APPLICATION OF FUZZY LOGIC FOR DIABETES MONITORING

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ABSTRACT

Diabetes is one of the most dangerous disease in the world; by 2025, at least 300 million people will have diabetes. The main objective of this research project is to apply fuzzy logic system for the purpose of monitoring diabetic patient's blood glucose level. The fuzzy logic system for monitoring blood glucose level was developed by using Matlab's fuzzy inference system editor. For this project, two input variables and one output variables with 12 linguistic rules were implemented to develop the fuzzy logic for diabetic monitoring. The data obtained from the system is then compared with the real condition. Based on the comparison done for this project, fuzzy logic system shows a promising potential to be used as a control strategy in monitoring patient's blood glucose level; the percent accuracy for the fuzzy logic system is 83%. In the future, the system can be integrated with blood glucose monitoring device and insulin pump; the combination is called artificial pancreas. With the advent of machine learning, the system can be further improved for benefits of diabetic patient.

Keywords: artificial intelligent, fuzzy logic, diabetes, blood glucose monitoring, obesity

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ABSTRAK

Penyakit diabetes adalah salah satu penyakit yang paling bahaya di seantero dunia; dijangka sekurang-kurangnya 300 juta orang akan menghadapi penyakit tersebut pada tahun 2025. Tujuan utama projek penyelidikan ini dijalankan adalah untuk menggunakan system logik kabur (*fuzzy logic)* untuk mengawasi kadar gula yang berada di dalam darah penyakit diabetes. *Fuzzy Inference System* editor yang terdapat di dalam perisian Matlab telah digunakan untuk mencipta system logic kabur khusus untuk mengawasi kadar gula di dalam darah penyakit. Untuk projek ini, 2 masukan berubah-ubah dan 1 keluaran berubah-ubah disertai dengan 12 peraturan linguistik telah digunakan untuk mencipta system logik kabur untuk mengawasi kadar gula di dalam darah penyakit. Data yang diperoleh dari sistem tersebut akan dibandingkan dengan keadaan sebenar. Berdasarkan kajian yang dibuat dalam projek ini, sistem logik kabur ini memperoleh 83% ketepatan. Pada masa hadapan, sistem yang dicipta dari matlab ini dapat disatukan dengan pam insulin dan alat pengawal gula di dalam darah; gabungan ini dipanggil pankreas buatan. Dengan kemunculannya teknik pembelajaran mesin, sistem ini dapat meningkatkan prestasinya dan menolong penyakit diabetes mengawal dan mengawasi kandungan gula di dalam darah mereka.

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LIST OF SYMBOLS AND ABBREVIATIONS

BMI	Body Mass Index
FIS	Fuzzy Inference System
DM	Diabetes Mellitus
ADA	American Diabetes Association
HR	Heart Rate
BP	Blood Pressure
PV	Pulse Volume
SD	Standard Deviation
FLMS	Fuzzy Logic Monitoring System
SVM	Support Vector Machine
HbA1c	Glycated Haemogoblin
SMBG	Self-Monitoring Blood Glucose

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CHAPTER 1: INTRODUCTION

1.1 Overview

Diabetes is one of the most dangerous diseases in the world. According to Horton (2009), approximately 333 million people will have diabetes by 2025. Based on statistic produced by Malaysia's Ministry of Health, 3.6 million Malaysian has diabetes (Bernama, 2017). A person is diagnosed with diabetes when his/her blood glucose level is more than 126 mg/dl if he/she is fasting; when tested 2 hours after meal, a person is considered diabetic when their blood glucose level is more than 200 mg/dl. Diabetes occurred due to body pancreas either failed to produce insulin or it only produce little amount of it; another reason is mainly due to insulin resistance where patient's body does not respond appropriately to insulin.

Diabetes can be categorized into two types; the first type is called Type 1 diabetes. This type of diabetes is mainly hereditary and it occurs due to insulin producing cell called Beta cell in pancreas being destroyed by the immune system; thus, patients with Type 1 diabetes need to constantly monitor and maintain their blood glucose at optimal level. The second type is called gestational diabetes and this type of diabetes occurs to pregnant patients who are over 25 years old and their body mass index (BMI) is above their normal level; according World Health Organization, this type of diabetes occurred in 4% of all pregnancy. The most common diabetes is Type 2 diabetes; out of 333 million that will have diabetes by 2025, 90-95% of the diabetic patients will have type 2 diabetes. This type of diabetes mainly occurs due to poor lifestyle choices such as diet rich in sugar and lack of exercise. While most type 2 diabetes patients are overweight or obese, it can also occur to non-obese patients (Heianza et al., 2014,).

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1.2 Problem Statement

Patients with diabetes required constant blood glucose monitoring. Traditional method, where blood glucose is monitored manually, can be a burden to patients; monitoring blood glucose level before meal, after meal, while patient is fasting, and before bedtime are required to prevent hypoglycemia or hyperglycemia. There are many control strategies used in diabetes monitoring, but the technique used is either never been described by the researcher because it is a trade secret or requires deep understanding of mathematical concept.

1.3 Report Organization

This report consists of 5 chapters and they are: introduction, literature review, methodology, result and discussion, and conclusion. The introduction part will briefly explain the overall state of the disease and discuss the problem statement and overall objective of this project. The literature review chapter discusses the cause and effect of diabetes and briefly explains the concept of fuzzy logic and its application in diabetes and other medical field; then, this chapter discuss and analyse other control strategy used by experts in the field. The methodology section explains the step taken to develop and modify the system. The result and discussion chapter will discuss about the data obtained from the system by comparing it to real condition. The conclusion chapter will summarize all the findings of the report.

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1.4 Objective

The aim of this study is to develop a fuzzy logic model in order to monitor the blood glucose level of diabetic patient. While research in the application of fuzzy logic into diabetes monitoring has been done, the technique used is either never been described by the researcher or requires deep understanding of mathematical concept; thus, the objectives of this project are:

1. To use Matlab's fuzzy inference system (FIS) editor to simulate the application of fuzzy logic into diabetic monitoring.
2. Analyse the accuracy of the fuzzy logic system with real life condition.
3. To understand the benefits of artificial pancreas, a system that integrate control strategy system such as the fuzzy logic system with insulin pump and diabetic monitoring devices.
4. To briefly mentions the integration of artificial pancreas with machine learning algorithm.

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CHAPTER 2: LITERATURE REVIEW

2.1 Cause of Diabetes

There are differences in the cause of incurring type 1 and type 2 diabetes and thus thorough understanding of both types of diabetes are needed in order to integrate it with the fuzzy logic model.

2.1.1 Type 1 Diabetes

Type 1 diabetes occurs mainly due to genetic disorder; patients with type 1 diabetes cannot produce insulin because beta cell, a type of cell that is responsible in the production of insulin, is destroyed by the immune system.

2.1.2 Type 2 Diabetes

Type 2 diabetes is the most common diabetes incurred by diabetic patients and it mainly occurs due to poor lifestyle choices such as unhealthy diet and infrequent exercise. Many diabetic patients have body mass index (BMI) that is 25 and above and thus can be categorized as overweight or obese, yet the correlation between obesity and incurring diabetes is slightly blurred. It can be deduced that obesity occurs mainly due to poor lifestyle choices, but not all overweight or obese subject has diabetes. Even so, Heianza et al. (2014) argued that obese subject has higher chances of incurring diabetes; for instance, it was found that metabolically healthy but obese individuals “had a significantly increased HR [hazard ratio] for diabetes” as compared to metabolically healthy and normal BMI individuals (p. 2422). The hazard ratio was calculated using Cox regression analysis. Furthermore, individuals that has hypertension, hypertriglyceridemia, and low HDL cholesterol concentration will have higher chances of incurring diabetes even though the BMI indicates that the person is not obese.

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Type 2 diabetes is a progressive disease and thus has devastating deteriorative affect; initially, it can be combatted by having a healthy diet followed by regular exercise. But Khan, St. Peter, Breen, Hartley, and Vessey (2010) warns that "intervention [in diabetic patients' activities] must be balanced with potential risk" (p. 46). As the disease progress, the diet and the exercise must be altered (Khan et al., 2010).

2.2 Consequence of Diabetes

Diabetic patients need to constantly monitor their blood glucose level to avoid diabetic complications due to hyperglycemia. According to Cade (2008), the aftereffect of hyperglycemia can be categorised into two vascular complication; some of the effect related to microvascular complications are diabetic neuropathy, nephropathy, and retinopathy; the other is related to macrovascular complications such as coronary artery disease, peripheral disease, and stroke.

In addition to hyperglycemia, diabetic patients may also experience hypoglycemia. Kavakiotis et al. (2017) mentioned that hypoglycemia occurs "mainly due to anti-diabetic treatment and [it] has a great impact among DM [Diabetes mellitus] patients" (p. 109). The insulin-producing drugs consumed in order to increase the level of insulin in patient's body system may sometime result in dramatic decrease in blood glucose level that is below the accepted level. According to Feldman-Billard, Massin, Meas, Guillausseau, and Heron, hypoglycemia may cause the increase of blood pressure, which increase the chance of diabetic patient to incur cardiovascular related disease.

2.3 Glycemic Control

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Table 2.1: Relationship between HbA1c and blood glucose level (AmericanDiabetesAssociation)

A1C % (mmol/mol)	Mean Plasma Glucose (mg/dl)	Mean Fasting Glucose (mg/dl)	Mean Premeal Glucose (mg/dl)	Mean Postmeal Glucose (mg/dl)	Mean Bedtime Glucose (mg/dl)
6 (42)	126 (100-152)				
5.5-6.49 (37-47)		122 (117-127)	118 (115-121)	144 (139-148)	136 (131-141)
6.5-6.99 (47-53)		142 (135-150)	139 (134-144)	164 (159-169)	153 (145-161)
7 (53)	154 (123-185)				
7.0-7.49 (53-58)		152 (143-162)	152 (147-157)	176 (170-183)	177 (166-188)
7.5-7.99 (58-64)		167 (157-177)	155 (148-161)	189 (180-197)	175 (163-188)
8 (64)	183 (147-217)				
8.0-8.5 (64-69)		178 (164-192)	179 (167-191)	206 (195-217)	222 (197-248)
9 (75)	212 (170-249)				
10 (86)	240 (193-282)				
11 (97)	269 (217-314)				
12 (108)	298 (240-347)				

Table 2.1 above shows the relationship between HbA1c and mean glucose level for diabetic patient compiled by the American Diabetes Association (ADA). The table

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above is used by clinician for glycemic control purposes; clinician uses the A1c to determine the appropriate glucose level for fasting, premeal, postmeal and before bedtime. The mean glucose level is based on the data of 507 adults that either has type 1 diabetes, type 2 diabetes and no diabetes; the association also mentioned that 2700 readings was taken per A1c column. The table above was not being taken into consideration in designing the fuzzy logic system because it is not reliable; in the same report, the ADA mentioned that "in a recent report, mean glucose [level] measured with CGM [continuous glucose monitoring] versus central laboratory-measured A1c in 387 participants in three randomized trials demonstrated that A1c [laboratory measured test] may underestimate or overestimate mean glucose" (p. 557) even though the association has determined that there are strong correlation (r=0.92) between the HbA1c and mean glucose level. Furthermore, it only shows the normal range of patient's blood glucose level and not range for hyperglycemia or hypoglycemia. The association suggested that blood monitoring device integrated with control strategy (i.e. continuous glucose monitoring) has the potential to help diabetic patient in improving their glycemic management.

2.4 Fuzzy Logic

Fuzzy logic is one of the branches that make up artificial intelligence. It was introduced by Lofti Zadeh, a researcher in the department of computer science at the University of California, Berkeley. Fuzzy logic is used to solve problems that has no definitive yes/no or black/white answer; in essence, system incorporated with fuzzy logic has the capabilities to obtain definitive solution based on vague and imprecise data (Grant, 2007).

