

Approach of a Mathematical Model for a Non-Invasive Glucometer

Luis Enrique Colmenares-Guillén*

Benemérita Universidad Autónoma de Puebla,
Facultad de Ciencias de la Computación, Puebla,
Mexico

enrique.colmenares@correo.buap.mx

Abstract. There are around 422 million adults with diabetes and 3.7 million worldwide deaths that are related to hyperglycemia. The objective of this research work is obtaining a mathematical model that can integrate into a non-invasive device for glucose measurement. In this study, the glucose measurement technique is exposed using a Galvanic Skin Response (GSR) sensor that is used for a non-invasive method. This research involves an experimental quantitative methodology of glucose samples. When comparing with the invasive method, a polynomial linear model with second-degree adjustment was obtained which provides an improvement in the percentage of error. Furthermore, glucose measurement with the GSR sensor coupled with the linear model proved favorable for integration into the prototype. In the future, the model will be incorporated into the prototype to guarantee the effectiveness of the glucose measurement by a non-invasive method with electrodermal activity and a machine learning algorithm will be developed to prevent high glucose levels with food and exercise preferences.

Keywords. Diabetes, electrodermal, galvanic, non-invasive.

1 Introduction

According to the World Health Organization, diabetes is defined as a serious chronic disease that occurs when the pancreas does not produce enough insulin (a hormone that regulates blood glucose) or when the body cannot effectively use insulin, which is produced by the pancreas [24].

In the Encuesta Nacional de Salud y Nutrición (ENSANUT) in the year 2020, there was a

prevalence of 10.6 percent of people with diagnosed diabetes in Mexico, according to information from the Ministry of Health [36], a trend that shows a progressive increase, thus placing the country, within the list of the 10 countries with the highest number of people living with this disease [32]; the world panorama also shows alarming facts, according to the latest data presented by the OMS, there are about 422 million adults with Diabetes, where approximately 3.7 million deaths are directly related to hyperglycemia [25], which is an effect of uncontrolled diabetes, and that the measurement of blood glucose concentration (monitoring) is a global health priority and one of the seven self-care behaviors, for people with diabetes [28], established by the American Association of Diabetes Educators (AADE).

In 2019, IDF (International Diabetes Federation) reported 12.8 million diabetics in Mexico and estimated that by 2045 the number would reach 22.9 million, occupying in both years the sixth place worldwide, after China, India, United States, Pakistan, and Brazil [13] and in 2021 IDF, reported 14.1 million diabetics in Mexico and estimated that by 2045 the number will reach 21.2 million, occupying seventh and eighth place respectively after the six countries mentioned above, with the addition of Indonesia and Bangladesh [14], as reported by the Center for Research in Food and Development (CIAD).

According to INEGI data (July 2021), the three main reasons for death nationwide last year were: heart disease, 218,885 (20.2 percent); COVID-19, 201,163 (18.5 percent); and diabetes mellitus (DM), 151,214 (13.9 percent) [10]. In 2018, 9 percent of the 20-year-old population in the state of Puebla had diabetes and 15.4 percent suffered

from hypertension, while 8.5 percent between 12 and 19 years of age presented obesity. In absolute numbers, patients with diabetes in that age group, totaled 362 thousand 927 in the entity, according to the Encuesta Nacional de Salud y Nutrición (Ensanut) 2018, elaborated by the Instituto Nacional de estadística y Geografía (Inegi).

In comparison with the other states of the Mexican republic, the mortality rate in the state of Puebla is in fourth place, both for females and males only below Coahuila, Tabasco, and Guanajuato for males [29]. The third place nationally with the highest number of hospitalizations due to diabetes is the position currently occupied by the state of Puebla in 2020.

Only in the first nine months of the year, 674 hospitalizations were recorded for this disease, ranking only below Tabasco (1,460) and Jalisco (905), this according to the report of the Hospital Epidemiological Surveillance System for Diabetes Mellitus Type 2 [17].

The research work is organized as follows: in section II, mathematical models, general considerations of diabetes and electronic elements that have been used for the development of the prototype. In section III, there are the results that were tested, the glucose concentration and the measurement of the GSR sensor.

In section IV, a comparison of the GSR sensor and other non-invasive techniques was made to understand the significance of the proposal and finally in section V, the conclusions, and challenges to improve this proposal.

2 Mathematic Models

There are a variety of mathematical models, statistical methods and computer algorithms in the literature that determine the physiology of diabetes [11], for example, in this research, testing insulin infusion algorithms and decision support systems and assessing glucose sensor performance, as well as the dynamics of glucose and insulin [6], based on differential equations are utilized to analyze the glucose-insulin regulatory system.

As there is an increasing emphasis on disorders of tissue sensitivity to insulin metabolism in pathologies such as diabetes, obesity, and cardiovascular disease, quantification

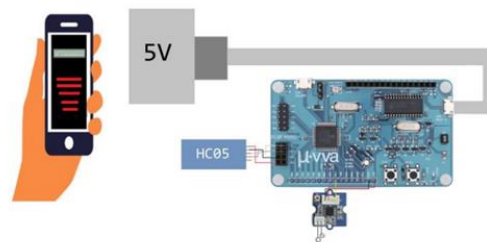


Fig. 1. Prototype of a non-invasive glucometer using GSR sensor

of insulin sensitivity from noninvasive tests has become more important in physiological research [40].

