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Review Article

Clinical Analysis for Haemoglobin, Glucose, Cholesterol, Uric Acid Level in Blood and Blood Pressure Using Biosensors

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ABSTRACT

Manual methods of clinical diagnosis are labour -intensive, costly, prone to error, and expose the caregiver to blood. To eradicate the disadvantage in manual methods we are going for the Biosensor technology (BT).BT offers several benefits over conventional diagnostic analysis. They include simplicity of use, specificity for the target analyze, speed to arise to a result, capability for continuous monitoring and ultiplexing, together with the potentiality of coupling to low-cost, portable instrumentation. Here we are going to design All in one Blood monitoring system which monitors the Blood Haemoglobin, glucose, cholesterol, uric acid, pressure level Using Enzyme electrodes and Pulse oximeter and the data acquisition is made easy by introducing a microcontroller and computed out.

Keywords: Amperometric enzyme electrode, pulse oximeter, microcontroller, blood monitoring system

1. INTRODUCTION

Amperometric biosensor for haemoglobin, glucose, cholesterol and uric acid analysis are widely used during real time analysis separately as each individual device. The performance of amperometric biosensor decided by stability of enzyme and its associated instrumention system [1]. Pulse oximeter use time-multiplexed red and infrared LEDs and a photodetector which detects the light attenuated by the perfused tissue. The probe is usually attached to the patient's fingertip, earlobe, forehead, or foot, i.e., to a region of tissue which is well perfused and translucent. The embodiment of the probe can be of transmissive or reflective type, which means that either the intensity of the transmitted light through the tissue or that of the backscattered light from the tissue is measured [2, 3].

2. BIOSENSOR

2.1. Amperometric Enzymatic Biosensors

Amperometry measures electric current between a pair of electrodes that are driving the electrolysis reaction. Oxygen diffuses through the membrane and a voltage is applied to the Pt electrode reducing O_2 to H_2 [1].

The Working and Counter electrode surfaces of the sensors are usually noble metal (Au, Pt) wire, plate, or foil with or without any modification. In some cases, different substrates, e.g., carbon electrode, silk fibroin membrane, or silicon/Pt microchip are used. The Reference electrodes are either Ag/AgCl or saturated calomel electrodes (SCE). Toward cost effective biosensors, inexpencive mass productive technologies and integration is very important [1, 4, 5].

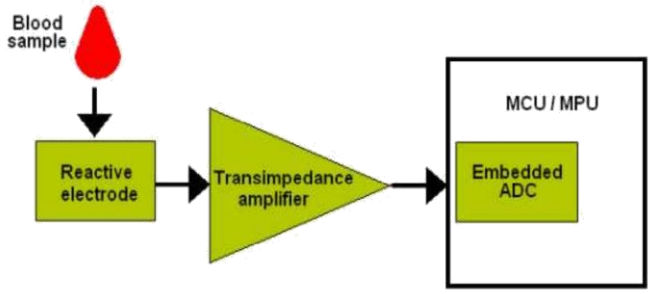

Fig. 1: Typical Block Diagram for Working of Biosensors

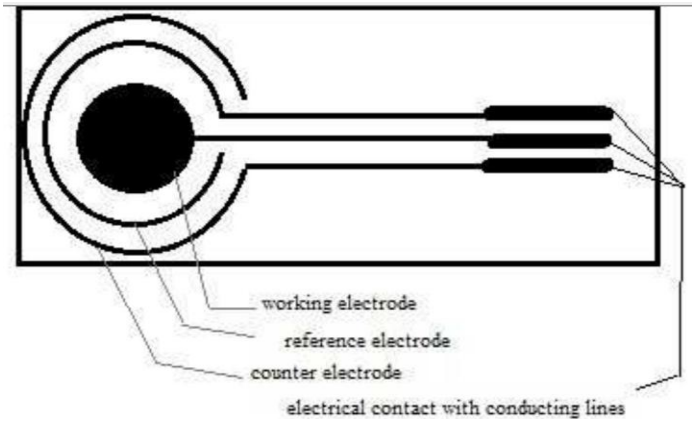

Fig. 2: Positions of different electrodes in biosensors. Immobilized enzyme reactions

