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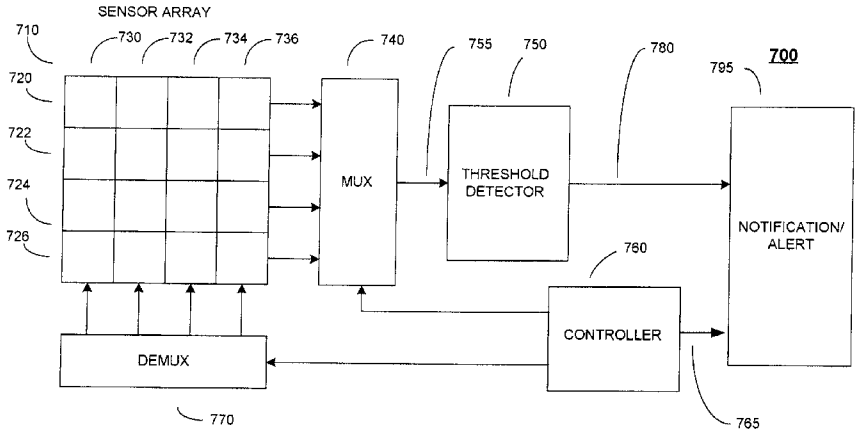

FIGURE 17

(57) Abstract: A methodology and an apparatus for the detection of biological substances employing the integration of multiple functions and units designed into and implemented in a sensor unit and system. The deployment of a set of sensor units as a group results in a distributed detecting, discriminating, and alerting system and network. Distribution of the sensor units facilitates real-time, in the field detection of different biological substances such as viruses, bacteria, spores, allergens, and other toxins that can be suspended in multiple media such as air, liquid, and blood. Besides detection/sensing, the system and individual sensor units perform: data acquisition, data development, data storage, statistical analysis, and data transmission.

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METHODOLOGY AND APPARATUS FOR THE DETECTION OF BIOLOGICAL SUBSTANCES

FIELD OF THE INVENTION

The present invention is directed to a miniaturized sensor and group of sensors sensitive to various biological substances such as viruses, bacteria, spores, allergens and other toxins as well as a system for analyzing the outputs of the sensors.

BACKGROUND OF THE INVENTION

Due to the increased level of terrorism in the world as well as increased globalization, there is a need to be able to reliably and quickly detect, analyze and report, in real-time the existence of biological substances such as viruses, bacteria, spores, allergens and other toxins within the environment and within the human and animal population.

In addition to detecting toxins that may be introduced to the environment and to the human and animal population as a result of biological warfare and terrorist attacks, there also exists a need for the detection of naturally occurring biological organisms that may also be harmful to world populations. For example, avian influenza is a viral infection of the respiratory and pulmonary system. It is classed as an influenza Type A, and like other Type A influenzas, it is subject to gradual mutations and sudden changes in its surface proteins. This class of influenza may cause major pandemics. Type A viruses that cause avian influenza are identified by differences in two surface proteins called hemagglutinin (H) and neuraminidase (N). There are 16 different hemagglutinin subtypes and 9 different neuraminidase subtypes. Hemagglutinin is a glycoprotein that binds the virus to a cell being infected and neuraminidase is an enzyme that helps the virus breach cell walls. They are both antigens that stimulate an immune response that results in the

production of antibodies. Detection may be accomplished indirectly by detection of antibodies produced and directly by detection of the antigens. The avian influenza virus is identified by the designation H5N1 because it includes a specific combination of hemagglutinin and neuraminidase subtypes. Other Type A viruses include but are not limited to H1N1, H2N2, H3N2, H3N8, H5N2 and H7N7.

Another example of requirements for detection of harmful biological substances is the detection of the presence of viral antigens in the blood. This approach may be used to diagnose HIV-1 Human immunodeficiency virus (HIV-1)) infection. One of the more prevalent antigens for this purpose is the capsid antigen, P24, a viral structural protein that makes up most of the HIV virus core particle. Because high titers of P24 antigen are present in the serum of acutely infected individuals during the short period between infection and seroconversion, P24 antigen assays are useful in the diagnosis of HIV-1 infection. The advantage of the P24 testing is that it can detect HIV infection days earlier, before antibodies develop and that it is a quantitative test that shows the intensity of HIV expression in the body which is a measure of how fast the disease is progressing. After seroconversion, the antigen is bound by P24-specific antibodies and becomes undetectable in the majority of infected individuals. For this reason, P24 antigen assays are not useful for diagnosing HIV-1 infection in otherwise healthy individuals who are thought to have established infection. However, later in the course of the disease, the serum P24 antigen again becomes detectable in 30-79% of patients. The presence of detectable P24 antigens is associated with an increased risk of clinical progression of the HIV-1 virus. Quantitative P24 assays are used to assess the antiviral activity of new drugs that are being tested to counteract the HIV-1 virus.

SUMMARY OF THE INVENTION

The problems associated with preventing the widespread use of biological warfare and in reliably and quickly detecting, analyzing and reporting, in real-time, the existence of biological substances such as viruses, bacteria, spores, allergens and other toxins within the environment and within the human and animal population are addressed by the present invention which utilizes a self-contained, regular-scale as well as millimeter-sized miniaturized -scale sensing and communication platform for a massively distributed sensor network with flexible network hierarchy and secure data flow. Individual sensor units in the form of chips are designed and manufactured, and can be miniaturized to be as small as the size of a grain of sand, and contain sensors, a processor unit, a memory, bi-directional wireless communications, and an internal power supply. Each sensor unit is controlled by a self-contained microcontroller in the form of a digital signal processor (DSP). This DSP controls both tasks performed by the sensor chip and, to conserve energy, power management between and for the various components of the system. Periodically, the DSP receives a reading from the sensor unit provided with one or more sensors contained on the chip, processes the data received from the sensors, and stores results in its memory. It also pseudo randomly activates the optical, acoustical and/or radio frequency (RF) transceiver provided on each sensor unit to monitor for incoming communication attempts. This communication may include new programs, data or messages from/to other sensor units or from/to a base station router(s) which controls the operation of a plurality of sensor units. In response to a message or upon initiation of a message, the DSP will use the RF transceiver, room re-transmitter (field operation station), or laser to transmit sensor data or a message to the router, another sensor unit or a centralized station. The router would also direct communication to or from the centralized station. To address the detection of different kinds of

biological substances such as viruses, bacteria, allergens, molds, proteins, and toxins (collectively, "targets"), the invention incorporates two classes of sensors with totally different manners of sensing and acquiring information.

The first of these sensors is acoustically based and may be used repeatedly without degradation. This sensor is functionally dependent on acoustical wave technologies. The sensor portion of the sensor unit is constructed as a micro-miniature mesh (net) on a silicon base, and has its own resonant frequency. For more accurate resonance readings other elements such as sapphire, quartz, or a germanium silica oxide (GSO) crystal, or a beryllium silica oxide (BSO) crystal may be used. The surface of the sensor unit is relatively small, approximately $1mm^2$ of working surface. To achieve greater sensor sensitivity and selectivity to the targets, both sides of the sensor unit base are charged by static electricity. The acoustically based sensor unit operates in three primary modes - collecting data, measuring data, and cleaning the sensor unit. During the collecting mode, targets come in proximity to the sensor. The static electricity applied to each sensor unit surface will draw the targets toward the surface of the sensor and will stick to the sensor unit surface due to molecular adhesion forces. After a time increment determined by a timer provided in the DSP, the sensor unit will be switched to the measurement mode. At this juncture, static electricity will be switched off and the sensor surface will begin to resonate with high frequency oscillation conditions. If there are no targets adhered to the sensor unit surface, the surface will resonate at a first frequency. The sensor surface will resonate at a second frequency, unequal to the first frequency in the presence of particular targets. The power and frequency of that oscillation will be a function of the physical properties of the target particles. The oscillation would result in the target particle leaving the surface of the sensor, resulting in the generation of a pulse. The acoustical nature of the pulse will be analyzed by the DSP and compared to

data contained in a data base provided in the memory of the DSP. If any matching properties are found, this information will be relayed to the centralized station which could issue an alert. During the cleaning mode, the surface of the sensor will be cleaned by the simultaneous application of static electricity depolarization and high power pulses, at a third frequency. After cleaning, all modes may be repeated as required.

Sensor units will be calibrated to known target signatures. If the air has a preponderance of targets exhibiting the same or similar signature (mass, adhesion factor, form factor, etc.), an alert will be triggered providing the micro-biological identity of the particles. This alert would be produced based upon communication between sensor units themselves, between communication with the routers and the sensing units and communication between the sensor units, the routers and the centralized system.

Each sensor unit will be manufactured from silicon wafers on a sapphire, quartz, BSO, or GSO crystal base substrate, such as those currently used for manufacture of microchips. All frontal surfaces will be used to produce and store energy.

The second type of these sensors would be a biological based sensor falling into two categories; bio pore sensors and the optical based sensors. Bio pore sensors are micro-miniature pools made up of pores containing substances (ligands) preferably in gels or other substances, and electro-sensing technologies. These bio pores contain the ligand in gel resting on electrodes that will react based on the presence of one simple molecule of a target. During the reaction, the bio pore will produce an electric signature pulse and static electricity, which will be analyzed and trigger an alert if a particular target is present. This analyzation would include comparing the electric signature pulse with a plurality of electro signature pulses stored in the memory of the DSP. This technology will require biological data sets documenting the reactive ligand for each target. This data will be used to choose the gel substances for the bio pores. In

all other ways, including data acquisition, data processing, and data communication, operational implementations are identical for any target.

Biological optical based sensors will have much in common with bio pore sensors. The main difference in their design is the integration of light-sensing micro-systems to detect and discriminate the sequence of photon bursts generated at the interaction of the target and ligand. These photon-bursts would be in the form of electro-optical signature pulses, compared to a plurality of electro-optical signature pulses stored in the memory of the DSP.

A particularly useful biological sensor configuration relies on the use of an array of bio pore sensors that is capable of detecting various antigens of Type A viruses that cause Type A influenza, such as the H5N1 (hemagglutinin and neuraminidase) strain of the avian flu virus. The array comprises at least one bio pore array element that is coated with a gel containing H5 antibodies (in the form of ligands) that are capable of generating a unique H5 electrostatic pulse signature signal when one or more of the H5 antigens attach to one or more of the H5 antibodies. The array also comprises at least one bio pore array element that is coated with a gel containing N1 antibodies (for example, in the form of ligands) that are capable of generating a unique N1 electrostatic pulse signature signal when one or more N1 antigens attach to one or more of the N1 antibodies. Thus, the presence of the H5N1 avian flu virus in close proximity to the two sensor array elements causes the H5 antigen to be captured by and bind with the H5 antibody and the N1 antigen to be captured by and bind with the N1 antibody such that a unique H5 electrostatic pulse signature signal is generated by the array element that captures the H5 antigen, and a unique N1 electrostatic pulse signature signal is generated by the array element that captures the N1 antigen. By detecting and storing each of these unique electrostatic pulse signature signals and comparing these signals to a library of stored electrostatic

pulse signature signals, and particularly a stored H5 electrostatic pulse signature signal and a stored N1 electrostatic pulse signature signal within the library, the presence of the H5N1 avian Flu virus may be readily detected. The process is similar for the detection of other toxins and diseases. For example, an antibody (for example, in the form of a ligand) for the P24 core protein can be used in the same way to detect the antigen HIV-1. Any disease or toxin in which an antibody exists (in the form of a ligand) that will bind with the corresponding antigen for that target disease or toxin may be detected using the sensor system of this invention.

The present system for determining the presence of a biological target comprises a sensor array comprising at least one sensor element, each sensor element further comprising: a plurality of ligands of at least one ligand type applied to a coating on the sensor element; an electrostatic output signal generated by the sensor element from an interaction when one of the plurality of ligands of the at least one ligand type binds to at least one biological target type; an electrostatic sensing surface, positioned in proximity to the at least one ligand for detecting the electrostatic output signal; and a measurement means for measuring the detected electrostatic output signal. The system further comprises a controller for controlling a sequencing of the selection of sensor elements within the array to sequentially select a column of the sensor array, to sequentially select each of the rows of the array and then to sequentially select and input a sample of the electrostatic output signal of each sensor element. The present invention further comprises a means for converting the electrostatic output signal of the sensor element from an analog signal to a digital equivalent signal by a digital-to-analog converter, the digital equivalent signal being stored in the controller. The digital equivalent sample signal is combined with other digital equivalent sample signals from the same sensor element and is stored in the controller to form a digital signature signal. The

digital signature signal is transmitted to a digital signal processor which compares the digital signature signal with a library of pre-stored signature signals representing known biological targets. An alert notification is generated when the digital signature signal matches a pre-stored signal type in the library of pre-stored signature signals that represents a signature generated when the at least one ligand type binds with the at least one biological target.

The system for determining the presence of a biological target in accordance with further comprises the binding of the at least one ligand with the at least one biological target, the detecting and measuring of the electrostatic output signal, the controlling of the sequencing of the selection of sensor elements within the array and selecting of the electrostatic output signal of each sensor element, the converting of the electrostatic output signal to the digital equivalent signal, the transmitting and the comparing of the digital equivalent signal to the library of pre-stored signature signals representing known biological targets, and said binding, detecting, measuring, controlling, converting, transmitting and comparing occurs in real-time.

The system comprises at least one ligand type that is an antibody for a protein hemagglutinin subtype H5, or at least one ligand type that is an antibody for a protein neuraminidase subtype N1, or at least one ligand type that is an antibody for a protein P24 or a similar toxin.

The system may have at least one ligand type of a first sensor element selected from the group consisting of an antibody for a protein hemagglutinin and at least one ligand type of a second sensor element selected from the group consisting of an antibody for a protein neuraminidase.

The system may have a sensor element within the sensor array comprising at least one ligand type selected from the group consisting of antibodies for a protein P24.

The system further comprises at least one biological target type that may be antigens of the protein hemagglutinin

subtype H5 that bind with the at least one ligand type antibody for the protein hemagglutinin subtype H5.

The system further comprises at least one biological target type that may be antigens of the protein neuraminidase subtype N1 that bind with the at least one ligand type antibody for the protein neuraminidase subtype N1.

The system further comprises at least one biological target type that may be antigens of the protein p24 that bind with the at least one ligand type antibody for the protein p24.

The system further comprises a first sensor element of the sensor array wherein the first sensor element comprises a plurality of ligands of a first ligand type that is an antibody for hemagglutinin subtype H5, a second sensor element of the sensor array wherein the second sensor element comprises a plurality of ligands of a second ligand type neuraminidase subtype N1, means for detecting a first electrostatic output signal when an influenza virus containing an hemagglutinin subtype H5 antigen is introduced in proximity to the first sensor element, means for detecting a second electrostatic output signal when an influenza virus containing a neuraminidase subtype N1 antigen is introduced in proximity to the second sensor element, means for controlling the sequencing of the selection of the first and second sensor elements to read samples of the first and second electrostatic output signals, means for converting the first and second electrostatic output signal samples to first and second digital equivalent sample signals, means for combining a plurality of first digital equivalent sample signals from a same sensor element to form a first digital signature signal and combining a plurality of second digital equivalent sample signals from a same sensor element to form a second digital signature signal, means for transmitting the first and second digital equivalent signals to a digital signal processor which compares the first and second digital signature signals to the library of pre-stored signature signals containing a first pre-stored signature signal representing a binding event when the first

ligand type for hemagglutinin subtype H5 binds with a hemagglutinin subtype H5 antigen and a second pre-stored signature signal representing a binding event when the second ligand type for neuraminidase subtype N1 binds with a neuraminidase subtype N1 antigen, and means for generating an alert upon matching both the first digital signature signal with the first pre-stored signature signal and the second digital signature signal with the second pre-stored signature signal.

The system further comprises a first sensor element of the sensor array wherein the first sensor element comprises a plurality of ligands of a first ligand type that is an antibody for hemagglutinin subtype H5, a second sensor element of the sensor array wherein the second sensor element comprises a plurality of ligands of a second ligand type that is an antibody for neuraminidase subtype N1, means for detecting a first electrostatic output signal when an influenza virus containing an hemagglutinin subtype antigen selected from the group consisting of H1 through H4 and H6 through H16 is introduced in proximity to the first and second sensor elements, means for detecting a second electrostatic output signal when an influenza virus containing a neuraminidase subtype antigen selected from the group consisting of N2 through N9 is introduced in proximity to the first and second sensor elements, means for controlling the sequencing of the selection of the first and second sensor elements to read samples of the first and second electrostatic output signals, converting the first and second electrostatic output signals to first and second digital equivalent sample signals, means for combining a plurality of first digital equivalent sample signals from a same sensor element to form a first digital signature signal and combining a plurality of second digital equivalent sample signals from a same sensor element to form a second digital signature signal, means for transmitting the first and second digital signature signals to a digital signal processor which compares the first and second digital signature signals to a library of pre-stored signature

signals containing binding events representing a binding of an antibody for hemagglutinin subtype selected from the group consisting of H1 through H4 and H6 through H16 and representing a binding of an antibody for neuraminidase subtype selected from the group consisting of N2 through N9, and means for indicating that the antigen hemagglutinin subtype selected from the group consisting of H1 through H4 and H6 through H16 and the antigen neuraminidase subtype selected from the group consisting of N2 through N9 have been detected.

The system further comprises a first sensor element of the sensor array wherein the first sensor element comprises a plurality of ligands of a first ligand type that is an antibody for hemagglutinin subtype H5, a second sensor element of the sensor array wherein the second sensor element comprises a plurality of ligands of a second ligand type that is an antibody for neuraminidase subtype N1, a third sensor element of the sensor array wherein the third sensor element comprises a plurality of ligands of a ligand type that is an antibody for hemagglutinin with a subtype selected from the group consisting of H1 through H4 and H6 through H16, a fourth sensor element of the sensor array wherein the fourth sensor element comprises a plurality of ligands of a ligand type that is an antibody for neuraminidase with a subtype selected from the group consisting of N2 through N9, means for detecting multiple electrostatic output signals when an influenza virus containing a protein of hemagglutinin subtype selected from the group consisting of H1 through H16 is introduced in proximity to the sensor elements and an influenza virus containing a protein neuraminidase subtype selected from the group consisting of N1 through N9 is introduced in proximity to the sensor elements, means for controlling the sequencing of the selection of the sensor elements to read samples of the electrostatic output signals, means converting the electrostatic output signal samples to digital equivalent sample signals, means for combining a plurality of digital equivalent sample signals from each sensor element to form digital signature

signals; means for transmitting the digital signature signals to a digital signal processor which compares the digital signature signals to a library of pre-stored signature signals containing binding events representing a binding of an antibody for hemagglutinin with a hemagglutinin antigen with a subtype selected from the group consisting of H1 through H16 and representing a binding of an antibody for neuraminidase antigen with a subtype selected from the group consisting of N1 through N9, and means for using the comparison to the library of pre-stored signature signals to identify the antigen that has been detected selected from the group consisting of hemagglutinin H1 through H16 and the antigen that has been detected selected from the group consisting of neuraminidase N1 through N9.

The system further comprising a first sensor element of the sensor array wherein the first sensor element comprises a plurality of ligands of a p24 ligand type representing an antibody of a p24 antigen, means for detecting a first electrostatic output signal when the p24 antigen is introduced in proximity to the first sensor element, means for controlling the sequencing of the selection of the first sensor element to read samples of the first electrostatic output signal, means for converting the first electrostatic output signals to a first digital equivalent sample signal, means for combining a plurality of digital equivalent sample signals from each sensor element to form digital signature signals; means for transmitting the first digital signature signal to a digital signal processor which compares the first digital signature signal to a library of pre-stored signature signals containing a first signature signal representing a binding event when the p24 ligand type binds with the p24 antigen, and generating an alert upon matching the first digital signature signal with the first pre-stored signature signal representing a p24 binding event.