Among the various physiological models proposed, the following two are the most important:

- Minimal model: Composed of two parts, the first describes the time evolution of plasma glucose concentration, i.e., kinetics and the second describes the pancreatic insulin release in plasma, reflected in concentration as a function of time [4].
- Ackerman Model: In the 1960s Ackerman and his team developed the linear model as a method for the identification of diabetes [1].

However, the search for a model to represent glucose and insulin metabolism is complex, due to the number of parameters that must be considered. A simple model has proven to be sufficient to perform a good analysis, as demonstrated by the models in the research work [8]. The objective of the present research work was to obtain a simple linear polynomial model that can be integrated in a non-invasive device for the development of a technological prototype.

2.1 General Considerations of Diabetes and Electronic Elements

In this section, the following are considered: the definition and behavior of diabetes mellitus or non-insulin-dependent diabetes, the metabolic cycle of blood glucose regulation, and the GSR sensor including galvanic current, electrodermal activity, and operating characteristics in the circuit.

2.1.1 Diabetes Mellitus (DM) Type II or Non-Insulin Dependent Diabetes Mellitus (NIDDM)

Type II diabetes represents more than 90 percent of patients with DM [7]. Physiologically, patients with DM II, develop resistance to the insulin that the pancreas produces, which raises plasma glucose, again stimulating insulin secretion, until the β -cell reserve is exceeded, generating a constant cycle of elevated glucose values and frequent high insulin values.

In this situation, the plasma insulin concentration is almost always high rather than low. By the high blood glucose concentration over time, it severely damages nerves and blood vessels, as well as pancreatic islets, liver, musculoskeletal tissue, and other organs [37].

2.1.2 Metabolic Cycle of Blood Glucose Regulation

Glucose ($C_6H_{12}O_6$) is an indispensable energy molecule in the human organism. When ingested, it can have three main destinations: to be used immediately, to be stored as glycogen in the liver or to be converted into fat. It is a primary fuel for all body tissues, so its homeostatic control is of great importance, it involves a series of hormones and a specific gland: the pancreas (with α and β cells) that acts in conjunction with the pituitary gland and the liver.

The pancreas is responsible for the digestion of fats, proteins, and long-chain carbohydrates by means of its exocrine function (enzyme production) and through its endocrine function regulates the blood glucose level by producing two hormones: insulin (hypoglycemic secreted by the β cells) and glucagon (hyperglycemic secreted by the α cells) [38].

Regarding the IDF Diabetes Atlas, it mentions that Glycogen is a form of glucose used to store energy in the liver and muscles. If blood glucose levels decrease, the hormone glucagon causes the body to convert glycogen into glucose and release it into the bloodstream [14].

There are also several other factors that can stimulate the autonomic nervous system via the adrenal medulla, thereby releasing adrenaline or noradrenaline, which also raise the blood glucose concentration.

Table 1. Glucose values

Glucose (mmol/L)	Glucose (mg/dL)
2	36.036 036
2.2	39.639 639 6
2.5	45.045 045
2.8	50.450 450 5
3	54.054 054 1
3.1	55.855 855 9
3.4	61.261 261 3
3.5	63.063 063 1
3.6	64.864 864 9
3.9	70.270 270 3
4	72.072 072 1
4.2	75.675 675 7
4.5	81.081 081 1
4.8	86.486 486 5
5	90.090 090 1
5.3	95.495 495 5
5.5	99.099 099 1
5.6	100.900 901
6	108.108108
6.2	111.711 712
6.5	117.117 117
6.7	120.720 721
6.9	124.324 324
7	126.126 126
7.2	129.729 73
7.5	135.135 135
7.8	140.540 541
8	144.144 144
8.4	151.351 351
8.5	153.153 153
8.9	160.360 36
9	162.162 162
9.5	171.171 171
10	180.180 18
10.1	181.981 982
10.5	189.189 189
10.6	190.990 991
11	198.198 198
11.2	201.801 802
11.5	207.207 207
12	216.216 216
12.3	221.621 622
12.5	225.225 225
13	234.234 234
13.4	241.441 441
13.5	243.243 243
14	252.252 252
14.5	261.261 261
14.6	263.063 063
15	270.270 27

15.5	279.279 279
15.7	282.882 883
13	234.234 234
13.4	241.441 441
13.5	243.243 243
14	252.252 252
14.5	261.261 261
14.6	263.063 063
15	270.270 27
15.5	279.279 279
15.7	282.882 883
16	288.288 288
16.8	302.702 703
17	306.306 306
17.9	322.522 523
18	324.324 324
19	342.342 342
20	360.360 36
20.2	363.963 964
21	378.378 378
21.3	383.783 784
22	396.396 396
22.4	403.603 604
23	414.414 414
23.5	423.423 423
24	432.432 432
24.6	443.243 243
25	450.450 45
25.8	464.864 865
26.8	482.882 883
28	504.504 505
30	540.540 541
33.6	605.405 405
35	630.630 631
40	720.720 721
44.8	807.207 207
50	900.900 901
56	1 009.009 01

According to the National Glycohemoglobin Standardization Program (NGSP) and the International Federation of Clinical Chemistry (IFCC), normal glucose levels (normoglycemia) in a person fasting for 8 h range from 70 mg/dL to 109 mg/dL or from 3.9 mmol/L to 6.1 mmol/L.

These values will vary under conditions such as food intake, exercise, emotions, among others. These results will vary under different conditions such as food intake, exercise, emotions, among others, and values greater than or equal to 200 mg/dL or 11.1 mmol/L are diagnostic of NIDDM (hyperglycemia) [15].