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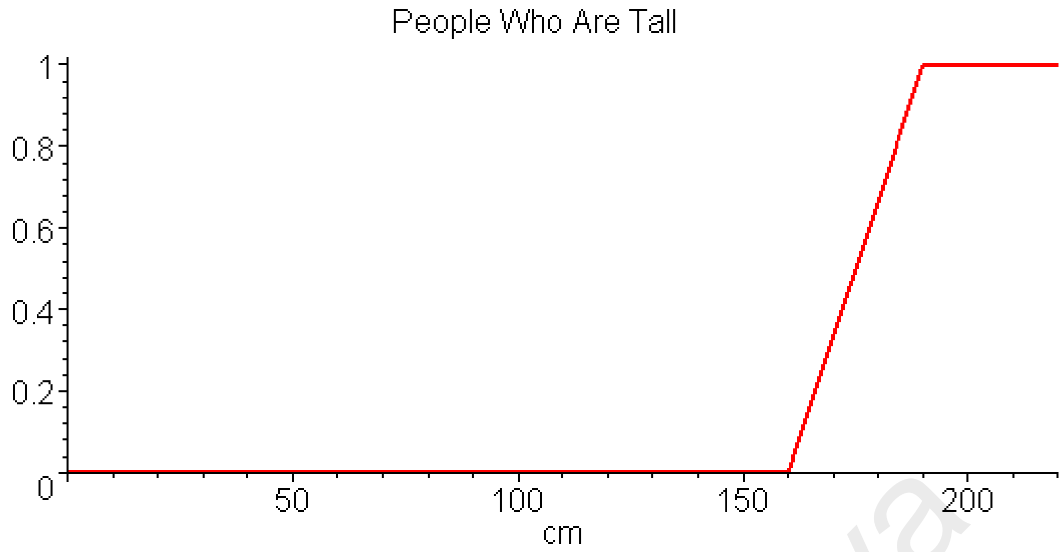

Figure 2.1: Example of Fuzzy Logic Graph (Maplesoft)

Fuzzy logic utilized multi valued logic instead of the binary Boolean logic and it is represented in the y-axis as shown in figure 2.1; the y-axis is called the degree of membership. The x-axis is called the universe of discourse; it is the range of all possible value of chosen variable. The graph in the figure 2.1 is called the membership function and it defines how each value of the universe of discourse is correlated to the degree of membership. For instance, people who are 180 cm is considered "sort of" tall because its degree of membership is 0.6 while people who are 190 cm is considered tall because degree of membership is 1. In terms of the shape of the membership function, it can be of any shape but the triangle, trapezoidal, and bell shape are most commonly used.

In addition to graph, fuzzy logic system also utilizes linguistic variable to represents the universe of discourse of the input and output variable in linguistic term. For instance, the range from figure 2.1 can be described linguistically as short, slightly tall, sort of tall, and tall for the 100-160, 160-169, 170-189, and 190-200 cm range, respectively. The linguistic representation of the value is called hedges. Turning the range of the input and output variables into linguistic variable is important in order to create fuzzy rule (linguistic rule).

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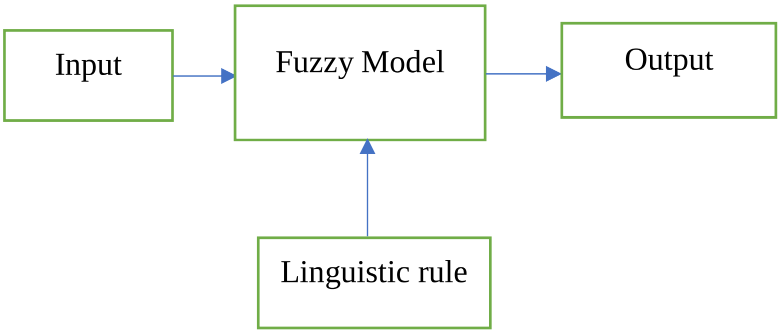

Figure 2.2: Basic Fuzzy Logic Model

Based on the example shown above, it can be deduced that fuzzy logic system requires input variables, output variables, linguistic rule and membership function. Figure 2.2 above shows the basic process of fuzzy logic system. The input variables can be more than one and the linguistic rule comes in the form of IF-THEN rule. For example, the 100-160 cm range is considered short, so the linguistic rule is written as “if the height is 100-160, then the person is short”. The example shown in figure 2.1 is a basic fuzzy logic example; more complicated fuzzy logic system involves more than one membership function in one input and multiple linguistic rule.

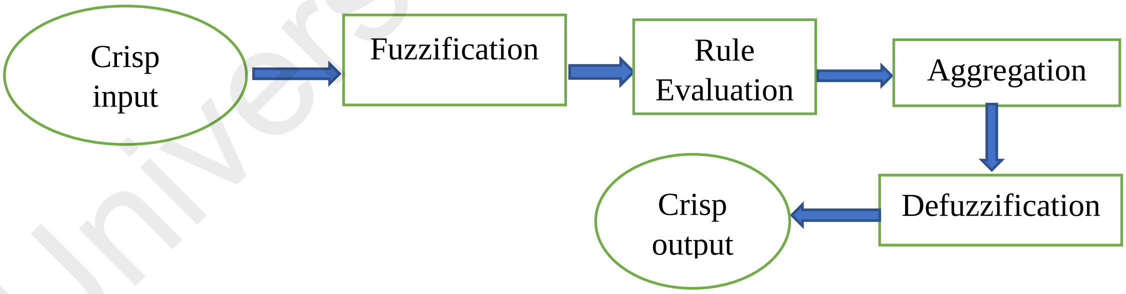

Figure 2.3: Mamdani Method

In fuzzy logic system, the numerical value of the input variables will be fuzzified, meaning that the crisp number will be inserted into its appropriate fuzzy sets in order to determine its degree of membership; but the output of the fuzzy logic system need to be in a crisp number; thus, the fuzzified input will need to undergo defuzzification. There are two methods that can be used for defuzzification purposes; one of the methods are the

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Mamdani method and the other is Sugeno method. For this project, the Mamdani method will be used. Flow chart above shows the fuzzification-defuzzification process using Mamdani method. As mentioned above, the crisp input will first be fuzzified. The next step is to determine the linguistic rule; if there is more than one antecedent (i.e more than one input), the AND/OR operator can be applied. The OR operator represents a union or the maximum value among the fuzzified input; it is used to determine the disjunction of the rule antecedents. In contrast, the AND operator represents an intersection or the minimum value among the fuzzified input and it is used in order to determine the conjunction of the rule antecedents. After determining and implementing the operator, the maximum/minimum value is correlated to the consequent (output) membership function via clipping method. For example, if the fuzzified input of A and B are 0.1 and 0.2, respectively, and the linguistic rule uses AND operator, then the fuzzified output is 0.1. The example given represents only one fuzzified output and in fuzzy logic system there are more than one output because more than one linguistic rules are required to mimic the real life condition; thus, all the rule's output will be aggregated into a single fuzzy set. Finally, the fuzzified output is defuzzified by using the centroid technique; the technique basically divides the output fuzzy set into two equal areas. The point that divides the area is the crisp output of the fuzzy system.

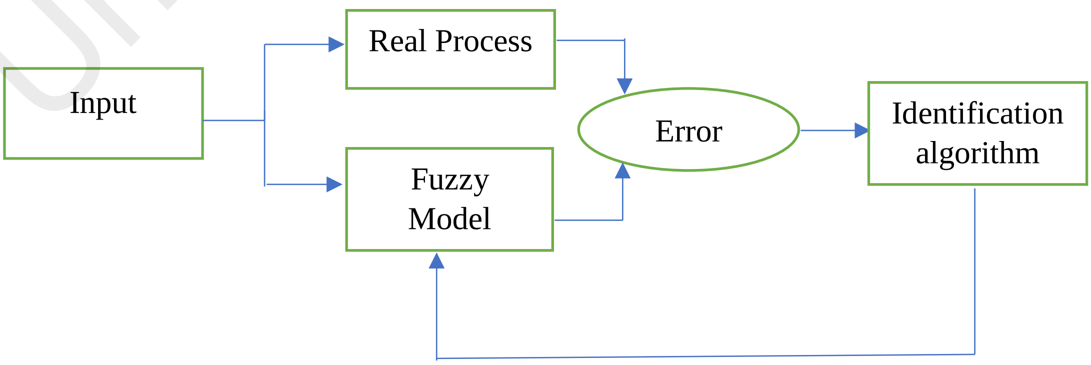

Figure 2.4: the "General Scheme of Identification Procedure" (Vachov, 2000, p. 52)

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Identifying the number of input and output variable and determining the linguistic rule of the system require knowledge of the subjects and implementing iterative learning algorithm so that the system best mimic the real process. Figure 2.4 above shows the iterative process to mimic the real process. It shows the process of identifying and changing the input, output, and linguistic rule by minimizing the error of the fuzzy model; the procedure is done by comparing it with the real process and then identification algorithm will determine where the error occurs. There are three level of identification that can be utilized to minimize the error between the real process and fuzzy model. The first level is the structure identification; in this level, the number of linguistic rule (i.e IF-THEN rule) and the number of input variable is adjusted. It is on this level where addition or reduction of linguistic rule and input variable is considered. The next level is the antecedent parameters identification, where the shape and range of the membership function will be adjusted; the former and the latter are fine-tuned so that it can correctly represent the linguistic rule in numerical terms. The final level is the consequent parameters identification; this level determines the number of output and identifying the range and shape of the membership function of the fuzzy model (Vachov, 2000).

The next subsection will first introduce the application of fuzzy logic in medical field followed by the application of fuzzy logic in monitoring diabetic patients.

2.4.1 Fuzzy Logic Application in Medical Field

Many medical devices have incorporated fuzzy logic theory into its system to increase the efficiency of healthcare providers in monitoring their patient; for instance, fuzzy logic system has been incorporated into anaesthetic monitoring device to help improve anaesthetist performances. Mirza and GholamHosseini (2010) lamented that "human errors in anaesthesia account for more than 80% of the preventable mishaps" (p. 3974). This mainly because anaesthetist depends on their experience and intuition when

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making decisions and in most of the circumstances, these "intuitive decision-making fails to achieve the optimal balance under competing or conflicting care delivery demands" (p. 3974). There is built-in alarm in medical devices that helps anaesthetist monitor the patient, but the system rigidity sometimes causes error that might harm patients. Mirza and GholamHosseini mentioned that "the frequent alarms are not only a nuisance for patients and caregivers but can also compromise patient safety and the effectiveness of care" (p. 3975). The rigidity of the classical system is mainly due to its dependent on exact mathematical analysis.

Table 2.2: Standard Deviation for Hypovolaemia (Mirza and GholamHosseini,2010, p. 3976)

Hypovolaemia	Mild	Moderate	Severe
Heart Rate (SD)	1.75-3	3-5	5 & >
Blood Pressure (SD)	2.75-5	5-6	6 & >
Pulse Volume (SD)	4-6	6-8	8 & >

Fuzzy logic theory was used to solve the rigidity of the classical system; with the implementation of fuzzy logic, the medical device has the capabilities to strategize that resembles human strategic thinking. This system is called fuzzy logic monitoring system (FLMS); the system was developed by using Matlab's fuzzy logic tool box. The three physiological parameters that it measured are heart rate (HR), blood pressure (BP), and pulse volume (PV). The system detects and classify hypovolaemia into three stages; the stages are mild, moderate and severe. In order to test the system, the first was step was to obtain patients' data; it was obtained from an anaesthesia monitor called S/5 Datex-Ohmeda located in the operating theatre; data acquisition from the monitor was approved by the local ethics communities. Then, the data was converted into digital format via DOMonitor.net. The various intra-operative procedures occurred during anaesthetic resulted in the raw digital data's waveforms incur high noise content; filtering technique

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such as variance-based filtering, low pass filtering and threshold-based noise rejection was used to filter the noise. After the filtration of noise, the system will be ready to be configured; there are 3 principles the system will follow before the system's alarm turned on. These 3 principles are in order; the first principle makes sure that the system will only accept HR, BP and PV input; system will announce alarm status as false if one of the inputs is missing and it will wait for the next data set that is obtained for the next 15 minutes. The second principle is setting limitation on the membership functions. The limits are classified as mild, moderate, and severe by calculating the standard deviation values for each parameter; table 2.2 above shows the standard deviation value of all three inputs classified as mild, moderate, and severe. This classification is done after the system is trained to analyse the input of 10 model patients' data and testing it with 10 random patients' data by using adaptive neuro fuzzy inference system technique; figure 2.5 below shows the FLMS structure. If both first and second principle are true (i.e. all three inputs are present and parameter exceed the SD limit), then principle 3 will check the validity of the system by applying the IF-THEN rule as shown in figure 2.6. The results shown in FLMS will then be compared with anaesthetist via Kappa analysis. Early research shows the system in agreement with anaesthetist majority of the time, but the author suggest more research is needing to increase the validity of the result.

