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ELECTROCHEMICAL SENSORS AND BIOSENSORS FOR THE PHARMACEUTICAL AND ENVIRONMENTAL ANALYSIS

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Abstract

Electro chemical sensors are used to determine the concentration of various analytes in testing samples such as fluids and dissolved solid materials. Electro chemical sensors are frequently used in occupational safety, medical engineering, process measuring engineering, environmental analysis, etc. Electro chemical sensors have electrode arrays with two, three or more electrodes, which are called Auxiliary electrodes, Reference electrode, and working electrodes. Electro chemical gas sensors are well known for detecting and quantifying toxic gases such as carbon monoxide, hydrogen sulfide, nitrogen oxides, chlorine, sulfur dioxide and the like. The electrodes of an electro chemical sensor provide a mechanism whereby the ionic conduction of an electrolyte solution in contact with the electrodes is coupled with the electron conduction of each electrode to provide a complete circuit for a current.

Key Words: Electrochemical sensors; Oxygen sensor detection principle.

Introduction

Electro analytical chemical sensor can play an important role in the protection of our environment. Electro chemical sensors are very attractive for onsite monitoring of priority pollutants, as well as for addressing other environmental needs. Such devices satisfy many of the requirements for onsite environmental analysis¹.

They are inherently sensitive and selective towards electro active species, fast, accurate, portable, and inexpensive. Such capabilities have already made a significant impact on decentralized clinical analysis.

Characteristics

There are different ways that electrochemical sensors are constructed, depending both on the gas to be detected as well as the manufacturer. However, the main characteristics of the sensors are essentially very similar. Following are some of the common characteristics¹ of electrochemical sensors.

Electrolyte within the sensor cell is an aqueous solution separated by a hydrophobic barrier which will not allow the aqueous solution to leak out. However, water vapor can pass through, just as other gas molecules can. In high humidity conditions, prolonged exposure can cause excessive water to build up and create leakage. In low humidity conditions, the sensor can dry out. Sensors that are designed to monitor high gas concentrations have less porous barriers to limit the amount of gas molecules that pass through, and therefore are not affected by the humidity as much as sensors that are used to monitor low gas concentrations, which have more porous barriers and allow a more free exchange of water molecules.

Pressure and Temperature:

In general, when the temperature is above 25°C, the sensor will read higher, when it is below 25°C, it will read lower. The temperature effect is typically 0.5% to 1.0% per degree centigrade, depending on the manufacturer and type of sensor.

Selectivity:

Electrochemical sensors are generally fairly selective to the target gas they are designed for. The degree of selectivity depends on the type of sensor, the target gas, and the concentration of gas the sensor is designed to detect.

Life Expectancy:

The life expectancy of an electrochemical sensor depends on several factors, including the gas to be detected and the environmental conditions in which the sensor is used. In reality, the life expectancy will be highly dependent on the total amount of gas exposed to the sensor during its life, as well as other environmental conditions, such as temperature, pressure and humidity. Typical gases and the range of measurements of electrochemical sensors are shown in table 1.

Table 1. Typical gases and the Range of Measurements of Electrochemical Sensors.

GAS NAME	PPM RANGE
Ammonia NH ₃	10
Arsinic Hydrochloride, ArH ₃	1
Bromin, Br ₂	30
Chlorine dioxide, Clo ₂	5
Hydrogen H ₂	2000

Major Components

An electrochemical sensor consists of the following major components¹:

Gas Permeable Membrane (hydrophobic membrane):

This is used to cover the sensor's sensing (catalyst) electrode and, in some instances, to control the amount of gas molecules reaching the electrode surface. Such barriers are typically made of thin, low-porosity Teflon membranes. Such sensors are called membrane clad sensors. Alternatively, the sensing electrode is covered with a high-porosity Teflon and the amount of gas molecules reaching the electrode surface is controlled by a capillary. Such sensors are referred to as capillary-type sensors. Besides offering a mechanical protection to the sensor, the membrane performs the additional function of filtering out unwanted particulates. Selecting the correct pore size of the membrane and capillary is necessary to transfer the proper amount of gas molecules. The pore size should be such as to allow enough gas molecules to reach the sensing electrode. The pore size should also prevent liquid electrolyte from leaking out or drying out the sensor too quickly.

