	NONE	