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Wireless Tear Glucose Sensor

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Abstract

This paper presents a novel wireless tear glucose level sensor for diabetes patients. The miniaturized sensor can be worn non-invasively under the eye lid. It is composed of a chronoamperometric glucose sensor and an ASIC set with integrated potentiostat and transponder circuits. Wireless energy and data transmission according to the passive transponder standard ISO18000-3 is used to power and readout the sensor. A special coil shape enables high comfort for the patient. High integration level is achieved by a combination of antenna and sensor electrode wires. A complete demonstrator system including ASIC and sensor fabrication as well as assembly was manufactured and the function is demonstrated.

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Keywords: Diabetes, Glucose Sensor, Amperiometry, Electrodes, Glucose Oxidase, Wireless, Transponder

1. Introduction

Diabetes is a widespread disease with approximately 285 million cases worldwide as of 2013 [1]. The patients have to determine not only blood glucose levels at set points during the day but they should also be alerted to the onset of sudden changes in the levels of glucose. Today, the majority diabetics control glucose levels by needle pricks and subsequent blood glucose strip testing. It is widely accepted but is painful and does not enable continuous monitoring. For the reasons mentioned researchers are looking for an alternative solution like minimally invasive sensors placed through the skin [2]. However these methods have additional drawbacks such as infection and gradual loss of sensitivity. A promising approach is to take advantage of the effect that the glucose level in tear fluid correlates well with the blood glucose level [3][4]. In this paper we describe a novel wireless glucose sensor for monitoring of glucose levels in the basal tear fluid present in the eye.

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2. Sensor Principle

The reports of [5] with that of [6] and [3] indicated that tears are not all equal in concentration of glucose and therefore a method to directly measure “normal” or basal tear production is essential. Based on this a method to measure base tear production directly under the bottom eyelid have been developed. In order to develop a device that not only fits into the lower eye lid but also has the capacity to conform to the surface of the eye and to eliminate the requirement to have any wires in or out of the lower eyelid a coil shaped device was chosen. A coil represents a device of high flexibility perpendicular to the short axis that is able to adapt to the shape of an eye whilst presenting an ideal device to act as an antenna for wireless data and power (figure 1b). To be able to measure glucose levels amperometrically, two or three electrodes are coiled in parallel to form an amperometric cell while a forth wire is used to facilitate wireless data and power transfer. Figure 1a illustrates the concept of the wireless glucose sensor that can be worn under the eye lid.

Fig 1: (a) Application; (b) Flexible coil shaped electrodes

The sensor uses a well-established and robust enzymatic detection of glucose (figure 2a). The enzyme glucose oxidase is a homodimeric glycoprotein, with a flavin adenine dinucleotide (FAD) cofactor. FAD plays an important role in the oxidation of glucose to gluconolactone, and in the course of the reaction, FAD is reduced to $FADH_2$. The $FADH_2$ is subsequently oxidized back to FAD by molecular oxygen, producing H_2O_2. The H_2O_2 produced is detected on a working electrode using chronoamperometrical measurement (figure 2b). This is a technique, where the current is measured as a function of time, directly after the introduction of a change in potential.

