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Improvement of Biocompatibility and Cross-sensitivity Elimination of Amperometric Enzyme Glucose Sensors

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ABSTRACT. This paper represents an experimental analysis of cross-sensitivity, which is the main problem that usually faces one of the most important glucose sensors which is the amperometric enzyme electrode. The elimination of cross-sensitivity is based-on experimental determination of correction factors. Moreover, the solution for biocompatibility problem is discussed. Then, these solutions were electronically implemented.

1. Introduction

The measurement and control of blood glucose concentration is very important specially for diabetics who suffer from "juvenile-onset" or "insulin-dependent" diabetes in which the pancreas produces very little-if any-insulin at all. The diabetes effects about 5% of the public in the world and it reaches 10% in the developed countries.

The most severe form of diabetes is the so-called type 1 diabetes where, as a consequence of damaged beta cells, no insulin is available for secretion. The diabetic must thus resort to exogenous insulin in order to restore normoglycemia. Of course, the conventional therapy which is based on multiple daily subcutaneous injections of insulin, had failed to achieve a good control of blood glucose specially in brittle (unstable) diabetics. For this reason, new artificial insulin infusion systems were developed[1,4].

The development of insulin infusion systems has generally proceeded along three fronts: open-loop systems, closed-loop systems and semiclosed-loop systems. These systems deliver insulin to the blood according to a special algo-

rithm that controls the operation of the device. The most accurate system is the closed-loop system, sometimes referred to as an artificial beta cell or artificial pancreas. The artificial pancreas, implied a sensor-controlled insulin delivery system with an implantable, reliable, stable, sensitive selective biocompatible, reproducible and durable glucose sensor as a prerequisite[5]. The most appropriate glucose sensor that fulfils these requirements is the amperometric enzyme electrode. However, practical experience soon confirmed the fear that the amperometric enzyme electrode as a glucose sensor poses two main problems: the biocompatibility and cross-sensitivity. These problems limit the required long-term stability of the closed-loop insulin infusion systems.

The cross-sensitivity of amperometric enzyme glucose electrode practically means that this electrode is not sensitive only to measured blood glucose, but also to other substances present in blood and body fluids. The effort in this paper is directed mainly toward eliminating these interfering influences.

2. Development of Glucose Sensors

Precise measurement and continuous control of the blood glucose level are fundamental requirements for brittle diabetes. There is a variety of glucose sensors based on different mechanisms, including optical glucose sensors[6,7], ion-selective electrodes[8] and enzyme electrodes[9].

The optical glucose sensors are based on absorption spectroscopy in the infrared region. The main drawback of these sensors is their bad selectivity. This is because the pure water has an intrinsic high background absorption in the infrared region. Moreover, the reproducibility of ion-selective sensors is weak which limits their application for glucose measurements. This is why the enzyme electrodes form the most commonly used sensors for blood glucose control and measurements. In the enzyme sensor, H_2O_2 is detected as a result of the conversion of glucose and O_2 to H_2O_2 and gluconolactone, which is turn hydrolyses in the presence of water to gluconic acid.

The amperometric enzyme electrode is a common type of glucose enzyme electrodes. The amperometric enzyme sensors comprises at least one sensing electrode, a working electrode (plus a secondary reference electrode). Glucose oxidase has been studied extensively in enzyme electrodes.

$$\text{glucose} + O_2 \xrightarrow{\text{GOD}} \text{glucose lactone} + H_2O_2$$

Detection of either O_2 or the H_2O_2 generated in the enzyme reaction is possible at the working electrode, which may be made of Carbon or Platinum polarized at – 0.60v or + 0.65 (versus Ag/AgCl) depending on wither oxygen or H_2O2 is the measured species[10].

This approach of employing a specific enzyme still leaves the inherent problems of electrochemical interferences at the transducer made worse by the high overpotentials often needed. In addition, a low ambient oxygen frequently moves rate limiting for oxidase-based enzyme electrodes. The first approach to addressing these problems was to interpose gas permeable (for O_2) membranes or low molecular weight cut-off membranes. Furthermore, external covering membranes are frequently employed, designed to increase biocompatibility and reduce surface fouling and provide a substrate diffusion limiting barrier. An alternative approach to modifying behavior is to change the enzyme reaction chemistry. Electron mediators for oxidase enzyme electrodes to transfer electrons from the enzyme to the electrodes have been developed; these have included soluble (ferryanide) or immobilized (ferrocenebased) electron mediators[11]. These sensors wholly avoid the dependence on Oxygen as the mediator takes the role of the electron acceptor, coupling the redox reaction to the working electrode.