The system for determining the presence of a biological target further comprises at least one sensor element, each sensor element further comprising: a plurality of ligands of at least

one ligand type applied to a coating on the sensor element, an electrostatic output signal generated by the sensor element from an interaction when one of the plurality of ligands of the at least one ligand type binds to at least one biological target type, an electrostatic sensing surface, positioned in proximity to the at least one ligand for detecting the electrostatic output signal, and a measurement means for measuring the detected electrostatic output signal. The system further comprises a controller to select and input the electrostatic output signal samples of each sensor element, means for converting the electrostatic output signal samples of the sensor element from an analog signal to a digital equivalent signal sample by a digital-to-analog converter, the digital equivalent signal sample being stored in the controller, means for combining a plurality of digital equivalent sample signals from each sensor element to form digital signature signals; means for transmitting the digital equivalent signal to a digital signal processor which compares each digital signature signal with a library of pre-stored signature signals representing known biological targets, and means for generating a notification alert when the digital signature signal matches a pre-stored signal in the library of pre-stored signature signals that represents a signature generated when the at least one ligand type binds with the at least one biological target type.

The system further comprises a system in which the digital signature signal is a time domain signature signal which is compared to pre-stored time domain signature signals using cross-correlation techniques to determine a match. The system further comprises a system in which the digital signature signal is converted to a frequency spectrum and then compared to pre-stored frequency spectrum signature signals using cross-correlation techniques to determine a match.

An embodiment of the present invention comprises at least one sensor element where each sensor element further comprises a plurality of ligands of at least one ligand type

applied to a coating on the sensor element, a voltage change generated by the sensor element from an interaction when one of the plurality of ligands of the at least one ligand type binds to at least one biological target type, a sensing surface positioned in proximity to the at least one ligand for detecting the voltage change and a detection means for detecting the voltage change. The system further comprises a controller to select and input samples of the voltage change of each sensor element and means for indicating that a biological target has been detected when the voltage change of a sensor element exceeds a threshold voltage. The detection and measurement means may be an FET. In another embodiment of the present invention, the sensor elements may be an array of sensor elements.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing generalized description of the invention will be better understood from the following detailed description of preferred embodiments of the invention with reference to the drawings that include the following:

Figure 1A is a diagram of an acoustical based sensing unit;

Figure 1B is a diagram of the acoustical based sensing unit of Figure 1A in the collecting mode;

Figure 1C is a diagram of the acoustical based sensing unit of Figure 1A in the analyzation mode;

Figure 1D is a diagram of the acoustical based sensing unit of Figure 1A in the cleaning mode;

Figure 1E is a diagram of two acoustical based sensing units, each in a different mode of operation;

Figure 2 is a diagram illustrating a single bio pore sensing unit;

Figure 3 is a diagram of several bio pore sensing units and a field effect transistor (FET) that form a basic structure of a bio pore sensing element used to sense a reaction between one or more ligand and one or more specific target;

Figure 4 shows the basic structure of a bio pore sensing element of Figure 3 with ligands encased in a gel;

Figure 5 shows an alternate embodiment of the bio pore sensing element illustrated in Figures 3 and 4;

Figure 6 illustrates another alternate embodiment of a bio pore sensing element having two electrodes;

Figure 7 illustrates another alternate embodiment of a bio pore sensing element having multiple nanotubes;

Figure 8 represents a top view of a bio pore sensing element having nanotubes formed between two electrodes;

Figure 9 is a side view of the bio pore sensing element shown in Figure 8;

Figure 10 illustrates a biologically optical based sensing unit;

Figure 11 illustrates a typical DSP and its relationship to other elements of a sub-system, according to the present invention;

Figure 12 illustrates an embodiment of a system according to the present invention;

Figure 13A illustrates a sensor array in a system configuration where the elements in the array may be selected from one of the embodiments of the sensor elements shown in Figure 2 through Figure 9 above;

Figure 13B shows an example of how ligands may be distributed on the sensor array shown in Figure 13A;

Figure 14A - Figure 14E show typical responses from bio pore sensing elements coated with H5, N1 And P24 antibodies and being subjected to H1,N1, N5, H5 and P24 antigens;

Figure 15 shows an alternate structure of a bio pore sensing element of Figures 2-9 with multiple ligand types encased in a gel; and

Figure 16 illustrates process steps required to implement an embodiment of the present invention.

Figure 17 illustrates an embodiment of a sensor array in a system configuration where the elements in the array may be selected from one of the embodiments of the sensor elements shown in Figure 2 through Figure 9 above.

Figure 18 illustrates process steps required to implement an embodiment of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

Each of the chips used as a sensor unit will be manufactured from silicon wafers on a sapphire, quartz, or BSO or GSO crystal base substrate or similar material, such as those currently used for manufacture of microchips. All frontal surfaces of the sensor units (except the bio pores) will be used to produce and store energy. The operationally integrated sensor units will act as a massively distributed sensor network. This network will function as a monolithic unit, providing a de-facto three dimensional real time sensing of the presence of biological substances. For instance, some clusters of sensor units could form a synchronous group executing on the same working cycles, thereby increasing the sensitivity and reliability of the system, and creating special features such as a distributed antenna. The invention lends itself to customization, and is readily adaptable to diverse operational configurations. For example, clusters of units could be aligned to monitor a statically charged air pump

which will move air, which could include targets, in one specific direction. This will increase the sensor sensitivity because the target particles will be brought into closer proximity with the sensor units. This system exhibits reliable capabilities to sort all targets using static electricity. This invention capitalizes on the fact that all target particles saturated in the air do not react equally to the polarity of the static electricity charge. Groups of the sensor units will change polarity together, generating additional information about the target distribution in air, such as how the air in a ventilation system is moving. This will create the basis for relational databases mapping the nature of the target to atmospheric conditions.

Referring to the drawings, Figure 1A illustrates an acoustical based sensor **1** having a sensor unit **2** comprising a plurality of micro resonators **3** on the surface of the sensor unit, thereby forming an oscillating web. Figures 1B, 1C and 1D illustrate the operation of the acoustical based sensor **1** in the collecting mode shown in Figure 1B, the analyzation mode illustrated in Figure 1C and the cleaning mode detailed in Figure 1D. The acoustical based sensors as well as all of the other sensors described in the present invention are adapted to be applied to the surface of a product, such as medical equipment, clothing or food or are adapted to be air borne. Regardless of whether the acoustical based sensors or biological based sensors are affixed to an object or are drifting in air, the purpose is to detect the presence of one or more of a plurality of biological substances denoted as "targets" **24** which would be harmful to humans and/or animals. These targets **24** would generally be air borne along with various other floating matter such as protein strings **5** and dust particles **6**. The acoustical based sensor **1** would be characterized as a sensor unit **2** having a surface onto which the various particles **5**, **6** and **24** would settle. The surface unit would be connected to a DC current source **7** having a battery **8**. Two switches **9a**, **9b** would be

attached in parallel to the source of electricity. Therefore, in the collecting mode as shown in Figure 1B, electricity would be applied to the surface of the sensor unit **2**, allowing the sensor unit to oscillate at a first frequency. The switches would be in the position shown in Figure 1B to apply a first current level to the surface of the sensor unit to allow that sensor unit to oscillate at that first frequency and power. As shown by the arrows attached to each of the air borne elements **5**, **6** and **24** shown in Figure 1B, these air borne elements would become attracted to the surface of the sensor unit.

Once these particles **5**, **6** and **24** become attached, or rest upon the surface **2** of the sensor unit, switch **9a** moves to the position shown in the analyzation mode shown in Figure 1C, thereby removing the source of electricity from the surface of the sensor unit. At this time, the air borne particles which would include target particles **24** would begin to oscillate at a second frequency, different than the frequency in which the surface of the sensor unit would oscillate in Figure 1B. A DSP including a bidirectional wireless communication, an internal power supply as well as a memory would sense the particular resonating frequency. This frequency would be compared to frequencies stored in the memory of the DSP, indicative of particular targets. If a match is made between the oscillating frequency of the target or targets and the oscillating frequency stored in the memory of the DSP, this match would be noted and stored in the memory of the DSP. At that time, or at a later time, this information would be transmitted utilizing the particular communications capacity of the sensors to adjoining sensors, to one or more routers, or to a centralized station in which a decision regarding the presence of toxic biological substances, indicative of a bio terrorist attack would then create the appropriate alert.

Once the analyzation step is complete as illustrated in Figure 1C, the surface of the sensor unit **2** would be cleaned by

moving switch **9b** to the position shown in Figure 1D. At this point, the surface of the sensor unit would oscillate at a third frequency, thereby ejecting all of the air borne material **5, 6** and **24** from the surface of the sensor unit as shown by the arrows included in Figure 1D.

Figure 1E shows two adjacent sensor units in differing phases such as the cleaning phase or the collection phase. The collection phase is illustrated by the sensor unit on the left and the cleaning phase is illustrated by the sensor unit on the right. The inclusion of the cleaning phase shown in Figure 1D would result in enabling repeated use of the acoustical base sensor unit.

Figure 2 shows a single bio pore sensing unit including a ligand **22** in the presence of a biological target **24**. Additionally, an optional biological amplification unit **20** can be affixed to a non-sensing surface of the ligand **22**. The ligand **22** may be an ion or molecule that reacts to form a complex with another molecule. The target **24** may be the molecule bound specifically by the ligand. Each ligand operates in conjunction with a specific target, of which there are a multitude of possible ligand/target pairs. The target may be a single molecule such as a protein, glycoprotein, saccharide, or lipid. The target may also be an organism such as bacteria or its spore, a virus, fungus, mold, or yeast. The ligand **22** and target **24** bind together with high affinity and specificity. Examples of ligand/target pairs are an antibody and whatever macromolecule the antibody was generated against, a cellular receptor and whatever substance specifically binds and activates the receptor, or a surface feature on a microorganism such as hemagglutinin on an influenza virus and an antibody or molecule (such as sialic acid in the influenza example) that binds the surface feature. It is important to note that a target will only completely attach itself to only one type of ligand. An interaction by the ligand with a target to which it should not bind completely, would

result in, at best, only a partial binding, for an instant of time.

Interactions between a ligand and its target arise from intermolecular attractions that include complementary conformations, charges, polarities, Van der Waals interactions, and reordering of the water molecules in the surrounding millieu. These attractive forces are cooperative and accumulate as the target and ligand come in proximity. Each target/ligand interaction has a specific kinetic and thermodynamic signature that can be characterized and quantified:

$$\text{Ligand + Target} \underset{k_{off}}{\overset{k_{on}}{\varpi \sim \omega}} \text{Ligand/Target Complex} \qquad (1)$$

The equilibrium constant is derived from the relation of the on and off constants:

$$K_{eq} = k_{on}/k_{off} \qquad (2)$$

K_{eq} is related to free energy by $\Delta G = \Delta GE + RT \ln K_{eq}$, and at equilibrium $\Delta G = 0$, so:

$$\Delta G = -RT \ln K_{eq}$$

For $K_{eq} = 1$, $\Delta GE = 0$

For $K_{eq} = 10$, $\Delta GE = -1.4$ Kcal/mole

For $K_{eq} = 10^5$, $\Delta GE = -7$ Kcal/mole (3)

with R = universal gas constant

T = temperature (Kelvin Scale)

The K_{eq} for avidin-biotin interaction is approximately $10^{15}M^{-1}$, and for a "typical" antigen-antibody interaction is approximately $10^{12}M^{-1}$. Thus the energy released from a mole of avidin-biotin interaction is approximately 21Kcal/mole and for

antigen-antibody approximately 16 Kcal/mole. The unique pattern of energy release is a function of the interaction signature for each ligand/target pair.

The single bio pore sensing unit shown in Figure 2 is based on micro-miniature pores of ligands generally, but not necessarily embedded within aqueous gels on sensing element surfaces with electro-sensing technologies cumulatively called bio pores. Each bio pore is filled with one or more ligands in gel and will react to the presence of one single molecule of a specific target for that ligand. During reaction, the reaction between the ligand and the specific target molecule will produce an electric pulse signature and static electricity which will be analyzed and trigger an alert if the proper target is present. This technology will require biological data sets describing the electrostatic signature generated by binding of each ligand/target pair. This data will be used to differentiate among targets. In all other ways, including data acquisition, data processing, and data communication, all implementations may be identical to other ligand/target pairs.

The materials and methods disclosed herein provide an effective manner for the mass production of uniform micro fabricated units. To customize a deployment of units to a particular targets of interest (Hepatitis C, Salmonella, Anthrax, etc.), the bio pores will contain the appropriate and unique reactive ligands. More specifically, each sensor element comprising a sensing unit of the present invention comprises a signal-converting element, a transducer, a responsive element, and the ligand shown in the sensing unit of Figure 2. Conversion circuits will include electron sensitive circuits, single electron transistors, photosensitive based circuits, acoustic sensitive based circuits, and inductivity sensitive detection circuits, based upon the type of sensor utilized. Depending on the application, specific bio-amplification elements may be used. The signal-converting element is comprised of an active moiety and signal-transforming domain. The ligand-specific moiety

specifically recognizes a selected target. A sensing unit used with the ligand shown in Figure 2 would require software and hardware to monitor and detect specific targets. Depending on the preliminary detector conversion circuits, the bio-amplification or device **20** may or may not be used. For instance, in some cases, when dealing with an extremely low energy ligand/target interaction, a sensing unit with amplifier **20** such as enzymatic fluorescence or chemiluminescence generation, with a photon-sensitive detector can be employed. In this case, after detection by the sensing unit, an electrical pulse will be converted to a photon stream, which will be detected by a sensitive photo-detector.

Figure 3 represents the use of a field effect transistor (FET) **30** with a sensing gate **32** as a measurement device awaiting integration of the gel and molecules of ligand **31**. The ligand **31** is placed on or close to the gate **32** as possible, such that any ligand/target interaction will generate a current from the source area **34** through the gate **32** to a drain area **36**. The FET is provided on a semiconductor base **38**. A layer of insulation **39** is provided over the gate **32**, the source **34** and the drain **36**. This FET structure will be implemented in several formats as will be discussed. The FET structure can take the form of a miniature extra sensitive field effect transistor (ESFET).

Figure 4 depicts the FET **30** with gel **33** incorporated in the design. The gel utilized should exhibit the properties of remaining moist, having optical sensitivity and allowing the targets to pass through the gel and to bind to the ligand. There are several ways to place the ligand in operational proximity to the gate area. For instance, the surface of the gate **32** can be coated with aminosilane. The ligand is tethered to the amino groups via a variety of cross linkers, for example, disuccinimidyl suberate, Bhydroxy disuccinimidyl suberate, etc. The cross linkers can be chosen with specificity to selected

functional groups on the ligand to achieve the desired orientation.

Figure 5 depicts an alternative embodiment of the FET approach. This FET **40** includes a silicon base **48** on which a source area **46** and a drain area **44** are provided. A gate **50** is provided on an insulator **42**. A number of ligands **52, 54, 56, 58** and **60** are associated with the FET **40**. These ligands are captured with a DC field produced by a DC current source **62** and an electrode **64**. AS was true with the FET shown in Figure 4, a similar gel **66** will be incorporated in the design. This facilitates orientation of the sensing elements to provide optimal sensing capability.

Figure 6 depicts an alternative approach FET **70** to facilitate orienting the ligands **72, 74, 76, 78** and **80**, electrostatically prior to introduction of the gel **90**. Besides orienting the ligands, the dual electrode configuration including a DC current source **92**, an upper electrode **94** and a lower electrode **96** in proximity to the gate area **98** will facilitate movement of the ligands to the gate area **98**, ultimately attaching them to the lower electrode **96** in the area of the gate area. The sensor unit includes a silicon base **82**, a source area **84** and a drain area **86** and a layer of insulation **88**. The lower electrode **96** will then completely dissolve, permitting the FET to function normally. Alternatively, the lower electrode will be only partially dissolved, facilitating a bias feedback capability.

Figure 7 depicts an advanced FET sensor **100** incorporating one or more catalyst islands **120** positioned on the FET gate electrode **110** in the area at the gate **122**. The catalyst island is capable of growing nanotubes **114, 116, 118**. The FET **100** includes a silicon base **102**, a drain area **104**, a source area **106** and an insulation coating **108**. The catalyst island **120** consists of chemical ingredients which form a base for growing the nanotubes. Nanotubes typically grow in a chaotic manner.

Their ultimate quantity and volume are managed by controlling time and temperature. The responsiveness to time and temperature are dependent on the ingredients of the catalyst. Generally, multiple nanotubes will be grown. The surface of the nanotubes can be customized using alternative methods to modify their properties. Modification can be achieved using chemical solutions to etch the nanotubes surfaces. Alternatively, the nanotubes can be coated with chemicals. The primary configuration for this invention will include coating the nanotubes with conductive or semi-conductive materials. This will be followed by application of the gel. This dramatically increases the surface area for target detection without increasing the linear surface of the detector. Operationally, after the ligand/target interaction, the signal will come through the surface of the nanotubes to the gate of the FET. Since the nanotubes are indirectly in contact with the gate of the FET, and the ligands would adhere to the surface of the walls of the nanotubes, more ligands would indirectly be in contact with the measurement device, i.e. the gate area. Operation then proceeds as previously described.

Figure 8 presents one possible implementation of the bio pore sensor **130**. In this case, the pore **132** has been created on the silicon chip surface. In the bio pore, nanotubes **134, 136, 138** generally extend between two electrodes **140** and **142**. All surfaces of the nanotubes will be covered with metal (clayed or plaque). The result is a dense electrode mesh. The pore is filled with many ligand elements connected to the nanotubes. When contact between a ligand and a target is achieved, a signal will be propagated over the nanotube mesh and to the electrodes **140, 142**. Electrodes are connected to the registration circuits (not shown).

Figure 9 depicts a side view of the bio pore **132** and a multidimensional perspective of the relative locations of the electrodes **140, 142** and the nanotubes within the pore. There are

multiple configurations for the various components that constitute a bio pore. The optimal configuration is a function of the planned deployment. These configurations will not be limited by availability of materials. It has been shown that available materials retain their film-forming properties even when non-latex water-soluble components (e.g., proteins, enzymes, polysaccharides such as agarose, or synthetic polymers) comprise up to approximately 25% by weight of the material. This alleviates a significant consideration related to a micro fabrication process for the production of biosensors; the established film adheres effectively to a planar substrate even in the presence of large amounts of additives (i.e., enzymes). Particle latex materials have been used traditionally to immobilize all manner of biologically active materials. Thus, the biosensor units of the present invention provide a flexible, generic system that can be adapted to recognize any selected biological substances.

A biological optical based sensor is shown in Figure 10. It is based on micro-miniature bio pores made up of pores of gel **152** containing ligands **154, 156, 158** and a light-sensing detector **160**. During the interaction of the target with the ligand, a sequence of photon bursts or signatures will be generated and detected by the light-sensing micro-system including detector **160**. The micro-systems will be built based on Avalanche Diodes type, Charge Coupled Devices (CCD), or other light-sensing technologies. Upon detection, a comparative analysis of the newly observed data and data stored in the DSP memory will be performed in the manner previously described with respect to the acoustical based and the non-optical based biological sensors.

Optical techniques have been successfully used in the field of sensors, monitoring reactions by measuring changes in absorption, fluorescence, scatter, and refractive index. In particular, for the biological optical based sensor, a layer

which undergoes an optical change is integrated onto the surface of the device so that the evanescent field of the light penetrates the sensing layer. Monoclonal antibodies may be used as the sensing layer, with high specificity to defined targets, then changing the sensing layer composition. Any reactions occurring at the sensing layer affect the evanescent field and hence the optical properties of the device.