There are other indicators of the amount of glucose in the blood, such as the glycosylated hemoglobin test (HbA1c), which gives results as a percentage. If the percentage is higher, the blood glucose level will also be higher. Normal values for a healthy person are below 5.7 percent according to the American Diabetes Association [2].

The most common measurement units used in the basic techniques of primary health care for blood glucose measurement are in terms of molarity (mmol/L) and in lesser use, although of equal importance in other parts of the world such as in the United States of America, the mass concentration (mg/dL) is used.

For performing the unit conversion, is presented below in equation (1), which is established in the specification sheet provided by the provider SPINREACT [35], of the reactive, and in addition, is used for the characterization of glucose concentration by resistance reading resulting from the Galvanic Skin Response sensor (GSR brand Grove, product version grove-sensor_GSR V1.0 from Shenzhen, China), which establishes that:

$$\text{mmol/L} = \text{mg/dL} * 0.0555. \quad (1)$$

2.1.3 Galvanic Skin Response (GSR) Sensor

Galvanic current

In medical applications galvanic current is used whose characteristics are continuous, uninterrupted, low voltage (60 V to 80 V) and equally low constant intensity (200 mA maximum).

The generation of galvanic current requires two terminations or poles: positive and negative; being direct continuous current, does not present pulses, nor waveform which produces two types of effects: polar (produced under the electrodes) and interpolar (produced inside the organism in the organic segment located between the two poles) [33].

Electrodermal activity

The skin presents an electrodermal activity (also called galvanic skin response) product of the variation of the resistance in her, which is produced by the change that the sweat glands produce, by secreting sweat increases the permeability of the membranes of the skin cells and this facilitates the

exchange of ions and therefore, improving the conductivity [34, 3].

GSR sensor

Such electrical activity can be monitored through a GSR sensor that, according to its specifications, allows measuring the electrical conductance of the skin. The model used "Grove-GSR Sensor V1.0" [16], has an operating voltage of 3.3 V to 5 V, with a sensitivity adjustable by means of a potentiometer (model 3009P-1-502LF, Bourns brand, mounting type, in Łódź, Poland), the input signal is resistance and the output signal can be voltage or an analog signal, which allows the result obtained to be processed and interpreted [9].

Circuit proposal

The first prototype is part of a bachelor's thesis research work [18]. The second prototype was made on a circuit board. At this stage, the final size of the circuit was established. Which was 5.1 cm long and 3.9 cm wide; so, the first step to prepare the board was to cut it following these measures.

The integrated components were an independent PIC18f2550 (previously programmed), with an 8MHz crystal oscillator, a pair of 22 pF ceramic capacitors, a Bluetooth module HC05 (pairing key 6969) and male pins for the connection of the GSR sensor.

Once, the tests to the GSR sensor were performed with the use of the microcontroller PIC18f4550 [21] integrated in the Miuva development board [22], and the Bluetooth communication module HC05 [5], has the following circuit proposal, shown in Figure 1.

3 Results and Discussion

3.1 Relationship Between GSR Sensor Results and Glucose Concentration

The most useful feature in this case is that, under the search for accurate alternatives that represent less stress [3], and/or risks for the patient compared to invasive methods for glucose monitoring [23], the GSR sensor through the measurement of electrodermal activity obtains a resistance response that can be related to a blood glucose concentration, allowing a non-invasive monitoring with its implementation.

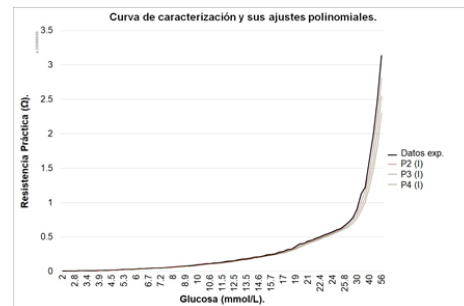


Fig. 2. The characteristic curve of the resistance result for each glucose value

Table 2. Values obtained from the characterization for GSR sensor

Glucose (mmol/L)	Resistance (Ω)	Conductance (G)
2	40 000	0.000 025 000 000
2.2	48 400	0.000 020 661 157
2.5	62 500	0.000 016 000 000
2.8	78 400	0.000 012 755 102
3	90 000	0.000 011 111 111
3.1	96 100	0.000 010 405 827
3.4	115 600	0.000 008 650 519
3.5	122 500	0.000 008 163 265
3.6	129 600	0.000 007 716 049
3.9	152 100	0.000 006 574 622
4	160 000	0.000 006 250 000
4.2	176 400	0.000 005 668 934
4.5	202 500	0.000 004 938 272
4.8	230 400	0.000 004 340 278
5	250 000	0.000 004 000 000
5.3	280 900	0.000 003 559 986
5.5	302 500	0.000 003 305 785
5.6	313 600	0.000 003 188 776
6	360 000	0.000 002 777 778
6.2	384 400	0.000 002 601 457
6.5	422 500	0.000 002 366 864
6.7	448 900	0.000 002 227 668
6.9	476 100	0.000 002 100 399
7	490 000	0.000 002 040 816
7.2	518 400	0.000 001 929 012
7.5	562 500	0.000 001 777 778
7.8	608 400	0.000 001 643 655
8	640 000	0.000 001 562 500
8.4	705 600	0.000 001 417 234
8.5	722 500	0.000 001 384 083
8.9	792 100	0.000 001 262 467
9	810 000	0.000 001 234 568
9.5	902 500	0.000 001 108 033
10	1 000 000	0.000 001 000 000
10.1	1 020 100	0.000 000 980 296
10.5	1 102 500	0.000 000 907 029
10.6	1 123 600	0.000 000 889 996
11	1 210 000	0.000 000 826 446
11.2	1 254 400	0.000 000 797 194
11.5	1 322 500	0.000 000 756 144