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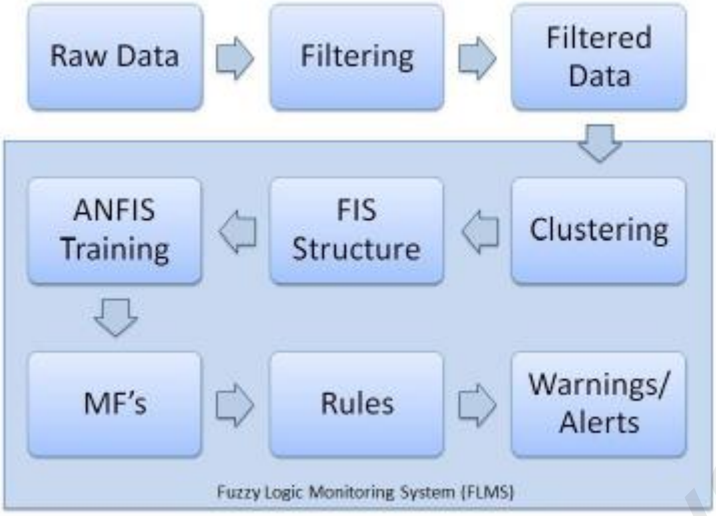

Figure 2.5: Fuzzy Logic Monitoring Structure (Mirza and GholamHosseini, 2010, p. 3976)

i. If (ECG-HR is mild) and (BP is mild) and (PV is mild) then (HYPOVOLAEMIA is mild).
ii. If (ECG-HR is moderate) and (BP is moderate) and (PV is moderate) then (HYPOVOLAEMIA is moderate).
iii. If (ECG-HR is severe) and (BP is severe) and (PV is severe) then (HYPOVOLAEMIA is severe).
iv. If (ECG-HR is mild) and (BP is mild) and (PV is moderate) then (HYPOVOLAEMIA is moderate).
v. If (ECG-HR is mild) and (BP is moderate) then (HYPOVOLAEMIA is mild).
vi. If (ECG-HR is mild) and (BP is mild) and (PV is severe) then (HYPOVOLAEMIA is moderate).
vii. If (ECG-HR is mild) and (BP is severe) and (PV is moderate) then (HYPOVOLAEMIA is moderate).

Figure 2.6: IF-THEN Rule Structure (Mirza and GholamHosseini, 2010, p. 3976)

Similarly, de Schatz (2015) uses fuzzy-neural based tool to monitor and predict patients' condition (p. 2580). Although the research done by de Schatz focused on patients under the intensive care unit, the method used is applicable to diabetic patient. Neural network is a branch of artificial intelligence where the computer system mimics the learning behaviour of human brain by feeding the system with data. Integrating fuzzy

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logic with neural network will increase the capabilities of the system, but the system will have both the drawbacks of neural network and fuzzy logic. In addition to the drawbacks of fuzzy logic, Adidela, Devi, Suma and Allam (2012) mentioned that the process of developing artificial neural network is complex and requires knowledge from expert in the field of artificial intelligence.

The anaesthetic monitoring device was reviewed extensively here because even though anaesthetic monitoring is not relevant in monitoring blood glucose level, the technique used to monitor heart rate, blood pressure, and pulse volume is applicable in monitoring blood glucose level.

2.4.2 Fuzzy Logic Application in Diabetes

Research has been done in trying to apply Grant (2007) proposed an approach to incorporate fuzzy logic to monitor and maintain patient's blood glucose level. Figure 2.7 shows the engineering diagram of a closed loop feedback system.

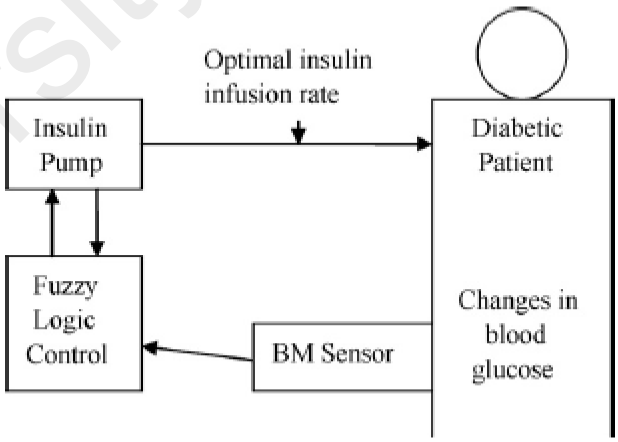

Figure 2.7: Closed Loop Feedback System for Diabetic Monitoring Device (Grant, 2007, p. 826)

Grant mentioned that some patients able to withstand high or low blood glucose level while some patients does not have the capabilities to do so; thus, the monitoring device that incorporate closed loop feedback system as shown in figure 2.7 will be able to solve problem mentioned above. The closed loop feedback system will recognise changes occur in blood glucose level. When changes occur, blood monitoring sensor will send the data to the fuzzy logic control system and the system will decide the optimal insulin infusion rate needed to be pumped into patients' system or it will not do anything if it's a false alarm. The key issue with Grant's article is it did not present the technology that it used to utilize the fuzzy logic system. Knowing the program or application used is important to estimate the cost of creating the simulation and eventually obtaining the necessary license to use the technology in a physical product.

In contrast with Grant, Adidela et al. (2012) included the technology used to monitor blood glucose level. Adidela et al. (2012) proposed a more advanced fuzzy logic algorithm called Fuzzy ID3; it is an "extension of ID3 (The Interactive Dichotomizer 3) technique…[and] it is most widely used decision tree algorithm" (p. 542). While the incorporation of fuzzy logic system into diabetes monitoring device will greatly improve patients' life, Adidela et al cautioned that proficiency in fuzzy logic theory is needed to develop the system. The main difficulty in applying Adidela et al. (2012) technique is the need to understand the abstract mathematics presented in the article; thus, developer and physician need to be proficient in abstract mathematics in order to use the Fuzzy ID3.

The differences between this project and those mentioned above is that this project will use Matlab's fuzzy inference editor to create the fuzzy logic system for blood glucose monitoring. Using programming language such as Matlab will help in simplifying the fuzzification and defuzzification steps and developer does not necessary need advanced mathematical knowledge to develop the fuzzy logic system.

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2.5 Artificial Pancreas

Artificial pancreas is a technological device that can help improves the life of diabetic patients. It is the integration of sophisticated control strategy such as fuzzy logic to monitor blood glucose level. All of the artificial pancreas is currently in the clinical stage, pending FDA approval. The differences between each artificial pancreas is the control strategy used to monitor patient's blood glucose level; for instance, Dassau et al (2017) uses G4 Share AP [Artificial Pancreas] with 505 algorithm developed by Dexcom, a company based in San Diego, California. The system shows promising result; after 12 weeks of using the artificial pancreas device, it was found that all 29 patients showed improvement in their HbA_{1c} percentage. HbA_{1c} percentage is the percentage of non-enzymatic attachment of glucose to proteins, in this case the haemoglobin found in human blood and it is directly proportional to patients' blood glucose level. The only issues with the method used by Dassau et al is the cost of the technology used in this research and it will take longer time for the technology to reach 3rd world countries.

Khan, Masud, and Mamun (2017) proposed a method that can help patient manage their blood glucose level in a novel, efficient and in convenient ways; this was done by using mathematical models and patients' previous self-monitoring blood glucose value to predict patients blood glucose value on the next day. The mathematical models used are support vector regression model, linear regression model, and Weilbull distribution model. The accuracy of all three predictions model were compared to each other by using root mean square error. Based on the root mean square error calculated, Khan et al were not convinced that all three mathematical models yield accurate prediction. The main reason why predictions were not accurate is because data used for this research came from the UCI machine learning repository; It was indicated in the article that data variation is one of the main reasons why all three mathematical models yield different prediction.

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Khan et al believes that all three of their models will work if they are used in real data from patients and they will initiate the research in the near future. Once the research is complete, Khan et al plans to develop an app that will incorporate one of the prediction models. One of the main weaknesses found in Khan et al methods are the mathematical model used are complicated and unnecessary when emerging method such as machine learning will soon be readily available and able to monitor blood glucose level in a much more efficient manner.

Recently, there is growing application of machine learning method towards blood glucose monitoring; for instance, Sudharsan B et al. uses Random Forest, support vector machines (SVM), k-nearest neighbour, and naïve Bayes to predict hypoglycemia for type 2 diabetes patient (as cited by Kavakiotis et al., 2017, p. 109). Similarly, George et al. (2013) uses support vector regression to predict hypoglycemia. While the findings of both Sudharsan B et al. and George et al. are promising, it only able to predict hypoglycemic cases and not hyperglycemia.

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CHAPTER 3: METHODOLOGY

3.1 Introduction

This chapter highlight the steps taken to design the fuzzy logic system for the purpose of monitoring blood glucose level. First, the variables that need to be included in the fuzzy logic system is discussed. Then, it is followed by the step by step process of implementing variable and linguistic rule into Matlab's fuzzy inference editor. Finally, the method in obtaining the data is discussed.

3.2 Design Criteria

The main purpose of designing the fuzzy logic system is to eventually be implemented in a non-invasive blood monitoring device for diabetic patient to monitor their blood glucose level for daily usage; thus, only relevant variables were included in developing the fuzzy logic system for this project. In subsection 3.2.1, the method in obtaining the variables is discussed; furthermore, the basic diabetes monitoring flowchart is shown in figure 3.1.

3.2.1 Variable

Determining the input variable is important in order to determine whether a diabetic patient experienced hypoglycemia or hyperglycemia. The most important variable is the blood glucose level; the range of blood glucose level will correspond to the action that diabetic patient will take (i.e. inject more or less insulin and/or visit their doctor). According to American Heart Association, the blood glucose range in determining whether a diabetic patient has hyperglycemia depends on prescription by doctor; thus, it is difficult to generalize the blood glucose range because each individual diabetic patient may have different range. For the purpose of this project, the blood

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glucose range to diagnose diabetic patient was used. The range of the blood glucose level can be easily change depending on clinician prescription.

Furthermore, the relationship between blood glucose level and patients experiencing hyperglycemia depends on whether patient is fully nourished or fasting. According to the American Diabetes Association (ADA), patient need to measure their blood glucose level before and after meal, before bedtime, and when they are fasting ("6: Glycemic Target: Standards of Medical Care in Diabetes -2018", 2018); thus, the second variable that need to be included is the time after a patient has their meal. Table 3.1 below shows the blood glucose range for fully nourished and fasting diabetic patient and the corresponding dependent variable.

Table 3.1: Blood Glucose Range for Fasting and 2 hours Glucose Tolerance Test (WHO)

conditions	Hypoglycemia (mg/dl)	Normal (mg/dl)	Impaired Glucose tolerance (mg/dl)	Hyperglycemia (mg/dl)
Fasting	≤ 72	74-109	110-125	≥126
2 hours Glucose Tolerance Test	≤ 72	73-139	140-199	≥200

As mentioned above, monitoring blood glucose level of a diabetic patient depends on whether the patient is fasting or fully nourished; higher blood glucose level is considered normal in the first 2 hours after meal. Figure 3.1 below shows the flowchart in monitoring diabetic patient's blood glucose level.

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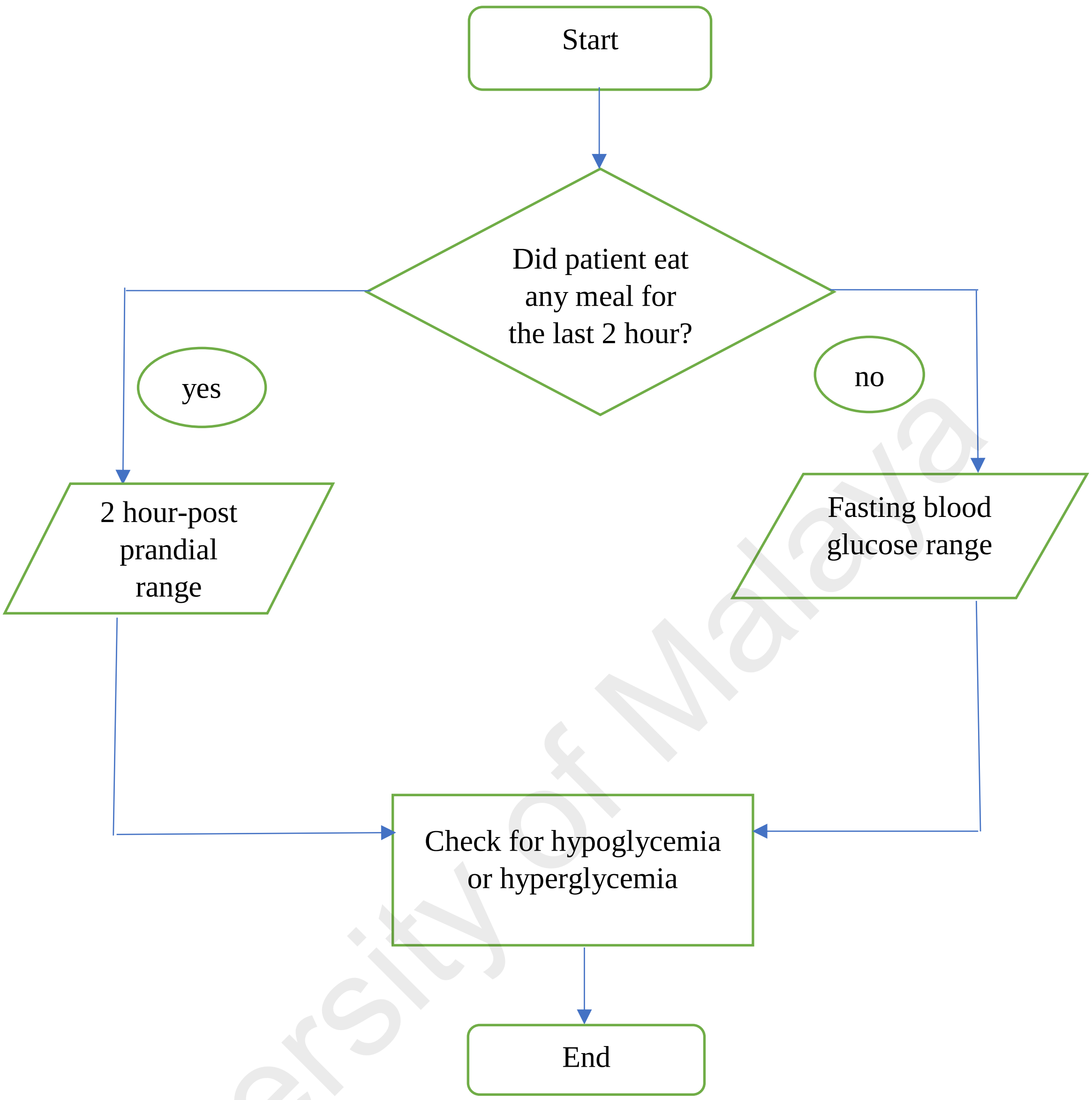