This biological optical based sensor will take advantage of interaction energy conversion to fluorescence, detecting the emitted light after interaction. The gel and the ligands in this detector will be located based on descriptions accompanying Figures 5 and 6.

As previously described, each of the various types of sensor units would be provided with a DSP **170** as shown in Figure 11.

Each sensor unit has a dedicated input/output channel **202** for initial power-up, charging the main storage capacitor, programming, and performance of test procedures. Connection to this channel will be done over dedicated devices, during initial test procedures. The input/output channel allows communication from each of the sensor units, such as the bio pore or bio optical sensor **172** and the acoustical sensor to a CPU **176**, through a communication controller **204**. Each unit has three additional channels: a near range (NR) communication channel including an acoustical antenna **208**, a radio frequency (RF) channel including an RF antenna **206**; and an optical channel including an optical antenna **210**. The NR communication channel has an ultrasonic transmitter/receiver. This communication channel allows each sensor unit to communicate with nearby sensor units. In other words, the sensor units start to sense each other, exchange data packets, and even convey information data packets, as well as to coordinate the various operational modes employed by the acoustical based sensor unit.

The RF channel is intended to be used for middle range communication and cluster definition. This channel is faster and can convey more information in a given period of time. In some circumstances this channel could be used to communicate between sensor units, thus it is anticipated incorporating an RF processor to manage the data flow between sensor units.

The optical channel is mainly intended to partially, or in some circumstances, totally substitute for the main RF channel during long-range communication with the router or with large cluster-to-cluster communications as well as to the centralized station. If RF spectrum pollution is experienced, this channel, along with the NR channel, becomes the communication media.

Based upon the distances between the sensor units, the router and the centralized station including a computer, each of the aforementioned manner of connections can be used to disseminate information between the sensor units, the router and the centralized station computer.

A non-alterable memory read only memory (ROM) or an EEPROM **190** is provided in the DSP and consists of Programmed Logical Matrix (PLM) and controlling circuits. The primary intended use for the memory is to hold all operational programs and instructions. Additionally, the memory will hold some sample signature patterns of a number of targets. These signature patterns can be tailored to the type of sensor unit employed, or could include all of the possible signature patterns, regardless of the sensor unit.

A random access memory (RAM) **188** is also included in the DSP. The RAM **188** is used to hold variables, acquired data, temporary data, temporary variables, and other miscellaneous data.

A flash memory (not illustrated) is provided in the DSP. It is divided into functional groups including: a stack and stack pointer, variables and current states, additional program files, and data files. This memory is mainly used by an

arithmetic logic unit (ALU) **182** for internal operations of the DSP. The ALU **182** can be used along with the EEPROM **190** and the RAM **188** to compare a measured signature with the signatures contained in the EEPROM **190**.

The sensor units have some potential sources of interruption provided in the DSP. These sources of interruption include a watchdog timer **194**, a wake-on-change **196**; a real-time clock, various counters such as time counters **198** and a program counter **186**, and overflow interrupts **196**. Each of the above-mentioned events generates a special signal to interrupt program flow and switch to the respective special attention functions. The watchdog timer **194** is the first tier of defense if an irresolvable DSP situation or any other event causes an unpredicted condition. This would be expected to occur most frequently if the processor is overwhelmed with different tasks and the power source capacity would not allow it to perform all functions simultaneously. Conceivably, the DSP could become trapped in an infinite loop with no normal manner to extricate itself. In this case the watchdog timer **194** will generate a high level interrupt to stop the loop and restart the DSP. Sensors and I/O channels produce a wake-on-change interrupt even during the power-saving sleep mode to allow the DSP to wake-up from an energy saving mode and assume the full operational mode. Overflow interrupts occur if corresponding flags in a special function register are enabled. The real-time clock is the main source of time synchronization. This interrupt allows performance of sequential operations with the DSP, its peripheral.

The sensor unit contains a 4-bit or 8-bit general-purpose ALU **182** performing arithmetic and Boolean functions between data in a working registers **184** and any register file such as instruction register **192**.

The register files are divided into two functional groups consisting of special function registers and general-purpose registers. The special function registers are used by

the DSP and peripheral components to control the operation of the device. The special function registers include the working register, a timer register, the program counter **186** and I/O registers. In addition, special function registers are used to control the I/O port configuration. The general-purpose registers are used for data and control information under command of the instructions.

The functions of the macro access controller (MAC) will be performed by the DSP. This will save power and space on the crystal, to optimize timing and avoid communication delays.

A bus **200** is included in the CPU **176** to allow for transfer of data to and from the components therein as well as to communicate with the I/O channel **202**.

An RF processor in communication with the DSP provides synchronous and asynchronous communication modes for each sensor unit. The RF processor receives an RF synchronization sequence, determines the required action, adjusts receiving and transmission parameters, and receives and transmits data. The RF processor also optimizes power acquisition procedures.

Primarily for purposes of energy conservation, all RF related circuits are designed based on resonance based ideology, and are incorporated in close proximity on the chip. The current design includes compatible or semi-compatible spectrum and frequency requirements, as per IEEE 802.1xx standard, which will allow use of existing communication capabilities. There will be additional advantages for power acquisition in the given frequency range.

All amplification of signals is done at the minimum levels necessary to receive and transmit signals. Since there are strict power limitations, we assume all data transmissions include some data-loss. All data correction will be done within the DSP and its software. Thus, power conservation is the cornerstone of all operation and design.

The antenna field on each unit is symmetrical and occupies all available space on the chip's surface. Likewise, the antenna assumes the shielding function for all internal sub units. The size of the antenna and its geometry are functions of the frequency spectrum, proposed sensitivity, and transmission power level. The transmission power level will be in the range of microwatts, thus thick antenna metallic layers will not be required. Thicknesses are expected to be in the range of 5 to 10 nm. Recent developments in surface etching show promise for the use of multilayer antenna wiring, which will increase antenna surfaces many fold. Switching facilities will facilitate low power, low loss, and CMOS types of serial/parallel switches to achieve extremely low energy loss. Considering the low power required for switching, power requirements are optimized (minimized) through fast switching capabilities. Even separate elements of the same antenna facilities will have incorporated switches for multiple segment switching. This allows optimization of total antenna capacitance and inductivity resulting in transmitting and achieving high quality resonance reception. Cumulatively, this leads to power conservation.

As previously indicated, information is communicated between individual sensor units, between the sensor units and one or more router units and also between a centralized system computer and the routers and the centralized system computer. During a communication cycle, each data package will consist of a preamble, data, and signature. If the package is not designated, it is directed to the centralized system computer. If the centralized system computer does not send confirmation in the established time frame, the centralized system computer will try to transmit the package via nearby sensor units. In this case, the end of the transmitted package will have a designation mark for chain communication. This mark will trigger any nearby sensor units to receive the package, and immediately retransmit with the same designation mark. In this way, the centralized system computer will receive the package by multiple paths, from

other sensor units, and perhaps many times. After receiving the first package, if no errors are present, the centralized system computer will form and transmit a response package with specific information as to which package has been successfully received. This will interrupt all other transmissions of the same package. All units will then switch to the normal operating mode.

For long-range communication each sensor unit can communicate with any and all sensor units. During initial handshake procedures, the sensor units are synchronized and are capable of generating and transmitting data packages simultaneously, forming phase antenna fields on the carrier frequency. During the transmission process, while data is being acquired by one sensor unit, all sensor units from the group will be involved. Before transmission, all members of the group will be assigned unique group numbers. After transmission, the first unit of the group will form a package of data, consisting of preamble, data, and signature. Then, each sensor unit provides package encryption and adds a designation descriptor. The sensor chip transmits these packages to other sensor chips. When another sensor unit(s) receives a package with a destination mark, the mark will be analyzed. If the destination mark prescribes a data package to be transmitted via the long-range communication mode, each sensor unit from the group will receive and place the data package in a special holding queue. All group members then start the RF synchronization cycle and when synchronization is achieved; all group members will transmit one single data package simultaneously, thus increasing the communication distance. After initial data from one of the units is transmitted, the second unit of the group will transmit their own package with a designation signature to all group members and the cycle will then repeat, until all data from all group members has been successfully transmitted. The main receiving unit will form and transmit a confirmation receipt for each package transmitted by the group. If any errors are acquired, the

package will be retransmitted a reasonable number of times until error free transmission is achieved.

The power facilities are distributed over and among different circuits. They include antenna facilities; receive, with all distributed amplification; RF processor; power management facilities; and power storage devices.

Each sensor unit has a unique input/output channel for initial power-up, charging the main storage capacitor, programming, and performing test procedures, some of which are activated through a power recovery and storage unit **212**. Connection to this port will be accomplished during initial test procedures. During normal operation, meaning operation in an open environment, the sensor unit will not be connected to any external power source for charging and operations. For power acquisition, the sensor unit collects power from the environment, including, but not limited to a solar battery **218**. The sensor unit is designed specifically to allow optimal use of unit volume and all system properties for acquisition, storage, and power management. The main power source is the electromagnetic radiation available in the complete radio frequency range received by RF receiver **216**. This type of energy is widely available in all places where there is human activity. These sources include radio transmitters in all AM/FM bands; radio receivers, because their converter circuits generate RF waves; police radar-based speed detectors; military or civilian radar; computer monitors, which are a significant near-field RF source; computer networks; and wires within the power grid. Secondary sources of energy are also available and each unit has designated facilities to acquire that energy. Mainly there are X-ray band and Gamma band sources as shown by receiver **220**, which are widely available in medical facilities screening facilities in airports, railroad and train stations, etc. Another source of repeatable energy may be motion of the object or surface upon which the unit is installed. An ultrasonic receiver **214** such as a piezoelectric

genomic element, will absorb this type of energy. Scenarios locating the unit on a surgical glove or surgical dressing could incorporate these ultrasonic receivers capable of absorbing temperature gradients and producing other health status parameters.

The RF band will be used as following: Power acquisition begins with the idle cycle of the main DSP processor. The DSP will advise the RF processor to open all receiving circuits and start to acquire signals in the wide spectrum. The RF processor will search the complete frequency range and attempt to determine the available energy. If any is available, all input circuits will be optimized on that specific frequency range. Detection and storage of the energy is done by multiple stages of detection and charging of the main capacitors. An optical sensor is the ideal because it collects any energy in the optical or close range bands. This additional function will not degrade main sensor functionality. Energy collected in the x-ray and Gamma-ray bands will be used on the reverse side of the unit. The chip volume in this scenario works like a massive filter of optical rays, allowing detection of only x-ray or Gamma rays. These rays freely penetrate silicon substances. An additional benefit of such a detector and power acquisition element is that the sensor unit will collect information about radiation background and/or radiation bursts.

The main storage capacitors are located on the lower layer of the sensor unit. The capacitors are configured in large fields of non-electrolyte, dry capacitors.

Power management facilities incorporate on/off and hibernation functionality. These circuits are principally designed for monitoring the main load circuits, stages of power consumption, and facilitating a power consumption prediction algorithm. Together with the main software on the DSP, power management software modules will detect the shortfalls of stored power and will re-allocate depending on power cycles. This allows decreased peak consumption and power-related heat

consumption. Additionally, the power management unit allows determination of maximum power storage peaks and allocates the maximum consumption at that specific moment, to maximize output transmitting performance. Information about power status is included in each block of data, and in this way the main unit can determine when it needs to run the main charging cycle to restore (replenish) power.

In the case of a new sensor unit or a sensor unit which has totally lost power, all circuits are designed such that receiving circuits switch to maximum power and the power storage cycle is active. In this way, if an operator or the main unit initiates unit activation, they are ready to acquire energy and recharge their power facilities. The replenishment cycle will be postponed until all capacitors are fully charged, and power management facilities will then initiate first wake-up procedures. During wake-up procedures, the DSP runs a simple self-test and then performs a testing of peripheral elements. After the test is successful, the DSP will initiate a short transmission session to check the RF channel. After all this is complete, a status code will be recorded in the memory along with the date and time. If the wake-up status is allowed, the DSP will switch to the normal acquisition and analysis phase. If the wake-up procedures generate a different code, that code will be sent to the main unit for further analysis and subsequent operational instructions. To enhance energy saving during the normal functioning modes, the power management system will power-up only those sensors and systems, needed at that particular moment. In the mode "collect or wait for an event", most of the system is in the power-saving mode. If some facilities are damaged during transportation or from improper previous usage, all possible codes will be stored in the unit memory for detailed scanning. Scanning can be performed with an external device to determine overall power status.

Power conservation is explicitly integrated in the operational power system. All circuits in the sensor unit allow

power management in a multiple stage conservation process. The circuits of the sensor units will be monitored for excessive power consumption. If this happens, a status flag of excessive power consumption will be generated and the centralized computer will further analyze that event.

The low power consumption stage is mainly designed to switch non-critical processes to low power, which will make execution time longer, but will provide enhanced power.

A super low power consumption stage will be activated when absolutely non-critical scenarios are encountered. The performance cycles will switch to the minimum possible operating level for very slow continuous operations, with minimum operations needed for survival of the chip, but not crucial for that specific environment. An example of such an event could be long-term survival, when no RF power sources are available, but there is a need to maintain operations to acquire possible energy bursts.

Hibernation of all circuits is not related to power conservation but will reduce the amount of consumed power. Usually hibernation is predictable, controllable, and will often be used during normal operation.

Each of the sensor units will be in the power-off stage when delivered from the factory. There is insufficient power to initiate operational and initialization tests. during this stage all power facilities are oriented to collect and conserve power. No calculations or transmissions are executed.

Figure 12 illustrates the system of the present invention in which a plurality of groups of sensor units **230** are dispersed in various locations. As previously indicated, each of the sensor units within each group **230** can transmit and receive information from any of the sensor units within that group. Each of the sensor units within each of the sensor groups or clusters **230** would also be in communication with a router **232**. This communication is generally wireless in nature and would utilize

the three types of transmitting technologies previously described. Some of the routers are provided with a switch **234** and a server **236** for transmitting information wirelessly or through an internet, VPN or internet system **238** to a centralized computer system **240**. This centralized computer system would receive and transmit data to and from the routers, as well as the individual sensor units. Based upon the information received by the centralized computer system **240**, a decision is made as to whether toxic biological substances are prevalent in one or more areas as well as whether this would constitute a bio terrorist attack. This decision making process is done either automatically utilizing an appropriate computer, or in conjunction with individuals reviewing the output of the centralized computer based upon information received from the groups of sensor units **230**.

Figure 13A illustrates a sensor array **310** in a typical system configuration **300**, where the elements in the array may be selected from one of the embodiments of the sensor elements shown in Figure 2 through Figure 9 above or may be some other type of sensor element such as a single electron transistor. The controller **360** controls the sequencing of the selection of sensor elements within the array **310** by controlling the demultiplexer **370** to sequentially select one of four columns **330, 332, 334, 336** of the sensor array **310**. When one of the four columns **330, 332, 334, 336** is selected, the controller **360** commands the multiplexer **340** to sequentially select each of the four rows **320, 322, 324, 326** of the array **310**. As each row **320, 322, 324, 326** is selected by the multiplexer **340**, a sample of the output of the sensor element located at the selected row and selected column is selected by the multiplexer **340** and sent to a digital-to-analog (D/A) converter **350** for conversion to a digital equivalent signal sample **355** that is stored in the controller **360**. As this sequence progresses, the output of each sensor element is

digitized and stored in the controller **360**. This process of sampling and digitizing outputs from the sensors and reconstructing a digital signature signal using time division multiplexing is well-known to those skilled in the relevant art of digital signal processing. The controller **360** combines a plurality of digital equivalent signal samples from each sensor element in the sensor array **310** to form a digital signature signal for each element in the array **310**. The digital signature signal **365** from each sensor element is then transmitted to a digital signal processor (DSP) **390**, which compares each digitized sensor output signature signal **365** with a library of pre-stored signature signals **380** representing known targets that may match the ligand coating on each sensor element in the array **310**. In this manner, any detected target that matches any one of the ligand coatings on at least one of the sensor elements is sensed and processed in real-time. When a match is found by the DSP **390** between a digitized sensor signature signal **365** and at least one of the pre-stored signature signals in the signal library **380**, a notification and alert are generated **395** for notification of appropriate personnel.

When the DSP **390** receives a digitized sensor signature signal **365**, it may process the signals using several alternate process embodiments. One process embodiment is to sequentially compare each of the time domain digitized sensor signature signals **365** with each of the pre-stored time domain signature signals in the signal library **380** using cross-correlation techniques to determine a match. Another process embodiment is to sequentially convert each received digitized sensor signature signal **365** to a frequency spectrum and then sequentially compare each of the frequency domain digitized sensor signature signals with each of the pre-stored frequency domain signature signals in the signal library **380** using cross-correlation techniques to determine a match.

An example of how ligands or antibodies may be distributed on a sensor array **310** is shown in Figure 13B. As a first example, assume that the sensor element located at column 1 **330** row 1 **320** of the sensor array **310** is coated with an H5 antibody (ligand). If the sensor array **310** were exposed to an H1 antigen, a response from the sensor located at column 1 **330** row 1 **320** shown in Figure 14A would result. Figure 14A shows a negative signature response characteristic indicating that an H5 antigen was not detected. If the sensor array **310** were exposed to an H5 antigen, a response from the sensor located at column 1 **330** row 1 **320** shown in Figure 14B would result. Figure 14B shows a positive signature response characteristic indicating that an H5 antigen was detected.

As a second example, assume that the sensor element located at column 4 **336** row 3 **324** of the sensor array **310** is coated with an N1 antibody. If the sensor array **310** were exposed to an N5 antigen, a response from the sensor element located at column 4 **336** row 3 **324** shown in Figure 14C would result. Figure 14C shows a negative signature response characteristic indicating that an N1 antigen was not detected. If the sensor array **310** were exposed to an N1 antigen, a response from the sensor element located at column 4 **336** row 3 **324** shown in Figure 14D would result. Figure 14D shows a positive signature response characteristic indicating that an N1 antigen was detected.

Another example is where the sensor element located at column 2 **332** row 1 **320** of the sensor array **310** is coated with a P24 antibody. If the sensor array **310** were exposed to a P24 antigen, a response from the sensor element located at column 2 **332** row 1 **320** shown in Figure 14E would result. Figure 14E shows a positive signature response characteristic indicating that an P24 antigen was detected.

It should be noted, for example, that simultaneous positive responses from a sensor element coated with H5

antibodies and a sensor element coated with N1 antibodies would indicate a presence of the H5N1 avian flu virus.

It should also be noted that although the sensor array **310** shown in Figures 13A and 13B is a four by four (4 by 4)square array, an array according to the present invention may take on numerous elements and array configurations. For example, an array may be a square array, a rectangular array, a three dimensional array, a circular array and the like. The array may also include any number of array elements.