Ideally, a mediator should operate at a low redox potential with a one- electron zero proton coupled process. The former feature help minimize the effects of interferants and the latter eliminates a pH dependence. Although the careful choice of mediator can improve the performance of enzyme electrodes, the use of mediators suffers several drawbacks :

a) loss of mediator to the bulk solution by leaching;
b) side chain reactions of the mediator with other constituents of the sample and, in particular, allowing electron mediation of other electrochemical active interferants
c) currents that are limited by the diffusion of mediator between the enzyme and electrode if the mediator is not immobilized.

To overcome these difficulties, various chemistries have been developed to modify mediator immobilization in some way[12]. These include:

1. chemical modification of the working electrode surface with covalently attached mediator,
2. direct attachment of the mediator to the enzyme such an approach offers facilitated electron transfer from the enzyme to the mediator,
3. entrapment of the enzyme within a polymer derivatised with redox active (mediator) groups.

Of course, the most extensively used mediators employed in enzyme electrodes are those based on ferrecene[12].

Although none of the sensors has been successfully applied in clinic for long-term monitoring due to the deposition of protein, fibriu and platelets on the ex-

ternal membrane, much progress has been achieved. In addition to the traditional method of using anticoagulant agents to prolong the life-time of the blood glucose sensor, other methods have also been reported in the literature[13]. Another glucose sensor is the needle type which is covered with a phospholipid-based copolymer as an external membrane, demonstrated a stable response for up to 72 h in undiluted blood[14].

3. Problem of Amperometric Enzyme Electrodes

The amperometric enzyme glucose sensors have enormous potential in health care, both for diagnosis and therapy. Various miniature enzyme sensors intended for in vivo measurement of glucose have been developed in the last two decades, but very few can be used successfully for in vivo measurement of glucose. This is caused by two main problems: biocompatibility and cross-sensitivity (selectivity) of the amperometric enzyme glucose sensor.

3.1. Biocompatibility

The issue of sensor biocompatibility primarily centers on the interactions between the sensor and biological surroundings. Good biocompatibility implies that the sensor neither harms nor adversely affects the cell with which it comes into contact, either directly or indirectly, and this must apply whether the sensor is used in tissues in vivo or in blood in vitro. At the same time, the living environment in which the sensor is placed should not react to the sensor surface so as to affect its characteristics. In this respect, the most important component of a sensor is the membrane in direct contact with the biological solution[15]. Of course, the membrane of invasive glucose sensor has three main functions. The first is to act as a protective ultrafiltration membrane by allowing only the target analyte and being measured to pass through it and preventing the interference of other components present in the biological environment. In this case, it is a requirement for the membrane to have high selectivity, for the target analyte and ideal a low affinity for undesirable interferents, such as proteins which may foul the membrane and lead to the malfunction of the sensor. The second function is diffusion control. Variations in "diffusion resistance" of the membrane thus lead to variations in response time and in analyte-consuming sensors, also produce variations in the dynamic measurement range and sensitivity of calibration. The third important function is biocompatibility. Thus, in invasive sensor design and development, in addition to the form, shape, size, and the construction of a particular sensor, the membrane material, and the fabrication and treatment of the membrane are crucial to achieve acceptable performance of the sensor for in vivo use.

The importance of the concept of biocompatibility of implant materials has become more evident as the interaction between the materials and their sur-

roundings determines their ultimate capability to function safely and effectively. The contact between synthetic materials and blood has always been one of these materials in the body. When translated into influences on sensors, the contact or surface interaction phenomenon leads to problems such as poor sensitivity, poor stability, poor reliability and questionable safety. Rapid growth in the polymer industry led to the utilization of these materials in medicine. The choice of technique for assessing biocompatibility remains difficult, due to the lack of knowledge and the variety of tests available. Many surface characteristics and electrochemical phenomena are believed to influence blood compatibility such as the shape of the polymer, surface tension, chemistry of the surface and the way in which it is presented to its milieu. Thus, the problem of biocompatibility is of primary importance in the development of polymers suitable for long-term usage in medical applications.

To solve the biocompatibility problem of glucose sensors, the surface of polymeric membranes must be modified. The usually used modification techniques for membrane surface are pharmacologically active agents (such as heparin, immobilized heparin or immobilized urokinase), albumin, coating, cell seeding or biolisation[5]. Selection of the appropriate technique allows to improve the biocompatibility of polymer membranes, of the glucose sensor.