12	1 440 000	0.000 000 694 444
12.3	1 512 900	0.000 000 660 982
12.5	1 562 500	0.000 000 640 000
13	1 690 000	0.000 000 591 716
13.4	1 795 600	0.000 000 556 917
13.5	1 822 500	0.000 000 548 697
14	1 960 000	0.000 000 510 204
14.5	2 102 500	0.000 000 475 624
14.6	2 131 600	0.000 000 469 131
15	2 250 000	0.000 000 444 444
15.5	2 402 500	0.000 000 416 233
15.7	2 464 900	0.000 000 405 696
16	2 560 000	0.000 000 390 625
16.8	2 822 400	0.000 000 354 308
17	2 890 000	0.000 000 346 021
17.9	3 204 100	0.000 000 312 100
18	3 240 000	0.000 000 308 642
19	3 610 000	0.000 000 277 008
20	4 000 000	0.000 000 250 000
20.2	4 080 400	0.000 000 245 074
21	4 410 000	0.000 000 226 757
21.3	4 536 900	0.000 000 220 415
22	4 840 000	0.000 000 206 612
22.4	5 017 600	0.000 000 199 298
23	5 290 000	0.000 000 189 036
23.5	5 522 500	0.000 000 181 077
24	5 760 000	0.000 000 173 611
24.6	6 051 600	0.000 000 165 246
25	6 250 000	0.000 000 160 000
25.8	6 656 400	0.000 000 150 231
26.8	7 182 400	0.000 000 139 229
28	7 840 000	0.000 000 127 551
30	9 000 000	0.000 000 111 111
33.6	11 289 600	0.000 000 088 577
35	12 250 000	0.000 000 081 633
40	16 000 000	0.000 000 062 500
44.8	20 070 400	0.000 000 049 825
50	25 000 000	0.000 000 040 000
56	31 360 000	0.000 000 031 888

This is because the stimulation of the autonomic nervous system in sympathetic division, in addition to regulating sweating, is closely related to blood glucose concentration, since this also regulates the adrenal glands, so that skin resistance variations based on this physiological mechanism can provide consistent information related to blood glucose concentration, which allows a clinical-mathematical correlation to be established.

3.2 Proposed Model

On Table 1, shows the equivalences between the glucose values in mmol/L and mg/dL of the values used for the characterization curve.

Figure 2 shows the characteristic curve of the relationship between the known blood glucose concentration in mmol/L units and the resistance measurement in Ohms units obtained with the GSR sensor. In the same Figure 2, the linear models with polynomial adjustment are represented: second degree polynomial represented by P2 (I), third degree polynomial P3 (I) and finally the fourth degree polynomial P4 (I).

Table 2 shows the values obtained from the characterization of the GSR sensor, with the values obtained from the curve, the shaded part highlights the ranges established as normal (3.9 mmol/L to 5.5 mmol/L) and the ranges that may be indicative of NIDDM (>11.2 mmol/L).

In the data was found that, to a value of glucose corresponds a single value of resistance and therefore of conductance. And conductance is the inverse of resistance and is measured in *siemens* concept used in Figure 3, which shows the relationship between known blood glucose concentration and the corresponding value of conductance.

After several tests with different functions, to make a proposal for the model, particularities were obtained, for example: measurements in the ranges established as normal, for plasma glucose concentration in blood in humans, show a linear behavior, and the same phenomenon occurs for the glucose data ranges whose diagnosis is an indicator of NIDDM.

On the other hand, the dispersion of data of the characteristic curve suggested linear behavior, which is why it was decided to perform a linear model with polynomial adjustment, which was programmed in MATLAB®, A polynomial adjustment of 2°, 3° and 4° was considered to compare them with each other, and to choose the closest to accuracy through the analysis of the correlation value, also obtained with the MATLAB program:

$$f(x) = 10000 * x^2 - 9.3132e^{-10*x} + 7.4506e^{-9}. \quad (2)$$

As shown in Table 3, the model with the best correlation coefficient is the one with degree two, therefore, will be the model to be used as a proposal. In equation 2, the value of Pearson's correlation coefficient resulting from the proposed model is significantly close to 1, which the

mathematical model reaches its objective, which is also reinforced with the minimum percentage error presented in Table 4, the average percentage error is 2.4137338270, obtained with the polynomial fit model degree 2 and the percentage error between them.

4 Discussions

Today, there is a need for the development of non-invasive medical devices that allow monitoring blood glucose concentration in an accessible, affordable, and efficient way. Throughout the search, innovation, and development of medical devices capable of providing glucose values that primarily allow adequate monitoring for the control of diabetes and at the same time are as minimally invasive as possible. With respect to devices, is required to have an end-user friendly experience both in terms of use and cost.

4.1 Comparison of the Use of the GSR Sensor and Other Sensors for Non-Invasive Glucose Measurement

A number of measurement techniques have been studied that are intended to be scaled to medical equipment and two types are highlighted: first, minimally invasive techniques that are also related to sensors such as microdialysis, subcutaneous implantable sensor, iontophoresis and sonophoresis that are based on the measurement of the concentration of glucose in the interstitial fluid (ISF) result that has been shown to be equivalent to the concentration of glucose in blood at steady state [27].