Figure 14A - Figure 14E show typical responses from bio pore sensing elements coated with H5, N1 And P24 antibodies and being subjected to H1,N1, N5, H5 and P24 antigens. If one of the sensor elements shown in Figures 2-9 and 13 were coated with H5 antibodies and exposed to an H1 antigen, a response from the sensor shown in Figure 14A would result. Figure 14A shows a negative signature response characteristic indicating that an H5 antigen was not detected. If one of the sensor elements shown in Figures 2-9 and 13 were coated with H5 antibodies and exposed to an H5 antigen, a response from the sensor shown in Figure 14B would result. Figure 14B shows a positive signature response characteristic indicating that an H5 antigen was detected. If one of the sensor elements shown in Figures 2-9 and 13 were coated with N1 antibodies and exposed to an N5 antigen, a response from the sensor shown in Figure 14C would result. Figure 14C shows a negative signature response characteristic indicating that an N1 antigen was not detected. If one of the sensor elements shown in Figures 2-9 and 13 were coated with N1 antibodies and exposed to an N1 antigen, a response from the sensor shown in Figure 14D would result. Figure 14D shows a positive signature response characteristic indicating that an N1 antigen was detected. If one of the sensor elements shown in Figures 2-9 and 13 were coated with P24 antibodies and exposed to a P24 antigen, a response from the sensor shown in Figure 14E would result. Figure 14E shows a positive signature response

characteristic indicating that a P24 antigen was detected. It should be noted, for example, that simultaneous positive responses from a sensor element coated with H5 antibodies and a sensor element coated with N1 antibodies would indicate a presence of the H5N1 avian flu virus.

Figure 15 shows an alternate structure of a bio pore sensing element **400** of Figures 2-9 with multiple ligand or antibody types **440-448** encased in a gel **420**. Figure 15 depicts the FET **410** with gel **420** incorporated in the design. The FET includes a gate region **430**, a source **432**, a drain **434**, a silicon base **436**, an insulator **438** over the source **432**, drain **434** and gate region **430**, and cross-linkers **412** over the gate region **430**. The gel **420** utilized should exhibit the properties of remaining moist, having optical sensitivity and allowing the target antigens **450 -456** to pass through the gel and to bind to the ligands or antibodies **440-448**. There are several ways to place the ligands or antibodies **440-448** in operational proximity to the gate area **430**. For instance, the surface of the gate **430** can be coated with aminosilane. The ligands are tethered to the amino groups via a variety of cross linkers **412**, for example, disuccinimidyl suberate, Bhydroxy disuccinimidyl suberate, etc. The cross linkers **412** can be chosen with specificity to selected functional groups on the ligands or antibodies **440-448** to achieve the desired orientation. The multiple antibody bio pore sensor element may replace the sensor array **310** shown in Figure 13A in some applications. Note that with multiple ligand or antibody types **440-448**, multiple target antigens **450-456** may be sensed. Therefore, the bio pore sensing element **400** having a coating of H5 and N1 antibodies would be capable of sensing the H5N1 avian flu virus. The resultant signature signal output from such a sensor element upon sensing the H5N1 virus would be a superposition of the H5 signature signal shown in Figure 14B and the N1 signature signal shown in Figure 14D, which could be

easily stored in the pre-stored signature signal library **380** shown in Figure 13 A.

Figure 16 illustrates process steps **500** required to implement a system embodiment of the present invention. The process is started **510** by cleaning the surface of the sensor **515**. This may be accomplished by mechanical chiseling, laser cleaning, chemically cleaning or thermally cleaning, so as not to affect the effectiveness of the sensor elements. The surface of the sensor elements are then treated with cross-linkers **520** to provide an appropriate orientation to the ligands or antibodies. The surface of the sensor elements are then coated with a selected ligand or antibody **525** capable of uniquely sensing a specific antigen, such as an H5 antibody and an N1 antibody **530** and may be suspended in a gel. The system is then deployed to expose the sensor elements to harmful antigens **535**. The system then looks for an output signature signal from the sensor elements **540**. If an output signature signal is detected, it is measured **545** and converted to a digital representation **550**. The output signature signal is then compared to a library of pre-stored signature signals **555** to determine if there exists a match to a known antigen **560**. If no match exists **560**, the system returns to sensing an output signal from the sensor elements **540**. If a match is found between the output signature signal and one or more pre-stored signature signals in the library **560**, an alert and notification is generated and sent to appropriate authorities **565**. It must then be determined if it is necessary to clean the sensor surface **570**. If the sensor surface requires cleaning **570**, the process then returns to the beginning for cleaning the sensor surface **515**. If the sensor surface does not require cleaning **570**, the system returns to exposing the sensor elements to harmful antigens **535**.

The real time detection of biological substances, to include pathogens, allergens, and microorganisms in multiple diverse environments requires the integration of several

scientific bodies of knowledge. As described, the present invention incorporates multiple technologies, demonstrates multiple functions, and has multiple applications.

Figure 17 illustrates a sensor array **710** in a typical system configuration **700**, where the elements in the array may be selected from one of the embodiments of the sensor elements shown in Figure 2 through Figure 9 above or may be some other type of sensor element such as a single electron transistor. The controller **760** controls the sequencing of the selection of sensor elements within the array **710** by controlling the demultiplexer **770** to sequentially select one of four columns **730, 732, 734, 736** of the sensor array **710**. When one of the four columns **730, 732, 734, 736** is selected, the controller **760** commands the multiplexer **740** to sequentially select each of the four rows **720, 722, 724, 726** of the array **710**. As each row **720, 722, 724, 726** is selected by the multiplexer **740**, a sample of the output at the sensor element located at the selected row and selected column is selected by the multiplexer **740**. If a ligand binds with its corresponding biological target, the sample output will be a change in voltage. The sample output **755** in the form of a voltage change is sent to a threshold detector **750** to determine if the voltage change that is detected exceeds a voltage threshold which indicates that a particular biological substance is preset. In an alternate embodiment, the threshold detector logic is contained in the controller. As this sampling of the sensor elements sequence progresses, the output of each sensor element is examined to determine if a biological target is present. This process of sampling outputs from the sensors is well-known to those skilled in the relevant art of signal sample processing. In this manner, any detected voltage change that exceeds a threshold voltage indicates that a ligand and target have interacted and that the biological target is present. This process of sampling the sensor elements and indicating a threshold has been exceeded is sensed and processed in real-time.

When the threshold is exceeded a notification is sent **780** and notification and alert are generated **795**.

Figure 18 illustrates process steps **800** required to implement a system embodiment of the present invention. The process is started **810** by cleaning the surface of the sensor **815**. This may be accomplished by mechanical chiseling, laser cleaning, chemically cleaning or thermally cleaning, so as not to affect the effectiveness of the sensor elements. The surface of the sensor elements are then treated with cross-linkers **820** to provide an appropriate orientation to the ligands or antibodies. The surface of the sensor elements are then coated with a selected ligand or antibody **825** capable of uniquely sensing a specific antigen, such as an H5 antibody and an N1 antibody **530** and may be suspended in a gel. The system is then deployed to expose the sensor elements to harmful antigens and biological substances **835**. The system then looks for a change in voltage from the sensor elements **840**. If voltage change is detected, it is then compared to a threshold for that sensor element **845**. If the sensor meets or exceeds the threshold **850**, an alert and notification is generated **860** indicating a biological substance has been detected. If the threshold has not been exceeded **860**, the next sensor element is selected and processing continues at step **840**. It must then be determined if it is necessary to clean the sensor surface **870**. If the sensor surface requires cleaning **870**, the process then returns to the beginning for cleaning the sensor surface **815**. If the sensor surface does not require cleaning **870**, the system returns to exposing the sensor elements to harmful antigens and biological substances **835**.

The multiple technologies may include micro miniature integrated circuitry with embedded sensing technologies that capitalize on the uniquely defining characteristics of the biological substances at hand. These characteristics include biochemical, electrochemical, physical, or thermodynamic

phenomenon. To enhance the sensitivity, nanotubes are grown in some units as an adjunct to electrodes upon which rest the ligands associated with the selected biological substances. After detection and discrimination, an alert is passed via the integrated circuitry to external receiving devices enabling a digitized alert of the biological substances' presence.

The units are multifunctional. Their functions include: detection, discrimination, amplification, digitizing, filtering, discrimination, energy acquisition from the environment, communication between units and to external routers and controllers, and network based sharing of information. This multiple functionality is possible because state-of-the-art biochemistry, information technology, and integrated circuitry are combined in such a way as to build a synergistic system oriented to the defining characteristics of the biological substances.

As can be appreciated, the individual sensor units and groups of sensor units can be utilized in many different types of environments and can be affixed to many different types of objects. These environments and objects could include their use in blood transfusion operations and blood plasma collection and storage operations as well as being employed with syringe needles. The sensor units could be attached to various types of gloves, such as used in surgery and drawing blood made from rubber and rubber substitutes. Similarly, condoms constructed from rubber and rubber substitutes and other pregnancy prevention devices could also have sensor units being attached thereto.

Various objects provided in a patient's room affixed to bedside point-of-care diagnostics, intensive care locations and hallways could also be utilized as a base for the individual sensor units. Furthermore, various HVAC ventilation systems and equipment could be provided with a plurality of sensor units as well as sensor unit groups. This would also include air moving equipment as well as local air filtration equipment, patient clothing and dressings, bed services, benches and other furniture

as well as face masks used by clinicians and patients. Furthermore, the present invention could be employed in toilet facilities for real time urine and excrement analysis or applied to the service or inside of dental and other human prosthetic fixtures. Furthermore, the present invention could be utilized in the animal or pet as well as fish environment.

The present invention has application in the food handling industry to include services of food processing equipment, conveyors, processing rooms, containers, silverware and other equipment including the inside surfaces of cans and containers, storage facilities and transportation equipment. The present invention has application in all aspects of the food chain, such as farms, food sources, waste management and packing houses.

The present invention has application in conjunction with organic materials used to manufacture produces such as leather products, cloth products and plastic products.

The present invention further has application in monitoring places in which the population gathers, such as train stations, airports, bus stations, offices, tunnels, bridges, terminals, distribution centers, stadiums, cafeterias, restaurants, bars and governmental facilities. The present invention would have application to be used in tickets, badges or passports or other identification documentation.

The present invention would also have application with units used in cabins of airplanes, train carriages, water craft, hovercraft, cars, trucks, and similar types of conveyances.

Given this disclosure, alternative equivalent embodiments as well as other uses will become apparent to those skilled in the art. These embodiments and further uses are also within the contemplation of the invention.

What is claimed is:

1. A system for determining the presence of a biological target, comprising:
   a. at least one sensor element, each sensor element further comprising:
      i. a plurality of ligands of at least one ligand type applied to a coating on the sensor element;
      ii. a voltage change generated by the sensor element from an interaction when one of the plurality of ligands of the at least one ligand type binds to at least one biological target type;
      iii. a sensing surface, positioned in proximity to the at least one ligand for detecting the voltage change;
      iv. a detection means for detecting the voltage change;
   b. a controller to select and input samples of the voltage change from each sensor element; and
   c. means for indicating that a biological target has been detected when the voltage change of a sensor element exceeds a threshold voltage.
2. A system for determining the presence of a biological target in accordance with claim 1 wherein:
   a. the binding of the at least one ligand with the at least one biological target;
   b. the detecting of the voltage change;
   c. the controlling of the selecting of the input sample of the voltage change for each sensor element; and
   d. said binding, detecting and controlling, occurs in real-time.

3. A system for determining the presence of a biological target in accordance with claim 1 further comprising generating a notification alert by the means for indicating that a biological target has been detected when the voltage change of a sensor element exceeds a threshold voltage.
4. A system for determining the presence of a biological target in accordance with claim 1 wherein the detection means is a field effect transistor (FET) provided with a source region, a gate region and a drain region.
5. The sensor unit in accordance with claim 4, wherein said FET is an electron sensitive field effect transistor (ESFET).
6. The sensor unit in accordance with claim 1, further comprising a biological amplification unit connected to at least one ligand type selected from the group consisting of a first ligand type and a second ligand type.
7. The sensor unit in accordance with claim 4, wherein each of the plurality of ligands comprises a ligand sensing surface and a ligand non-sensing surface opposite the ligand sensing surface, the non-sensing surface of at least a portion of the plurality of ligands is provided in proximity to the gate region of the FET.
8. The sensor unit in accordance with claim 4, further comprising a gel enveloping at least a portion of the plurality of ligands of the at least one ligand type in proximity to the gate region of the FET.
9. The sensor unit in accordance with claim 4, further comprising an electric current source connected between a

silicon base of the FET and a first electrode positioned opposite the gate region.

10. The sensor unit in accordance with claim 9, further comprising a dissolvable second electrode in proximity to the gate region, said second electrode connected to the electric current source.

11. The sensor unit in accordance with claim 10, further comprising a plurality of nanotubes provided between the first and second electrodes, wherein the non-sensing surfaces of the ligands attach to one of the nanotubes.

12. The sensor unit in accordance with claim 7, further comprising a catalyst provided on the gate region.

13. The sensor unit in accordance with claim 11, further comprising conductive or semi-conductive materials coating the surface of the plurality of nanotubes.

14. A system for determining the presence of a biological target, comprising:

a. a sensor array comprising:

i. at least one sensor element, each sensor element further comprising:

1. a plurality of ligands of at least one ligand type applied to a coating on the sensor element;

2. a voltage change generated by the sensor element from an interaction when one of the plurality of ligands of the at least one ligand type binds to at least one biological target type;

3. a sensing surface, positioned in proximity to the at least one ligand for detecting the electrostatic signal; and
4. a detection means for detecting the voltage change;

b. a controller for controlling a sequencing of the selection of sensor elements within the array to sequentially select a column of the sensor array, to sequentially select each of the rows of the array and then to sequentially select and input a sample of the voltage change of each sensor element; and

c. means for indicating that a biological target has been detected when the voltage change of a sensor element exceeds a threshold voltage.

15. A system for determining the presence of a biological target in accordance with claim 14 wherein:

a. the binding of the at least one ligand with the at least one biological target;

b. the detecting of the voltage change;

c. the controlling of the sequencing of the selection of sensor elements within the array and selecting of the voltage change of each sensor element; and

d. said binding, detecting and controlling, occurs in real-time.

16. A system for determining the presence of a biological target in accordance with claim 14 further comprising generating a notification alert by the means for indicating that a biological target has been detected when the voltage change of a sensor element exceeds a threshold voltage.

17. A system for determining the presence of a biological target in accordance with claim 14 wherein the detection means is a field effect transistor (FET) provided with a source region, a gate region and a drain region.

18. The sensor unit in accordance with claim 17, wherein said FET is an electron sensitive field effect transistor (ESFET).

19. The sensor unit in accordance with claim 14, further comprising a biological amplification unit connected to at least one ligand type selected from the group consisting of a first ligand type and a second ligand type.

20. The sensor unit in accordance with claim 17, wherein each of the plurality of ligands comprises a ligand sensing surface and a ligand non-sensing surface opposite the ligand sensing surface, the non-sensing surface of at least a portion of the plurality of ligands is provided in proximity to the gate region of the FET.

21. The sensor unit in accordance with claim 17, further comprising a gel enveloping at least a portion of the plurality of ligands of at least the first ligand type in proximity to the gate region of the FET.

22. The sensor unit in accordance with claim 17, further comprising an electric current source connected between a silicon base of the FET and a first electrode positioned opposite the gate region.

23. The sensor unit in accordance with claim 22, further comprising a dissolvable second electrode in proximity to the gate region, said second electrode connected to the electric current source.

24. The sensor unit in accordance with claim 23, further comprising a plurality of nanotubes provided between the first and second electrodes, wherein the non-sensing surfaces of the ligands attach to one of the nanotubes.

25. The sensor unit in accordance with claim 17, further comprising a catalyst provided on the gate region.

26. The sensor unit in accordance with claim 24, further comprising conductive or semi-conductive materials coating the surface of the plurality of nanotubes.

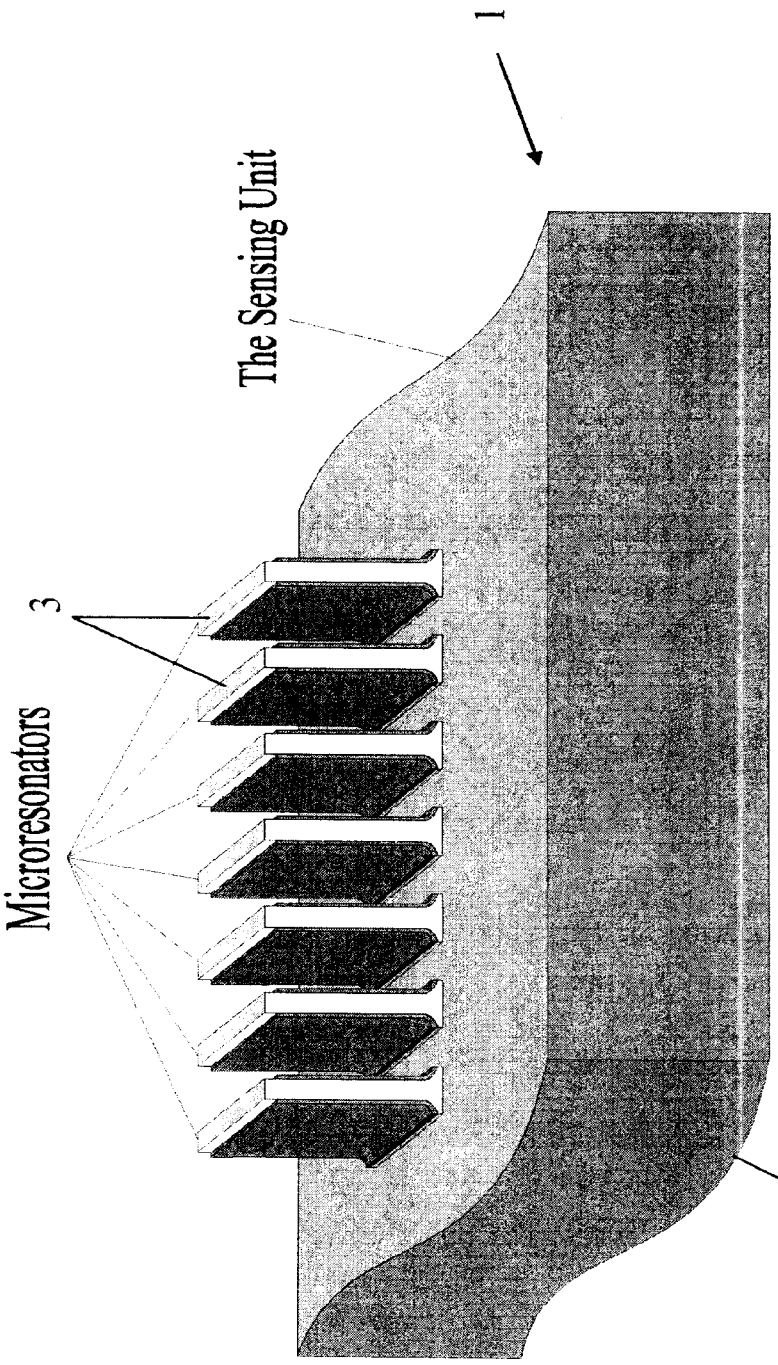

Figure 1A

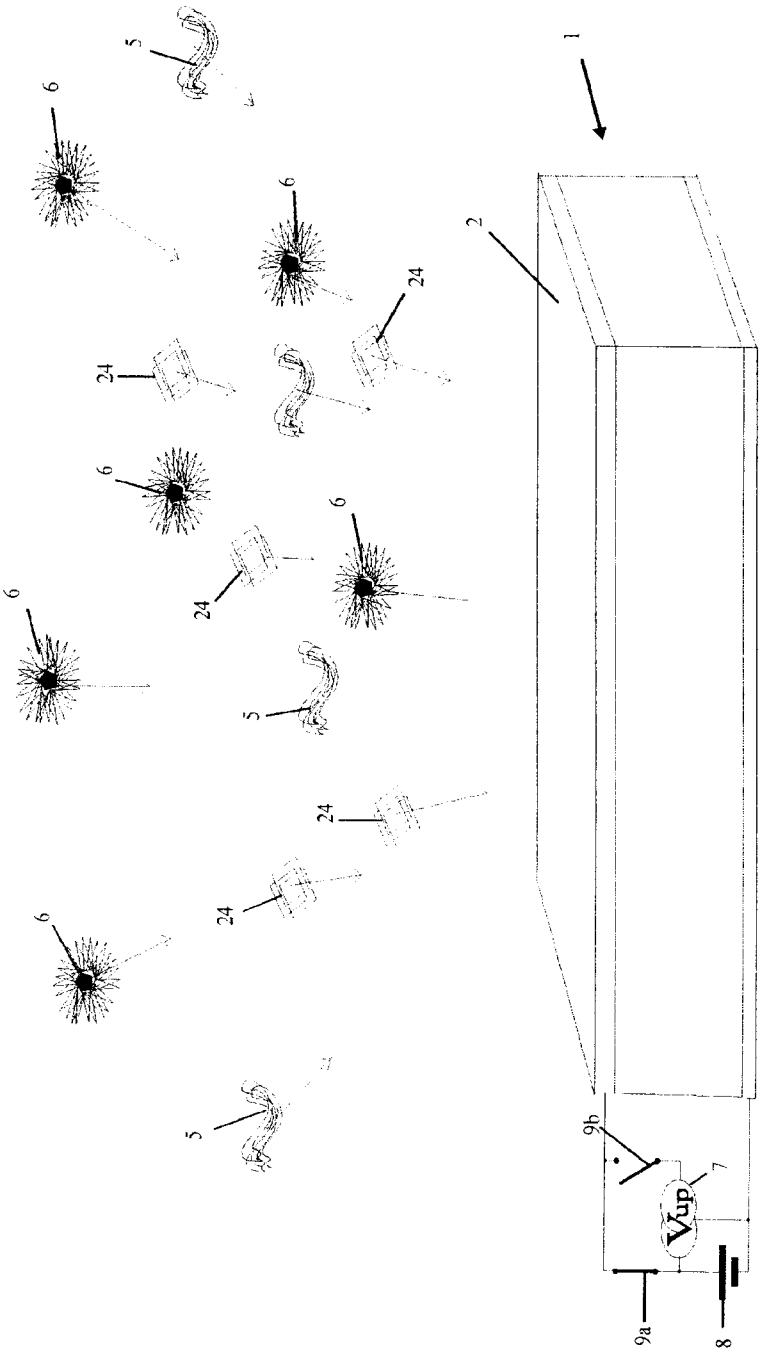

Figure 1B
Phase 1: Collecting.