Figure 3.1: Basic Diabetes Monitoring Flowchart

Other variables that were taken into consideration but not included in the simulation were HbA1c (glycated haemoglobin), systolic blood pressure, and body mass index. HbA1c was not included because the purpose of this simulation is to eventually be able to integrate the fuzzy system with self-monitoring or continuous glucose monitoring device that will be used at home. Furthermore, HbA1c check-up is mainly done by doctors and it is dependent on the situation of the diabetic patient; for instance, some patient who managed to effectively control their blood glucose level will only require 4-6 times HbA1c check-up per year while some will require regular (weekly or monthly) check-up

(HAP.org). Systolic blood pressure was not included because it is the dependent variable of patient's blood glucose level, specifically between hypoglycemia and increasing blood pressure; Feldman-Billard et al. (2010) mentioned that for type 2 diabetic patient experiences an increase in systolic blood pressure 20-30 minutes after hypoglycemic event. In relation to type 1 diabetes, it is still debatable whether the hypoglycemic event has an effect on systolic blood pressure (829). As mentioned in the literature review section, even though there is a strong correlation between high body mass index and diabetes, not all obese patient is diabetic. Thus, BMI index was not included as the input variable.

3.3 Simulation Steps

This section will demonstrate the process of designing fuzzy logic system for diabetic monitoring via matlab.

<u>Steps</u>

1. Open the Matlab software.
2. Open the fuzzy logic toolbox by typing "fuzzy" on the command window as shown in figure 10 below

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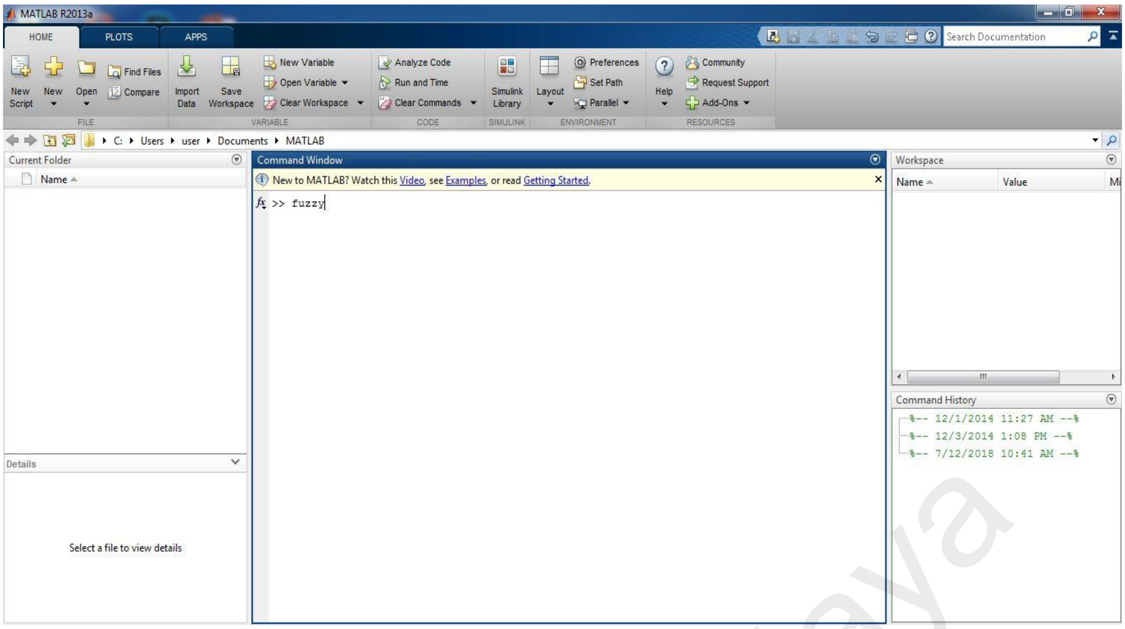

Figure 3.2: Command Window in Matlab

3. Fuzzy Inference System (FIS) editor will appear as shown in the image below. Adjust the number of input and output accordingly. For this project, there are two input and one output.

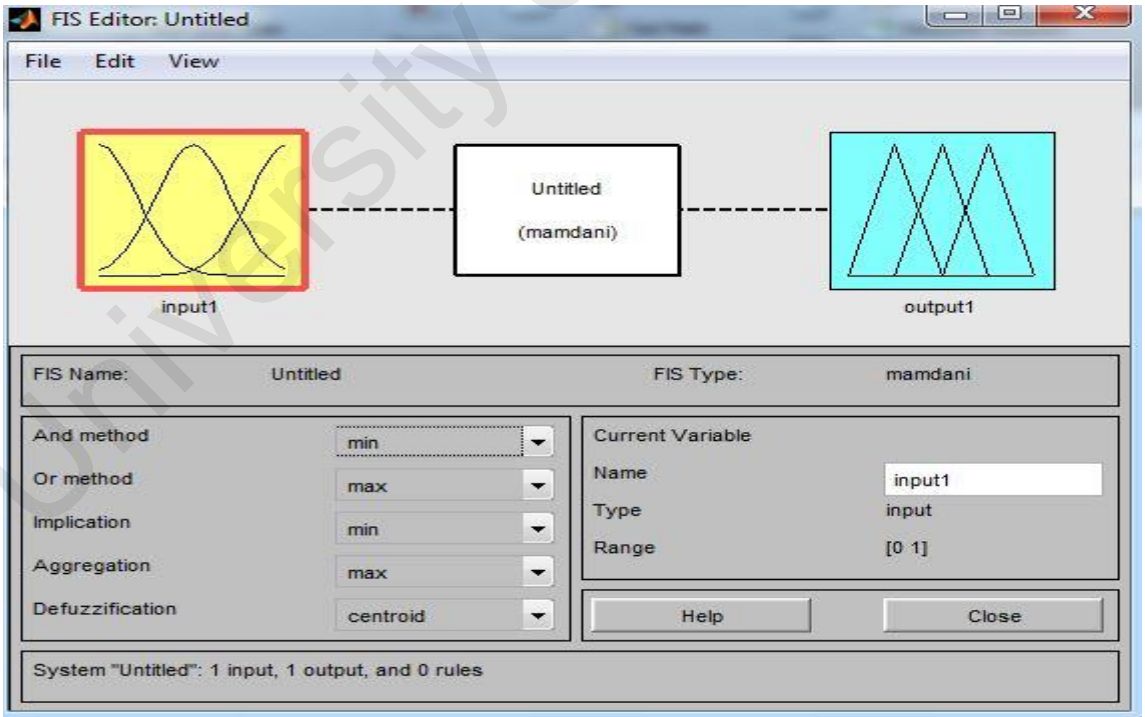

Figure 3.3: Fuzzy Inference System Editor

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4. The universe of discourse for both inputs is shown in table 3.2 and 3.3, respectively.

Table 3.2: Range for Blood Sugar (mg/dl)

Blood sugar (mg/dl)	Condition (level)
0-79	low
73-140	normal
125-199	caution
≥ 185	high

Table 3.3: Time After Meal (hour)

hour	condition
0-3	full
2-5	Slightly hungry
4-8	hungry

5. After filling the range of the inputs, the membership function's shape was determined. As shown in figure 3.4, the shape for blood sugar input are trapezoidal. The degree of membership is 1 until it reaches a certain point where fuzziness occurs; for example, 0-72 mg/dl is considered low but 73-79 is between low and normal level. The membership function's shape for time after meal is not uniform as compared to blood glucose level membership function. As shown in figure 3.5, the membership function's shape for time after meal consist of half triangle, an obtuse triangle, and trapezoidal. The shape mimics the condition of human hunger situation; the degree of membership for the first membership function (half triangle) indicate that there is no fuzziness whether patient is hungry 0 hours after meal, then the degree of freedom is slowly changes (lowered) until it reaches 3 hours after meal, where patient will start to experience slight hunger or the feeling of fully satiated is gone. As with the previous membership function, the feeling of slight hunger will be true up to certain point; for most individual, they may start experiencing it in between 4 to 5 hours after meal. The final membership function is

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trapezoidal in shape and it starts at 4 hours after meal; this is to take into consideration that some patient has high metabolism and thus will experience hunger much more quickly, yet it is still in the fuzzy region because it is not always true. For most individuals, regardless whether diabetic or non-diabetic patient, will start to feel hungry from 6 hours after meal onwards; thus, degree of freedom from 6 hours onward is 1.

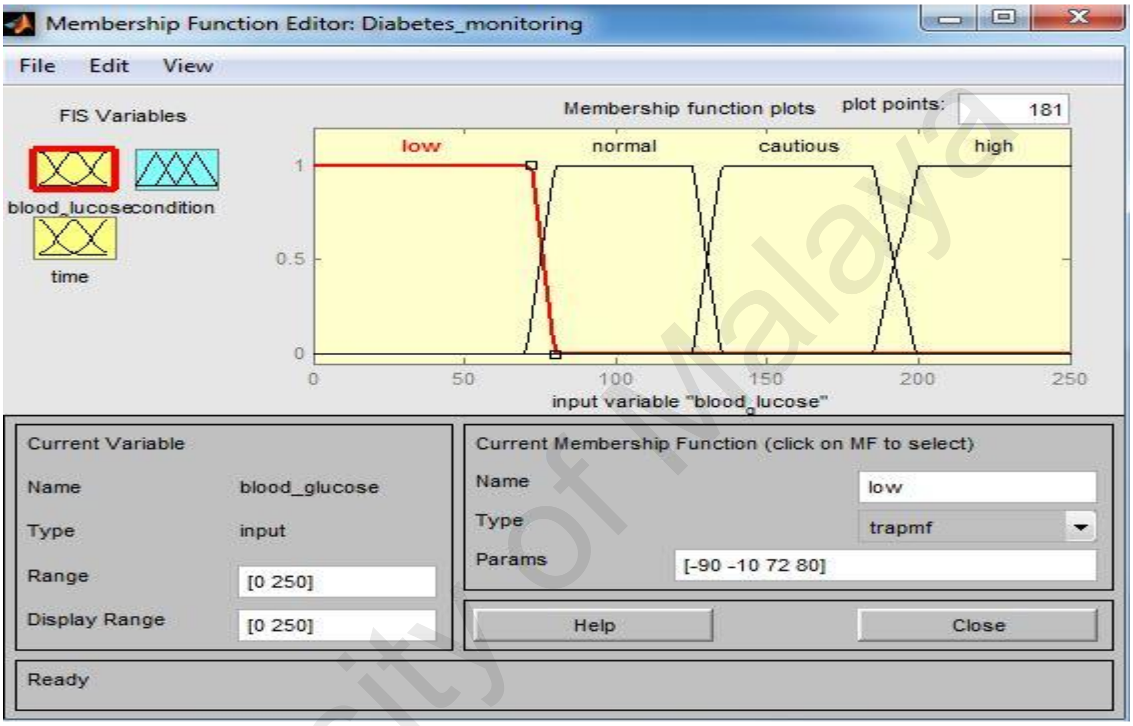

Figure 3.4: Membership Function for Blood Glucose Level

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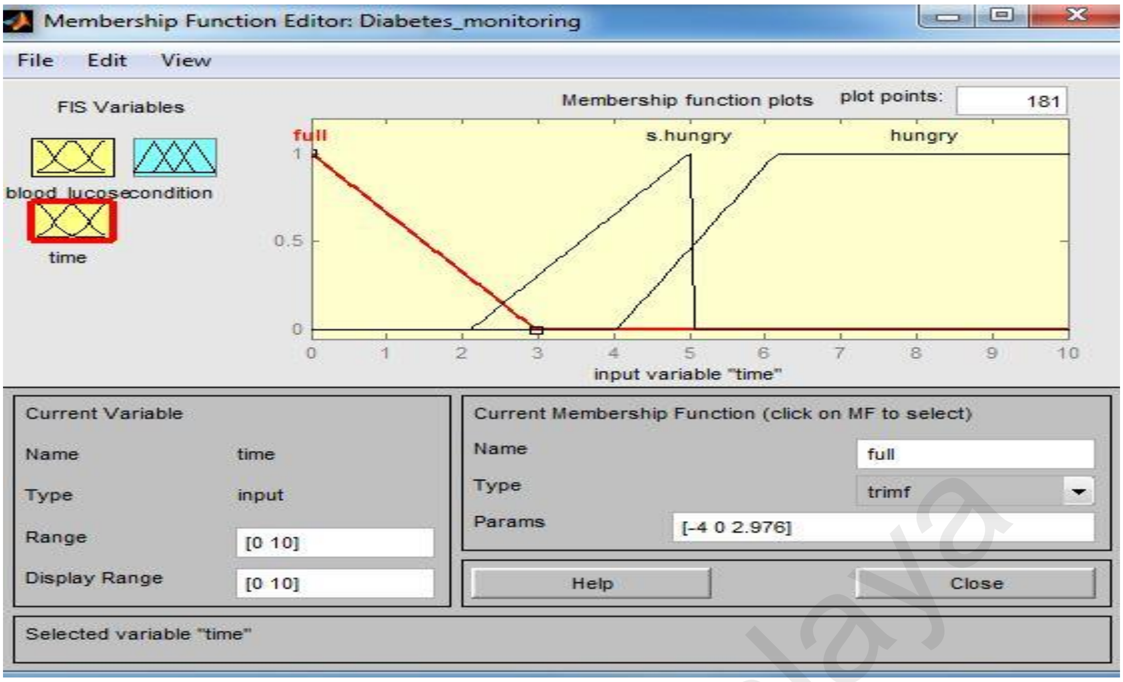