Second, non-invasive techniques, which are related to the types of sensors that exist, optical: Raman spectroscopy, polarimetry, optical coherence tomography [19], photoacoustic spectroscopy, impedance spectroscopy, mid-infrared spectroscopy, near-infrared spectroscopy [31], the electrical type using electromagnetism [30] and electrodermal as the GSR sensor.

There are also thermal and nanotechnology sensors [10], which are non-invasive techniques that are expensive due to the use of materials and laboratory tests that must be used for these devices.

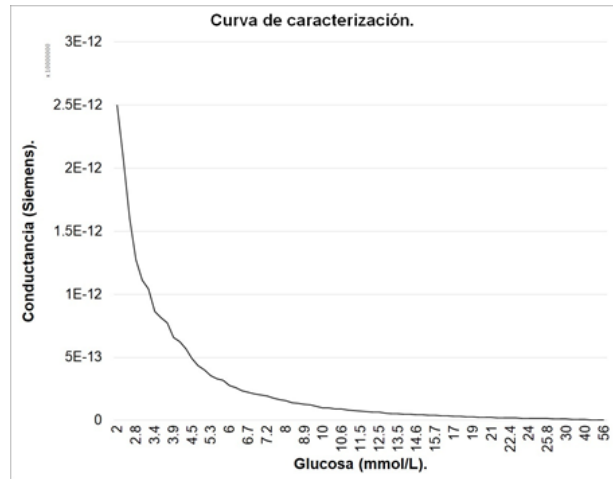


Fig. 3. The characteristic curve of the conductance result for each glucose value obtained

Table 3. Correlation values obtained for each polynomial degree

Polynomial	Correlation
Grade 2	0.999 999 999 999 999 999 999 999 999 999 997 54
Grade 3	0.999 999 999 999 999 999 999 999 999 999 999 112 95
Grade 4	0.999 999 999 999 999 999 999 999 999 999 751 909 03

Table 4. The practical resistance value and the comparison with the model resistance value

Practical Resistance (Ω)	Model Resistance (Ω)	Error percentage
40 000	4.000 E+04	2.299 E-06
48 400	4.840 E+04	1.900 E-06
62 500	6.250 E+04	1.471 E-06
78 400	7.840 E+04	1.173 E-06
90 000	9.000 E+04	1.022 E-06
96 100	9.610 E+04	9.568 E-07
115 600	1.156 E+05	7.954 E-07
122 500	1.225 E+05	7.506 E-07
129 600	1.296 E+05	7.095 E-07
152 100	1.521 E+05	6.045 E-07
160 000	1.600 E+05	5.747 E-07
176 400	1.764 E+05	5.212 E-07
202 500	2.025 E+05	4.541 E-07
230 400	2.304 E+05	3.991 E-07
250 000	2.500 E+05	3.678 E-07
280 900	2.809 E+05	3.273 E-07

302 500	3.025 E+05	3.040 E-07
313 600	3.136 E+05	2.932 E-07
360 000	3.600 E+05	2.554 E-07
384 400	3.844 E+05	2.392 E-07
422 500	4.225 E+05	2.176 E-07
448 900	4.489 E+05	2.048 E-07
476 100	4.761 E+05	1.931 E-07
490 000	4.900 E+05	1.876 E-07
518 400	5.184 E+05	1.774 E-07
562 500	5.625 E+05	1.635 E-07
608 400	6.084 E+05	1.511 E-07
640 000	6.400 E+05	1.437 E-07
705 600	7.056 E+05	1.303 E-07
722 500	7.225 E+05	1.273 E-07
792 100	7.921 E+05	1.161 E-07
810 000	8.100 E+05	1.135 E-07
902 500	9.025 E+05	1.019 E-07
1 000 000	1.000 E+06	9.195 E-08
1 020 100	1.020 E+06	9.014 E-08
1 102 500	1.102 E+06	8.340 E-08
1 123 600	1.124 E+06	8.183 E-08
1 210 000	1.210 E+06	7.599 E-08
1 254 400	1.254 E+06	7.330 E-08
1 322 500	1.322 E+06	6.953 E-08
1 440 000	1.440 E+06	6.385 E-08
1 512 900	1.513 E+06	6.078 E-08
1 562 500	1.562 E+06	5.885 E-08
1 690 000	1.690 E+06	5.441 E-08
1 795 600	1.796 E+06	5.121 E-08
1 822 500	1.822 E+06	5.045 E-08
1 960 000	1.960 E+06	4.691 E-08
2 102 500	2.102 E+06	4.373 E-08
2 131 600	2.132 E+06	4.314 E-08
2 250 000	2.250 E+06	4.087 E-08
2 402 500	2.402 E+06	3.827 E-08
2 464 900	2.465 E+06	3.730 E-08
2 560 000	2.560 E+06	3.592 E-08
2 822 400	2.822 E+06	3.258 E-08
2 890 000	2.890 E+06	3.182 E-08
3 204 100	3.204 E+06	2.870 E-08
3 240 000	3.240 E+06	2.838 E-08
3 610 000	3.610 E+06	2.547 E-08
4 000 000	4.000 E+06	2.299 E-08
4 080 400	4.080 E+06	2.253 E-08
4 410 000	4.410 E+06	2.085 E-08
4 536 900	4.537 E+06	2.027 E-08
4 840 000	4.840 E+06	1.900 E-08
5 017 600	5.018 E+06	1.833 E-08
5 290 000	5.290 E+06	1.738 E-08
5 522 500	5.522 E+06	1.665 E-08
5 760 000	5.760 E+06	1.596 E-08
6 051 600	6.052 E+06	1.519 E-08
6 250 000	6.250 E+06	1.471 E-08
6 656 400	6.656 E+06	1.381 E-08
7 182 400	7.182 E+06	1.280 E-08
7 840 000	7.840 E+06	1.173 E-08
9 000 000	9.000 E+06	1.022 E-08
11 289 600	1.129 E+07	8.144 E-09
12 250 000	1.225 E+07	7.506 E-09
16 000 000	1.600 E+07	5.747 E-09
20 070 400	2.007 E+07	4.581 E-09
25 000 000	2.500 E+07	3.678 E-09
31 360 000	3.136 E+07	2.932 E-09

