Proposal of Electrode for Measuring Glucose Concentration in Blood

Klara Fiedorova, Martin Augustynek, and Tomas Klinkovsky

Abstract

The article deals with the design of the electrode system and the appropriate measuring circuit for the measurement of blood glucose concentration, since the determination of the level of blood glucose is an integral part of many medical procedures for determining the state of the human organism. The aim of the concept is to create two functional devices with different design of the electrode system and to perform a series of measurements to verify the functionality and the data statistically process. There was used the principle of resistive sensing of non-electric quantities, so the designed systems using gold electrodes working as electrolytic sensors. The problem relating to the measuring circuit, which is the same for both electrode systems, has been solved by a microampere meter which can convert the generated signal to a suitable measured electrical signal. The signal is formed by the reaction of glucose and enzyme, the resulting value being directly proportional to the glucose concentration. At this work, created systems fully meet specified conditions and requirements. The research confirmed the functionality of the designed units. On the basis of obtained data is possible to compare and evaluate the constructed electrode systems and to make the basis for further development in the subject matter.

Keywords

Measurement of blood glucose concentration
Glucose meters • Basic principles of analyzers
Blood glucose • Diabetes mellitus
Glucose measurement sensors

1 Introduction

In clinical practice, blood glucose is used as an important indicator of the state of the human body, primarily used in patients affected by diabetes mellitus. The glycemic value affects the physical proportions of the individual, the time of day and also the diet. The determined value is also dependent on the source of the analyzed blood. Normal blood glucose levels range from 3.3 to 6.6 mmol/l in capillary blood, 6.9–5.5 mmol/l in venous blood, and 4.2–6.4 mmol/l in blood plasma. A fall in blood pressure below 3.3 mmol/l is referred to as hypoglycemia and values above 5.5 mmol/l are called hyperglycemia. The basic division of methods used to measure blood glucose is invasiveness of measurement. Invasive methods are more accurate and include laboratory tests, glucometers, and part of a continuous subcutaneous electrode method [3]. Many invasive methods are based on the chemical reaction of the enzyme or the chemical with glucose, electrochemical or photometric techniques are used to determine the blood sugar concentration with the chemical reactions mentioned. Invasive methods are nowadays insurmountable in terms of accuracy and market accessibility. In addition, non-invasive methods would be very convenient in terms of comfort, but they are only experimental processes that are in the development phase. The most notable non-invasive method is the NIR method utilizing infrared interaction along with glucose. Further, there is reverse iontophoresis or Raman spectroscopy [3, 6].

The work focuses on the development of a suitable electrode or electrode system that would be able to measure

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the blood glucose concentration. This is the development of a new blood glucose measurement technique for continuous measurement where the sensor should be incorporated into the catheter and then inserted into the body of the patient. In end use, the sensor should be used to detect glucose levels, and then the heart rate should be calculated from this value.

2 Methods

Before the actual design of the electrode system, the type of electrode sensor had to be determined. It was taken into account that the conductivity of the solution, which will correspond to the glucose concentration, will subsequently be measured. Therefore, the proposed system should behave like an electrolytic sensor. General information on this type of sensor is given in [1, 2, 5, 6]. It was also very important to include in the proposal the fact that the enzyme that is specific to its chemical reactions is used for the measurement. The exact procedure for enzymatic chemical reactions is disclosed in the publications [4]. To illustrate the nature of the electrochemical reaction:

$$GLUCOSE + GOx(FAD) \rightarrow GLUKAGON + GOx(FADH_2)$$
$$GOx(FADH_2) + O_2 \rightarrow GOx(FAD) + H_2O_2$$

This part of the chemical reaction produces hydrogen peroxide, which oxidizes at a potential of

$$H_2O_2 \underset{exotherm,s=4MJ/kg}{\overset{0.6\,V.}{\rightarrow}} 2H^+ + 2e^-$$

Based on the specificity of the enzyme measurement, the electrode system design was followed. The first step was to select a suitable material for all elements of the electrode system so that the material did not enter and did not affect chemical reactions. The best material for the electrodes would be platinum, but due to availability, gold-plated electrodes that are of sufficient quality were used. The electrodes have a diameter of 0.6 mm. Next, the material into which the entire system is built will be chosen and will serve as a container for the injection of test samples. Silicone has been chosen in the form of a tube, allowing for easy installation of electrodes that are electrically non-conductive and do not affect the measurement. The tube diameter is 0.4 cm, the height above the earth electrode is 0.5 cm. The size of the space for application of the solution is $25.13 * 10^{-8}$ l. The electrodes embedded in the tube are connected by means of copper wires with pinheads, which can be connected to the measuring circuit. The material for the earth electrode is copper wires in the insulator. The size of the diameter is chosen with respect to the size of the