2.2. Immobilized enzyme reactions

The enzymatric reaction will differ from each and every analysis we use, as follows:

- For glucose measurement, the immobilized enzyme used is glucose oxidase enzyme (GOd) catalyzes invivo oxidation of glucose in the presence of O_2 as a oxidizing agent, producing gluconic as the oxidation products of glucose and hydrogen peroxide as the reduction product of O_2.

$$\text{Glucose} + O_2 \xrightarrow{\text{glucose oxidase}} \text{gluconic acid} + H_2O_2$$

The amperometric determination of glucose can be made by electrochemical oxidizing the produced H_2O_2 [4-6].

$$H_2O_2 \longrightarrow O_2 + 2H^+ + 2e^-$$

- For uric acid measurement, the immobilized enzyme used is uricase (Uox) catalyzes invivo oxidation of uric acid in the presence of O_2 as a oxidizing agent, producing allantoin and CO_2 as the oxidation products of uric acid and hydrogen peroxide as the reduction product of the O_2.

$$\text{Uric acid} + O_2 + H_2O \xrightarrow{\text{uricase}} \text{allantonin} + CO_2 + H_2O_2$$

The amperometric determination of uric acid can be made by electrochemical oxidizing the produced H_2O_2 [4, 6, 7].

$$H_2O_2 \longrightarrow O_2 + 2H^+ + 2e^-$$

- For cholesterol measurement, the immobilized enzyme used is cholesterol oxidase (chox) and this reaction is followed by electrochemical oxidation of mediator (m1) on the electrode surface.

$$\text{Cholesterol} + m_{1ox} + m_{2red} \xrightarrow{\text{chox}} \text{Cholest - 4 – enome}$$

$$m_{1red} \xrightarrow{\text{electrode}} m_{1ox} + e^-$$

$$\text{Cholesterol} + O_2 + H_2O_2 \xrightarrow{\text{chox}} \text{Cholest - 4 – enome}$$

The oxygen is the physiological mediator for chox. in this case it measures either increase in speed (or) decrease in speed of the production of oxidation and reduction [6, 8, 9].

For hemoglobin level measurement, the haemoglobin is measured after detergent lysis of erythrocytes and conversion to the azido-met form. Reaction products are measured by reflectance optics in a porous membrane after the reaction reaches its end point [6].

2.3. Pulse oximeter

It uses time-multiplexed red and infrared LEDs and a photodetector which detects the light attenuated by the perfused tissue. The probe is usually attached to the patient's fingertip, earlobe, forehead, or foot, i.e., to a region of tissue which is well perfused and translucent. The embodiment of the probe can be of transmissive or reflective type, which means that either the intensity of the transmitted light through the tissue or that of the backscattered light from the tissue is measured [2, 3].

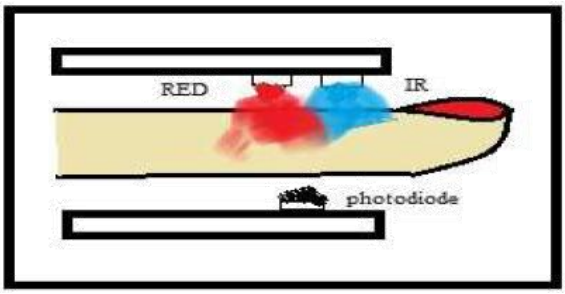

Fig. 3: Schematic Diagram of Pulse Oximeter

2.4. Selectivity by Amperometric sensors

The selectivity is always crucial in case of any sensor. When utilizing amperometric biosensors in blood, serum, or urine nonspecific interference of oxidizable analytes (for instance ascorbic acid, acetaminophen, D-fructose, dopamine, or uric acid) can occur, depending on the applied voltage. For the protection of the electrode surfaces from these analytes, the use of size-exclusion membranes [like Nafion, poly-(-phenilendiamin) or calixarene] is widely spread. These membranes do not let organic molecules to contact the polarized electrode surface, while smaller molecules like or can reach the electrode unhindered and can be detected [7].