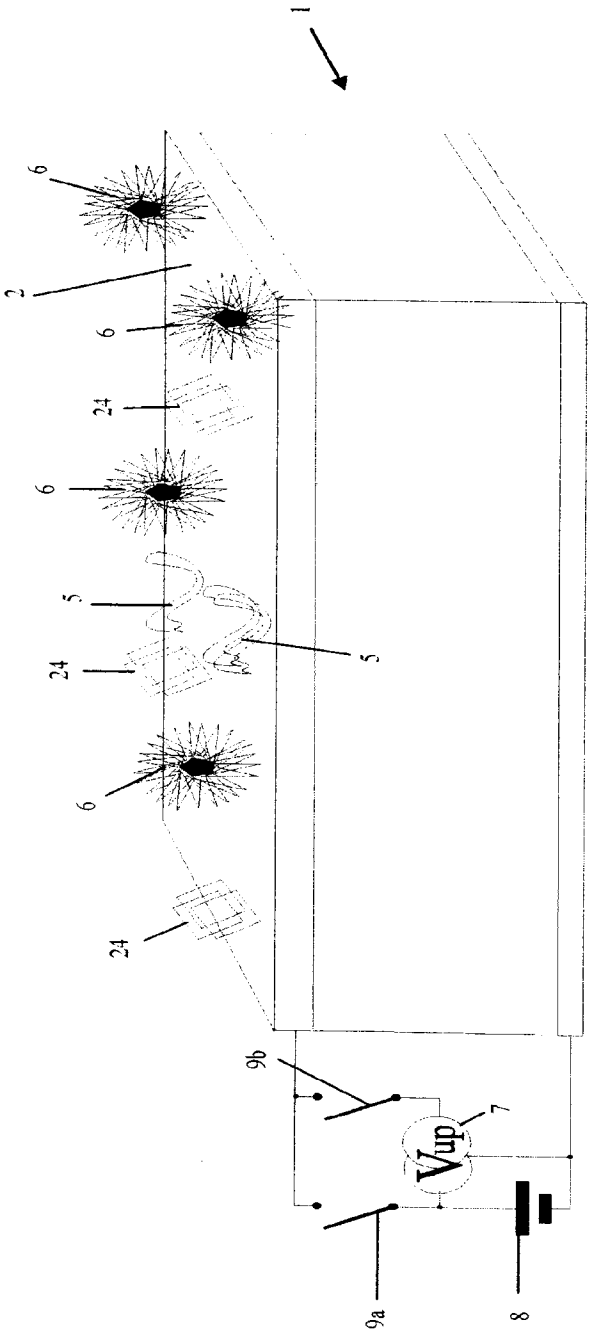

Figure 1C

Phase 2: Analyzing.

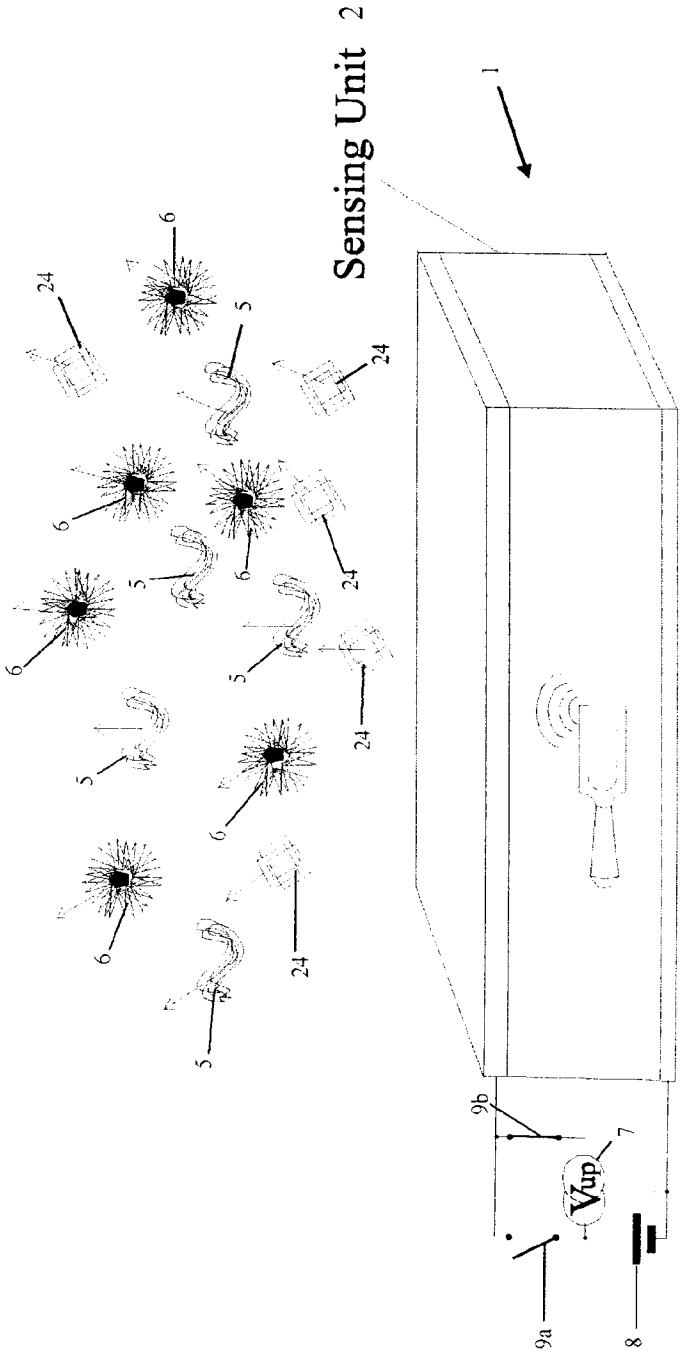

Figure 1D

Phase 3: Clean-up.
Acoustic and/or electrostatic shock.

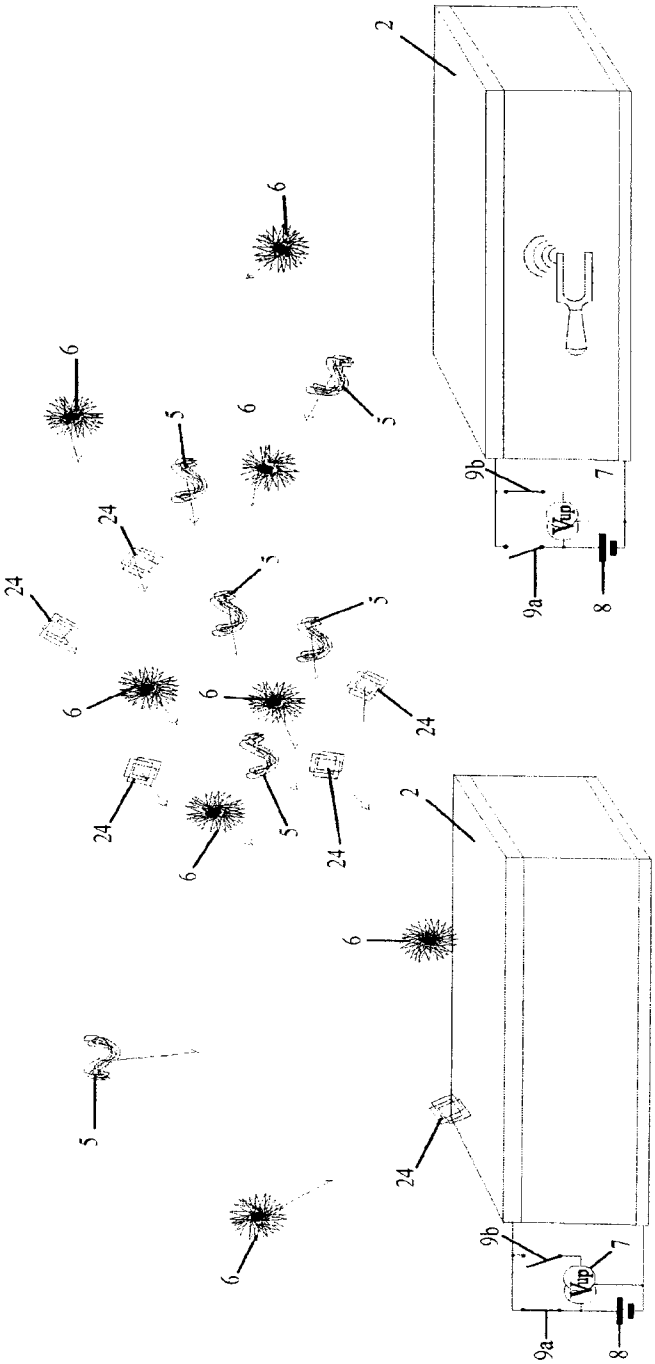

Figure 1E

Synchronous particles Transfer.
One sensing unit in phase 3 (cleaning)
another sensing unit in phase 2 (collection).

