Data Processing and Analysis of Glucose Concentration According to the Immittance Meter

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Abstract: This article proposes a method for measuring glucose concentration as a possible promising way to create a non-invasive glucometer. The dependence of the complex resistance of a solution of sodium chloride with different concentrations of glucose is investigated. In fist the glucose concentrations were calculated in saline to carry out these measurements. Further we prepared solutions (test samples) with a content of 3, 5, and 10 mmol per liter. We also created a board layout for measurements, that allowed us to vary solutions with different glucose concentrations. Using an immittance meter, we measured the complex resistance as a function of frequency in the range from 25 Hz to 1 MHz. At a medium frequency, we observed a resonance. We also found that at a frequency of 2 kHz there is a clear dependence of the complex resistance on the increase in glucose in solution. The obtained measurement data is of great interest for non-contact monitoring of glucose concentration in biological fluids.

1 INTRODUCTION

Monitoring glucose levels is an important indicator of normal human activities, especially for people with diabetes. The incidence of diabetes is increasing every year. Diabetes mellitus is a chronic disease in which blood sugar levels are elevated. This happens as a result of the fact that the pancreas either does not produce insulin, or the synthesized insulin cannot work effectively. The number of people with diabetes over the past 35 years has increased 4 times. Now more than 400 million people in the world have diabetes, and the prevalence of the disease continues to grow [1-5]. The World Health Organization estimates that diabetes will be the seventh leading cause of death by 2030. Possible methods of treatment include regulation of blood glucose levels by dietary methods, oral medication or insulin administration, all presented methods have an adverse effect on daily life [6-10].

Currently, it is recommended for patients with diabetes to regularly check their blood glucose with a glucometer. This practice can help closely monitor your blood glucose. In this way, patients with diabetes and their doctors can get a clear picture of blood glucose levels to optimize therapy. This is an indicator for adjusting the dose of insulin among patients with diabetes who need daily injections of insulin.

Typically, all blood glucose meters are invasive and require a finger puncture to take a blood sample. However, finger pricking to determine blood glucose levels for diabetics who check their blood sugar daily several times a day is difficult [11-14]. Puncture of a finger causes pain and subsequently leads to tissue damage. It also increases the risk of infection.

2 SUGGESTED MEASUREMENT METHOD

It is proposed to investigate the dependence of the complex resistance of a sodium chloride solution with different glucose concentrations.

2.1 Method for Calculating Concentrations in Solution

Molar concentration is the amount of solute (number of moles) per unit volume of solution. The molar concentration in the SI system is measured in mol / m^3, but in practice it is much more often expressed in mol / l or mmol / l. The test solution consists of saline (NaCl 0.9%) and glucose solution (C6H12O6 40%).

The level of glucose in the blood drops to 3.5 mmol per liter with hypoglycemia. This concentration of glucose in the blood leads to various disorders in the body. Normal blood glucose levels are on average between 3.5 and 5.5 mmol per liter. The level of glucose in the blood increases from 6.5 or more with hyperglycemia, it's negatively affects the body. We selected solutions according to all 3 states based on these data. You may notice that these data are too generalized. However, we believe that these extremes are enough for the first tests. At the first stage, it is important to understand the applicability of this approach - to understand sensitivity.

Solution calculation steps:

1) Calculate the molar mass of glucose. The chemical formula for glucose is C6H12O6. Molar mass of carbon - C = 12.011 Da. The molar mass of hydrogen is H = 1.008 Da. Molar mass of oxygen - O = 15.999 Da. Molar mass C6H12O6 = C * 6 + H * 12 + O * 6 = 72.066 + 12.096 + 95.994 = 180.156 Da. (weight 1 mol in grams).
2) 1 milliliter of glucose solution contains 0.4 grams of glucose therefore 0.00222 moles of C6H12O6.
3) Based on this, to obtain a solution with a content of 3 mmol per liter of C6H12O6, it is necessary to add 1.36 ml of a solution of 40% glucose in a 200 ml capacity with saline solution.
4) For a solution with a content of 5 mmol per liter of C6H12O6, it is necessary to add 2.25 ml of a solution of 40% glucose in a 200 ml capacity with saline.
5) For a solution with a content of 10 mmol per liter of C6H12O6, it is necessary to add 4.5 ml of a solution of 40% glucose in a 200 ml capacity with saline.