Electrode:

The selection of the electrode material is very important. It is a catalyzed material which performs the half cell reaction over a long period of time. Typically, the electrode is made from a noble metal, such as platinum or gold, and catalyzed for an effective reaction with gas molecules. Depending on the design of the sensor, all three electrodes can be made of different materials to complete the cell reaction.

Electrolyte:

The electrolyte must facilitate the cell reaction and carry the ionic charge across the electrodes efficiently. It must also form a stable reference potential with the reference electrode and be compatible with materials used within the sensor. If the electrolyte evaporates too quickly, the sensor's signal will deteriorate.

Filter:

Sometimes a scrubber filter is installed in front of the sensor to filter out unwanted gases. There is a limited selection of filters, each with different degrees of effectiveness. The most commonly used filter medium is activated charcoal. The activated Char coal filters out most chemicals with the exception of carbon monoxide and hydrogen gases. By properly selecting the filter medium, an electrochemical sensor can be made more selective to its target gases. Choosing the suitable materials for the above components, and arranging the geometry of all these components to determine the optimum operating performance presents a challenge to scientists. Minor variations in the details of the sensor design can have a profound influence on the sensor's accuracy, response time, sensitivity, selectivity, and life expectancy.

Principle of Operation

Electro chemical sensors operate by reacting with the gas of interest and producing an electrical signal proportional to the gas concentration¹. A typical electrochemical sensor consists of a sensing electrode (or working electrode), and a counter electrode separated by a thin layer of electrolyte.

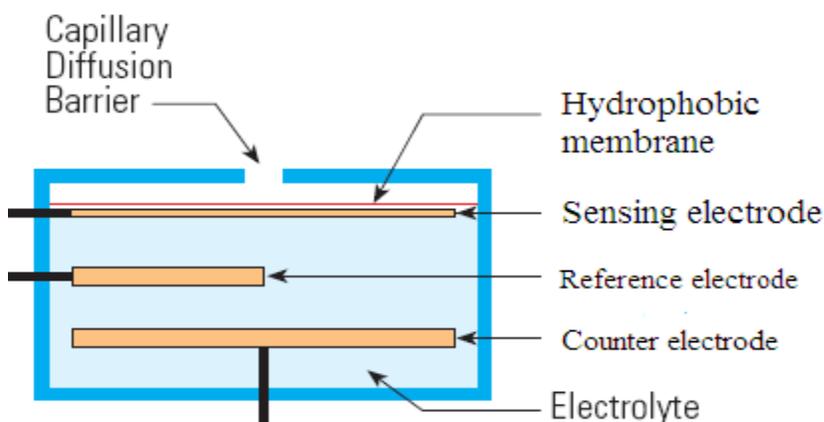


Fig.1. Block diagram of electrochemical sensor

Gas that comes in contact with the sensor first passes through a small capillary-type opening and then diffuses through a hydrophobic barrier, and eventually reaches the electrode surface. This approach is adopted to allow the proper amount of gas to react at the sensing electrode to produce a sufficient electrical signal while preventing the electrolyte from leaking out of the sensor, fig.1. The gas that diffuses through the barrier reacts at the surface of the sensing electrode involving either an oxidation or reduction mechanism. These reactions are catalyzed by the electrode materials specifically developed for the gas of interest. With a resistor connected across the electrodes, a current proportional to the gas concentration flows between the anode and the cathode. The current can be measured to determine the gas concentration. Because a current is generated in the process, the electrochemical sensor is often described as an amperometric gas sensor or a micro fuel cell.