Figure 3.5: Membership Function for Time After Meal

6. The universe of discourse for the output is shown in table 3.4 and the membership function plot is shown in figure 3.6.

Table 3.4: Output Range for Patient's Condition

Condition	Level
hypoglycemia	0-3
normal	2.5-5.5
Pre-diabetic	5-8
hyperglycemia	7.5-10

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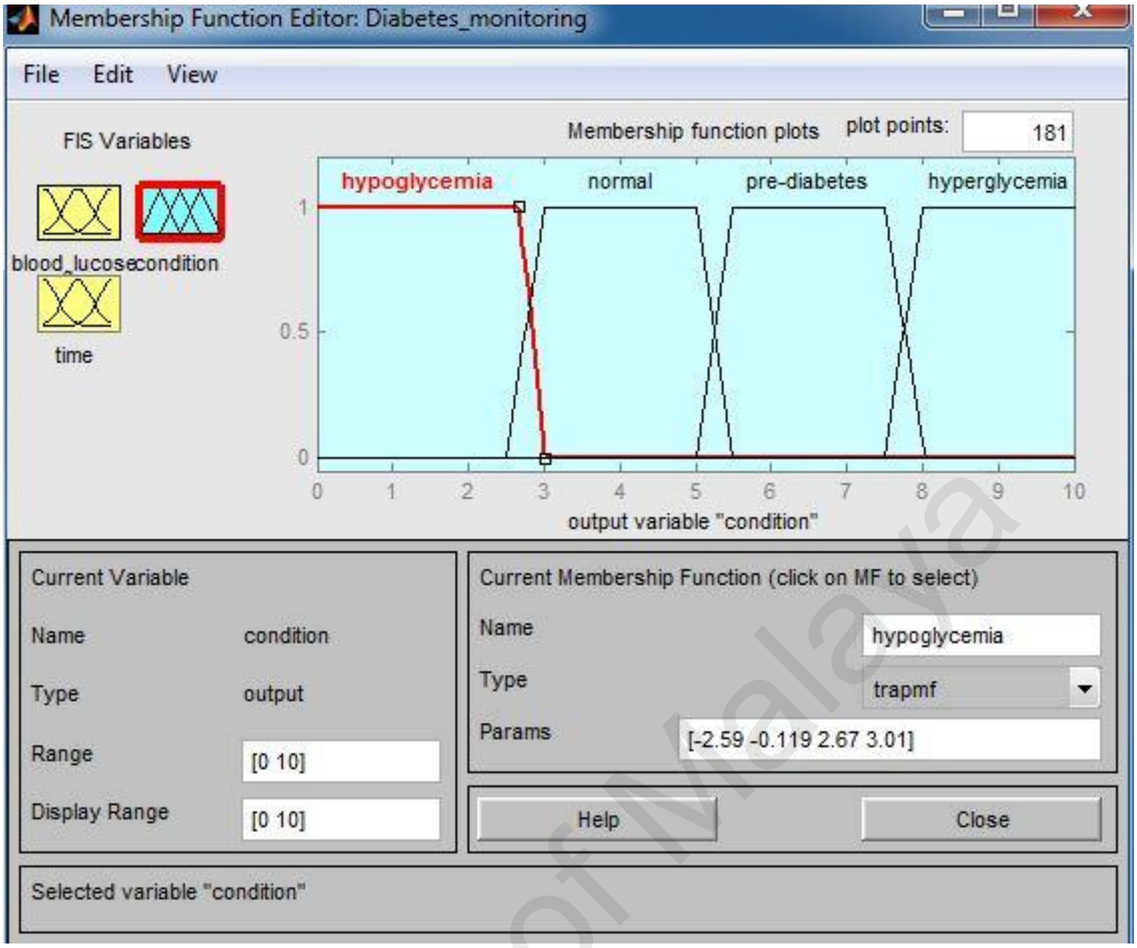

Figure 3.6: Membership Function for Patient Condition

7. After filling both the input and output, the type of method needs to be determined. The method used for this project is the Mamdani method. The defuzzification is done by using the centroid technique.

8. After filling both the input and output, the next step is to insert the linguistic rule into the system. The linguistic rule is shown below

I. If Blood Glucose is low and hour after meal is full, then patient has hypoglycemia
II. If Blood Glucose is low and hour after meal is slightly hungry, then patient has hypoglycemia
III. If Blood Glucose is low and hour after meal is fasting, then patient has hypoglycemia
IV. If Blood Glucose is normal and hour after meal is full, then patient is normal

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V. If Blood Glucose is normal and hour after meal is slightly hungry, then patient is pre-diabetes

VI. If Blood Glucose is normal and hour after meal is hungry, then patient has hyperglycemia

VII. If Blood Glucose is caution and hour after meal is full, then patient is pre-diabetic

VIII. If Blood Glucose is caution and hour after meal is slightly hungry, then patient is pre-diabetic

IX. If Blood Glucose is caution and hour after meal is fasting, then patient has hyperglycemia

X. If Blood Glucose is high and hour after meal is full, then patient has hyperglycemia

XI. If Blood Glucose is high and hour after meal is slightly hungry, then patient has hyperglycemia

XII. If Blood Glucose is high and hour after meal is fasting, then patient has hyperglycemia

9. Figure 3.7 below shows the linguistic rule on the matlab's software

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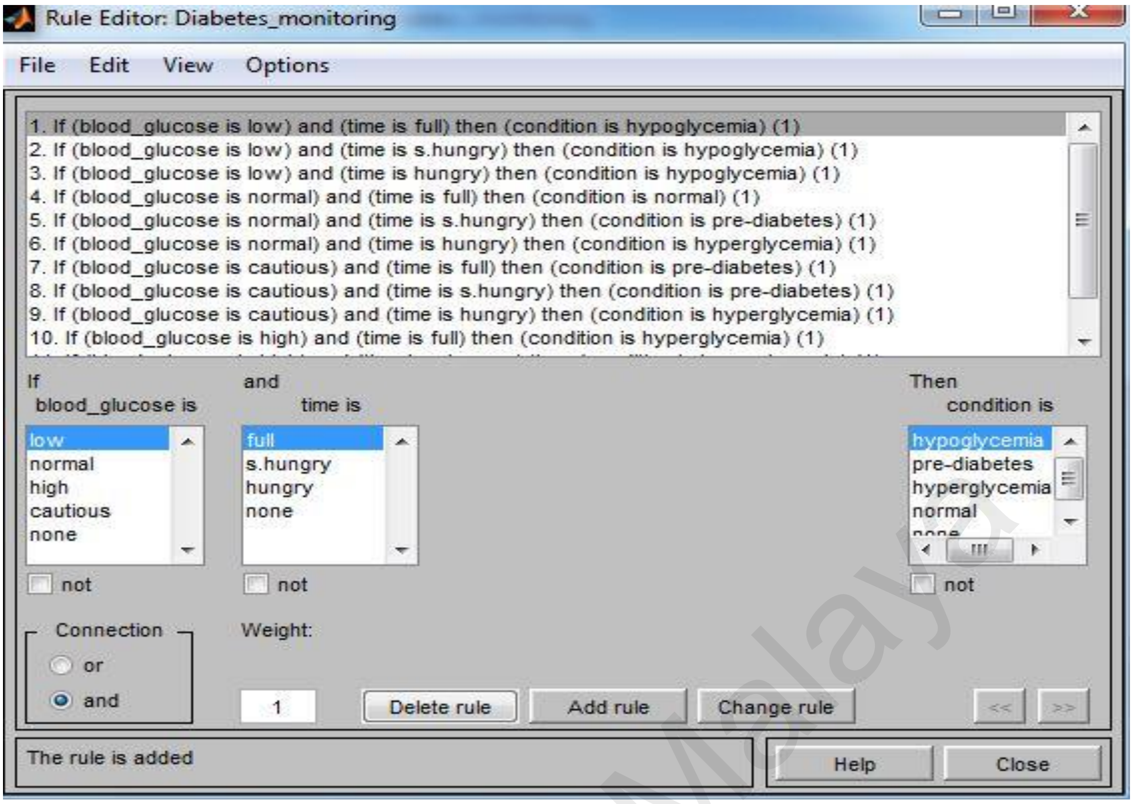

Figure 3.7: Linguistic Rule Input

10. To retrieve the file, open the fuzzy logic toolbox on Matlab and click the file button. Then, click the import button and search for the file.

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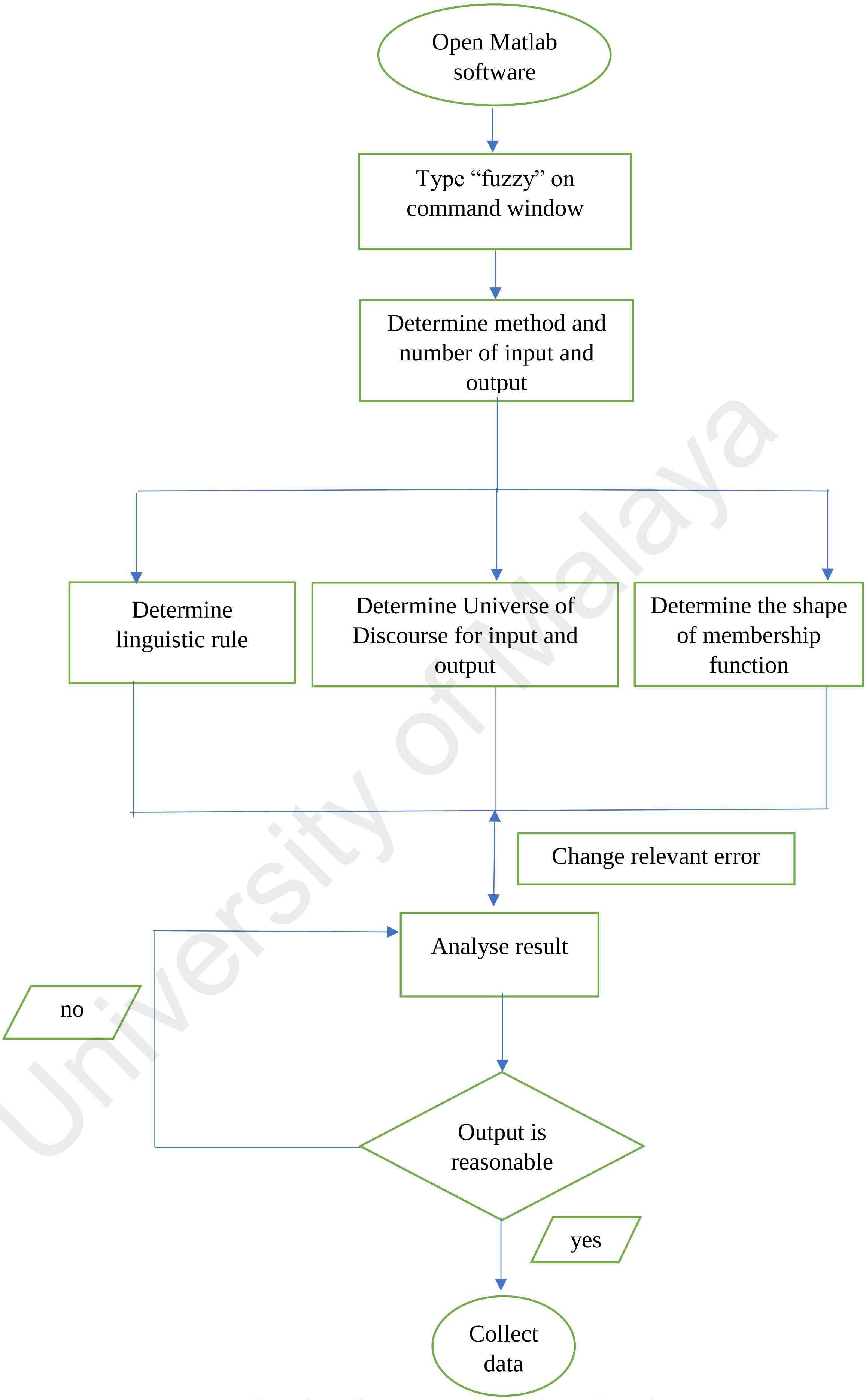

Figure 3.8: Flowchart for Setting Up and Analyse the System

11. Figure 3.8 above shows the flowchart of the process in designing and analysing the output of the system. The flowchart represents brief summary of the step taken above in designing the system. Furthermore, it also shows the iterative step taken in improving the system so that it can best mimic the real condition. If the output is not reasonable, then the system will be re-analysed in order to determine the error of the system; the error could come from insufficient linguistic rule, wrong universe of discourse (range) for the input and output variable, inaccurate membership function or all of them combined.