3.2. Cross-sensitivity

The sensitivity of amperometric glucose sensors is usually affected by the concentration of amino acids and urea[16,17]. This is because the molecules of these materials have very small size, which enables them to diffuse by the polymeric membrane of glucose sensors. The efforts of different researches are directed mainly toward eliminating these interfering influences. Two principles have been conceived and both have been utilized for this purpose: separation and differentiation by selectively permeable membranes (molecular size); and potential dependent reactivity of different plasma components at the electrode[18]. Of course, many researchers succeeded in suppressing adverse effect of amino acids to a tolerable limit of error by covering the electrode with a compact membrane. The simultaneous elimination of the interferences of amino acids and urea has also been possible, though with reduced accuracy. Lerner *et al.* [19], claimed the ability to measure glucose in the presence of amino acids and urea with an error less than 10%. From clinical norm point of view this error is significant[20]. This is because, according to Tonkse Criterion[20], the maximum allowable error for glucose measurements is 7.2%. The Tonkse criterion states that the maximum tolerable error for analytical measurements is 0.5 S_b where S_b is the biological standard deviation, which can be easily determined from the range of glucose clinical norm. The range of clinical norm for glucose in human

blood is 90-120 mg/dl (105 ± 2 S_b). Thus, the biological standard deviation S_b is equal to 7.5 mg/dl. Therefore, the maximum percentage tolerable error is 7.2%. This why in this paper, it is decided to find practically the correction factor for urea to eliminate its effects upon the output signal of amperometric glucose sensor.

3.2.1 Experimental Analysis of Urea Interferences

To determine the effect of urea concentration in blood upon the sensitivity of glucose sensor, a lot of experiments was carried out. The experiments were performed in vitro using the measuring stand shown in Fig. 1. The Yellow spring Instrument (YSI) laboratory glucose analyzer is a stander instrument for glucose measurements. It is used here to ensure that the designed electronic system for glucose measurements is correctly operated and to control the glucose concentration in the investigated blood samples.

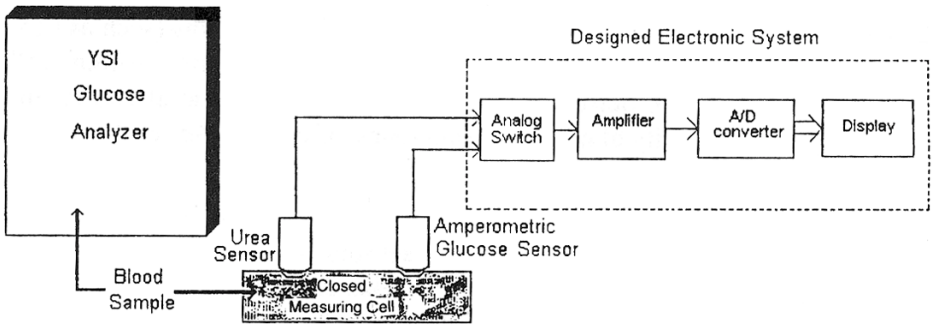

FIG. 1. Block diagram of measuring stand for investigation of influence of blood urea on the sensor's output signal.

The urea sensor is electrochemical sensor similar to amperometric glucose sensor. The only difference between them is that a polysulfone polymer membrane with a degree of sulfonation equal 0.175 is used in urea sensor instead of polymer membrane in the glucose sensor, while the rest parts of both sensors are identical.

Using polysulfone membrane, urea can be measured free from interference with good accuracy in the presence of glucose and indeed also in the presence of other larger molecules.

The operation of previous system (Fig. 1) is very simple. Both of urea and glucose sensors are in touch with the blood sample in the measuring cell, which is mixed with heparin to improve the biocompatibility of the sensors with the blood sample.

The measuring cell is closed to avoid the entrance of atmospheric gases to blood sample, which may affect also the sensitivity of glucose sensor. The range of the output signals (currents) of the glucose and urea sensors is 0 μA to 20 μA. The current of each sensor is converted into voltage using an op-amp based current-to-voltage (I/V) converter[21]. Then, the output signal (voltage) of the I/V converter is amplified with using a noninverting operational amplifier with a voltage gain (A_v) equal to 100. After this, the output voltage of the amplifier is digitized using the ICL 7107 A/D converter[22]. This A/D converter includes display/driver, thus allowing direct interface with three and half digits liquid crystal display.