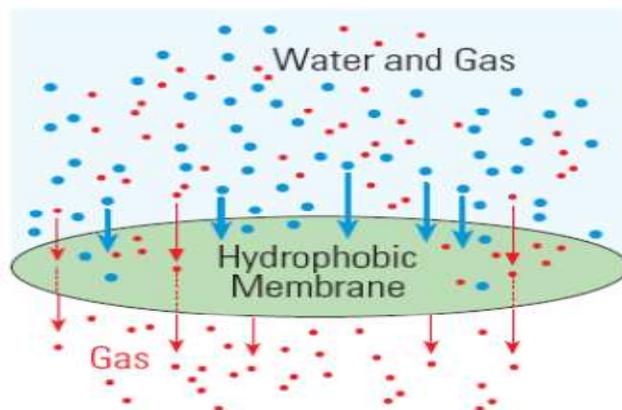


Fig.2. Diffusion through hydrophobic membrane.

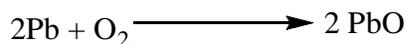
PRINCIPLES INVOLVED IN DIFFERENT TYPES OF ELECTROCHEMICAL SENSORS:

1. OXYGEN SENSOR DETECTION PRINCIPLE:

Most portable or survey instruments used for workplace evaluation of oxygen concentrations make use of "fuel cell" type oxygen sensors. "Fuel cell" oxygen sensors consist of a diffusion barrier, a sensing electrode (cathode) made of a noble metal such as gold or platinum, and a working electrode made of a base metal such as lead or zinc immersed in a basic electrolyte (such as a solution of potassium hydroxide)¹. Oxygen diffusing into the sensor is reduced to hydroxyl ions at the cathode. Hydroxyl ions in turn oxidize the lead (or zinc) anode.



This yields an overall cell reaction of:



Fuel cell oxygen sensors are current generators. The amount of current generated is proportional to the amount of oxygen consumed (Faraday's Law). Oxygen reading instruments simply monitor the current output of the sensor. An important consideration is that fuel cell oxygen sensors are used up over time. In the cell reaction above, when all available surface area of the lead (Pb) anode has been converted to lead oxide (PbO), electrochemical activity ceases, current output falls to zero, and the sensor must be rebuilt or replaced. Fuel cell sensors are designed to last no more than one to two years. Even when installed in an instrument which is never turned on, oxygen sensors which are exposed to atmosphere which contains oxygen are generating current, and being used up. Oxygen sensors are also influenced by the temperature of the atmosphere and are being used to measure. The warmer the atmosphere, the faster the electrochemical reaction.

For this reason oxygen sensors usually include a temperature compensating load resistor to hold current output steady in the face of fluctuating temperature. Another limiting factor is cold. The freezing temperature of electrolyte mixtures commonly used in oxygen sensors tends to be about 5° F (- 20 °C). Once the electrolyte has frozen solid, electrical output falls to zero, and readings may no longer be obtained. There are two basic variations on the fuel cell oxygen sensor design. These variations have to do with the mechanism by which oxygen is allowed to diffuse into the sensor. Dalton's Law states that the total pressure exerted by a mixture of gases is equal to the sum of the partial pressures of the various gases. The partial pressure for oxygen is that fraction of the total pressure due to oxygen. Partial atmospheric pressure oxygen sensors rely on the partial pressure (or $p\text{O}_2$) of oxygen to drive molecules through the diffusion barrier into the sensor.

As long as the $p\text{O}_2$ remains constant, current output may be used to indicate oxygen concentration. On the other hand, shifts in barometric pressure, altitude, or other conditions which have an effect on atmospheric pressure will have a strong effect on $p\text{O}_2$ sensor readings. Since there is less force driving oxygen molecules through the

diffusion barrier into the sensor, the current output is significantly lower. "Capillary pore" oxygen sensor designs include a narrow diameter tube through which oxygen diffuses into the sensor. Oxygen is drawn into the sensor by capillary action in much the same way that water or fluid is drawn up into the fibers of a paper towel. While capillary pore sensors are not influenced by changes in pressure, care must be taken that the sensor design includes a moisture barrier in order to prevent the pore from being plugged with water or other fluids.