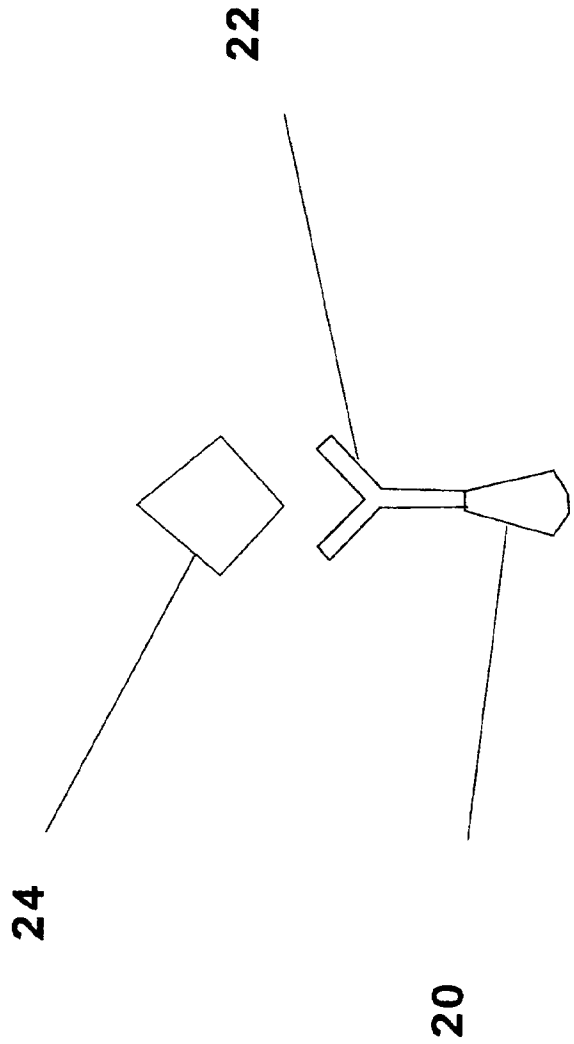

Figure 2

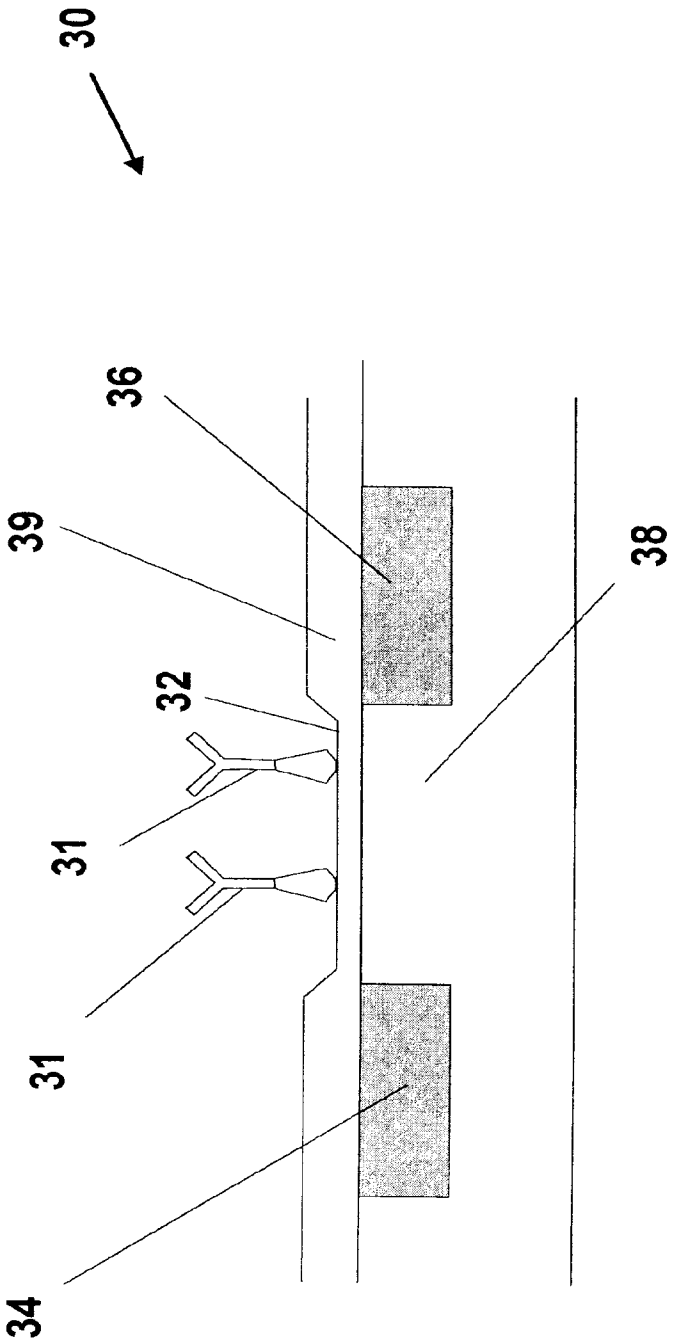

Figure 3

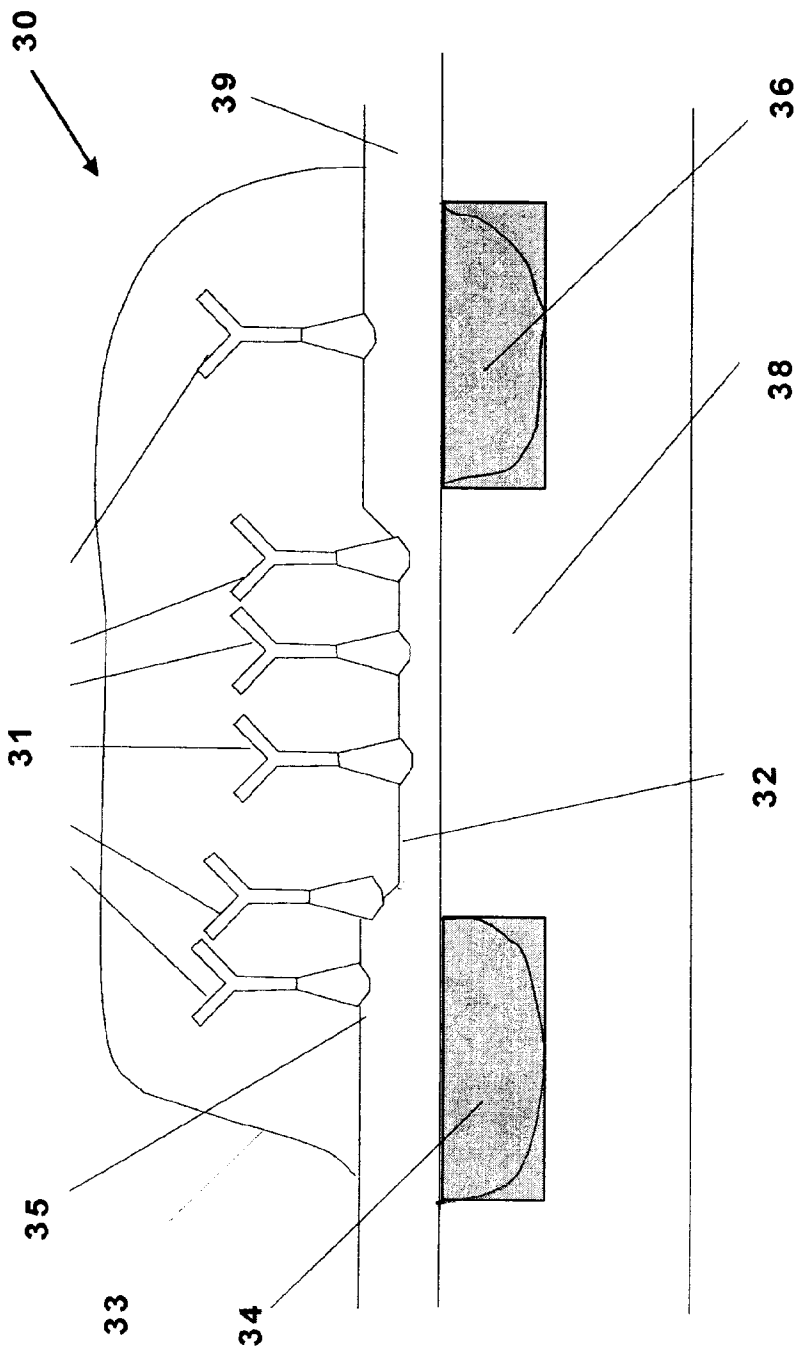

Figure 4

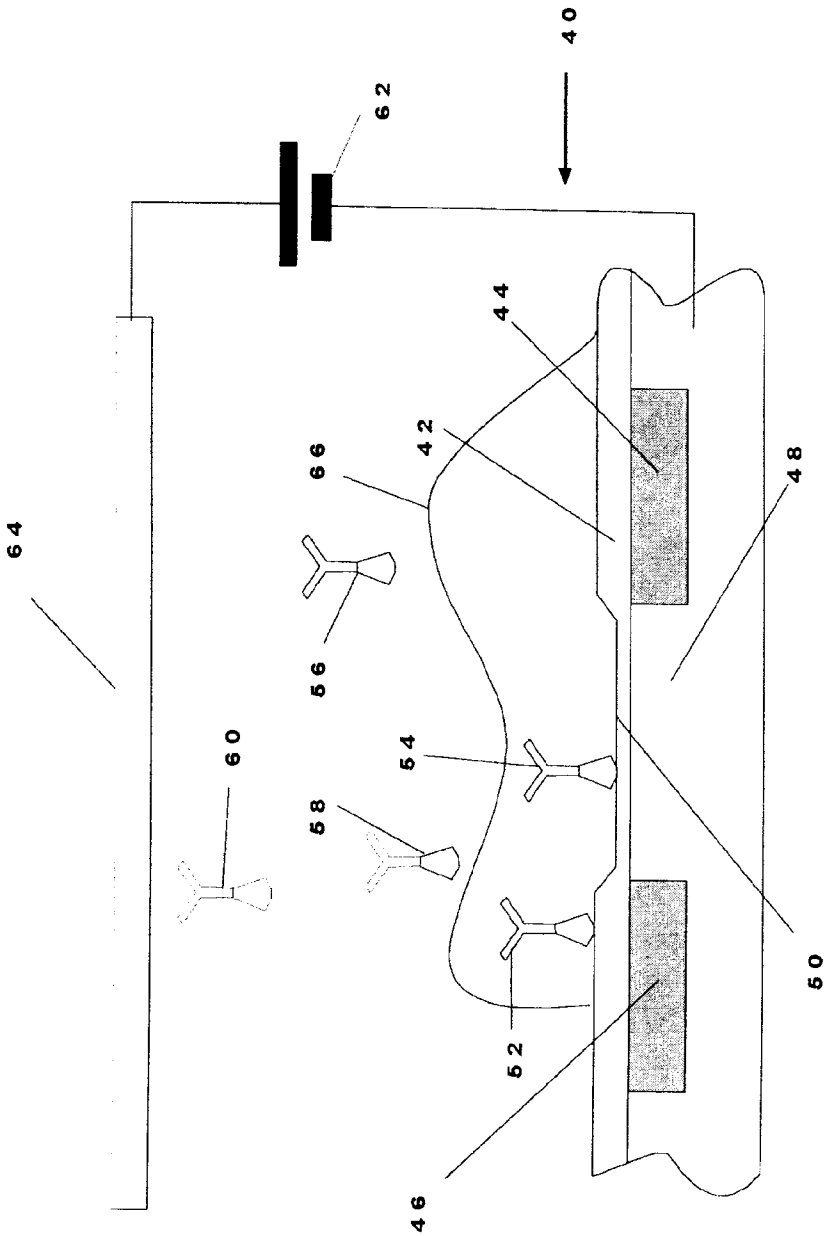

Figure 5

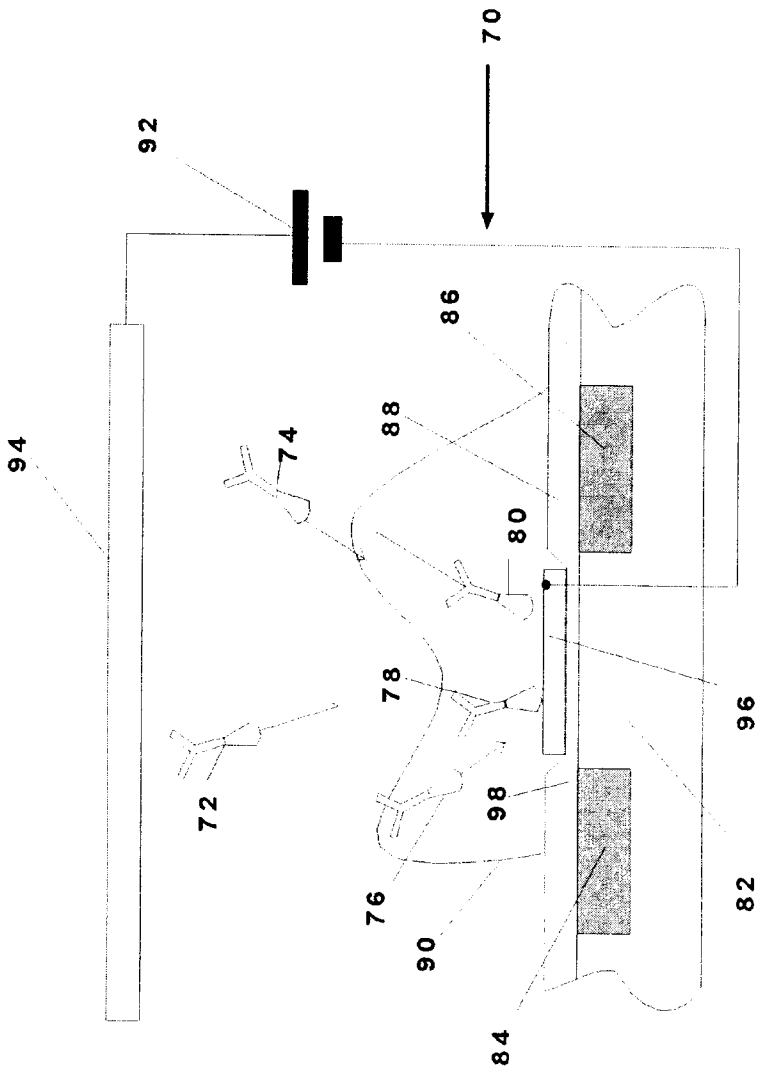

Figure 6

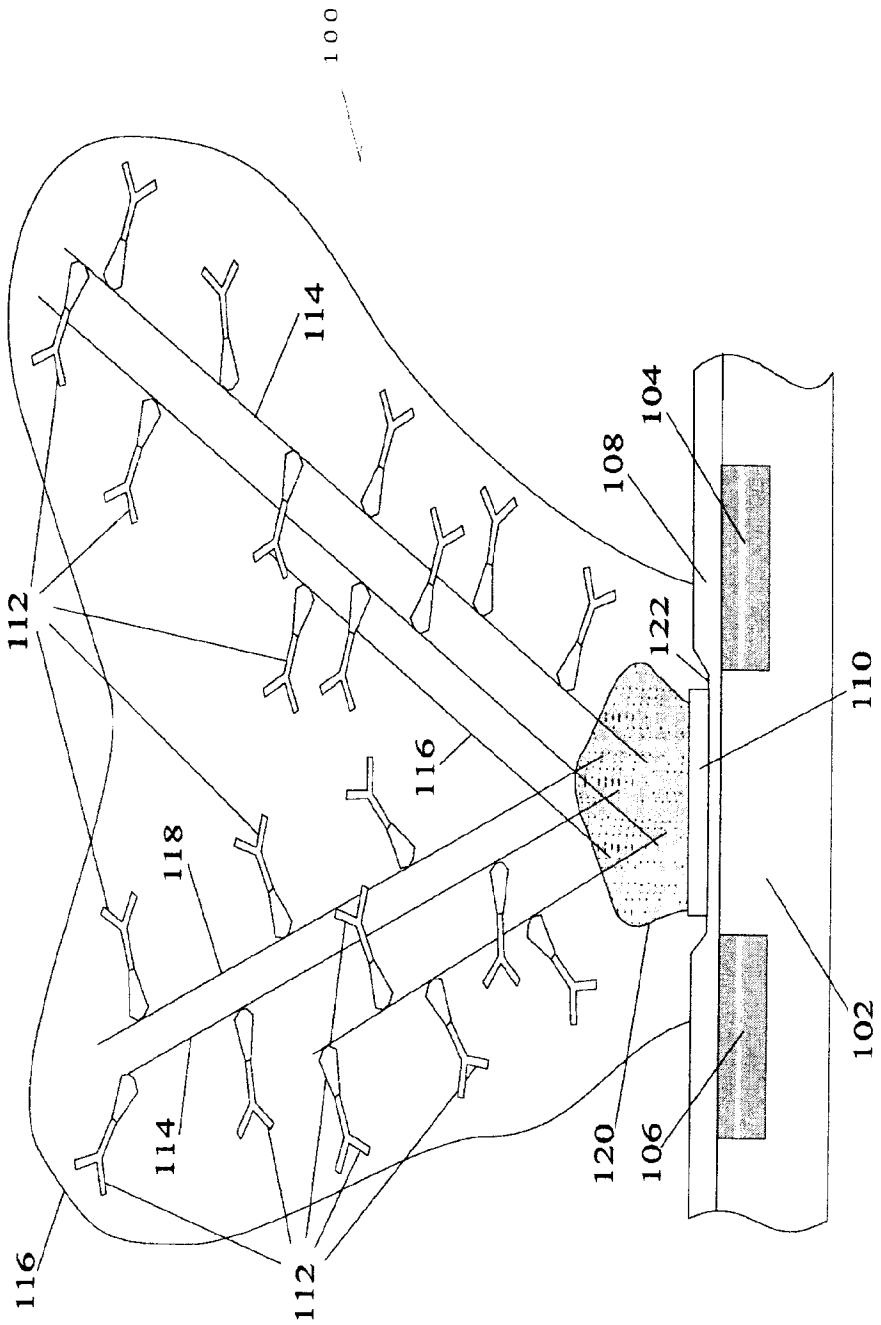

Figure 7

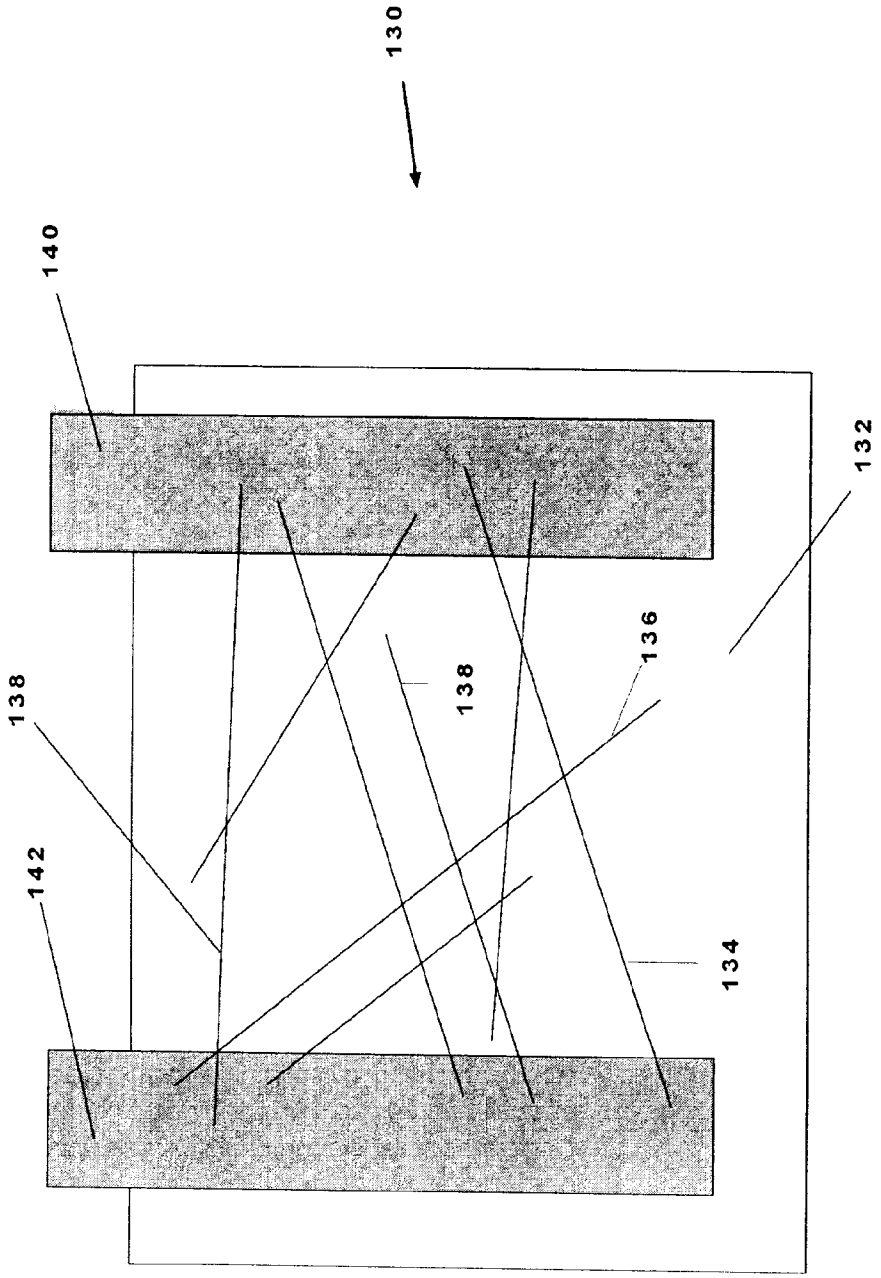

Figure 8

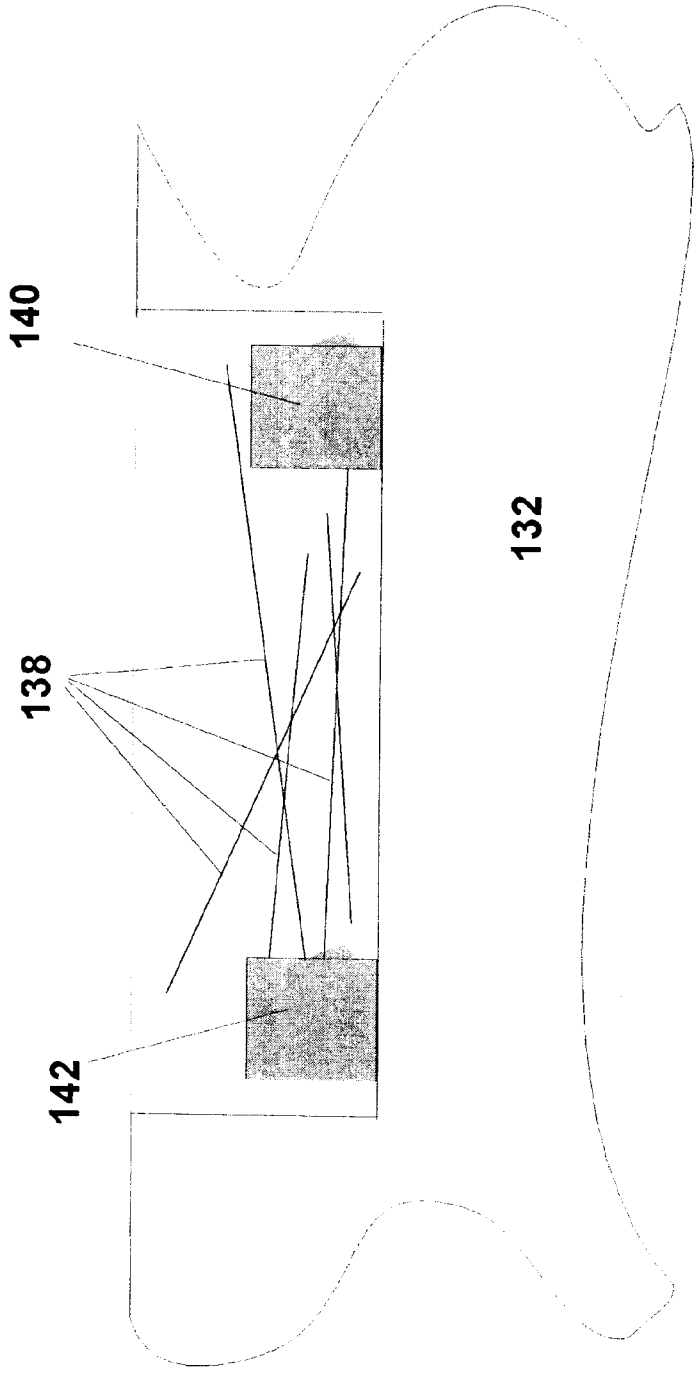

Figure 9

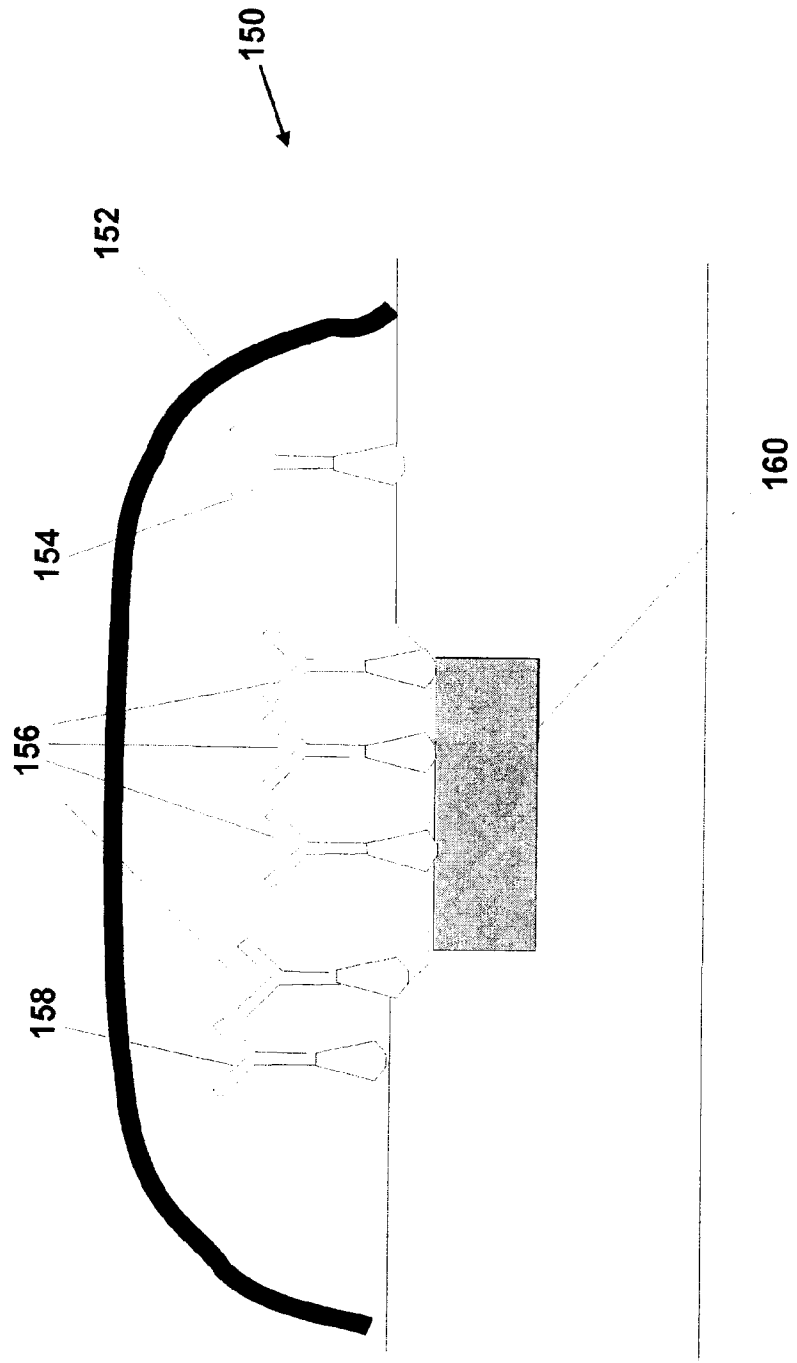

Figure 10

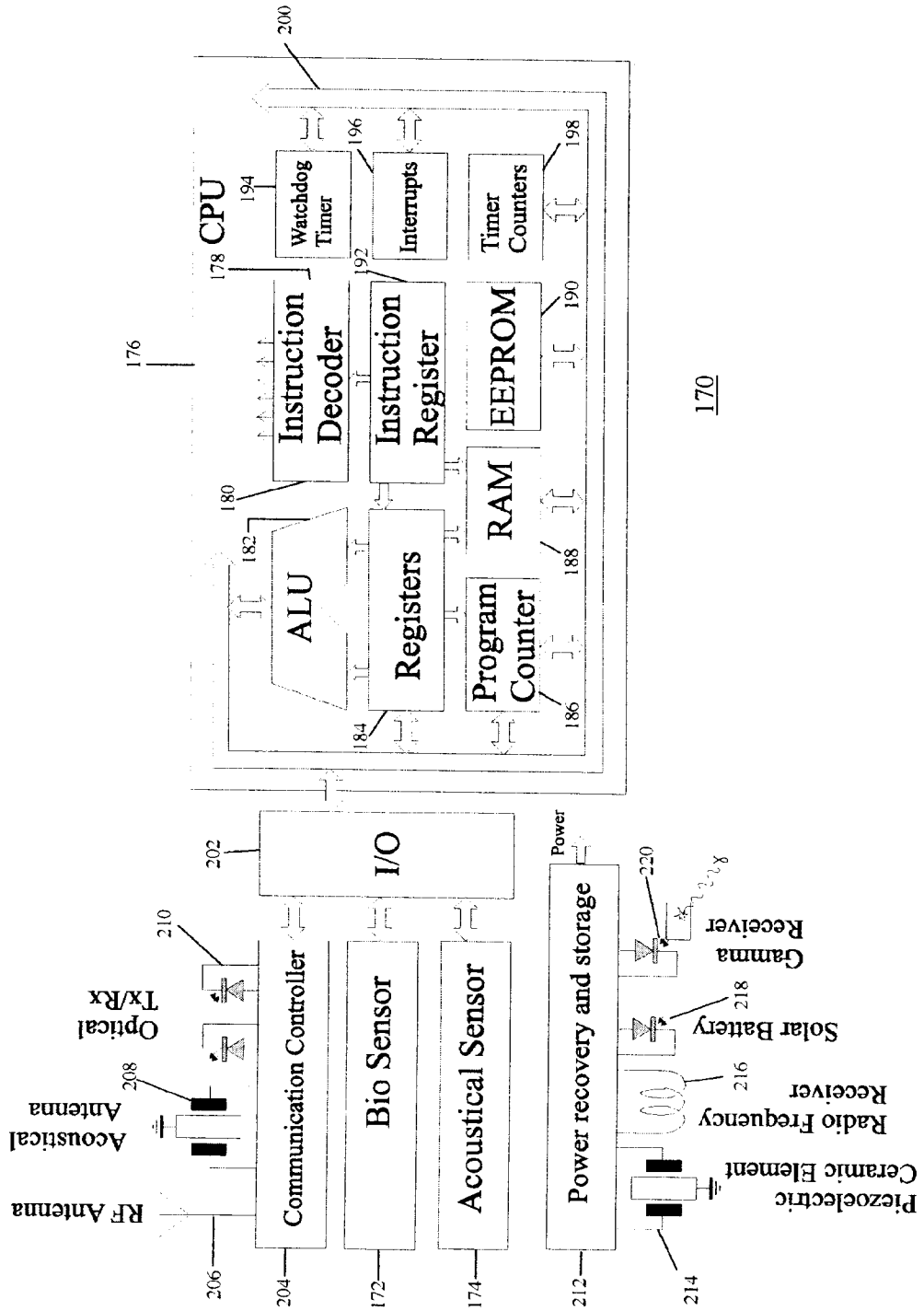
CPU
Watchdog Timer
Interrupts
Timer Counters
Instruction Decoder
Instruction Register
EEPROM
ALU
Registers
RAM
Program Counter
I/O
Communication Controller
Bio Sensor
Acoustical Sensor
Power recovery and storage
Power
RF Antenna
Acoustical Antenna
Optical Tx/Rx
