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Closed Loop System Design for Wireless Artificial Pancreas

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Abstract

Over the years diabetes has been a major cause of death due to its severe complications. Therefore, the artificial pancreas was introduced to help type 1 diabetic patients to automatically control their blood glucose level noninvasively by providing the substitute endocrine functionality of a healthy pancreas. The output voltage of the pulse oximeter was related to glucose using Microsoft Excel Regression Analysis Tool. The glucose level is then transmitted wirelessly through the radio frequency zigbee module. Afterwards, it was regulated according to the treat to range control algorithm within the sliding scale insulin protocol.

Although the artificial pancreas has managed to monitor blood glucose level and regulate it, its accuracy was found to be 89% compared to Accu-Chek glucometer. Not to mention its exceedingly inadequate size, time consumption and high expenses.

Keywords: Pancreas; Glucose; Insulin; Hypoglycemia; Hyperglycemia

Introduction

Diabetes from the Greek word meaning "a siphon‟ when the body is acting as a conduct for the excess fluid, and mellitus from the Greek and Latin for honey [1], which is a chronic disease that occurs when the pancreas is not producing enough insulin or when the body cannot effectively use the insulin it produces [2]. It is classified into four categories including: Type 1 which occurs when there is a Lack of insulin and requires insulin injections. While Type 2 occurs when there is insulin resistance (cells failure) and requires replacement. In addition, gestational diabetes occurs during pregnancy (might lead to type 2 diabetes). While pre-diabetes is when the glucose levels are higher than normal and lower than diabetic which eventually may lead to diabetes [3].

Type 1 diabetic patients must receive long acting basal insulin (Galrgine) before bedtime to take care of basal (steady-state) needs and rapid acting insulin (Lispro) before each main meal to compensate for meals or snacks. And the total daily dose (TDD) of the insulin must not exceed 0.5 units/kg, 40% of it is injected as long acting insulin while 60% is served as a rapid acting insulin divided into three meals a day (20% per meal) [4,5]. While Type 2 diabetes considered a milder form of diabetes because of its slow onset (pre-diabetes) and because it can be controlled with diet and medication [6].

The artificial pancreas (AP) is an externally worn medical device that mimics the endocrine function of the biological pancreas by monitoring blood glucose level (BGL). It infuses insulin and possibly glucagon according to an appropriate control law to regulate BGL to type 1 diabetic patient in a more automated fashion [7]. Offering mobility, reliability since it will automatically regulate and control glucose level by using digital communication techniques and advanced computer algorithms [8]. As well as avoiding hyperglycemia (raise in glucose levels) which over time contribute to complications development such as: nerve, kidney, eyes, muscle and foot damage, cardiovascular diseases and Alzheimer's [9,10], while hypoglycemia (drop in glucose levels) which can be distressing and can lead to coma or death [7].

Fundamental Theories

In the AP, the probe pulse oximeter's output voltage is detected non-invasively and glucose is calculated within the first processing unit (arduino UNO). Then glucose is transmitted wirelessly through zigbee module to the second processing unit, displaying it in a liquid crystal display (LCD) for user interface to gain patient's trust. According to the received glucose level and the treat to range control algorithm within the sliding scale insulin protocol the arduino UNO will inject insulin through an insulin pump composed of a DC motor (suction), insulin reservoir and infusion set during hyperglycemia, or do nothing if the glucose level is within the normal range. It will also notify the patient to eat something sweet in the case of hypoglycemia or get immediate help in the case of severe hyperglycemia by activating an alarm and locating the patient with a global positioning system (GPS) module **(Figure 1)**.

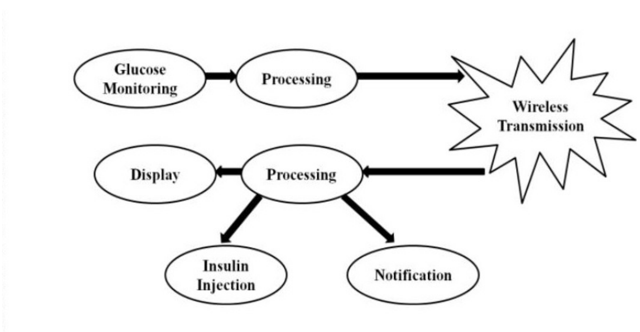


Figure 1 Artificial pancreas working principle.