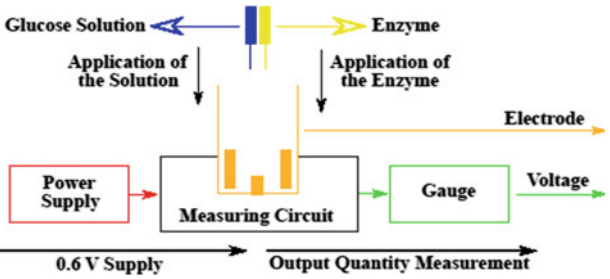

Fig. 1 Diagram of design principle of the proposed system

silicone tubing to provide a seal for the tube. Its main function is to eliminate the interference of the entire measuring system. It consists of a system of copper wires in an insulator.

To measure the blood glucose concentration, it was essential to construct a suitable circuit that would supply a required 0.6 V source voltage to the electrode and allow a suitable signal to be measured to match the glucose concentration. Since the assumed signal is assumed to be small, the circuit must be capable of capturing it. The whole is shown in Fig. 1.

The concept of conductivity, which is one of the methods for determining the concentrations of electrical conductivity of solutions, is applied in this issue. Here we take into account the given biosensor parameters, such as the cross-section and the distance that we calculate the resistance of the given system (Tables 1 and 2).

Based on the above parameters, the system resistance is calculated.

$$R = \rho * {}^{l}/_{S} \quad (1)$$

$$G = {}^{1}/_{R}[S] \quad (2)$$

$$\rho = Specific\ Resistance, l = Distance\ of\ electrodes$$
$$S = Cross\ Section\ of\ electrode;$$
$$G = k * C, C = S/l, k = Specific\ Conductivity$$

3 Results

The blood glucose level was measured under constant, unchanging conditions. For illustration and orientation in glucose analysis, blood was not used but aqueous solutions with a known glucose concentration of 3 mM, 7 mM, 12 mM, 18 mM with a volume of 0.3 ml. The measurement was carried out in two phases, the first phase being measured only with a pure glucose solution. Based on the fact that aqueous glucose solutions are made up of distilled water, we

Table 1 Overview of electrode system parameters

Electrode system	Cross section [mm]	Distance [mm]	Specific resistance [Ω cm]	Length [mm]
1	0.6	0.47	2.35 μ	4

Table 2 Overview of electrode system parameters

Electrode system	Resistance [Ω]	Conductivity [S]
1	$0.02 * 10^{-6}$	$50 * 10^{6}$

can assume that when the electrical voltage is applied to the solution, it will be possible to measure the current proportional to the glucose concentration in the solution. During the measurement, the value was recorded at the specified time point. In the second step, 0.01 g of the enzyme was added to the 10 s solution and the reading was read at the time point before the enzyme was added and at the time of enzyme application. Subsequently, there was a violent change in the voltage caused by the chemical reaction, and the response time was read off, the voltage value was again read off after the steady state. Each sample was measured 10 times. The voltage was recorded at certain time points in order to fully understand the nature of the measurements and the principle of chemical reactions.

A detailed description of the measured values presented in tables and graphs with statistic data analysis can be found in the literature. Tables 3 and 4 show the selected representatives of the measured groups, Table 3 characterizing the measurement of the pure glucose solution and Table 4 with the enzyme measurement. From both tables it is possible to read that the measured voltage value increases with increasing glucose concentration. Enzyme measurement is very characteristic of its course as the chemical reaction between glucose oxidase and glucose is fully applied here.