Piezoelectric Ceramic Element
Radio Frequency Receiver
Solar Battery
Gamma Receiver
170
176
178
180
182
184
186
188
190
192
194
196
198
200
202
204
206
208
210
212
214
216
218
220

Figure 11

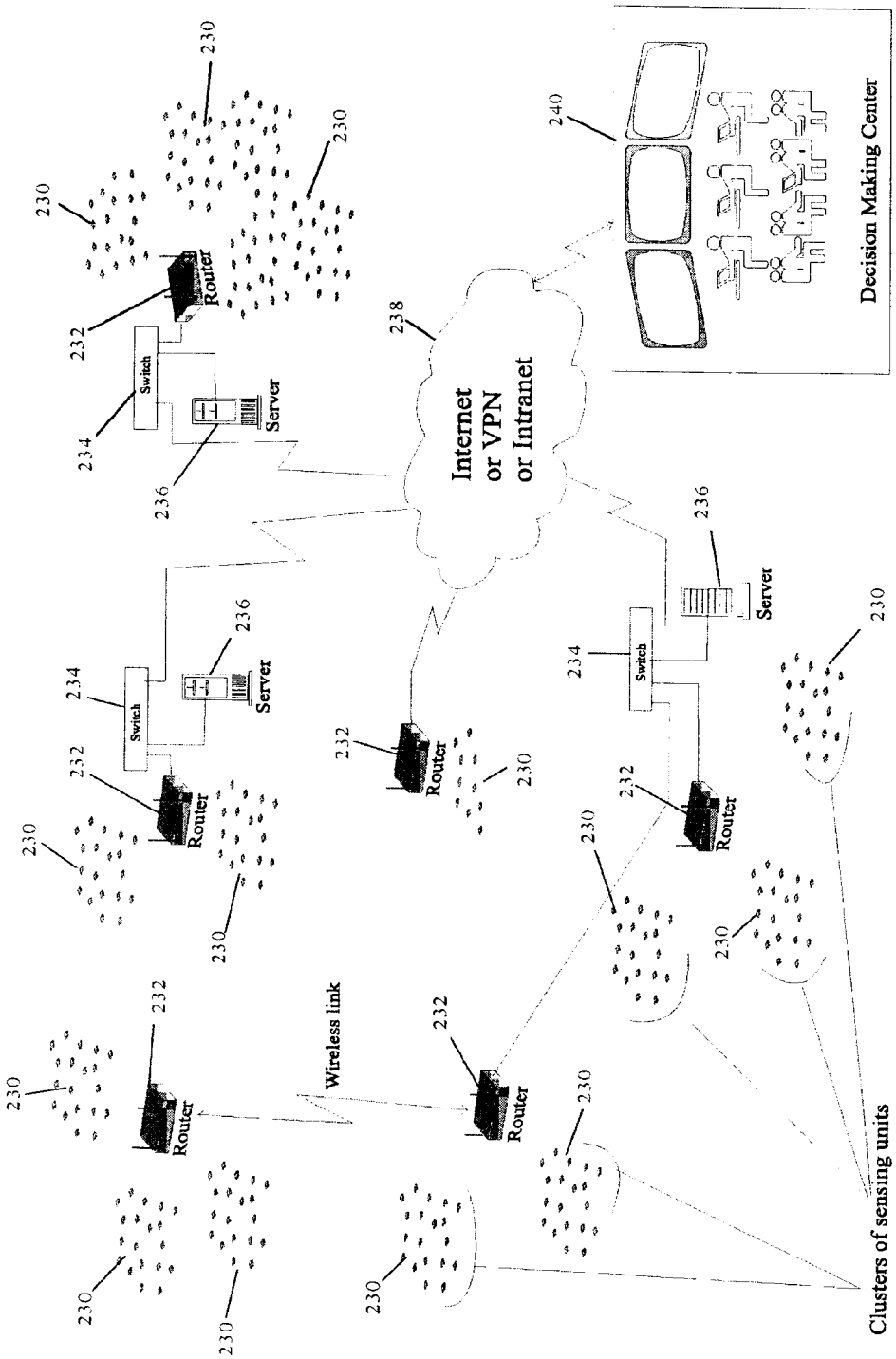
Internet
or VPN
or Intranet
Decision Making Center
Router
Switch
Server
Wireless link
Clusters of sensing units
230
232
234
236
238
240

Figure 12

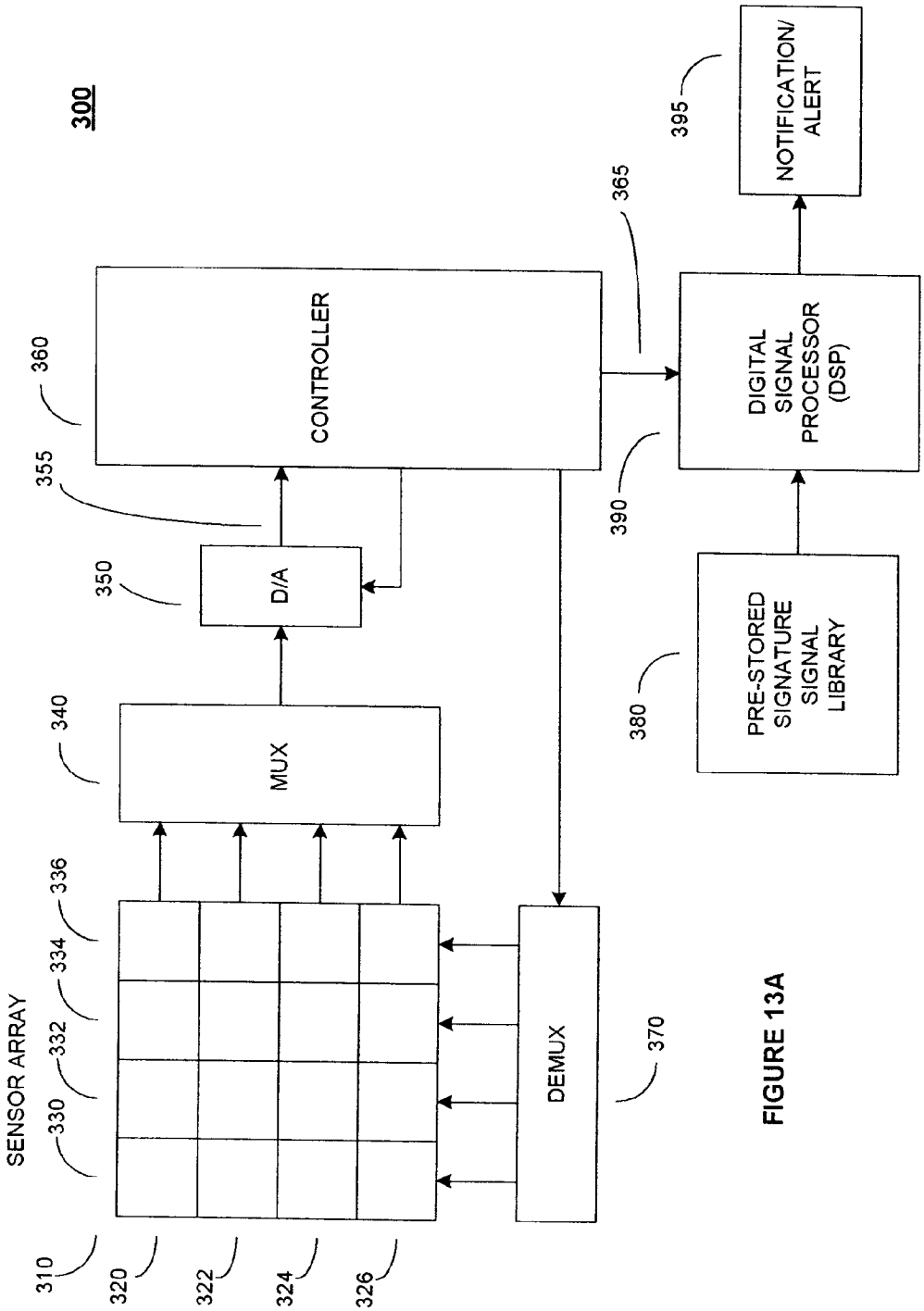
300
NOTIFICATION/ ALERT
395
365
CONTROLLER
360
DIGITAL SIGNAL PROCESSOR (DSP)
355
390
D/A
350
PRE-STORED SIGNATURE SIGNAL LIBRARY
380
MUX
340
336
334
332
330
SENSOR ARRAY
DEMUX
370
310
320
322
324
326

FIGURE 13A

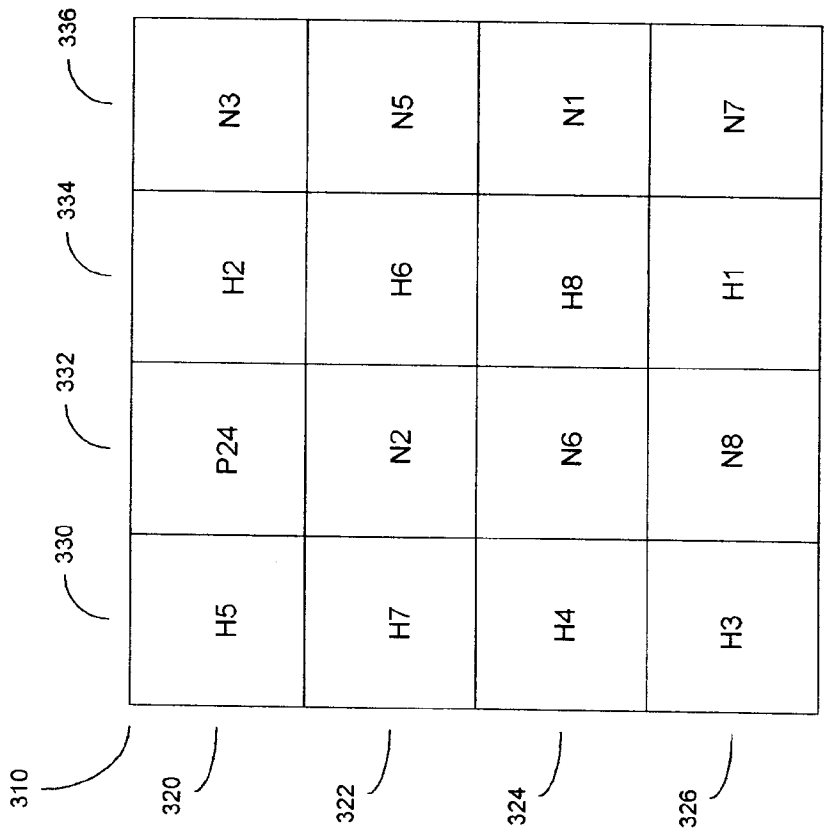
310
320
322
324
326
330
332
334
336
H5
P24
H2
N3
H7
N2
H6
N5
H4
N6
H8
N1
H3
N8
H1
N7