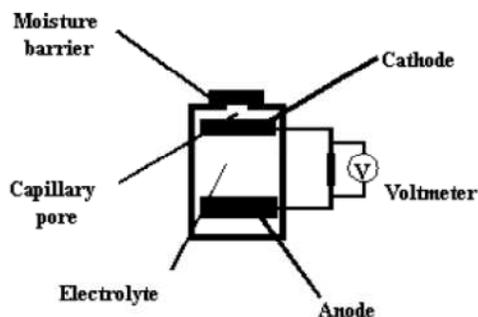


Fig. 3. Capillary pore oxygen sensor

2. EFFECTS OF CONTAMINANTS ON OXYGEN SENSORS:

Oxygen sensors may be affected by prolonged exposure to "acid" gases such measured in many cases to 0.1 ppm. The chief limitation of electrochemical sensors is the effects of interfering contaminants on toxic gas readings. Most substance-specific electrochemical sensors have been carefully designed to minimize the effects of common interfering gases. Substance-specific sensors are designed to respond only to the gases they are supposed to measure. The higher the specificity of the sensor the less likely the sensor will be affected by exposure to other gases which may be incidentally present. For instance, a substance-specific carbon monoxide sensor is deliberately designed not to respond to other gases which may be present at the same time, such as hydrogen sulfide or methane. Even though care has been taken to reduce cross-sensitivity, some interfering gases may still have an effect on toxic sensor readings. In some cases the interfering effect may be "positive" and result in readings which are higher than actual. In some cases the interference may be negative and produce readings which are lower than actual. Electrochemical sensor designs may include a selective external filter designed to remove interfering gases which would otherwise have an effect on the sensing electrode. The size and composition of the filter are determined by the type and expected concentration of the interfering contaminants being removed. Depending on the nature of the reaction each

gas has with the sensor, the effect can either decrease the signal (negative cross sensitivity) or increase the signal (positive cross sensitivity). Most oxygen sensors are not recommended for continuous use in atmospheres which contain more than 25% CO₂.

3. SUBSTANCE-SPECIFIC ELECTROCHEMICAL SENSORS:

One of the most useful detection techniques for toxic contaminants is the use of substance specific electrochemical sensors installed in compact, field portable survey instruments. Substance-specific electrochemical sensors consist of a diffusion barrier which is porous to gas but nonporous to liquid, reservoir of acid electrolyte (usually sulfuric or phosphoric acid), sensing electrode, counter electrode, and (in three electrode designs) a third reference electrode. Gas diffusing into the sensor reacts at the surface of the sensing electrode. The sensing electrode is made to catalyze a specific reaction. Dependent on the sensor and the gas being measured, gas diffusing into the sensor is either oxidized or reduced at the surface of the sensing electrode. This reaction causes the potential of the sensing electrode to rise or fall with respect to the counter electrode. The current generated is proportional to the amount of reactant gas present. This two electrode detection principle presupposes that the potential of the counter electrode remains constant. In reality, the surface reactions at each electrode causes them to polarize, and significantly limits the concentrations of reactant gas they can be used to measure. In three electrode designs it is the difference between the sensing and reference electrode.

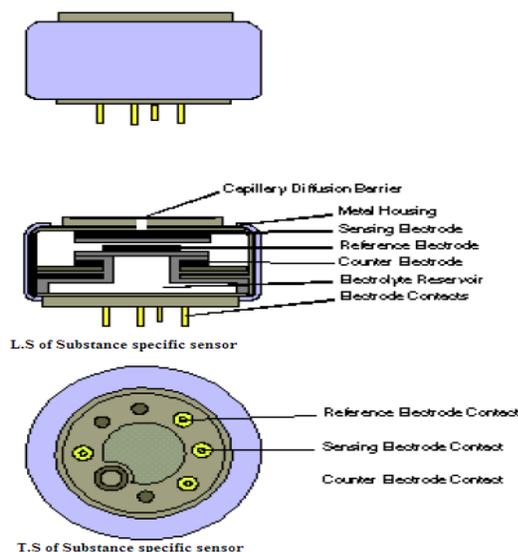


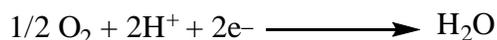
Fig. 4. Substance specific electrochemical sensor.