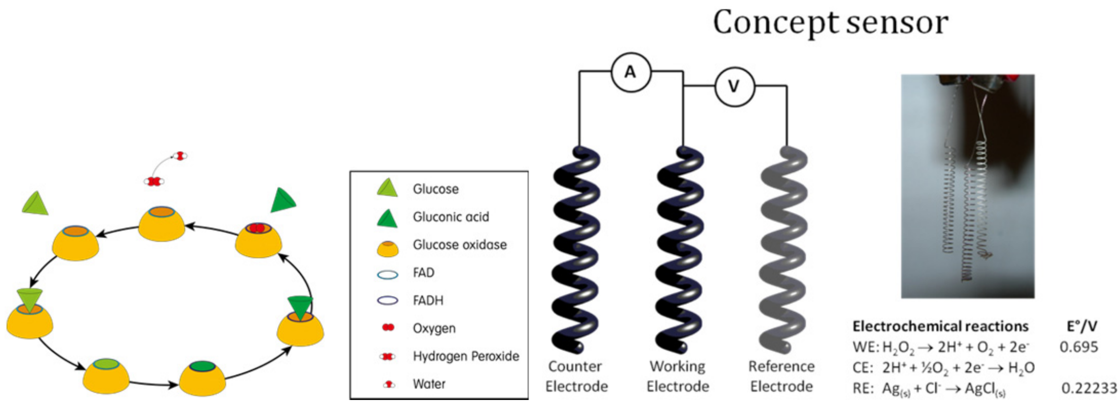

Fig 2. (a) Glucose Oxidase; (b) Amperoemtric measurement.

A passive transponder system is well suited for level monitoring where quasi continuous measurements with sample times in the order of a few minutes to a few hours are sufficient. Therefore a passive transponder coupled to an amperometric glucose sensor was developed. This makes a wireless readout of the glucose sensor placed under the eye lid possible. Thus the battery-free operation enables miniaturization and allows the sensor to be placed unobtrusively under the lower eyelid.

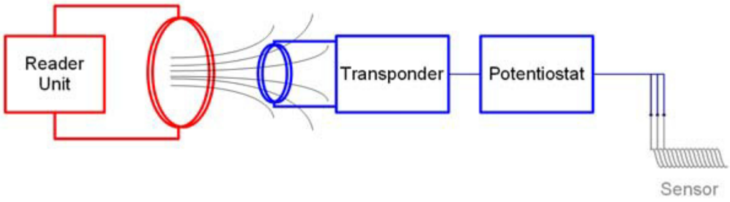

Fig 3: Transponder System

Fig 33 illustrates the glucose level monitoring system. It consists of the reader unit and the sensor unit. The reader unit generates a magnetic field in order to provide the sensor unit with energy. It receives and processes the measurement data captured by the sensor unit. Further it has a user interface to display the measurement result. The sensor unit is composed of a transponder and a potentiostat circuit. The potentiostat circuit performs an amperometric measurement with the help of the sensor by applying a constant voltage to the electrodes and measuring and digitalizing the current. The task of the transponder is to generate a stable supply voltage for the potentiostat and handle the communication between the reader unit and the potentiostat circuit.

3. Realization

An ASIC-Set (figure 4a) is developed that includes the potentiostat and the transponder circuit. The potentiostat performs the chronoamperometric measurement. An operational amplifier to generate a controlled potential as well as a trans-impedance amplifier with an ADC to gather and digitalize the electrode current are integrated on chip. The transponder circuit adds the wireless energy and data transmission capability to the device. The passive 13.56 MHz RFID standard (ISO 18000-3) is used. For this purpose it has a rectifier connected to the antenna coil. Between the transponder and the potentiostat there is a digital SPI interface. Hence the transponder system acts as a bridge between the reader and the potentiostat. With the help of the SPI interface the potentiostat can be controlled and digitalized sensor currents can be read out.

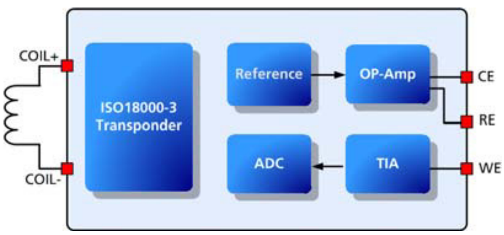

Fig. 4. (a) Readout ASIC-Set; (b) Assembled Sensor Unit Prototype (length approximately 15 mm)

The ASICs, fabricated in 350 nm CMOS technology and the helix are assembled in a first prototype shown in figure 4b. It has a length of approx. 15 mm. The ASICs are bonded on a flexible PE film using flip chip technique. The helix wires are connected to the PI film using conductive adhesive. An encapsulation protects the ASICs against liquids.