FIGURE 13B

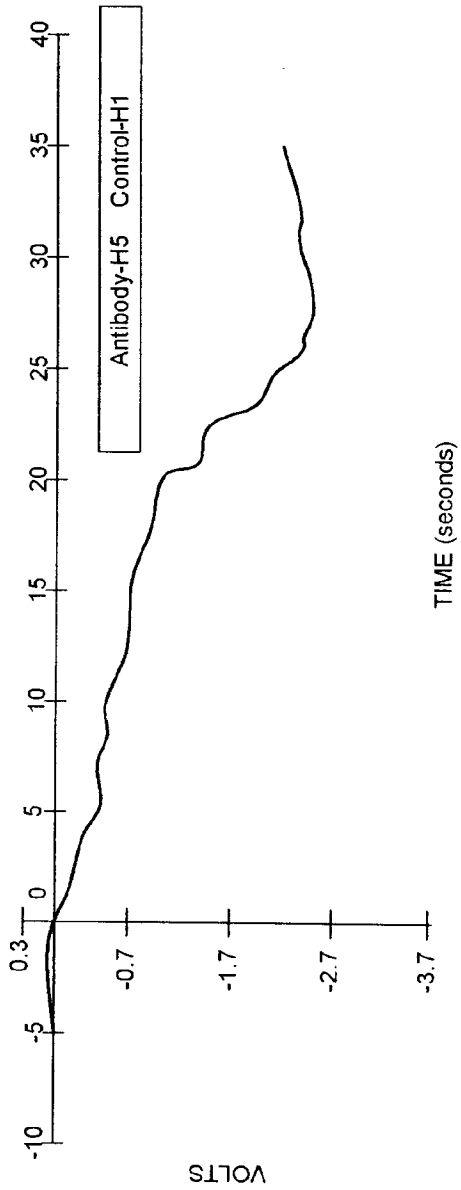

FIGURE 14A

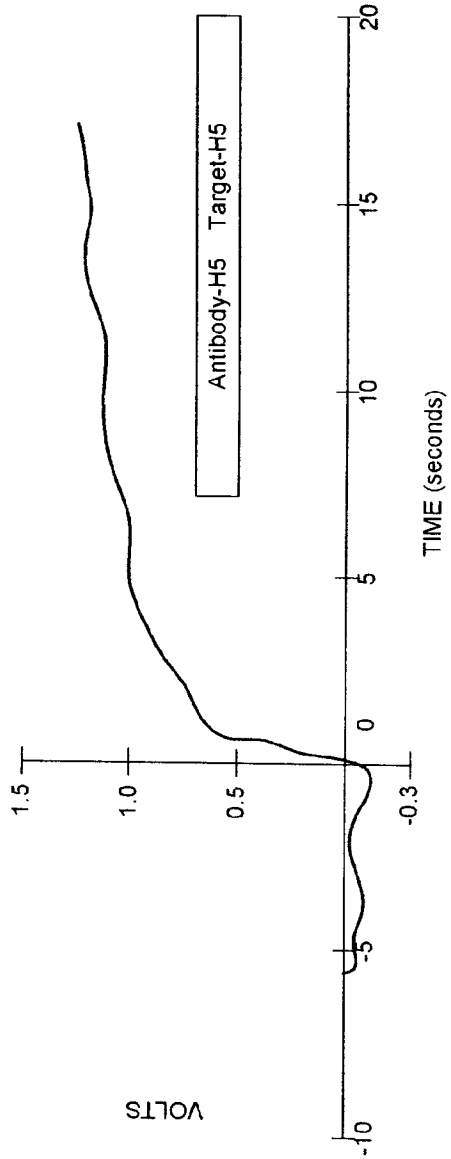

FIGURE 14B

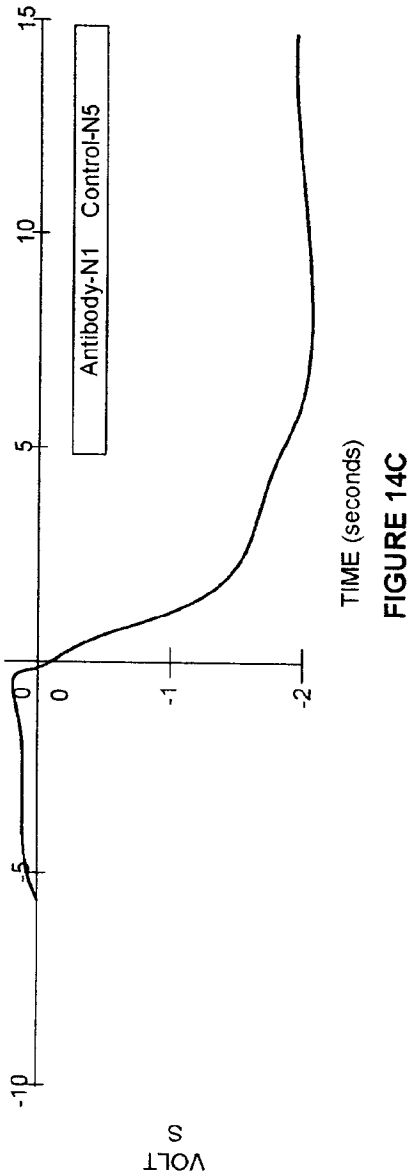

FIGURE 14C

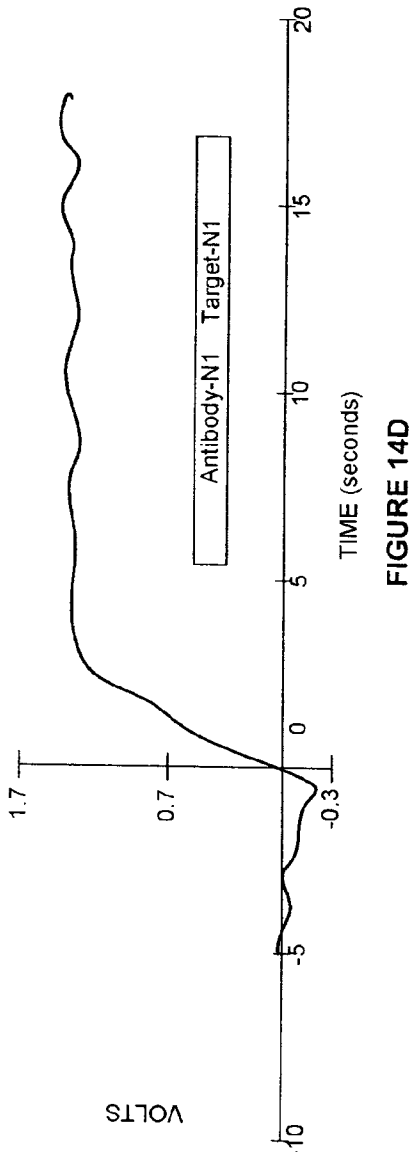

FIGURE 14D

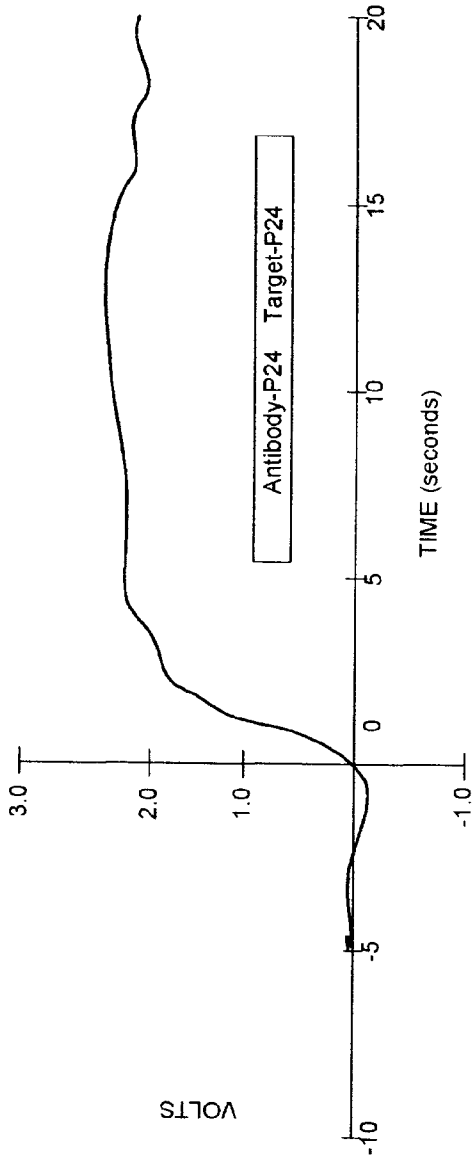
Antibody-P24 Target-P24
VOLTS
TIME (seconds)
3.0
2.0
1.0
-1.0
-10
-5
0
5
10
15
20

FIGURE 14E

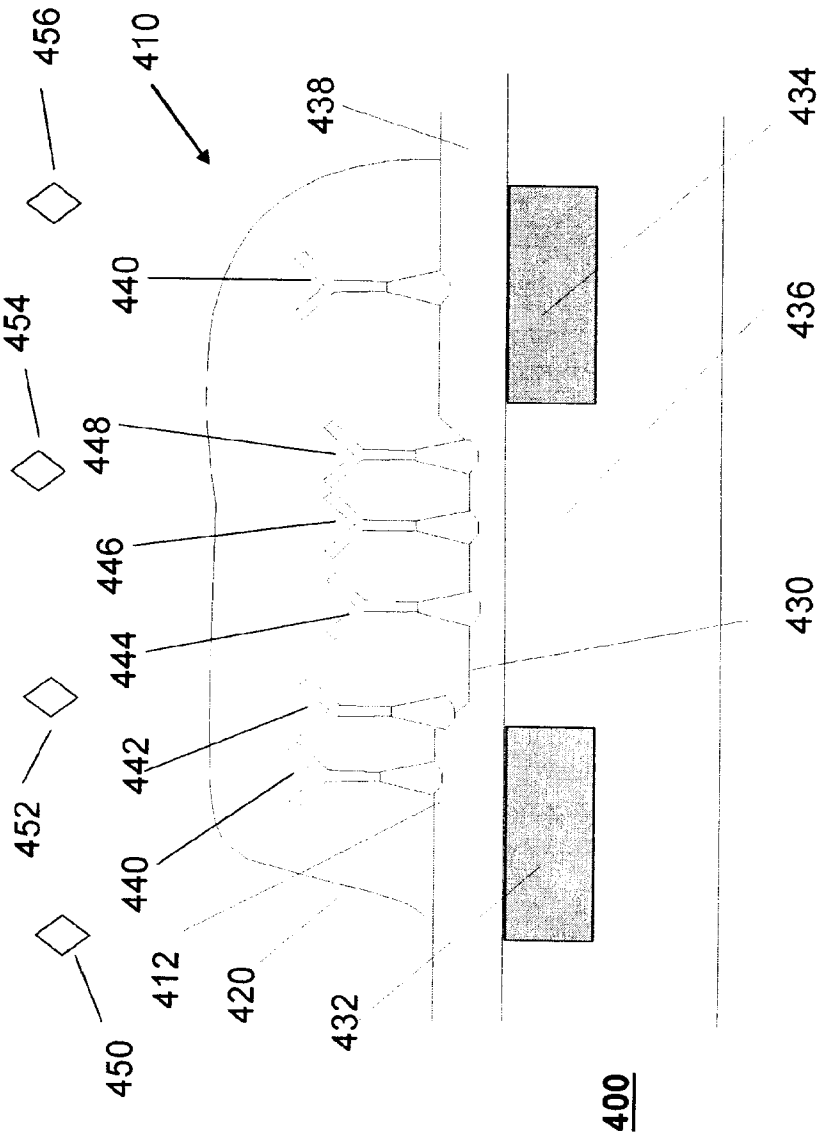
456
410
438
434
454
440
436
448
446
444
430
442
452
440
412
420
432
450
400

FIGURE 15

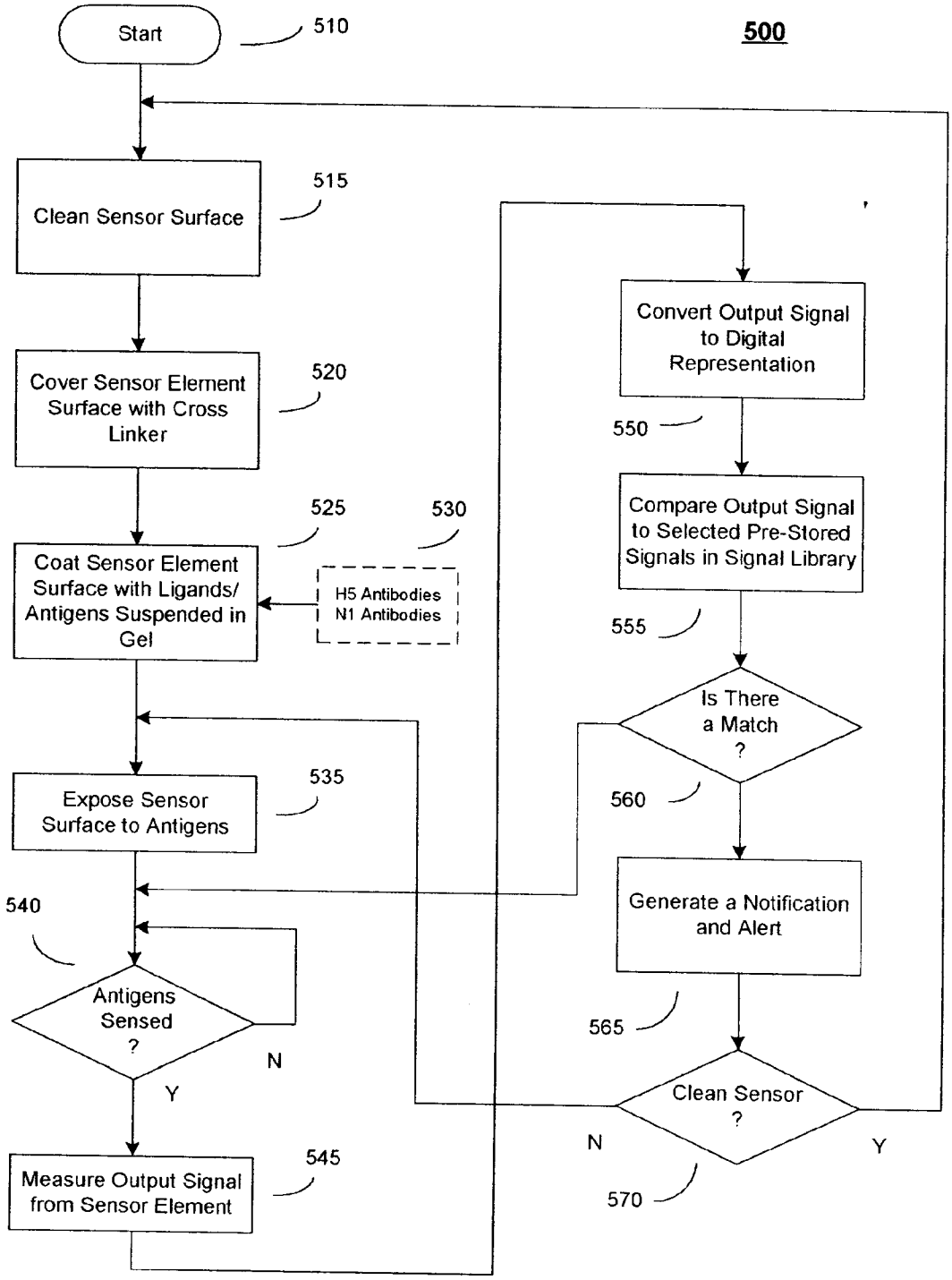
Start
510
500
Clean Sensor Surface
515
Cover Sensor Element Surface with Cross Linker
520
Coat Sensor Element Surface with Ligands/ Antigens Suspended in Gel
525
530
H5 Antibodies
N1 Antibodies
Expose Sensor Surface to Antigens
535
540
Antigens Sensed ?
N
Y
Measure Output Signal from Sensor Element
545
Convert Output Signal to Digital Representation
550
Compare Output Signal to Selected Pre-Stored Signals in Signal Library
555
Is There a Match ?
560
Generate a Notification and Alert
565
Clean Sensor ?
N
Y
570

FIGURE 16

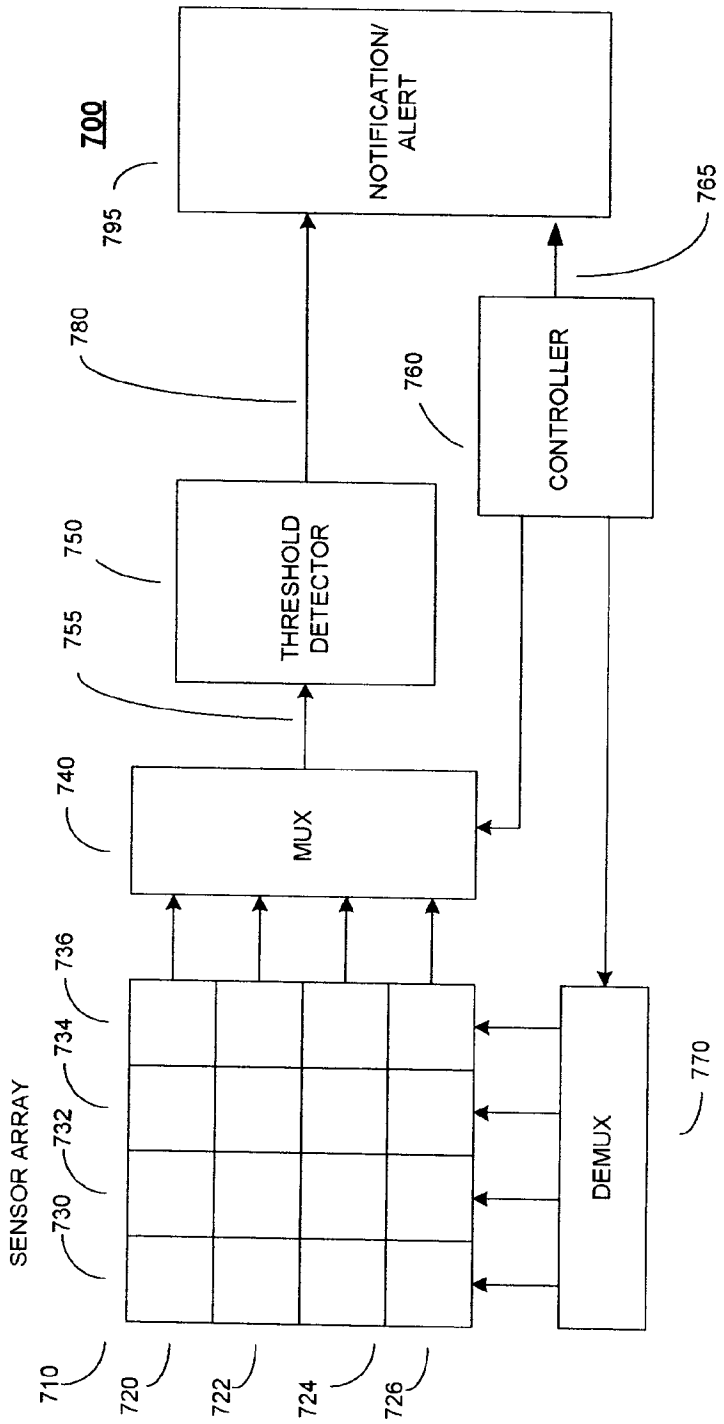
700
NOTIFICATION/ ALERT
795
765
780
760
CONTROLLER
THRESHOLD DETECTOR
750
755
740
MUX
736
734
732
730
SENSOR ARRAY
DEMUX
770
710
720
722
724
726

FIGURE 17

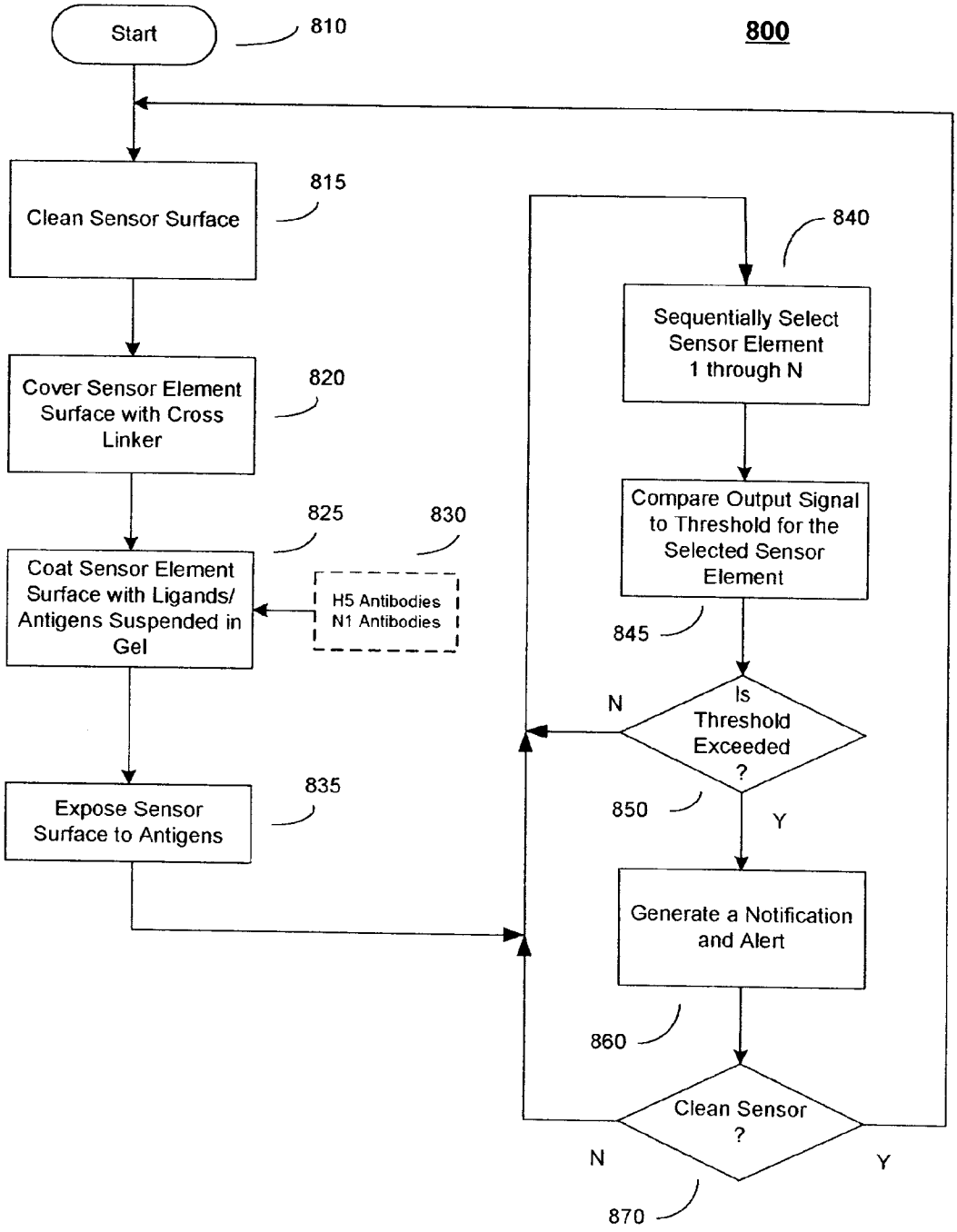
Start
810
800
Clean Sensor Surface
815
Cover Sensor Element Surface with Cross Linker
820
Coat Sensor Element Surface with Ligands/ Antigens Suspended in Gel
825
830
H5 Antibodies
N1 Antibodies
Expose Sensor Surface to Antigens
835
840
Sequentially Select Sensor Element 1 through N
Compare Output Signal to Threshold for the Selected Sensor Element
845
Is Threshold Exceeded ?
N
850
Y
Generate a Notification and Alert
860
Clean Sensor ?
N
Y
870

FIGURE 18