Considering the analysis of the physiology in blood glucose regulation, the pathophysiology of NIDDM and the physical operation principle of fun, the relationship between electrodermal activity or galvanic response of the skin and blood glucose concentration was argued.

After the analysis, the characteristic curve of the relationship between GSR sensor results in terms of resistance and glucose concentration, a linear behavior was found in the most important parameters for NIDDM control (normoglycemia and hyperglycemia), the same phenomenon found in the data dispersion.

Based on the potential for these developments and after a bibliographic research, accuracy, versatility, adaptability, costs, and a series of factors to be considered for the construction of a medical device were analyzed in these scientific articles.

Two non-invasive glucose measurement sensors (a widely used optical type such as near infrared spectroscopy and electromagnetic) were selected for comparison with the galvanic skin response (GSR) sensor technique.

The process of calibration and validation of the GSR sensor was performed the patent title *Proceso de Medición de glucosa no Invasivo in México* (No. de Patent MX 361747 B) in which was decided why to use the GSR sensor and also in the bachelor thesis of Aldo Enrique Aguila. Table 5 shows a comparison analysis between the different techniques with sensors, which can be used as alternatives for noninvasive glucose measurement.

5 Conclusions

In conclusion, a linear model with polynomial adjustment was proposed in the work, where the second-degree polynomial presented a correlation of 0.999 999 999 999 999 999 999 999 999 999 999 999 999 997 54, being more accurate compared to the 3rd and 4th degree polynomial adjustments, with an average error percentage in the proposed model of 2.4137338270. The challenge of the second-degree polynomial with respect to the device proposed in the design will be the integration that determines the degree of error and the

Table 5. Comparative summary of noninvasive techniques for glucose measurement

Technique	Advantages	Challenges
Galvanic Response Skin	<ul style="list-style-type: none"> – Continuous monitoring by direct measurement on skin [34]. – Samples without pretreatment before analysis. – Relatively low construction costs. – Linear behavior in normoglycemia and hyperglycemia demonstrated in this paper. – Sensor compatible to development boards with A/D converter [9]. – Affordable and accessible development tools, multiplatform and flexible programming [9]. – Signal quality depends on sensor-skin contact [34] – Intuitive and user-friendly interface. 	<ul style="list-style-type: none"> – Variations between states: stable, under tension and physical exercise due to humidity changes [9]. – Studies around the GSR sensor only focused on the stress level [3]. – Requires characterizations with control groups, under different situations to refine the model.
Near-Infrared Spectroscopy	<ul style="list-style-type: none"> – The penetration depth of IR light into the skin impinges on interstitial fluids [31]. – Samples without pre-treatment before analysis [39]. – High variety of components on the market. – Well-known mathematical model (Lambert and Beer's law) [20]. – Repeatable results. – Numerous studies around the use of this technique [39]. – Linear response in hypoglycemia and hyperglycemia values [39]. 	<ul style="list-style-type: none"> – Interference from other fluids [26]. – Easy alteration of results due to: pressure, temperature and humidity [26]. – Errors in hyperglycemia ranges or due to changes in tissue components. – Limited coupling.
Electromagnetic Sensing	<ul style="list-style-type: none"> – Results proportional to concentration and type of analyte [30]. – Use of a single frequency for the analyte (minimizes interference) [30]. – The sensor is simple and inexpensive. 	<ul style="list-style-type: none"> – Easy alteration of results due to temperature [30]. – Few studies of the technique. – Non-ergonomic coupling.

identification of the valid data that associates the glucose level in each patient. This is a significant advance with respect to non-invasive devices because there is a first model that approximates a glucose measurement with the contribution of a GSR sensor.

After comparing the advantages and challenges between non-invasive techniques, glucose measurement using the GSR sensor was found to be favorable, detecting that there are still technological challenges to be solved, aimed at improving the proposal for the development of the prototype. For future work, a machine learning

algorithm will be developed to prevent high glucose levels with food and exercise preferences. Additionally, communication and monitoring of the patient database will be synchronized with glucose measurements with a real-time library (RTI - real time innovation).

Acknowledgments

This article is part of the project: Analysis and development of healthcare technology, automating the delivery of medical services, and monitoring

patient care, funded by the Vicerrectoría de Investigación y Estudios de Posgrado (VIEP) of the Benemérita Universidad Autónoma de Puebla. The research of the non-invasive glucometer is being developed in the Faculty of Computer Science, in which the research was done in collaboration with the Biomedical Engineer Maira Aideé Gutiérrez Vargas from the National Polytechnic Institute, having a professional stay and being an important part for the proposal of the model and creating this synergy of collaboration with universities in the country.