3.4 Collecting Data

The result developed by the system can be viewed as surface viewer or rule-based window as shown in figure 3.9 and 3.10, respectively. The surface viewer represents the relationship between the input and output. In figure 3.9, the x and y axis represent blood glucose and hour after meal while z axis represents patient's condition. By choosing any value from blood glucose level and time after meal, the graph can be used to find the condition of the patient. But throughout the project, the rule-based window was used to obtain data. The value of blood glucose level and time after meal is change by adjusting the red line on both the input variable; the condition will correspond to the change made by the adjustment the blood glucose level and/or time after eaten variable. Alternatively, both the input value can be adjusted by changing the input value manually via the input column.

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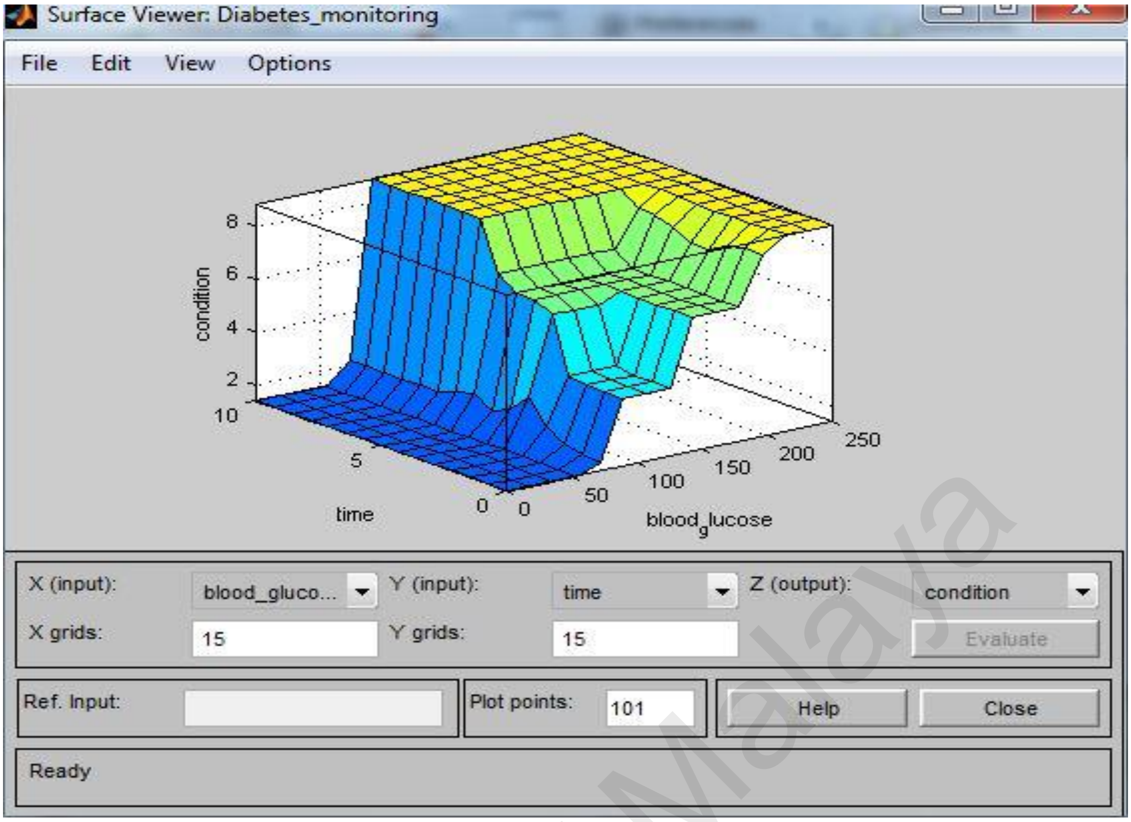

Figure 3.9: Surface Viewer Window

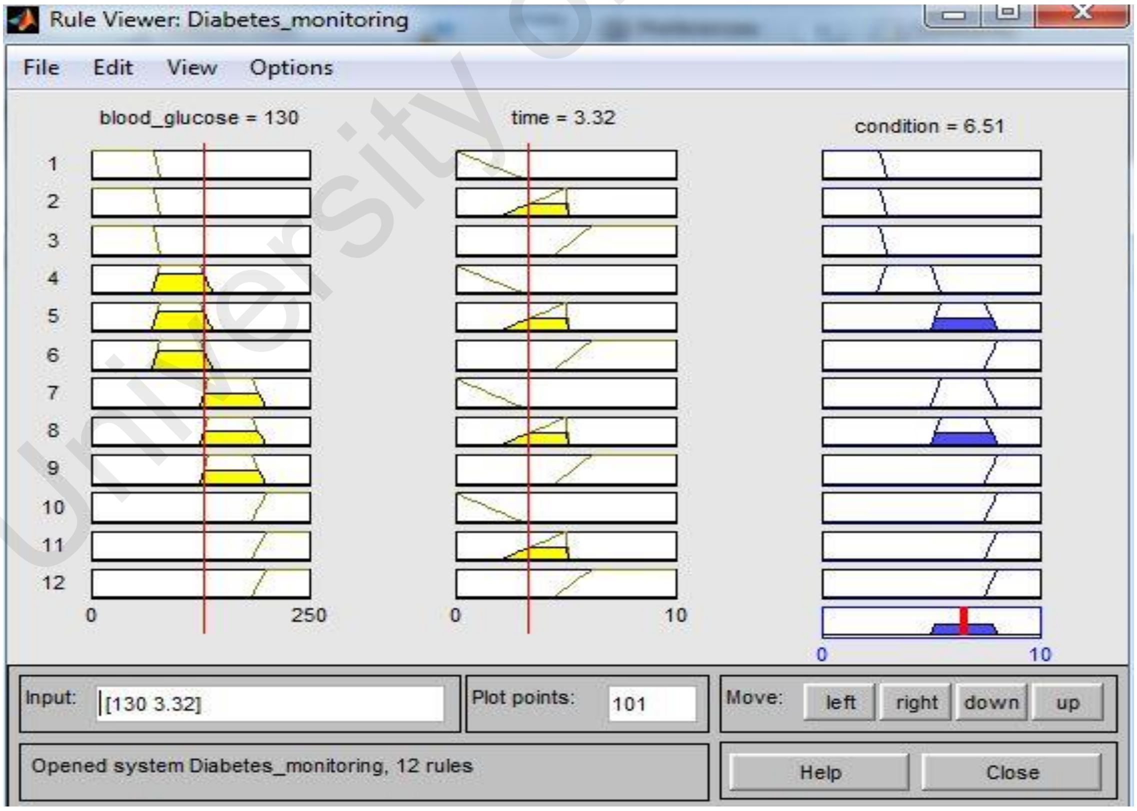

Figure 3.10: Rule Viewer Window

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CHAPTER 4: RESULT AND DISCUSSION

4.1 Introduction

This chapter will discuss the result obtained from the fuzzy logic system; furthermore, it will discuss about the integration of the system with blood glucose monitoring device and insulin pump to form an artificial pancreas. Then, it will discuss about the benefits of artificial pancreas and the effect of technological advancement towards diabetes monitoring.

4.2 Result

Table 4.1 below shows 12 random data obtained after initially setting up the system on Matlab. The screenshot of the data obtained from Matlab as shown on the table can be found on the appendix. The output was then compared to the real condition based on table 3.1 in chapter 3. For instance, between 0-2 hours after meal the 2 hours glucose test will be used as comparison and the fasting glucose test will be used as comparison for ≥ 4 hours after meal.

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Table 4.1: Result Obtained from the System

Number	Blood Glucose	time	output	condition	Real condition
1	67.7	0.136	1.4	hypoglycemia	hypoglycemia
2	67.7	3.59	1.43	hypoglycemia	hypoglycemia
3	67.7	8.05	1.4	hypoglycemia	hypoglycemia
4	130	0.136	5.1	normal	normal
5	130	3.32	6.51	Pre-diabetic	Normal/pre-diabetic
6	130	7.77	8.86	hyperglycemia	hyperglycemia
7	212	0	8.9	hyperglycemia	hyperglycemia
8	212	4.5	8.88	hyperglycemia	hyperglycemia
9	212	8.05	8.9	hyperglycemia	hyperglycemia
10	125	5	7.01	Pre-diabetes	Pre-diabetes
11	125	7.86	8.9	hyperglycemia	Quasi-hyperglycemia
12	37.8	0.0455	1.4	hypoglycemia	hypoglycemia

Based on the preliminary data, the system performed well relative to the real condition, with the system yielding 83% accuracy rate; for instance, the output of data 1 to 3 correctly show that patient experiencing low blood sugar level is experiencing hypoglycemia, regardless whether patient just consumed their meal or they are fasting. The output for data 1,2, and 3 are 1.4,1.43, and 1.4, respectively; based on the output range outlined in table 4.1, all three value dictates that patient is experiencing hypoglycemia and the hypoglycemia membership function from figure 3.6 shows that the degree of membership for all three data is 1; this indicate that there is no fuzziness and that patient is experiencing hypoglycemia. Similarly, the output for data 7,8, and 9

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correctly shows that patient who has high blood sugar level is experiencing hyperglycemia, regardless of whether he/she just consumed their meal or they are fasting. The output value for data 7,8, and 9 are 8.9,8.88, and 8.9, respectively; based on the hyperglycemia membership function shown in figure 3.6, the degree of membership for all the three data is 1, meaning that there is no doubt that patient is experiencing hyperglycemia.

The only error occurred in data 5 and 11. In terms of data 5, it lies in the region between fully satiated and hungry (time after meal is 3.32 hours). The condition based on the output is 6.51, indicating pre-diabetic; but the real condition is difficult to decipher because it's in the slightly hungry range; the real condition could be in between normal/pre-diabetic range. For data 11, 125 mg/dl and 7.86 hour after meal is still considered to be in pre-diabetic region, but it is entering the hyperglycemia region as the value of hyperglycemia for fasting is 126 mg/dl and above. Thus, the output value should be on the region of pre-diabetes (5-8), or more specifically between 7.5-8, which is the fuzzy region between pre-diabetes and hyperglycemia (quasi-hyperglycemia); yet the output value for data 11 is 8.9, indicating it's a hyperglycemia condition with degree of membership of 1.

The small error occurred is mainly due to the blood glucose level range and/or knowledge base (linguistic rule) input. To further analyse the system, data of blood glucose level at 126 mg/dl and 140 mg/dl at various time after meal was used. The main reason the former and latter were picked is because both of the value represent different condition at different time; for instance, 126 mg/dl blood glucose level is considered normal for fully satiated diabetic patient but hyperglycemic for fasting diabetic patient.