To investigate the effect of urea upon the sensitivity of amperometric glucose sensor, the concentration of urea in blood sample (with fixed glucose concentration) is changed from 0 to 600 mg/dl and recording the output signal (current) of glucose sensor for each change in urea concentration. This range of urea concentration change covers the normal (10-55 mg/dl) and pathological ranges (more than 55 mg/dl) for human. The in vitro change of urea in blood sample is done by adding different known concentrations of urea to this sample. The measurements of sensor's current during the change of urea concentration is done at constant glucose concentration in blood sample. The obtained results of glucose sensor's current (i_{sen}) and urea concentration (c_{urea}) coincide in Fig. 2.

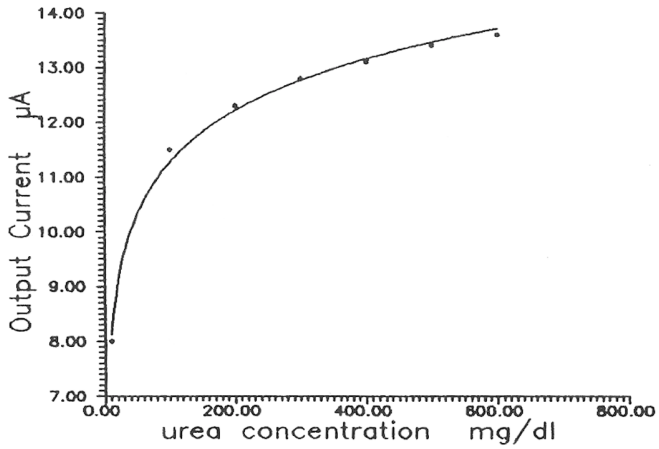

FIG. 2. The influence of blood urea on the output signal of the glucose sensor.

Of course, the glucose sensor's current is first measured for the blood sample with a constant glucose concentration with no urea. Then, the urea is added to the blood sample and the current is measured for each change in urea concentration. From Figure 2, it can be concluded that the current of glucose sensor is increased if the urea in blood is increased. Thus, the sensitivity of the glucose sen-

sor will be changed and the amount of this change depends on the urea concentration in investigated blood sample.

From the obtained experimental results, the correction factor that represents the influence of urea concentration on the sensor's current can be determined. This factor is found to be 0.05 μA/mg% for the urea concentration in the range 10 to 100 mg% and 0.01 μA/mg% for urea concentration in the range 100 to 600 mg%.

Unfortunately, the electronic implementation of these two correction factors requires first a measurement of urea concentration in investigated blood sample. This means that, the measurement of glucose in blood requires two sensors : a glucose sensor and a urea sensor. This is because to correct the output signal of the applied glucose sensor from the influence of urea, the urea concentration must be measured (using a urea sensor). Then, the influence of urea concentration upon the current of glucose sensor can be eliminated using the following relationships:

$$i_{corr} = c_{urea} * \text{correction factor} \quad (1)$$

$$i_{true} = i_{glucose\text{-}sensor} - i_{corr} \quad (2)$$

where

i_{corr} – correction current that represents the influence of urea upon the current of glucose-sensor.

c_{urea} – Actual urea concentration in investigated blood sample.

$i_{glucose\text{-}sensor}$ – the actual value of the current of glucose-sensor.

i_{true} – the true value of glucose-sensor current that is free of urea concentration influences.

The value of correction factor must be selected depending on the range of measured urea concentration. The electronic realization of previous equations is very simple specially if the glucose-analyzer composes microprocessor. Therefore, these equations and correction factors will be stored in an EPROM in a form of a short program written in assembly language. Furthermore, only the current i_{true} determined from equation 2 can be used to find glucose concentration in investigated blood sample instead of the actual current obtained directly from glucose-sensor. Using the previous procedure, the problem of cross-sensitivity of glucose-sensor toward urea concentration in blood is solved.

4. Electronic Implementation of Cross-sensitivity Solution

The solution for the cross-sensitivity problem of the amperometric enzyme glucose sensor is used to design an instrument for measurement of glucose concentration in blood (Fig. 3). This instrument is built up from amperometric glu-