References

1. **Ackerman, E., Rosevear, J. W., McGuckin, W. F. (1964).** A mathematical model of the glucose-tolerance test. *Physics in Medicine and Biology*, Vol. 9, No. 2, pp. 203–213. DOI: 10.1088/0031-9155/9/2/307.
2. **ADA (2020).** ADA, American Diabetes Association Resumen de clasificación y diagnóstico de la diabetes. Wordpress.com. <https://sinapsismex.files.wordpress.com/2020/02/resumen-de-clasificac3b3n-y-diagn3b3stico-de-la-diabetes-american-diabetes-association-2020.pdf>.
3. **Bakker, J., Pechenizkiy, M., Sidorova, N. (2011).** What's your current stress level? Detection of stress patterns from GSR sensor data. *IEEE 11th International Conference on Data Mining Workshops*. pp. 573–580. DOI: 10.1109/ICDMW. 2011.178.
4. **Bergman, R. N. (2005).** Minimal model: perspective from 2005. *Hormone Research*, Vol. 64. pp. 8–15. DOI: 10.1159/000089312.
5. **Bluetooth (2017).** Módulo Bluetooth HC05. Naylamp Mechatronics-Perú. <https://naylampmechatronics.com/inalambrico/43-modulo-bluetooth-hc05.html>.
6. **Chalishajar, D., Geary, D. Cox, G. (2016).** Review study of detection of diabetes models through delay differential equations. *Applied Mathematics*, Vol. 7, pp. 1087–1102. DOI: 10.4236/am.2016. 710097.
7. **Chatterjee, S., Khunti, K., Davies, M. J. (2017).** Type 2 diabetes. *Lancet*, Vol. 389, No. 10085. pp. 2239–2251. DOI: 10.1016/s0140-6736(17)30058-2.
8. **Cisneros, I. A. (2014).** Modelos matemáticos para la diabetes. Universidad de Cantabria, <https://n9.cl/6pwfv>.
9. **Colmenares-Guillen, L. E., Ruiz, M. C., Niño, E. H. (2015).** Aplicación de cómputo móvil y pervasivo para el monitoreo no invasivo de la diabetes en tiempo real. *European Scientific Journal*, Vol. 11, No. 33. pp. 130–147.
10. **Coulman, S. A., Anstey, A., Gateley, C., Morrissey, A., McLoughlin, P., Allender, C., Birchall, J. C. (2009).** Microneedle mediated delivery of nanoparticles into human skin. *International Journal of Pharmaceutics*, Vol. 366, No. 1–2, pp. 190–200. DOI: 10.1016/j.ijpharm.2008.08.040.
11. **Dalla-Man, C., Raimondo, D. M., Rizza, R. A., Cobelli, C. (2007).** GIM, simulation software of meal glucose—insulin model. *Sage Journals*. Vol. 1, No. 3. DOI: 10.1177/193229680700100303.
12. **DGCS-UNAM (2021).** En aumento, los casos de diabetes en México. Unam.Mx.https://www.dgcs.unam.mx/boletin/bdboletin/2021_966.html.
13. **FID (2019).** Atlas de la diabetes de la FID (Federación Internacional de la Diabetes). *Diabetesatlas.org*. https://diabetesatlas.org/upload/resources/material/20200302_133352_2406-IDF-ATLAS-SPAN-BOOK.pdf.
14. **FID (2021).** IDF Diabetes Atlas. *Diabetesatlas.org*. https://diabetesatlas.org/idfawp/resource-files/2021/07/IDF_Atlas_10th_Edition_2021.pdf.
15. **Granada-Ybern, M. L., Martínez-de-Osaba, J. B. (2012).** Criterios actuales diagnósticos de diabetes mellitus y otras alteraciones del metabolismo hidrocarbonado. Educación Continuada en el Laboratorio Clínico.
16. **GSR (2014).** GSR, galvanic skin response sensor, grove biomedicine. *Seedstudio.com*. https://files.seedstudio.com/wiki/Grove-GSR_Sensor/res/Grove-GSR_Sensor_WiKi.pdf.
17. **Hernández, M. (2020).** Diabetes posiciona a Puebla en el tercer lugar nacional con más hospitalizaciones. *El Sol de Puebla, Noticias Locales, Policiacas, sobre México, Puebla y el*