3. SYSTEM DESIGN

3.1. Basic principle

Sample handling is complished by capillary fluidics in the cartridge. For glucose and cholesterol, the blood sample is filtered to remove erythrocytes before analysis. For glucose and cholesterol, the analyte is converted to hydrogen peroxide with an oxidase, and the peroxide is converted to coloured product by peroxidise [1].

3.2. Basic Block diagram

The proposed measurement engine consists of the Following components:

3.2.1. Test strip

The blood is placed in the test strip through capillary action which is converted into varying current by using ADC.

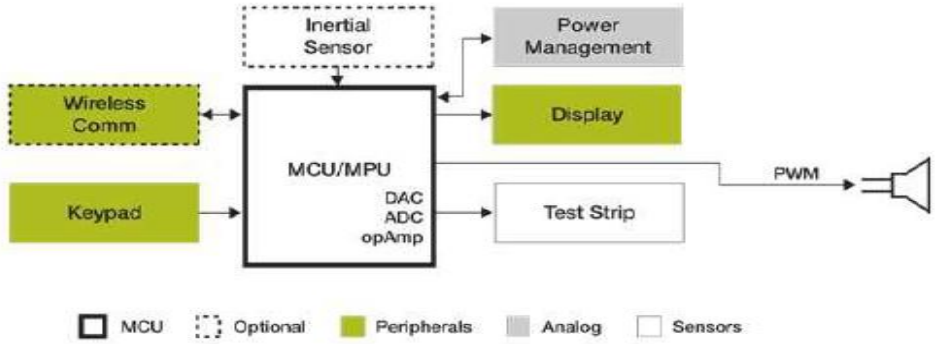

Fig. 4: Typical Block Diagram of Amperometric Sensors

3.2.2. Digital to analogue Converter (DAC)

Provides the signal biasing. The DAC outputs specific voltages to bias sensors (strips). A critical parameter on the DAC is settling time, which must be lower or equal to 1 microsecond for high power mode and 5us for low power mode. Monotonicity must be able to allow the proper wave forms to bias the biosensor.

3.2.3. Transimpedance Amplifier

Used to convert the current inputs into voltages that can be read by the ADC, it performs signal conditioning. A critical parameter is bias current which must be below 500 picoamperes to measure small changes produced in the biosensor during the chemical reaction.

3.2.4. Operational Amplifiers

Compare mode set for "greater than range" that initiates the measurement algorithm. The compare mode set for "inside range" easily identifies the peak of the chemical reaction. A critical parameter for general purpose amplifier is the bias current which must be below or equal to 2uA to allow the proper design of unity gain buffers, low pass filter, gain amplifiers, inverter and non-inverter programmable gain amplifier (PGA).

3.2.5. Analogue to Digital Converter (ADC)

This allows the measurement of small signals in the biosensor. The signal which picked up from the biosensor will vary depending upon the time periodically. To make it compact and easy to analysis it must be converted into digital and the measured value is to be shown out through the display.

3.2.6. Additional modules (VREF, Programmable Delay Block and Time of Day)

The VREF is a trimmable voltage reference used as a reference for analogue peripherals. The Programmable Delay Block is the glue logic that controls the timing and trigger of ADC and DAC modules. The programmable delay block, along with the ADC, are used to perform measurements at preset time intervals and calculate the levels of the measuring apparameters. A time of day module is used to keep track of time and therefore log the time at which a measurement was taken [1, 5].

3.3. Data management

Connectivity through USB and wireless are also desirable since data management is key forthephysician. It is very important to analyse the data of the patient who is using this clinical analyzer and connecting to a computer to graph measurement information is also made. The interface should be easy for the patient to use but powerful enough to allow the doctor to obtain as much information as possible through the connectivity interfaces. Wireless connectivity is more important not only for easy access to the information but also to connect with other devices which interact with the clinical measurements ex., glucose measurement needs to interact with such as an insulin pump to assist the user in administering the appropriate insulin dosage. Keypads and a human machine interface can be implemented through buttons and segment LCD to touch sensing interfaces and graphical LCDs, all which are also managed through the microcontroller. Another basic component of the system is the measurement engine which is a group of analogue and digital IP modules which interact with the sensors to deliver a voltage to the microcontroller and process the measurement [1].