Glucose calculations

Since the pulse oximeter probe is used as a non-invasive mean for monitoring glucose. Therefore, a relation between its analog to digital conversion (ADC) output voltage and glucose must be identified. The simplest way for understanding this relation is by deriving a mathematical equation that correlates both of them using regression [11]. As shown in the equation below:

Equation 1: Glucose-Voltage Relationship:

$$G = \varepsilon * S + \lambda * A + (\alpha * V) - \beta$$

Where:

S: Sex of the patient "male=0 or female=1".

A: Age of the Patient "years".

G: Glucose concentration in the blood "mg/dl".

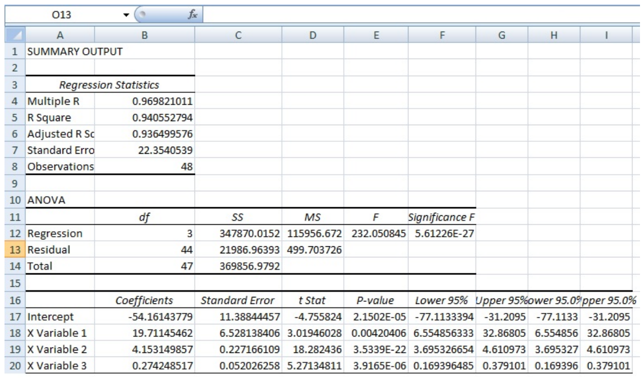
V: ADC output voltage "volt".

ε , λ, α and β are constants, where ε=19.71, =4.15, α=0.27 and β=54.16.

Equation 1 was done by monitoring glucose levels of random population using ACCU CHECK glucometer. By comparing its readings with pulse oximeter's output voltage the equation was identified using Microsoft Excel regression analysis tool. And the analysis output is summarized in **Figure 2**.

Control algorithm

As seen in **Table 1**, the arduino will react with every specific level of glucose, following a treat to range (TTR) control algorithm based on the sliding scale insulin protocol [12].



SUMMARY OUTPUT

Regression Statistics	
Multiple R	0.969821011
R Square	0.940552794
Adjusted R Sc	0.936499576
Standard Erro	22.3540539
Observations	48

ANOVA

	df	SS	MS	F	Significance F
Regression	3	347870.0152	115956.672	232.050845	5.61226E-27
Residual	44	21986.96393	499.703726		
Total	47	369856.9792			

	Coefficients	Standard Error	t Stat	P-value	Lower 95%	Upper 95%	ower 95.0%	pper 95.0%
Intercept	-54.16143779	11.38844457	-4.755824	2.1502E-05	-77.1133394	-31.2095	-77.1133	-31.2095
X Variable 1	19.71145462	6.528138406	3.01946028	0.00420406	6.554856333	32.86805	6.554856	32.86805
X Variable 2	4.153149857	0.227166109	18.282436	3.5339E-22	3.695326654	4.610973	3.695327	4.610973
X Variable 3	0.274248517	0.052026258	5.27134811	3.9165E-06	0.169396485	0.379101	0.169396	0.379101

Figure 2 The output summary of regression.

Table 1 Artificial pancreas control algorithm.

Blood Glucose Level, mg/dl	Insulin Endured, IU	Action Requested	
0-80	0	Alarm ON, GPS Activation	**Hypos**
81-100	0	No action	**Normal**
101-150	0	No action	**T2DM**
151-200	2	No action	
201-250	4	No action	
251-300	6	No action	**T1DM**
301-350	8	No action	
351-400	10	No action	
>401	12	Alarm ON, GPS Activation	**Hyper**

To convert IU (Insulin Unit) to mL divide by 100 to reduce 50 mg/dl [4].