- Mundo. <https://www.elsoldepuebla.com.mx/doble-via/salud/diabetes-posiciona-a-puebla-en-el-tercer-lugar-nacional-con-mas-hospitalizaciones-dia-mundial-de-la-diabetes-2020-issstep-inegi-complicaciones-de-la-diabetes-6015897.html>.
18. **Huerta, N. E. (2015).** Aplicación de cómputo móvil y pervasiva para el monitoreo de la diabetes en tiempo real. Benemérita Universidad Autónoma de Puebla. <https://repositorioinstitucional.buap.mx/handle/20.500.12371/9358>.
 19. **Lan, Y. T., Kuang, Y. P., Zhou, L. P., Wu, G. Y., Gu, P. C., Wei, H. J., Chen, K. (2017).** Noninvasive monitoring of blood glucose concentration in diabetic patients with optical coherence tomography. *Laser Physics Letters*, Vol. 14, No. 3, pp. 035603. DOI: 10.1088/1612-202x/aa58c0.
 20. **López-Toctaguano, V. L., Oñate-Amaguaña, W. P. (2014).** Diseño e implementación de un glucómetro no invasivo basado en la ley de Lambert Beer y longitud de onda cercana al infrarrojo (NIR), con interfaz de comunicación bluetooth a dispositivos con sistema operativo Android (Bachelor's thesis). Repositorio Institucional de la Universidad Politécnica Salesiana.
 21. **Microship (2009).** PIC18F2455/2550/4455/4550 data sheet 28/40/44-pin, high-performance, enhanced flash, USB microcontrollers with nanoWatt technology. Microchip.com. <https://ww1.microchip.com/downloads/aemDocuments/documents/OTH/ProductDocuments/DataSheets/39632e.pdf>.
 22. **Miuva (2021).** Tarjeta de desarrollo Miuva. INTESC. <https://intesc.mx/productos/tarjeta-de-desarrollo-miuva>.
 23. **Monsod, T. P., Flanagan, D. E., Rife, F., Saenz, R., Caprio, S., Sherwin, R. S., Tamborlane, W. V. (2002).** Do sensor glucose levels accurately predict plasma glucose concentrations during hypoglycemia and hyperinsulinemia? *Diabetes Care*, Vol. 25, No. 5, pp. 889–893. DOI: 10.2337/diacare.25.5.889.
 24. **OMS (2016).** Informe mundial sobre la diabetes. OMS, Organización Mundial de La Salud, <https://apps.who.int/iris/bitstream/handle/10665/254649/9789243565255-spa.pdf>.
 25. **OMS (2022).** Diabetes. OMS, Organización Mundial de La Salud, <https://www.who.int/news-room/fact-sheets/de-tail/diabetes>.
 26. **Páez-Roa, A. A., Villamizar-Mejía, R. (2012).** Medición no invasiva del nivel de glucosa en la sangre usando espectroscopia con infrarrojo cercano. *Estado del arte, Revista UIS Ingenierías*, Vol. 11, No. 1, pp. 21–33.
 27. **Páez, X., Mazzei-Dávila, C. A., Hernández, L. (2003).** Microdiálisis subcutánea: una técnica simple para monitorizar el ambiente bioquímico extracelular. Combinación con electroforesis capilar y detección mediante fluorescencia inducida por láser. *Investigación clínica*, Vol. 44, No. 3, pp. 227–239.
 28. **Pilar-Hevia, V. E. (2016).** Educación en diabetes. *Revista médica Clínica Las Condes*, Vol. 27, No. 2, pp. 271–276. DOI: 10.1016/j.rmclc.2016.04.016.
 29. **Ramírez-Sierra, D. V. (2019).** Frecuencia de diabetes tipo 2, complicaciones y factores asociados en pacientes mayores de 30 años de la consulta externa de medicina interna del Hospital Universitario de Puebla del 2017. Benemérita Universidad Autónoma de Puebla.
 30. **Robaina, R. R., González, J. L., Trujillo, H., Cruz, J. C. (2006).** Detección de cambios de glucosa en sangre por método electromagnético no invasivo.
 31. **Palomo, I. R., Romero, P. L. M. R., Hernández, D. N. (2016).** Mejora del diseño de un prototipo de sensor no invasivo para la medida de glucosa en sangre. *Escuela Técnica Superior de Ingeniería Universidad de Sevilla*.
 32. **Rojas, M. R., Basto-Abreu, A., Aguilar-Salinas, C. A., Zárate-Rojas, E., Villalpando, S., Barrientos-Gutiérrez, T. (2018).** Prevalencia de diabetes por diagnóstico médico previo en México. *Salud pública de México*, Vol. 60, No. 3, pp. 224–232. DOI: 10.21149/8566.
 33. **Sahoo, R., Sethi, S. (2015).** Functional analysis of mental stress based on physiological data of GSR sensor. Springer International Publishing, *Emerging ICT for*

- Bridging the Future-Proceedings of the 49th Annual Convention of the Computer Society of India (CSI), Advances in Intelligent Systems and Computing, Vol 337. DOI: 10.1007/978-3-319-13728-5_12.
- 34. Sharma, M., Kacker, S., Sharma, M. (2016).** A brief introduction and review on galvanic skin response. International Journal of Medical Research Professionals, Vol. 2, No. 6. DOI: 10.21276/ijmrp.2016.2.6.003.
- 35. Spinreact (2013).** Determinación cuantitativa de glucosa. Importadores exclusivos: Lab center de Mexico S.A. de C.V.
- 36. SS (2021).** Encuesta Nacional de Salud y Nutrición 2020 sobre Covid-19 Resultados Nacionales. SS, secretaria de Salud, <https://ensanut.insp.mx/encuestas/ensanutcontinua2020/doctos/informes/ensanutCovid19ResultadosNacionales.pdf>.
- 37. Torrades, S. (2006).** Diabetes mellitus tipo 2. Elsevier.es. <https://www.elsevier.es/es-revista-offarm-4-pdf-13088620>.
- 38. Velásquez, S., Velásquez, R., Leyton, M., Borjas, J., Custodio, A. (2013).** Modelado del control de la regulación de Glucosa. Universidad, ciencia y tecnología, Vol. 17, No. 66, pp. 11–18.
- 39. Villena, G. W., Mobashsher, A. T., Abbosh, A. (2019).** The progress of glucose monitoring- A review of invasive to minimally and non-invasive techniques, devices, and sensors. Sensors (Basel, Switzerland), Vol. 19, No. 4, p. 800. DOI: 10.3390/s19040800.
- 40. Zamarrón-Sobrinos, C. (2021).** Modelos matemáticos del sistema regulador glucosa-insulina en pacientes diabéticos con retraso de tiempo.

Article received on 14/04/2024; accepted on 15/06/2024.

*Corresponding author is Luis Enrique Colmenares-Guillén.