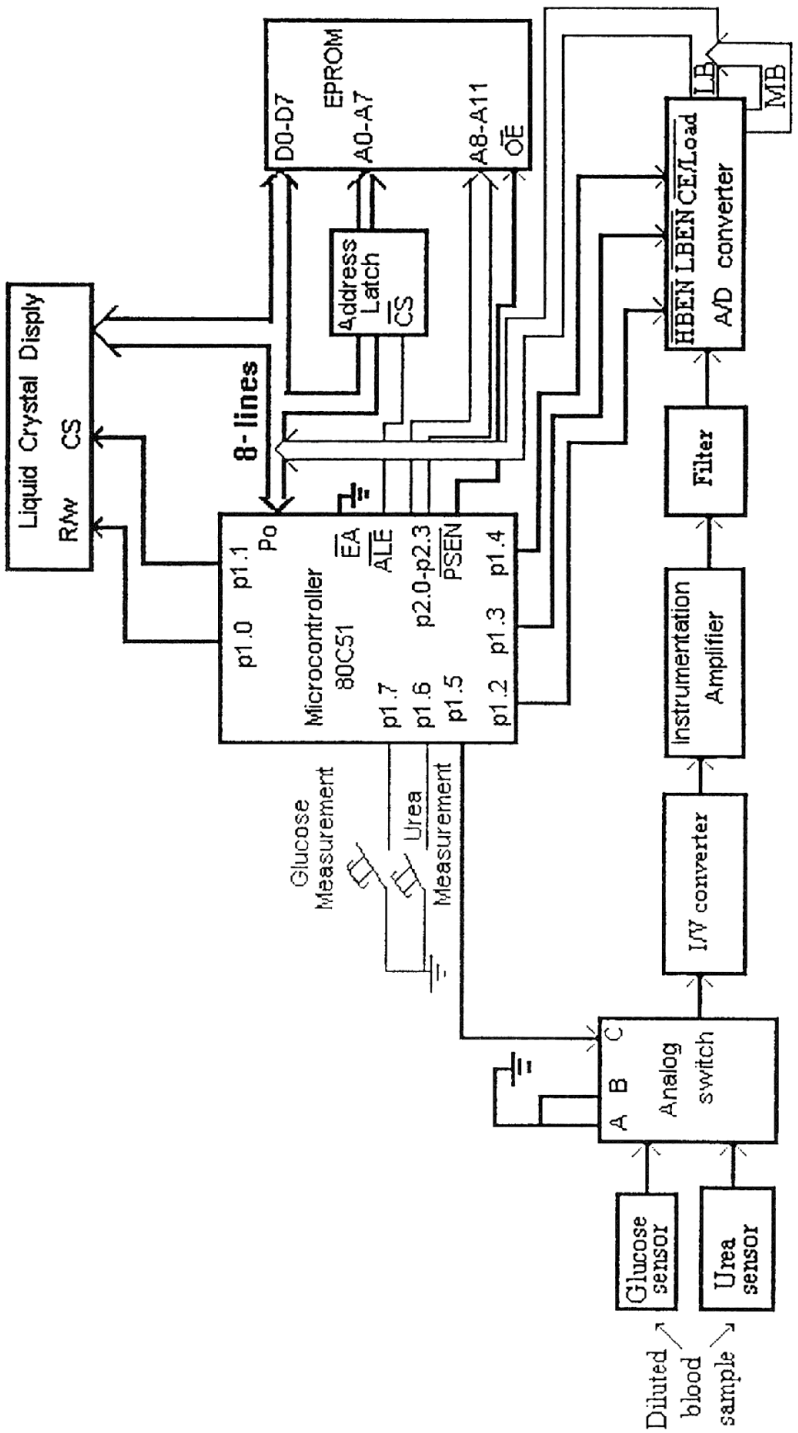

FIG. 3. Simplified block diagram of designed microprocessor-based glucose concentration analyzer.

cose sensor, urea sensor, amplifier, A/D converter and a microprocessor system. It is designed to measure the glucose concentration in the range 0 to 700 mg/dl and urea concentration in the range 0 - 600 mg/dl. These ranges cover the normal and pathological ranges of blood glucose and urea concentrations[20].

4.1. Glucose and Urea Sensors

The calibration plots of selected amperometric enzyme glucose and urea sensors are shown in Figure 4[23].