The oxidation of carbon monoxide in an electrochemical sensor provides a good example of the detection mechanism:

Carbon monoxide is oxidized at the sensing electrode:



The counter electrode acts to balance out the reaction at the sensing electrode by reducing oxygen present in the air to water:



Similar reactions allow for the electrochemical detection of a variety of reactant gases including hydrogen sulfide, sulfur dioxide, chlorine, hydrogen cyanide, nitrogen dioxide, hydrogen, ethylene oxide, phosphine and ozone. A bias voltage is sometimes applied to the counter electrode to help drive the detection reaction for a specific contaminant. Biased sensor designs allow for the detection of a number of less electrochemically active gases such as hydrogen chloride and nitric oxide. Several other contaminants (such as ammonia) are detectable by means of other less straight forward detection reactions.

In some cases, cross sensitivity is used to deliberate advantage. Carbon monoxide and hydrogen sulfide are the two most common toxic gases associated with confined space entry. In addition to "substance specific" sensors designed to measure these toxic hazards, several manufacturers offer a dual purpose sensor designed to detect both carbon monoxide and hydrogen sulfide. Dual purpose sensors of this kind are useful in situations requiring use of a single sensor to monitor simultaneously for both toxic hazards. It should be pointed out that since dual purpose sensors have been designed to respond to both hazards at the same time, they cannot determine which of the two hazards is producing the reading. A dual purpose sensor cannot determine which hazard is present in what specific concentrations, but may still be capable of providing an immediate indication when conditions become unsafe. When a specific contaminant such as hydrogen sulfide is known to be potentially present, the best approach is usually to use a direct reading substance specific sensor.

4. METAL OXIDE SEMICONDUCTOR SENSORS:

Metal oxide semiconductor (or MOS) sensors may be used for toxic as well as combustible gas monitoring. As discussed previously in the combustible gas monitoring section, MOS sensing elements consist of a metal oxide semiconductor such as tin dioxide (SnO_2) on a sintered alumina ceramic bead contained within a flame arrestor. In clean air the electrical conductivity is low, while contact with reducing gases such as carbon monoxide or combustible gases increases conductivity. Sensitivity of the sensing element to a particular gas may be altered by changing the temperature of the sensing element.

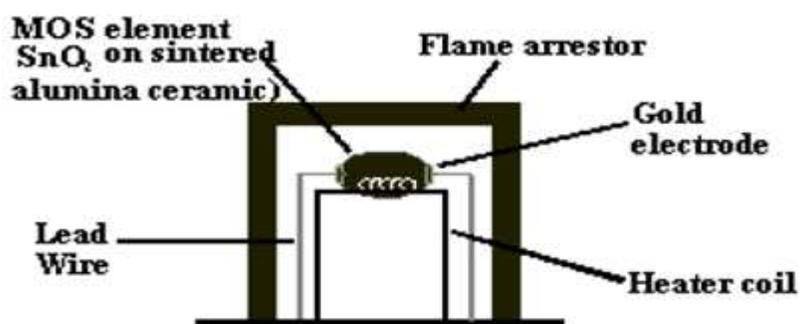


Fig. 5. Metal oxide semiconductor sensor

MOS sensors are "broad range" devices designed to respond to the widest possible range of toxic and combustible gases, including chlorinated solvent vapors and other contaminants difficult to detect by other means. This non specificity can be advantageous in situations where unknown toxic gases may be present and a simple go or no go determination of the presence of toxic contaminants is sufficient. Since sensitivity of the sensing element to a particular gas is mathematically predictable, a commonly used strategy is to preprogram the instrument with a number of theoretical specific response curves. If the exact nature of the contaminant is known, an identification code can be entered, and readings of the sensor will be adjusted to reflect the expected sensitivity of the sensor to the contaminant being measured. MOS sensors offer the ability to detect low (0 - 100 ppm) concentrations of toxic gases over a wide temperature range. The chief limitations concerning use of this kind of sensor are the difficulty in the interpretation of positive readings, the potential for false positive alarms, and the effects of humidity on sensor output.