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Table 4.2: Results for 126 and 140 mg/dl at Various Time

Data	Blood Glucose Level (mg/dl)	Time after meal (hr)	Output	Condition	Real Condition
1	126	0	4.27	normal	normal
2	126	4	6.51	Pre-diabetic	Normal/pre-diabetic
3	126	8	8.89	hyperglycemia	hyperglyemia
4	140	0	6.51	Pre-diabetic	Pre-diabetic
5	140	4	6.51	Pre-diabetic	Pre-diabetic/hyperglycemia
6	140	8	8.9	hyperglycemia	hyperglycemia
7	126	3.25	6.51	Pre-diabetic	Normal/pre-diabetic
8	126	9.2	8.89	hyperglycemia	hyperglycemia
9	140	3.25	6.51	Pre-diabetic	Pre-diabetic
10	140	9.2	8.9	hyperglycemia	hyperglycemia

Based on table 4.2 above, there were irregularity between the system condition and real condition when time after meal is between 3 to 4 hours. The output for data 2 and 7 is 6.51, which indicate that patient is experiencing pre-diabetic condition. But the real condition is difficult to decipher because the range is in between after the 2hr glucose tolerance test and before fasting (hungry) range. In the fuzzy logic system, 4 hours after meal indicates that a patient is slightly hungry, but the digestion of food depends on patient's metabolism and the metabolism of diabetic and non-diabetic patient are almost similar (diabetes.co.uk.); thus, some patient may be experiencing pre-diabetic while other is still in normal range. The same conclusion is true when blood glucose level is at 140 mg/dl; at 3-4 hours after meal, the system predicted that the patient is in the pre-diabetic

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range. But the real condition indicate that patient might be in between pre-diabetic and hyperglycemia range, depending on their metabolism.

The main weakness of the system is it did not take physical activities into consideration; the intensity of patient's physical activities has an effect towards their metabolism. Before developing system, it was assumed that patient will only perform low intensity physical activities and thus the effect of metabolism should be negligible; but it was later found that there are athlete who has diabetes, usually type 1 diabetes. The proposed solution is to add another input that represents the physical activities, but in order to do so, a deep knowledge in the field of sport science, nutrition, and metabolic biology are needed; in other word, the input of expert such as nutritionist, sport scientist, and doctors are required.

4.3 Integration of fuzzy logic system

The main purpose of this research project is to run a simulation of fuzzy logic system to monitor blood glucose level. At some point in the future, the findings from this project can be integrated with a blood glucose monitoring device and insulin pump to form an artificial pancreas. Flowchart below shows how a blood glucose monitoring device integrated with control strategy such as fuzzy logic system and insulin pump to monitor diabetic patient's blood glucose level.

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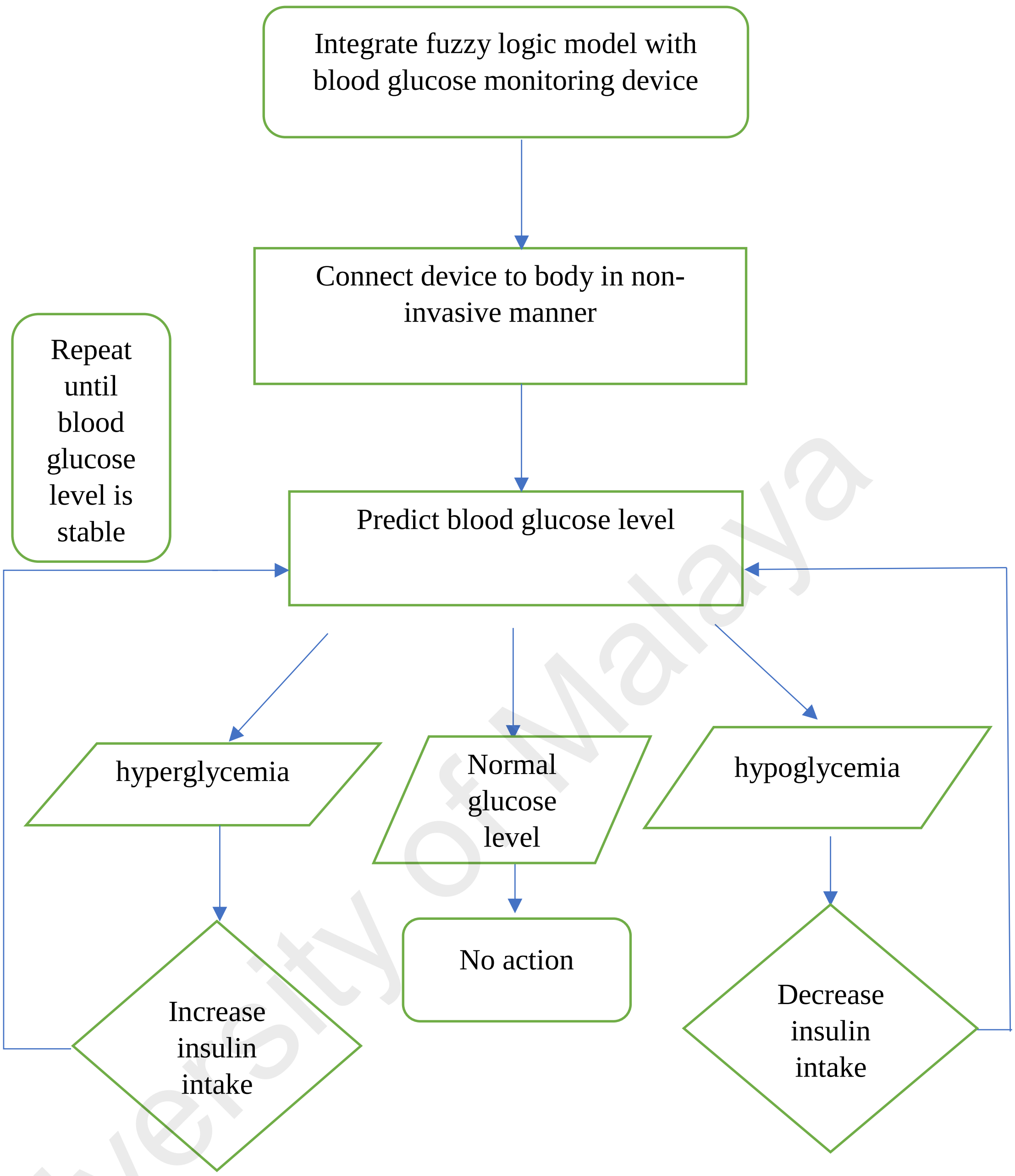

Figure 4.1: Flowchart for Artificial Pancreas Functionality

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4.4 Benefits and Challenges of Artificial Pancreas

The integration of blood glucose monitoring device, insulin pump and a control strategy are invariantly called artificial pancreas. Fuzzy logic system developed for this research project is one of many control strategies that can be used for the purpose of monitoring and maintaining optimal blood glucose level for diabetic patient.

Most of the research done in regards to artificial pancreas is still in clinical stage, but research done so far indicates the likelihood of artificial pancreas to replace the conventional method; for instance, Dassau et al. (2017) designed and conducted a study that tracks the performance of artificial pancreas in monitoring and maintaining blood glucose level in 29 type 1 diabetes patients. The studies lasted for 12 weeks and all 29 subjects used artificial pancreas to monitor and maintain their blood glucose level; subjects have to use the artificial pancreas 24/7 throughout the studies. The unique feature of the artificial pancreas designed by Dassau et al is the integration of controlling algorithm and cloud-based server into the devices; thus, patients' data will be automatically uploaded into the server. Based on the data, each patients' basal insulin delivery settings will be changed each week.

After 12 weeks of using the artificial pancreas device, it was found that all 29 patients showed improvement in their HbA_{1c} percentage. HbA_{1c} percentage is the percentage of non-enzymatic attachment of glucose to proteins, in this case the haemoglobin found in human blood and it is directly proportional to patients' blood glucose level. According to World Health Organization, a person is considered diabetic if their HbA_{1c} percentage is 6.5% or above. In the article, subjects HbA_{1c} improved from averaging $7.0 \pm 0.8\%$ to $6.7\% \pm 0.6\%$ after 12 weeks of using the artificial pancreas device. Even though it is still in the diabetic range, it showed a promising potential in maintaining patients' blood glucose level. Furthermore, the studies showed that subjects

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spent less time in the hypoglycemic range while using the artificial pancreas. Even though the system showed promising potential, it is still not yet perfect; Dassau et al. (2017) mentioned in the article that “10% of adaptation recommendation were manually overridden” (p. 1719).

Even with the initial success that artificial pancreas received, it is still not readily adaptable for recreational purposes; Turksoy et al. (2017) mentioned that monitoring blood glucose level while performing physical activities can be a major challenge in the development of artificial pancreas. Thus, it was proposed that biometric physiological variables such as heart rate, heat flux, skin temperature, near-body temperature, and galvanic skin response be included in the artificial pancreas system; the main objective was to find which biometric physiological variables has the strongest correlation with the changing of blood glucose level (Turksoy et al., 2017). The correlation was tested by using partial least square (PLS) regression and variable importance in projection (VIP) method. Out of all listed biometric physiological variables above, skin temperature was found to have the strongest correlation with blood glucose level. Turksoy et al. (2017) suggested that skin temperature should be considered to be included into artificial pancreas system.

Although most of the research associated with artificial pancreas lean towards type 1 diabetes patient, there are recent studies conducted in the application of closed loop artificial pancreas on type 2 diabetes patient. As mentioned above, Khan et al (2017) argues that continuous glucose monitoring and thus artificial pancreas is not compatible with type 2 diabetes “because of the fact that Type 2 diabetes patients are more likely to measure their BGL with self-monitoring blood glucose (SMBG) which are taken once or twice daily at home by the patients themselves” (p. 392). But researchers from the University of Cambridge did not agree to the argument proposed by Khan et al; Kumareswaran et al (2014) conducted a feasibility studies in regards to the application of

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closed loop insulin delivery on type 2 diabetes patient. In the article, Kumareswaran et al used the word closed loop insulin delivery to describe their method instead of artificial pancreas even though it is identical. The research conducted by Kumareswaran et al was initiated by having 12 subjects with type 2 diabetes to undergo two 24 hours visit; subjects underwent closed loop insulin delivery on their first visit while on the second visit subjects underwent a controlled treatment in which patients was treated via conventional method. 7 of the subjects are male with an average age and BMI to be 57.2 years and 30.5 kg/m^2, respectively; the average years of subjects having diabetes is 7.6 years. The result of both the closed loop and controlled treatment were then compared to each other; the feasibility study showed that using closed loop insulin delivery (artificial pancreas) increases the time (40% in 24 hours) that blood glucose level stays in normal range as compared to patient that did not used the closed loop insulin delivery (24% in 24 hours). In addition to that, there is no apparent risk of subjects having hypoglycemia when subjects underwent the closed loop insulin delivery therapy. Kumareswaran et al. (2014) mentioned that the most significant discovery obtained from the studies is the “overnight glycemic control [blood glucose range when subjects were asleep] achieved with closed-loop system was comparable to that previously shown in adults with type 1 diabetes (time in target 78 vs 76%)” (p. 1201). Even though the overall glycemic control (time in normal blood glucose range) between type 1 and type 2 diabetes patient is slightly different, the similarity in overnight glycemic control indicates that artificial pancreas may be suitable for type 2 diabetes patient; at the same time, more research is still need to be done in the compatibilities of artificial pancreas with type 2 diabetic patient.

Khan et al. proposed argument on the incompatibilities of artificial pancreas with type 2 diabetes patient occurs three years after the feasibility studies was conducted by Kumareswaran et al, yet the latter’s article was not mentioned in the former’s reference.

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Thus, it can be concluded that Khan et al may not be aware of the research done by Kumareswaran et al.

4.5 Improvement of Diabetes Monitoring

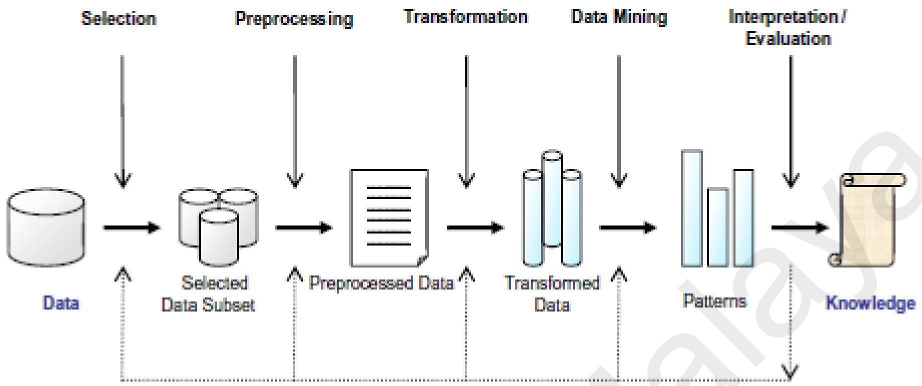

Figure 4.2: Knowledge Discovery in databases (KDD)process (Kavakiotis et al., 2017, 106)

The monitoring of blood glucose can be significantly improved by integrating artificial pancreas to machine learning mechanism. As shown above, Dassau et al. integrated the artificial pancreas with cloud computing in order to change patients' basal insulin delivery settings on a weekly basis without the intervention of clinician. Figure 4.2 above shows the knowledge discovery in databases (KDD) process; the process explains how data obtained from a patient is ultimately converted into knowledge. Out of the 5 steps outlined above, the most important step is the data mining because it is the step where the machine learning algorithm analyses the data; it processes the data and turn it into discernible pattern (Kavakiotis et al., 2017, p. 106). If the credibility of the developed machine learning algorithm is high, then this mechanism can be helpful to patient as they will not have to constantly monitor their blood glucose level.