Artificial pancreas construction

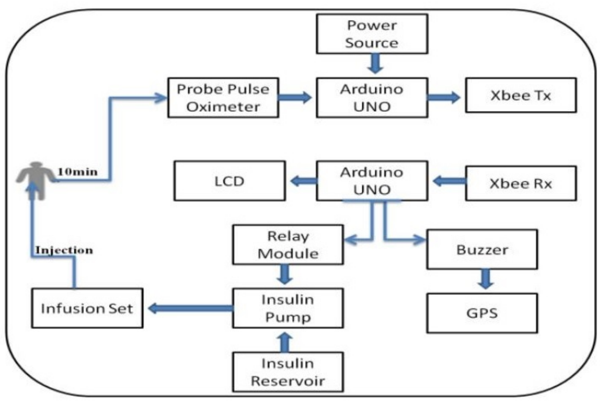


Figure 3 Methodology's block diagram.

The AP **(Figure 3)** consists of two separate parts connected wirelessly using radio frequency zigbee module. The first circuit consists of a non-invasive glucose sensor (probe pulse oximeter), arduino UNO for control and zigbee transmitter. While the second part of the AP consist of zigbee receiver, arduino UNO, GPS, buzzer, 1-channel relay module, DC motor, insulin reservoir and infusion set (IV drip) **(Figure 4)**.

Figure 4 Part one (Glucose monitoring).

The raw materials were collected and inspected, the Pulse Oximeter's Probe analog to digital conversion (ADC) signal was sent to the arduino through the analog pin A0, while the arduino was programmed to send the signal wirelessly *via* zigbee transmitter connected to its digital pins (2 and 3) **(Figure 5)**.

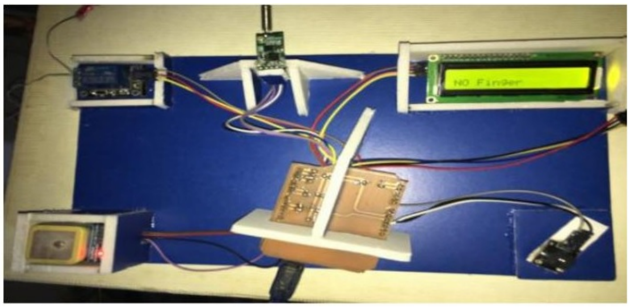


Figure 5 Part two (Glucose regulation).

The GPS was connected to digital pins 10 and 11 in the arduino, while the DC motor was derived by the 1-Channel Relay connected to pin 6 in the arduino to suction insulin from the insulin reservoir and deliver it to the patient through an infusion set inserted subcutaneously. In addition to that, LCD pins were connected with pin A4 and A5 (analog) in the arduino based on the standard connection. Noticing that, the arduino was powered *via* its USB interface.

Results and Discussion

Results were categorized into two scenarios: the first scenario (**Table 2**) was precisely used to reveal how the artificial pancreas will react to all possible BGLs. The arduino in the second part was adjusted to estimate random glucose levels every 30 seconds (50 mg/dl-420 mg/dl) and react to it by either injecting insulin, activating the alarm and GPS or resulting in absolutely nothing. According to the treat to range control algorithm mentioned in **Table 1** all the glucose ranges mentioned above will be displayed in the LCD. While in the second scenario shown in **Table 3** the probe pulse oximeter glucose level was compared to the readings of Accu-Chek glucometer for error calculations. As a result, the output of the second part will interact accordingly to the first scenario.

Table 2 First scenario.

Item no	AP's Readings "mg/dl"	LCD Message	Action Taken
1	50	Range 1	Buzer and GPS activation
2	90	Range 2	No Action
3	120	Range 3	No Action
4	160	Range 4	Insulin Injection (2 ml)
5	220	Range 5	Insulin Injection (4 ml)
6	260	Range 6	Insulin Injection (6 ml)
7	320	Range 7	Insulin Injection (8 ml)
8	360	Range 8	Insulin Injection (10 ml)
9	420	Range 9	Insulin Injection (12 ml), Buzer and GPS Activation

10 examples from a collection of 48 glucose samples are illustrated in **Table 3** summarizing the second scenario:

Table 3 Second scenario.