2.2 Preparing solutions (test samples)

Test samples were made on basis of the concentration calculation method presented above. For to appropriate concentrations (test samples) we mixed solution of 0.9% sodium chloride and 40% solution of glucose in the necessary proportions (Figure 1).

Figure 1: NaCl solution 0.9% and glucose solution 40%.

The procedure for the manufacture of solutions:

1) Removed the aluminium plug from the tank with NaCl solution.
2) Disconnect the top of the ampoule with 40% glucose solution.
3) Using a sterile syringe, the required amount of a 40% glucose solution was set for each sample and added to a container with a solution of 0.9% sodium chloride.
4) The contents of the sample containers were mixed and signed for measurements.

2.3 Making Layout for Measurements

The layout was created for measurements. The measuring model is a printed circuit board with a fixed latex tube on it. The prepared solutions of different glucose concentrations were supplied through this nylon tube. There are 4 contacts located at the same distance from each other on the printed circuit (Figure 2).

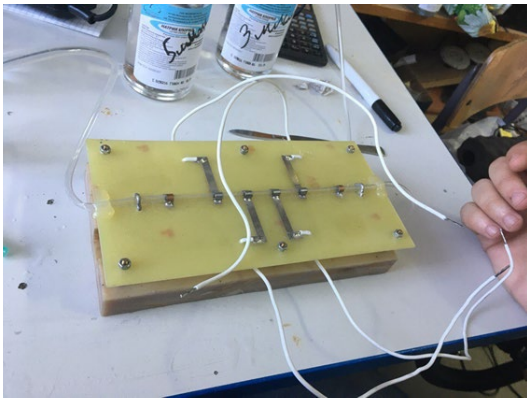

Figure 2: Measurement Layout.

The procedure for making the layout for measurements:

1) Production of printed circuit board in the copper sulfate.

2) The nylon tube was taken from a medical dropper.
3) The cylindrical contacts are soldered to the PCB.
4) 4 wires are soldered to the board for ease of use.

3 CARRYING OUT THE EXPERIMENT

The immittance meter E7-20 was used for measurements. E7-20 Immittance Meter (RLC) is a precision instrument of accuracy class 0.1, with a wide range of operating frequencies of 25 Hz - 1 MHz and a high measurement speed (up to 25 measurements per second) [5].

We researched the complex resistance module using the Immittance meter E7-20. The measurement layout and the E7-20 immittance meter were connected using a connecting device (CD) (Figure 3).

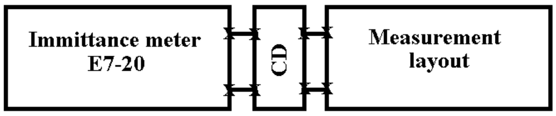

Figure 3: Scheme of the measurements.

To start work, it is necessary to carry out zero correction in open circuit mode and then in short circuit mode. Connected to the COM port of a personal computer and launched the program for measurements. We connected our model for measurements to the connecting device CD. Further we placed a test sample (solutions) in the model for measurements.

The measurements were carried out as follows. In the program, the frequencies for measurements were selected: 25, 50, 60, 100, 120, 200, 500, 1000, 5000, 10000, 20,000, 50,000, 100,000, 200,000, 500,000, 1,000,000 Hz. We used all frequencies at which E7 - 20 can measure to find the dependence of the complex resistance at frequencies on the glucose content in the samples.

At each frequency, measurements were performed 100 times for each sample. This number of measurements were made to establish the true average value. Since we know that the standard error of the mean is estimated as the sample standard deviation divided by the square root of the sample size:

$$\sigma_{\bar{x}} = \frac{s}{\sqrt{n}},$$

where s - corrected sample standard deviation:

$$s = \sqrt{\frac{1}{n-1}\sum_{i=1}^{n}(x_i - \bar{x})^2},$$

and n - size of the sample. It follows that the more measurements are taken, the easier it will be to identify the true average value:

$$\bar{x} = \frac{1}{n}\sum_{i=1}^{n} x_i .$$

After taking measurements, we started processing and analysing the measurement results.

4 RESULTS AND DISCUSSIONS

For data processing, we used the Microsoft Excel program, as it meets our requirements and is easy to use. As an example of the processed data, we took 3 frequencies: 25 Hz, 2 kHz and 50 kHz, that is, at low medium and high frequencies. We plotted probability density function for all data on the measurement frequencies (Figure 4).