4. WORK MODULE OF THE ELECTRODE

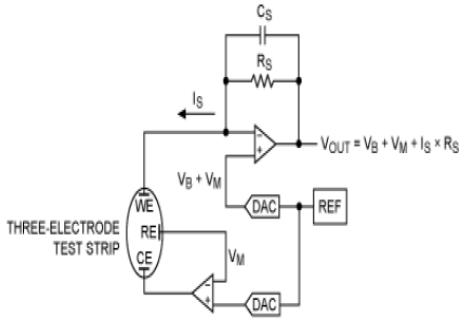

Fig. 5: Basic Circuit diagram for effective data acquisition (Using three electrode systems)

To eliminate nonspecific oxidation current of any oxidizable analyte, a bipotentiostatic measuring system have be used, which uses two symmetric and identically prepared working electrodes (W1 and W2 - with and without the enzyme). The only difference between them is the presence of the enzyme. During the measurement, the potentials of W1 and W2 are the same and the currents in the two circuits are measured simultaneously. The current of W2-C circuit (I2) is subtracted from the current of W1 C (I1).When using this method, the eventual interaction between the pNMPy covered electrode and the components of the sample solution in the electrochemical cell is negligible, because the difference of the currents can originate only from the enzyme reaction which is specific; thus, the measured current difference is related only to the concentration of the detected substrate [10].

5. PRESSURE LEVEL DETECTOR

The pulse oximeter is used as a pressure level detector in this clinical analyzer. This measures blood oxygenation by sensing the infrared and red light absorption properties of deoxygenated and oxygenated hemoglobin. It is comprised of a sensing probe attached to a patient's earlobe, toe or finger that is connected to a data acquisition system for calculation and display of oxygen saturation level, heart rate and blood flow. Light sources, typically light-emitting diodes, shine visible red and infrared light. Deoxygenated hemoglobin allows more infrared light to pass through and absorbs more red lights; highly oxygenated haemoglobin allows more red lights to pass through and absorbs more infrared light. The oximeter senses and calculates an amount of light at those wavelengths proportional to the oxygen saturation (or desaturation) of the hemoglobin. Because of the use of light in the absorbance measurement, the designer needs a true "light-to-voltage" conversion using current as the input signal. The classes of photodiode amplifiers suitable for pulse oximetry applications are the classical resistor-feedback transimpedance amplifier and the capacitorfeedback switched integrator. In either amplifier configuration, the resulting output voltage is read by an analog-to-digital converter and serialized for microcontroller [2, 3]. With that, the oxygen saturation of the human blood: R = Ratio of the Light Absorbance at the two different wavelengths.O_2

$$SaO_2 = \frac{[O_2 - Hb]}{2a[O_2 - Hb] + [Hb]}$$

5.1. Transimpedance Amplifier Requirements

Low input bias current over temperature range of interest.

- Low input capacitance relative to photodiode capacitance.
- High gain bandwidth product.
- Low voltage noise.
- For maximum precision, low offset drift over temperature.

For single-supply systems:

- Rail-to-rail input (including 0V) and output if operating the photodiode in photovoltaic (zero bias) mode.
- Rail-to-rail output only if operating the photodiode in photoconductive mode (biased).
- Shutdown and/or low supply current if battery powered system.

5.2. Audio

Audible indicators range from simple buzzers to more advanced talking meters for the vision impaired. A simple buzzer can be driven by one or two microcontroller port pins with pulse-width modulation (PWM) capability. More advanced voice indicators and even voice recording for test result notes can be achieved by adding an audio codec along with speaker and microphone amplifiers.

6. CONCLUSION

The manual method of analysing the level of haemoglobin, glucose, cholesterol, uricacid and blood pressure includes a lot of labour work and time. By using the clinical analyzer, we can able to measure all the above parameter easy at low cost which is a portable device and the result can be printed as a graph or stored in the memory of the device. Through the USB port the device can be interface with computer and other peripheral devices.

7. ACKNOWLEDGEMENT

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