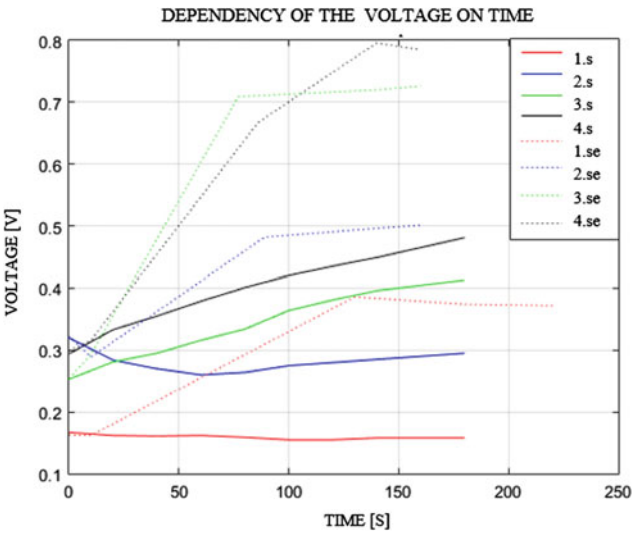

Fig. 2 Graphical representation of the measured values using the first electrode system (Color figure online)

At this point, the time of the chemical reaction was measured, and the value of the stress after the steadying was then read. From these values it is again seen that the value of the measured voltage with increasing concentration increased.

It can be seen from the graph of Fig. 2 that the measured voltage measured at certain time intervals increases as the concentration of the solution analyzed at that time increases. The solid lines correspond to pure glucose solutions, is no enzyme added. The dotted lines plot the samples with the added enzyme. For each solution concentration, whether pure solution or with added enzyme, one color is selected. Measurement with and without enzyme is distinguished only by line type. The blue curves record a course of 3 mM solution analysis. In both cases these are the lowest values. Therefore, the assumption is that samples with a 3 mM glucose solution should have the lowest strain. The red lines

Table 3 Table of readings of pure glucose solution obtained by the first electrode system

Solution (mM)	[V]	20 s/[V]	40 s/[V]	60 s/[V]	80 s/[V]	100 s/[V]	120 s/[V]	3 min/[V]
3	0.168	0.17	0.173	0.182	0.19	0.195	0.199	0.22
7	0.322	0.296	0.284	0.271	0.276	0.272	0.276	0.295
12	0.253	0.281	0.295	0.316	0.334	0.364	0.381	0.413
18	0.348	0.358	0.379	0.411	0.429	0.438	0.451	0.499

Table 4 Table of readings of the pure enzyme solution with the added enzyme obtained by the first electrode system

Solution (mM)	[V]	Enzyme 10 s/[V]	Reaction [s]	Change [V] [min]	2:20 min/[V]	2:40 min/[V]
3	0.173	0.183	20	0.387(1:55)	0.392	0.385
7	0.241	0.246	16	0.492(1:17)	0.478	0.443
12	0.262	0.274	14	0.616(1:21)	0.662	0.664
18	0.286	0.294	14	0.671(1:21)	0.766	0.782

ranged from 7 mM samples. These curves give higher voltages than blue, so the assumption is confirmed again. Green includes curves plotting the measured voltage from a solution of 12 mM. Again, these are higher voltage values than in previous situations. The black curves recorded samples measured at a concentration of 18 mM. These values are visibly the highest.

4 Discussion

In this work it was a creation of a functional unit consisting of an electrode system and a measuring circuit that could determine the value of the concentration of glucose in the aqueous solution. After the construction of the measuring unit, it was possible to test it. This took place in two cycles, when the stress value of the pure glucose solution was determined with different concentrations of this substance and then the enzyme tests were performed. During the initial measurement experiments, we have immediately confirmed the assumption that electrical energy can transfer even a pure glucose solution, is without a proper chemical reaction. After this verification, the final set of experimental measurements could be switched. From the measured values that were subjected to the graphical comparison, it is clear that the values obtained by analyzing the pure glucose solution are dependent on the concentration of the glucose solution used, as the increasing concentration increases the value of the measured voltage. This fact was confirmed by the second assumption. Another important assumption was that data measured by analysis of the enzyme solution using glucose should become higher in voltage. This was confirmed during the comparison of the individual voltages that were measured using the same glucose solution concentrations. This comparison clearly shows that the samples with the enzyme used show higher voltages. The course of these measurements is characterized by a rapid increase in voltage with a consequent rapid retreat. This phenomenon is associated with the chemical reaction and its saturation. However, when measuring the level of blood glucose, where many of the parts that are capable of transmitting electrical energy, we must accurately distinguish the electrical signal generated by the chemical reaction.

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