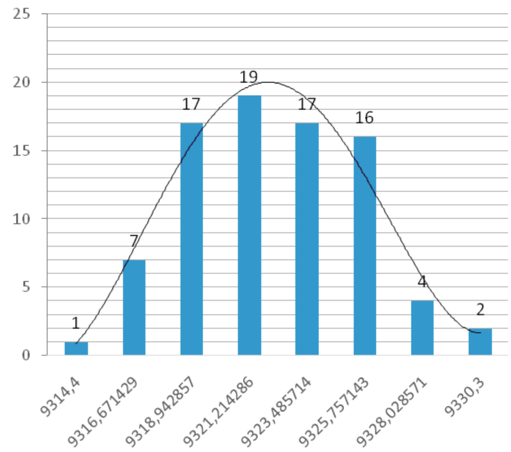

Figure 4: Histogram and density function for solution without glucose.

Density function was a normal distribution for all dataset. The normal distribution was parametrized in terms of the mean and the variance:

$$f(x;\bar{x},\sigma) = \frac{1}{\sqrt{2\pi\sigma^2}} e^{-\frac{(x-\bar{x})^2}{2\sigma^2}} .$$

At a frequency of 25 Hz, histograms of the distribution of the complex resistance module were obtained. From the results it was found that at a frequency of 25 Hz in a solution without glucose there is a high reading of the complex resistance modulus and a slight change when measuring solutions with glucose.

We examined the behaviour of the complex resistance module at a frequency of 2 kHz. The results showed that at a frequency of 2 kHz, with an increase in glucose concentration, the complex resistance modulus increases.

At a frequency of 50 kHz, the distribution of the complex resistance module was also obtained. From the results it became clear that at a frequency of 50 kHz, the complex resistance modulus does not explicitly depend on the frequency.

It can be seen in our measurements that the scatter of values is present, but this will not affect the average value of the repetition rate. To establish the law of distribution and a more accurate true value in the future, we will conduct more measurements.

To visualize the values of the readings of the complex resistance modulus at all frequencies, we plotted the dependence of the average value of the samples on the measurement frequency (Figure 5).

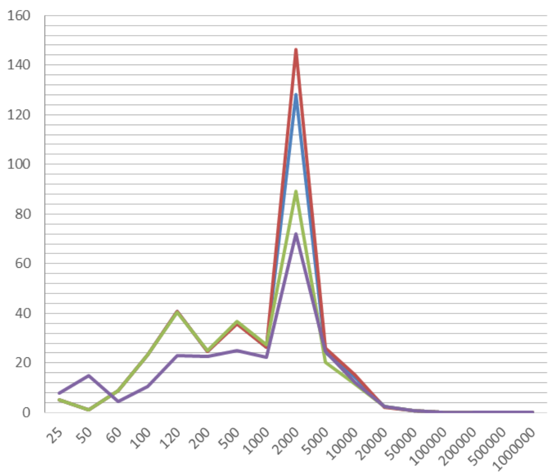

Figure 5: The graph of the true average module of complex resistance Z (vertical, MOhm) on measurement frequency (horizontal, Hz): lilac line - 0 mmol / liter; green line - 3 mmol / liter; blue line - 5 mmol / liter; the red line is 10 mmol / liter.

This graph shows that at a frequency of 2000 Hz we observe an unexplained resonance. This resonance will subsequently be investigated by us. It is also seen that at low frequencies we have a large scatter of values and the influence of glucose concentration on the frequency dependence of the complex resistance modulus is not observed, but at high scatter of values it is insignificant.

5 CONCLUSIONS

In this paper, we have shown the relevance of a non-invasive glucometer in the daily activities of a person with diabetes and the need to create it. We presented a method for measuring the level of glucose in the blood. We developed a model for measurements and made measurements and their processing.

The measurement results showed that the creation of such a glucometer can be implemented in practice. It can be seen from the above measurement results that it is not advisable to measure the complex resistance modulus Z at low and high frequencies. There are observe resonance at the middle frequency. Also, at a frequency of 2 kHz, the dependence of the complex resistance modulus Z on the increase in glucose concentration in the solution is observed.