As humidity increases sensor output increases as well. As humidity drops to very low levels, sensor output may fall to zero even in the presence of gas. In addition if a user keys in the preprogrammed response curve for a contaminant which is highly detectable by the sensor, but actually encounters one which is less detectable, the result may be erroneously low readings.

Mechanism

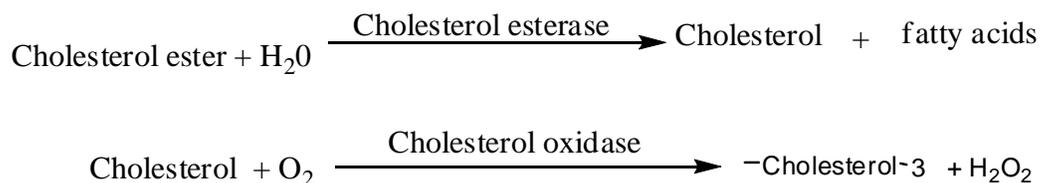
Electrochemical sensors are the largest group of chemical sensors, representing approximately 58% of the total chemical sensors. Other types include optical (24%), mass (12%) and thermal (6%). This division is based on the general transduction principle, general mechanism involved in this electrochemical sensor is Transduction mechanism². Electrochemical sensors are devices that extract information about sample from measurement of some electrical parameters³. It is easy to categorize by measuring their electrical parameters, as they are linked together by Ohms (i.e the potential difference in a circuit is equal to the product of the current and the resistance that is voltage = ampere time ohm). So, if we measure difference of two potentials we discuss about potentiometric sensors.

APPLICATIONS OF ELECTROCHEMICAL SENSORS ON CLINICAL ANALYSIS:

1. METABOLITES:

(a) Cholesterol:-

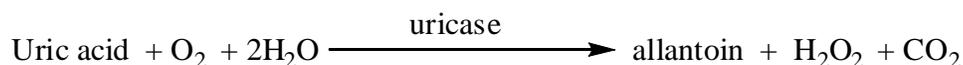
Determination of the cholesterol level in human blood is of great significance in clinical analysis/diagnosis. High cholesterol accumulation in blood serum is strongly correlated with coronary heart disease, arteriosclerosis, myocardial infarction, brain thrombosis, lipid metabolism dysfunction, hypertension, etc.⁴ Cholesterol determination is performed by enzymes, such as cholesterol oxidase (ChO_x) and cholesterol esterase. These together can be used to monitor both native and esterified cholesterol levels. Cholesterol esterase catalyzes the hydrolysis of cholesterol ester, which is important for determination of total cholesterol. The estimation of cholesterol is based on follows:



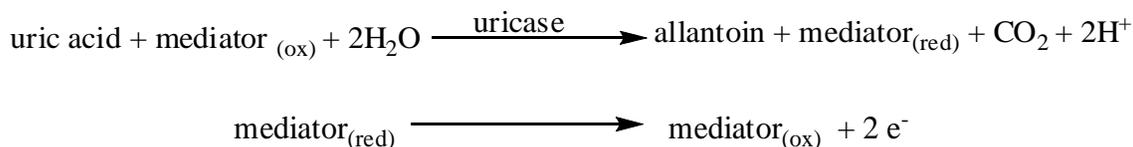
The production of hydrogen peroxide is oxidized at a high anodic potential (above +0.6 V)⁵. Some researchers used horseradish peroxidase (HRP)⁶ or electron transfer mediators, such as ferrocyanide⁷, and Prussian Blue^{8,9}, to measure hydrogen peroxide reduction current at lower potential and, thus, to avoid the influence of reductants. Nanostructures such as nano wires, nanoparticles and CNTs have been used as smart building blocks for emerging electronic and sensing devices.