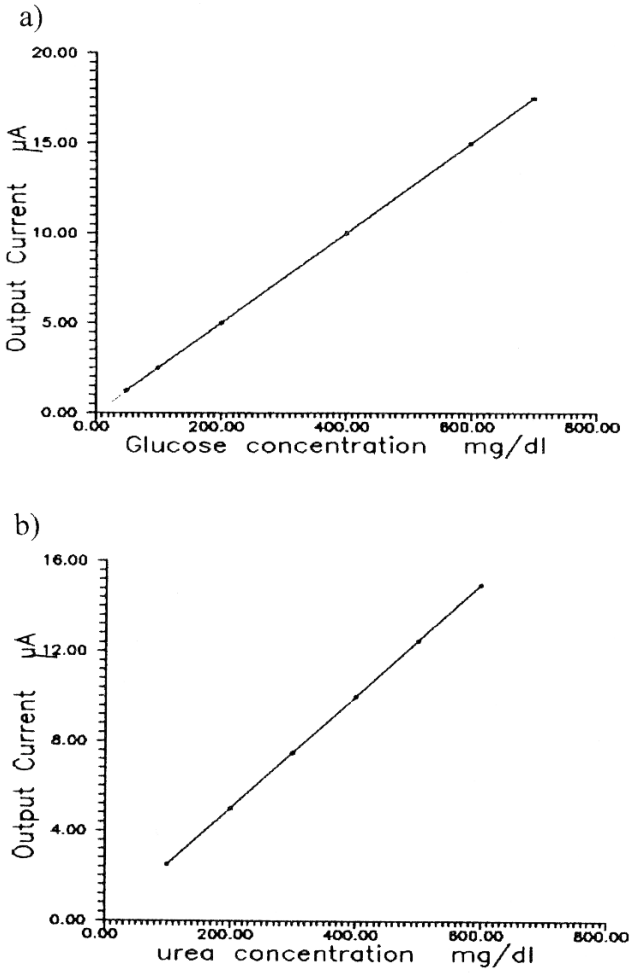

FIG. 4. Calibration plots for a- glucose sensor and b-urea sensor

From, the above plots it can concluded that the relationship between the output signal of glucose sensor and glucose concentration is linear. The same result can be concluded in case of urea sensor. Therefore, only two calibration points

are required. The sensitivity of the amperometric glucose sensor is 0.0292 μA/ mg/dl while the sensitivity of the urea sensor is 0.0237 μA/mg/dl.

4.2. Analog Part

The analog part of the designed instrument includes: current-to-voltage converter, amplifier, filter and A/D converter.

The analog switch is used to select one sensor (glucose or urea sensor) at a time. This switch is controlled by microprocessor. Then, the output signal (current) of each sensor is converted into voltage using op-amp-based I/V converter. Next, the output signal of I/V converter is entered to bioelectric amplifier. The designed amplifier must have high voltage gain (A_v), high input resistance (R_{in}) and high common mode rejection (CMRR) ratio[24]. These parameters can be fulfilled using the instrumentation amplifier shown in Fig. 5. The main parameters of this amplifier are: A_v = 100, CMRR= 110 and R_{in}= 33 MΩ).

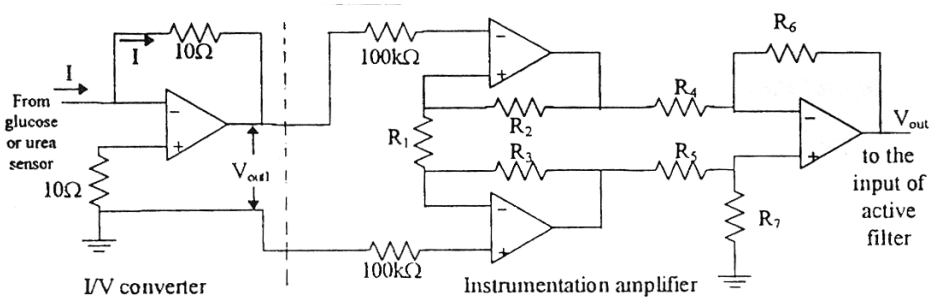

FIG. 5. Circuit diagram of I/V converter and instrumentation amplifier

The above circuit can be described mathematically by the following relationships:

$$V_{out1} = 10\ I \tag{3}$$

where I is the current from glucose or urea sensor

$$V_{out} = A_v\ V_{out1} \tag{4}$$

Of course, in the above amplifier the following condition is fulfilled $R_2 = R_3$, $R_4 = R_5$ and $R_6 = R_7$. Thus, the voltage gain can be expressed by:

$$A_v = \left(1 + \frac{2R_2}{R_1}\right)\left(\frac{R_6}{R_4}\right) \tag{5}$$

For Av =100, the following values of resistors were selected:

R2 = R3 = 1KΩ, R1 =220Ω, R4 = R5 = 1KΩ and R6 = R7 = 10 KΩ. The frequency response of this amplifier is experimentally found to be 0 Hz to 100 KHz.

Then, the output signal of the instrumentation amplifier is applied to a band stop type active filter[24]. The cutoff frequency of this filter is 50 Hz. Thus, the main aim of this filter is to eliminate the interference from the electrical main. The minimum attenuation in the stop-band of this filter is 70 dB while the maximum attenuation of the wanted signal in the pass band is 0.1 dB.