As shown in chapter 2 section 2.3, each percentage of HbA1c corresponds to different mean glucose level and in this project, and the diagnostic diabetes range was used for monitoring purposes because each patient hyperglycemic range varies; thus, machine learning algorithm such as artificial neural network can be combined with the fuzzy logic system to adjust patient’s blood glucose level range without physician’s consultation.

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CHAPTER 5: CONCLUSION

Fuzzy logic system developed in this project is shown to be able to monitor the blood glucose level of a patient by indicating the condition of the patient at certain level. The result shows that the system predicted condition is almost similar to the real condition, with the percent accuracy of 83%. The complication of this project occurred when it was found that every patient will have different hyperglycemic level and thus the blood glucose range for diagnostic purposes was used; nevertheless, the blood glucose range in the system can be easily change without deep understanding of abstract mathematics. Another complication occurred in the project is patient’s metabolism rate; physical activities affect the metabolism rate of a patient and thus affect the second input of the system, which is time after meal. The solution for this problem is to add a third input variable with the help of expert. Furthermore, the emerging of machine learning will help in adjusting the blood glucose range without physician’s input. In the future, the fuzzy logic system developed in this project can be combined with machine learning algorithm such as neural network system to improve patient’s blood glucose level.

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REFERENCES

Adidela, D. R., Devi G., L., Suma G., J., & Allam, A. R. (n.d.). Application of Fuzzy ID3 to Predict Diabetes. *International Journal of Advanced Computer and Mathematical Sciences,3*(4), 2012th ser., 541-545. Retrieved March 27, 2018.

American Diabetes Association. (2018). 6. Glycemic Targets: Standards of Medical Care in Diabetes 2018. *Diabetes Care,38*(Supplement_1), 55-64. doi:10.2337/dc15-s009

Baig, M. M., Gholamhosseini, H., Kouzani, A., & Harrison, M. J. (2011). Anaesthesia monitoring using fuzzy logic. *Journal of Clinical Monitoring and Computing,25*(5), 339-347. doi:10.1007/s10877-011-9315-z

Cade, W. T. (2008). Diabetes-Related Microvascular and Macrovascular Diseases in the Physical Therapy Setting. *Physical Therapy,88*(11), 1322-1335. doi:10.2522/ptj.20080008

Cryer, P., Davis, S., & Shamoon, H. (2003). Hypoglycemia in Diabetes. *Diabetes Care*.

Dassau, E., Pinsker, J. E., Kudva, Y. C., Brown, S. A., Gondhalekar, R., Man, C. D., . . . Doyle, F. J. (2017). Twelve-Week 24/7 Ambulatory Artificial Pancreas With Weekly Adaptation of Insulin Delivery Settings: Effect on Hemoglobin A 1c and Hypoglycemia. *Diabetes Care,40*(12), 1719-1726. doi:10.2337/dc17-1188

Diabetes: Your A1c Test. (2012). Retrieved May 23, 2018, from https://www.hap.org/

Definition and Diagnosis of Diabetes Mellitus and Intermediate Hyperglycemia(pp. 1-46, Rep.). (n.d.). World Health Organization.

Feldman-Billard, S., Massin, P., Meas, T., Guillausseau, P. J., & Heron, E. (2010). Hypoglycemia-Induced Blood Pressure Elevation in Patients With Diabetes. *Archives of Internal Medicine,170*(9), 829. doi:10.1001/archinternmed.2010.98

Ganji, M. F., & Abadeh, M. S. (2011). A fuzzy classification system based on Ant Colony Optimization for diabetes disease diagnosis. *Expert Systems with Applications,38*(12), 14650-14659. doi:10.1016/j.eswa.2011.05.018

Gestational diabetes. (2017, April 28). Retrieved April 13, 2018, from https://www.mayoclinic.org/diseases-conditions/gestational-diabetes/symptoms-causes/syc-20355339

Georga, E. I., Protopappas, V. C., Ardigò, D., Polyzos, D., & Fotiadis, D. I. (2013). A Glucose Model Based on Support Vector Regression for the Prediction of Hypoglycemic Events Under Free-Living Conditions. *Diabetes Technology & Therapeutics,15*(8), 634-643. doi:10.1089/dia.2012.0285

Ghazavi, S. N., & Liao, T. W. (2008). Medical data mining by fuzzy modeling with selected features. *Artificial Intelligence in Medicine,43*(3), 195-206. doi:10.1016/j.artmed.2008.04.004

Grant, P. (2007). A new approach to diabetic control: Fuzzy logic and insulin pump technology. *Medical Engineering & Physics,29*(7), 824-827. doi:10.1016/j.medengphy.2006.08.014

University of Malaya

Heianza, Y., Kato, K., Kodama, S., Suzuki, A., Tanaka, S., Hanyu, O., . . . Sone, H. (2014). Stability and changes in metabolically healthy overweight or obesity and risk of future diabetes: Niigata wellness study. *Obesity,22*(11), 2420-2425. doi:10.1002/oby.20855

Horton, E. S. (2009). Effects of Lifestyle Changes to Reduce Risks of Diabetes and Associated Cardiovascular Risks: Results from Large Scale Efficacy Trials. *Obesity,17*(N3s), 43-48. doi:10.1038/oby.2009.388

Kang, S. (2018). Personalized prediction of drug efficacy for diabetes treatment via patient-level sequential modeling with neural networks. *Artificial Intelligence in Medicine,85*, 1-6. doi:10.1016/j.artmed.2018.02.004

Kavakiotis, I., Tsave, O., Salifoglou, A., Maglaveras, N., Vlahavas, I., & Chouvarda, I. (2017). Machine Learning and Data Mining Methods in Diabetes Research. *Computational and Structural Biotechnology Journal,15*, 104-116. doi:10.1016/j.csbj.2016.12.005

Khan, M. A., Peter, J. V., Breen, G. A., Hartley, G. G., & Vessey, J. T. (2000). Diabetes Disease Stage Predicts Weight Loss Outcomes with Long-Term Appetite Suppressants. *Obesity Research,8*(1), 43-48. doi:10.1038/oby.2000.7

Khan, T. A., & Sievenpiper, J. L. (2016). Controversies about sugars: Results from systematic reviews and meta-analyses on obesity, cardiometabolic disease and diabetes. *European Journal of Nutrition,55*(S2), 25-43. doi:10.1007/s00394-016-1345-3

Khan, T., Masud, M. A., & Mamun, K. A. (2017). Methods to predict blood glucose level for type 2 diabetes patients. *2017 IEEE Region 10 Humanitarian Technology Conference (R10-HTC),*392-395. doi:10.1109/r10-htc.2017.8288982

Kovatchev, B., Tamborlane, W. V., Cefalu, W. T., & Cobelli, C. (2016). The Artificial Pancreas in 2016: A Digital Treatment Ecosystem for Diabetes. *Diabetes Care,39*(7), 1123-1126. doi:10.2337/dc16-0824

Kudva, Y. C., Carter, R. E., Cobelli, C., Basu, R., & Basu, A. (2014). Closed-Loop Artificial Pancreas Systems: Physiological Input to Enhance Next-Generation Devices. *Diabetes Care,37*(5), 1184-1190. doi:10.2337/dc13-2066

Kumar, P. S., & Pranavi, S. (2017). Performance analysis of machine learning algorithms on diabetes dataset using big data analytics. *2017 International Conference on Infocom Technologies and Unmanned Systems (Trends and Future Directions) (ICTUS)*. doi:10.1109/ictus.2017.8286062

Kumareswaran, K., Thabit, H., Leelarathna, L., Caldwell, K., Elleri, D., Allen, J. M., . . . Hovorka, R. (2013). Feasibility of Closed-Loop Insulin Delivery in Type 2 Diabetes: A Randomized Controlled Study. *Diabetes Care,37*(5), 1198-1203. doi:10.2337/dc13-1030

Lekkas, S., & Mikhailov, L. (2010). Evolving fuzzy medical diagnosis of Pima Indians diabetes and of dermatological diseases. *Artificial Intelligence in Medicine,50*(2), 117-126. doi:10.1016/j.artmed.2010.05.007

Li, D., Liu, C., & Hu, S. C. (2011). A fuzzy-based data transformation for feature extraction to increase classification performance with small medical data sets. *Artificial Intelligence in Medicine,52*(1), 45-52. doi:10.1016/j.artmed.2011.02.001

University of Malaya

Mathematical Introduction to Fuzzy Logic, Fuzzy Sets, and Fuzzy Controls. (2016). Retrieved April,2018,from https://www.maplesoft.com/applications/view.aspx?sid=1409&view=html

Number of smartphone users worldwide 2014-2020. Retrieved April 5, 2018, from https://www.statista.com/statistics/330695/number-of-smartphone-users-worldwide/

Otto, E., Semotok, C., Andrysek, J., & Basir, O. (2000). An Intelligent Diabetes Software Prototype: Predicting Blood Glucose Levels and Recommending Regimen Changes. *Diabetes Technology & Therapeutics,2*(4), 569-576. doi:10.1089/15209150050501989

Park, J., & Edington, D. W. (2001). A sequential neural network model for diabetes prediction. *Artificial Intelligence in Medicine,23*(3), 277-293. doi:10.1016/s0933-3657(01)00086-0

Qaisar, S. B., Khan, S. H., & Imtiaz, S. (2012). Neural Network and Physiological Parameters Based Control of Artificial Pancreas for Improved Patient Safety. *Computational Science and Its Applications – ICCSA 2012 Lecture Notes in Computer Science,97*, 120-127. doi:10.1007/978-3-642-31137-6_26

Sato, A., & Iwamoto, Y. (2013). Diagnostic criteria of diabetes. *Diabetol International,4*, 77-80. doi:10.1007/s13340-013-0110-6

Schatz, C. H., Schneider, F. K., Abatti, P. J., & Nievola, J. C. (2015). Dynamic Fuzzy-Neural based tool formonitoring and predicting patients conditions using selected vital signs. *Journal of Intelligent & Fuzzy Systems,28*(6), 2579-2590. doi:10.3233/ifs-151537

Simon, G. J., Caraballo, P. J., Therneau, T. M., Cha, S. S., Castro, M. R., & Li, P. W. (2015). Extending Association Rule Summarization Techniques to Assess Risk of Diabetes Mellitus. *IEEE Transactions on Knowledge and Data Engineering,27*(1), 130-141. doi:10.1109/tkde.2013.76

Steil, G. M., Rebrin, K., Darwin, C., Hariri, F., & Saad, M. F. (2006). Feasibility of Automating Insulin Delivery for the Treatment of Type 1 Diabetes. *Diabetes,55*(12), 3344-3350. doi:10.2337/db06-0419

Sudharsan, B., Peeples, M., & Shomali, M. (2014). Hypoglycemia Prediction Using Machine Learning Models for Patients With Type 2 Diabetes. *Journal of Diabetes Science and Technology,9*(1), 86-90. doi:10.1177/1932296814554260

Tsukamoto, Yuuki, et al. "Evaluation of a Novel Artificial Pancreas: Closed Loop Glycemic Control System With Continuous Blood Glucose Monitoring." *Artificial Organs*, vol. 37, no. 4, 2013, pp. 67–73., doi:10.1111/aor.12068.

Turksoy, K., Monforti, C., Park, M., Griffith, G., Quinn, L., & Cinar, A. (2017). Use of Wearable Sensors and Biometric Variables in an Artificial Pancreas System. *Sensors,17*(3), 532. doi:10.3390/s17030532

Tuomilehto, J. (2011). Diabetes Management: A new journal addressing the management issues of a complex disease. *Diabetes Management,1*(1), 1-3. doi:10.2217/dmt.10.7

Vachkov, G. (2000). *Fuzzy control: Synthesis and analysis*(pp. 47-72) (S. S. Farinwata, D. P. Filev, & R. Langari, Eds.). Chichester: Wiley.

University of Malaya

Wang, C., Li, L., Wang, L., Ping, Z., Flory, M. T., Wang, G., . . . Li, W. (2013). Evaluating the risk of type 2 diabetes mellitus using artificial neural network: An effective classification approach. *Diabetes Research and Clinical Practice,100*(1), 111-118. doi:10.1016/j.diabres.2013.01.023

Zheng, T., Xie, W., Xu, L., He, X., Zhang, Y., You, M., . . . Chen, Y. (2017). A machine learning-based framework to identify type 2 diabetes through electronic health records. *International Journal of Medical Informatics,97*, 120-127. doi:10.1016/j.ijmedinf.2016.09.014

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