(b) Uric acid:

One of the major problems in biological determinations of UA comes from electrochemical interferences such as ascorbic acid (AA), which has a similar oxidation potential, $E_{1/2} \approx 200$ mV versus SCE, at graphite electrodes, and is present at high concentrations in biological systems¹⁰. Removing the interference caused by AA is critical in UA sensor design. There are two methods for the measurement of UA, enzymatic and non-enzymatic. The enzymatic procedures using uricase (urate oxidase, EC 1.7.3.3, UOx), have been developed based on amperometric detection of H₂O₂ produced in the reaction below:



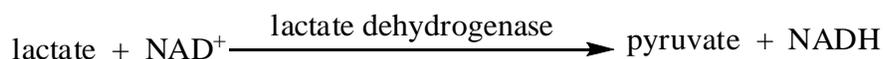
Other enzymatic procedures are based on electron transfer mediators, the reactions are as follows:

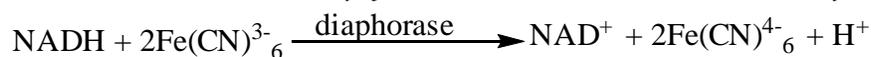


Much research into conducting polymer-based enzymatic sensors for detecting UA has been reported. In order to enhance the fixation and stability of UO_x and electron transfer mediators on the surface of electrode, polypyrrole and its derivatives such as dodecyl sulfate doped poly(N-methylpyrrole) were utilized^{11,12}.

(c) Lactate:

Reliable blood lactate measurements would also be of interest in sports medicine. Lactate can be measured based on the reaction using NAD⁺ dependent lactate dehydrogenase and ferricyanide.





2. Blood gases:

Biological body consumes oxygen and release carbon dioxide by gaseous exchange in alveolus and tissue. Partial pressure of carbon dioxide ($p\text{CO}_2$) and partial pressure of oxygen ($p\text{O}_2$) dominantly interact with physical conditions. Particularly, $p\text{O}_2$ reflects lung stress such as pulmonary embolism or pulmonary atelectasis and it is an indicator of blood oxygen levels, which is used for diagnosis, treatment and management of depressed respiration¹³.

3. Electrolytes:

A miniaturized electrochemical simultaneous multisensor array for K^+ , Na^+ , and Ca^{+2} in human whole blood, based on chemical vapor deposition technique, had been tested . This sensor array was composed of a four channel portable battery operated, reference electrode and simultaneous multi-sensing electronic system based on discrete electronic parts¹⁴. A ion-selective planar sensor for K^+ and Ca^{2+} , which was fabricated with bulk silicon micromachining techniques using a double-sided wafer process combined with polymeric membrane coatings, and the dimension of the chip is $1 \text{ mm} \times 5 \text{ mm} \times 0.5 \text{ mm}$. This potentiometric device had solid-state contacts and uses a hydrogel as an inner liquid electrolyte solution¹⁵. The sensors showed near Nernstian slope, good resolution, sufficient lifetime, and excellent reliability, but a larger drift, mainly in the start-up period.

4. DNA:

Deoxyribonucleic acid (DNA) is a very important biomolecule that has an essential role in the determination of hereditary characteristics, storing the genetic information necessary for the replication of living organisms¹⁶. DNA analysis is the most recent and most promising application of electrochemical sensors to clinical chemistry.

5. Other analyses:

These are also used for the measurement of Haemoglobin, Blood ketones (Ketone bodies, including β -hydroxybutyrate, acetoacetic acid and acetone, are produced by incomplete fatty acid metabolism within mitochondria of hepatocytes) and Nitric oxide (An electrochemical device for detecting exhaled NO based on a specially designed electrochemical sensor was developed).

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