4. Practical Verification

To analyze the performance and linearity of the glucose sensor a measurement with reference devices is done. Thereby a dummy cell composed of a resistor network with known impedances is used. Figure 5a shows the resulting ADC counter values over the calculated currents in the dummy cell. A good linearity can be seen in the target measurement range.

To demonstrate the working system, six sample tubes are prepared. In each a buffer solution with different glucose concentrations from 0.1 mMol to 1 mMol are filled in. The glucose sensor was dipped into each sample tube and a measurement was performed. The WE electrode current measured by the potentiostat is plotted in figure 5b.

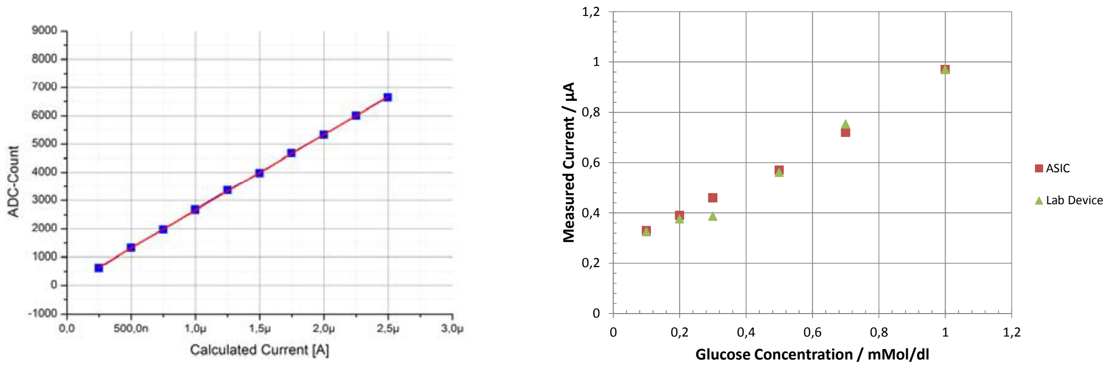

Fig. 5: (a) Potentiostat Linearity (b) Measurement with Sensor

For reference purposes a commercial lab potentiostat (from Autolab) was used to verify the measured currents. Each point of the figure represents a WE electrode current sampled 15 seconds after applying the potential to the CE electrode. As can be seen, the sensor unit provides acceptable results.

5. Conclusion

In this paper a novel tear glucose monitoring system was presented. It consists of a sensor unit composed of glucose sensor, potentiostat circuit and ISO 18000-3 transponder interface. A novel design of integrated antenna and electrode wires that enables high degree of miniaturization was presented. It was shown how such a device can be wirelessly powered despite the challenging boundary conditions. A complete demonstrator system was manufactured including ASIC fabrication. Finally the functionally laboratory environment was demonstrated.

The results were promising. After a re-design phase the system will be tested under clinically relevant conditions.

References

[1] Dixon JB; Zimmet P; Alberti KG; Rubino F; Bariatric surgery: an IDF statement for obese Type 2 diabetes; International Diabetes Federation Taskforce on Epidemiology and Prevention

[2] Sandeep Kumar Vashist; Continuous Glucose Monitoring Systems: A Review; Diagnostics 2013, 3, 385-412; doi:10.3390/diagnostics3040385

[3] N. J. Van Haeringen, Survey of Ophthalmology 1981, 26, 84-96; b) J. D. Lane, D. M. Krumholz, R. A. Sack and C. Morris, Current Eye Research 2006, 31, 895-901.

[4] Chu M et al 2011 Biomedical soft contact-lens sensor for in situ ocular biomonitoring of tear contents Biomed. Microdevices

[5] Tear Glucose Analysis for the Noninvasive Detection and Monitoring of Diabetes Mellitus, J. T. Baca, D. N. Finegold, S. A. Asher, The Ocular Surface, 2007, 5, 280-293.

[6] Dealing with the Delay, W. F. March, Diabetes Technology and Therapeutics, 2002, 4, 49-50.