The output signal of the filter is digitized using a 12-bit A/D converter (ICL 7109)[25]. The full scale range of this A/D converter is 2 V. Its resolution is equal to 0.488 mV, while the dynamic range is 72.2 dB. Moreover, the main feature of the selected A/D converter (ICL 7109) is that it consists of a three state output buffer which makes it suitable for direct interfacing of its output with the data bus of microprocessor. Of course, the used microcontroller 80C51 has 8-bit data bus, while the selected A/D converter is 12-bit. The binary data from A/D converter, least significant byte LB(bits 1 to 8) and most significant byte MB (bits 9 to 12) are sent to the microcontroller data bus under the control signals LBEN (least significant byte enable) and HBEN (most significant byte enable). The control signal LBEN and HBEN are sent from the microprocessor.

4.3. Digital Part

The digital part is composed of microcontroller 80C51, 4KB program memory EPROM (2732), address latch (74HCT573), and a liquid crystal display. The selected microcontroller poses an 80 bytes RAM. Its main advantage is that it performs a signal pin operation. The EPROM contains the program in a form of assembly code that controls the operation of the instrument.

4.4 Instrument Operation

The designed glucose analyzer is operated as follows. The actual glucose and urea concentration measurement in the investigated blood sample are made using glucose and urea sensors by pressing manually the keys for glucose and urea measurements. Electronically, this is done by the microcontroller control of the logic levels at pins 6 and 7 of port 1. (p1.6 & p1.7). The pin operation is one of the most important and useful advantages of the selected microcontroller (80C51). When the key of urea measurement is pressed, then a logic level 0 appears at p1.6. Therefore, the microcontroller sends logic level 0 at p1.5 (pin five of port 1), to the analog switch to select the urea sensor to perform urea concentration measurement. But, if the key of glucose measurement is pressed, then a logic level 0 appears at p1.7. Next, the microcontroller sends logic level 1 at p1.5 to the analog switch to select the glucose sensor to perform glucose concentration measurement. If both keys are pressed, then the instrument performs the measurement of urea and glucose concentrations, respectively. Of course, the glucose concentration measurement will not appear at the display until the urea concentration measurement is performed. Then, the output signal of each

sensor is converted into voltage using the I/V converter and then amplified using the instrumentation amplifier. After this, the signal is entered to the active filter and then digitized using a 12-bit successive-approximation A/D converter. The binary data of A/D converter is stored in the internal RAM of the applied microcontroller. Then a correction is made for the glucose concentration according to equation 2, to eliminate the influences caused by urea concentration in the blood sample. After this the glucose and urea concentrations are displayed via liquid crystal display. Of course, the glucose concentration measurement will not appear at the display until the urea concentration measurement is performed. The microcontroller serves many tasks that greatly simplify the use of this instrument. It controls the operation of all parts of the instrument, performs a mathematical processing for the obtained signals from urea and glucose sensors, stores the data in its internal RAM and controls the data transmission between this analyzer, and personal computer.

4.5. Testing the Instrument

The designed instrument is experimentally tested by performing measurements of glucose for different heparin diluted blood samples with different glucose concentrations prepared in vitro using this instrument and the YSI analyzer simultaneously.

The in vitro change of glucose concentration is done in the laboratory by adding glucose to the diluted blood keeping the urea concentration at fixed level (10 mg/dl). The glucose concentration is changed from the range 80 mg/dl to 700 mg/dl. This range covers the physiological 80-120 mg/dl) and pathological (121-700) ranges of blood glucose concentration. For each change, the blood glucose concentration is measured by designed instrument and YSI analyzer.

Then the urea concentration is set to a new level (50 mg/dl) and the previous measurements of glucose concentration is repeated. The previous procedure is repeated for five additional different urea concentration settings (100 mg/dl, 200 mg/dl , 300 mg/dl, 400 mg/dl and 500 mg/dl) that cover the physiological and pathological ranges of blood urea. The obtained results are shown in Table 1. From these results, it can be concluded that the maximum error is less than 2% which is few times less than the permissible error for glucose measurements. For a comparative study, the previous procedure of measuring glucose concentrations in heparin diluted blood for different settings of urea concentration are repeated. The actual measured glucose concentration is displayed without elimination of the cross-sensitivity using eqn.2. the obtained results led to result that the maximum error is about 12% for urea concentration less than 100 mg/dl and about 8% for urea concentration bigger than 100 mg/dl.