In the future, it is planned to study the results in more detail. It is necessary to increase the number of measurements in order to reveal a clear dependence of the measured parameters on glucose. In addition, accuracy is important in such measurements (measurement error should not exceed 10-15 percent). Therefore, it is necessary to study the errors that can affect the measurement results, the influence of skin layers and other physiological data of a person. However, we believe that the results obtained now are important and have the prospect of further development.

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REFERENCES

[1] The official website of the World Health Organization media center. [Online]. Available: http://www.who.int/mediacentre/factsheets/fs312/en/ Date of access: 09.10.2018.

[2] Official site MedicineNet, Definition of a puncture of a finger. [Online]. Available: http://www.medi-cinenet.com/script/main/art.asp?articlekey=39540 Date of access: 09/10/2018.

[3] S. Gozani, “Nerve damage in diabetes”, Bulletin of the Harvard Institute of Neurology. D. Mahoney, The Brain Magazine, no. 5, 1996, pp. 44-56.

[4] Diabetes mellitus standards for diabetes care, diabetes treatment, 39 supplement. 1, 2016, pp. 4-42.

[5] V.M. Lozovsky, A.G. Varakomsky and V.V. Bahur “Immitance meter E7-20”, Operation manual, OJSC "MNIPI", 2006, pp.4-13.

[6] World Health Organization (WHO). Diabetes. [Online]. Available: http://www.who.int/news-room/fact-sheets/detail/diabetes (accessed on 3 October 2018).

[7] Healthline. “The Effects of Low Blood Sugar on Your Body”. [Online]. Available: https://www.healthline.com/health/low-blood-sugar-effects-on-body#6 (accessed on 2 October 2018).

[8] L.C. Clark and C. Lyons, “Electrode systems for continuous monitoring in cardiovascular surgery”. Ann. N. Y. Acad. Sci., no 102, 1962, pp. 29-45.

[9] C.-F. So; K.-S. Choi; T.K.S. Wong and J.W.Y. “Chung, Recent advances in noninvasive glucose monitoring”. Med. Dev. (Auckl.), no 5, 2012, pp. 45-52.

[10] Y. Uwadaira and A. Ikehata, “Noninvasive Blood Glucose Measurement”. In Nutritional and Therapeutic Interventions for Diabetes and Metabolic Syndrome, 2nd ed.; Bagchi, D., Nair, S., Eds.; Academic Press: San Diego, CA, USA, 2018; pp. 489-504.

[11] N.H. Cho, J.E. Shaw, S. Karuranga, Y. Huang, J.D. da Rocha Fernandes, A.W. Ohlrogge and B. Malanda, “IDF Diabetes Atlas: Global estimates of diabetes prevalence for 2017 and projections for 2045”. Diabetes Res. Clin. Pract. no. 138, 2018, pp. 271- 281.

[12] J. Lin, T.J. Thompson, Y.J. Cheng, X. Zhuo, P. Zhang, E. Gregg and D.B. Rolka, “Projection of the future diabetes burden in the United States through 2060”. Popul. Health Metr., no. 16, 2018, pp. 1-9.

[13] A. Tura, S. Sbrignadello, D. Cianciavicchia, G. Pacini and P. Ravazzani, “A Low Frequency Electromagnetic Sensor for Indirect Measurement of Glucose Concentration: In Vitro Experiments in Different Conductive Solutions”. Sensors, no. 10, 2010, pp. 5346-5358.

[14] C. Chen, X.-L. Zhao, Z.-H. Li, Z.-G. Zhu, S.-H. Qian and A.J. Flewitt, “Current and Emerging Technology for Continuous Glucose Monitoring”. Sensors, no. 17, 2017, p. 182.

[15] T. Lin, A. Gal, Y. Mayzel, K. Horman and K. Bahartan, “Non-invasive Glucose Monitoring: A Review of Challenges and Recent Advances”, Curr. Trends Biomed. Eng. Biosci, no. 6, 2017, pp. 1-8.

[16] B.J. Van Enter, E. von Hauff, “Challenges and perspectives in continuous glucose monitoring”. Chem. Commun, no. 54, 2018, pp. 5032-5045.

[17] O.S. Khalil, “Spectroscopic and Clinical Aspects of Noninvasive Glucose Measurements”. Clin. Chem. no. 45, 1999, p. 165.