Patient No	Gender	Age	O/P Voltage "V"	AP Readings "mg/dl"	Glucometer Readings "mg/dl"	Error "%"	Action Requested
1	Female	21	207	108	105	3	No Action
2	Male	25	225	110	111	1	No Action
3	Female	22	213	114	119	4	No Action
4	Male	25	229	113	120	7	No Action
5	Female	21	202	107	108	1	No Action
6	Male	59	247	258	212	18	Insulin Injection

7	Female	21	212	110	114	4	No Action
8	Male	24	213	103	109	6	No Action
9	Female	48	248	231	224	3	Insulin Injection
10	Female	21	220	112	129	13	No Action

As shown in **Figure 6**, the actual glucose levels computed using the artificial pancreas and the desired glucose levels conducted *via* the ACCU-CHEK glucometer were plotted together to clarify their correlation, due to voltage-glucose relation.

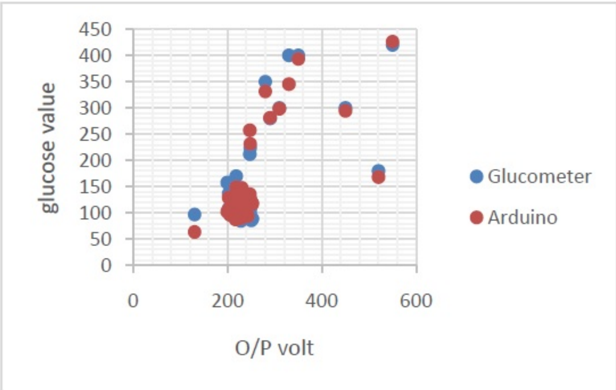


Figure 6 Artificial pancreas and Accu-Chek glucometer correlation.

Conclusion

The artificial pancreas has managed to monitor the glucose level by calculating it from the probe pulse oximeter's output voltage, using an equation derived with Microsoft Excel Linear Regression Technique. The glucose level was successfully regulated non-invasively, based on the signal received from the glucose meter wirelessly. As well as the control algorithm built on the treat to range sliding scale insulin protocol with an accuracy of 89%.

Recommendations

1. The AP should be patient specific because it is affected by various physiological features. Therefore, a physiological model including age, gender and weight must be considered to reduce the regression equation standard error as much as possible.

2. The smaller the device the more acceptability it will receive from patients, as it offers mobility. To minimize the size of the artificial pancreas microelectronics, integrated circuits (ICs) or nanotechnology can be used. If nanotechnology is used the system can simply be composed of a nano-glucose sensor working in cooperation with the biological pancreas, to emphasize its endocrine function activating it by transmitting electrical signals to control insulin production into the blood stream.

3. The artificial pancreas can be enhanced to endure multiple hormones not only insulin. It can also be used to deliver chemo/cryotherapy for pancreatic cancer patients since these surgeries cannot be done easily. The AP might also kill the cancer cells or reduce them without the need for high risk surgeries.

4. The AP system can be constructed as a glucose sensor in form of a ring consisting of a light emitting diode (LED) transmitter and photodiode to detect and measure glucose. While the insulin part "connected to the ring using wireless connection" may be constructed as a watch to display glucose level, calculate the exact dose of insulin and inject it directly to the vein behind the watch, putting into consideration that mobility issues must be controlled.

5. Follow up of diabetes should be accompanied with a backup storage to keep the weekly/monthly/annual readings. The daily glucose level graphs can be emerged to help health care professionals in statistics, diabetes researches and checking the clinical improvement per patient through their electronic medical record. There also should be a power backup and notification to the patient that his/her batteries need to be replaced as soon as possible.

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