Of course, before the measurements of glucose concentration in the diluted blood sample, the glucose and urea sensors are calibrated. These sensors have linear calibration curves. Thus, two calibration points were required. The calibration is performed by measuring the output currents of both urea and glucose sensors for two diluted blood samples. In these samples, the urea and glucose concentrations are precisely known. In the first sample, the urea concentration is 10 mg/dl while the glucose concentration is 50 mg/dl. In the second blood sample, the urea concentration is 600 mg/dl and the glucose concentration is 700 mg/dl. Measuring the output signals at urea and glucose sensors and knowing the concentrations of the urea and glucose in the two diluted blood samples, the actual sensitivity of these sensors can be determined. This actual sensitivity is then taken into account by the program stored in the EPROM. After this, the sensors are connected to the designed instrument and it will be ready for glucose and urea measurements. Of course, it is important to note that the designed instrument is denoted to be used for in vitro measurements of blood glucose and urea concentrations. Thus, if the instrument will be used for in vivo measurements of glucose, then new calibration factors or actual sensitivity for glucose and urea sensors must be determined experimentally in a similar procedure as in case of previous in vitro applications of the sensors.

TABLE 1. The obtained results of blood glucose concentration measurements for different settings of urea concentration.

Blood glucose concentration measured by YSI analyzer [mg/dl]	Blood glucose concentration [mg/dl] measured by designed instrument for different urea settings Curea [mg/dl] using eqn.						
	C_{urea} = 20 mg/dl	C_{urea} = 50 mg/dl	C_{urea} = 100 mg/dl	C_{urea} = 200 mg/dl	C_{urea} = 300 mg/dl	C_{urea} = 400 mg/dl	C_{urea} = 500 mg/dl
50	50.2	50.3	50.5	50.6	50.8	50.9	50.9
100	100.6	100.9	101.2	101.4	101.5	101.6	101.7
200	201.0	201.3	201.7	202.0	202.2	202.3	202.4
300	301.0	301.6	302.1	302.3	302.6	302.7	302.7
400	401.6	402.1	402.5	402.8	403.0	403.1	403.1
500	501.9	502.5	502.9	503.2	503.5	503.6	503.7
600	602.1	602.8	602.4	602.7	602.9	603.0	603.1
700	702.4	703.2	703.8	703.4	703.9	704.1	704.2

5. Conclusion

From the experimental results illustrated in Table 1, it can be concluded that the used procedure for elimination of cross-sensitivity which is based on the ap-

plication of eqn. 2 is very effective and clearly improves the selectivity of the amperometric enzyme glucose sensor.

As a result of cross-sensitivity elimination, the obtained results of glucose measurements by the designed instrument and the YSI analyzer for different settings of urea concentrations are strongly correlated. Moreover, if the equation 2 is not used to eliminate the cross-sensitivity of the amperometric enzyme sensor, then a significant error will occur. This error depends on the urea concentration. At low blood urea concentration (less than 100 mg/dl) the changes of urea concentration are strongly influenced by the output of glucose sensor. However, at concentrations bigger than 100 mg/dl, the current of glucose sensor inhibited relatively small changes with increasing of urea concentration.

The results of blood glucose concentration measurements obtained by the designed instrument that takes into account the solutions of biocompatibility and cross-sensitivity have a percentage error less than 2%, which satisfies the clinical requirements. Practically, this means that the electronic implementation of the biocompatibility and cross-sensitivity solutions ensures their effectiveness for improvement of the amperometric enzyme glucose sensors parameters.

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تحسين التوافقية الطبية والتقليل من الحساسية تجاه المؤثرات الخارجية لمجسات الجلوكوز

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المستخلص . يناقش هذا البحث مشاكل مجسات الجلوكوز والمستعملة لقياس نسبة تركيز الجلوكوز في الدم وهذه المشاكل هي : حساسية المجس إلى تركيز اليوريا (urea) في الدم والتوافقية الطبية . والتخلص من هذه المشاكل يحسن نوعية المجس وبالتالي يسمح بقياس دقيق لنسبة الجلوكوز في الدم بما يحقق المعايير الطبية . وللتخلص من هذه المشاكل تم إجراء تجارب عمليه للتوصل إلى علاقة تمثل رياضيا تأثير تركيز اليوريا في الدم على الإشارة الخارجة من مجس الجلوكوز ، وبعد استخراج هذه العلاقة الرياضية تم تصميم جهاز لقياس الجلوكوز في الدم استخدمت فيه هذه العلاقات الرياضية على شكل برنامج مخزن في ذاكرة الجهاز ، وبعد فحص الجهاز ومقارنة نتائجه بنتائج الأجهزة المعيارية لقياس الجلوكوز في الدم تبين أن دقة هذا الجهاز تحقق المعايير الطبية مما يدل على فعالية العلاقة الرياضية المستخرجة للتخلص من تأثير تركيز اليوريا في الدم على مجس الجلوكوز .