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Design Fuzzy Control System for Blood Glucose Level for Type-I Diabetes Mellitus Patients Using GA

A Simulation Study

تصميم المتحكم الضبابي للتحكم في نسبة مستوى سكرالدم لدى مرضى السكري من النوع الاول بإستخدام الجينات اللوغاريتمية

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إقـــــرار

أنا الموقع أدناه مقدم الرسالة التي تحمل العنوان:

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بناءً على موافقة شئون البحث العلمي والدراسات العليا بالجامعة الإسلامية بغزة على تشكيل لجنة الحكم على أطروحة الباحث/ **أحمد سليمان عبدالكريم بشير** لنيل درجة الماجستير في **كلية *الهندسة*** **قسم الهندسة الكهربائية – أنظمة التحكم** وموضوعها:

تصميم المتحكم الضبابي للتحكم في نسبة مستوى سكر الدم لدى مرضى السكري من النوع الأول باستخدام الجينات اللوغارتمية

Design Fuzzy Control System for Blood Glucose Level for Type-I Diabetics Mellitus Patients using GA

وبعد المناقشة التي تمت اليوم السبت 28 شوال 1438هـ، الموافق 2017/07/22م الساعة الثانية عشر ظهراً في قاعة مبنى القدس، اجتمعت لجنة الحكم على الأطروحة والمكونة من:

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وبعد المداولة أوصت اللجنة بمنح الباحث درجة الماجستير في **كلية *الهندسة*/ قسم الهندسة الكهربائية – أنظمة التحكم.**

واللجنة إذ تمنحه هذه الدرجة فإنها توصيه بتقوى الله ولزوم طاعته وأن يسخر علمه في خدمة دينه ووطنه.

والله ولي التوفيق،،،

نائب الرئيس لشئون البحث العلمي والدراسات العليا

أ.د. عبدالرؤوف علي المناعمة

Abstract

Biomedical instrumentation is an interesting and demanding area in which many fields are available to be discover and explore. Diabetes mellitus disease is one of the main segments of research area which is being addressed for the decades. One of the main functions of the pancreas is to regulate blood glucose concentration through releasing insulin enzyme. As a results of this deficiency blood glucose level concentrations (BGL) increased. Many researchers are working for diagnosing and treating diabetes mellitus disease. Mathematical models of blood glucose and insulin dynamics are used for this purpose. Through my work a simple mathematical model of the dynamics of glucose and insulin interaction in the blood system developed by Stolwijk and Hardy is used. By using Stolwijk and Hardy model, a closed-loop feed-back system which regulates and manages the blood glucose-insulin will be designed, implemented and analyzed using Matlab/Simulink. Mamdani fuzzy logic algorithm controller (FLC) type is designed for exogenous insulin infusion pump. The control algorithm used expert knowledge about this disease treatment by using Mamdani-type to regulate the blood glucose level (BGL) for type I diabetes mellitus patient (TIDM). The used control strategy based on a continuous insulin infusion closed-loop control system to avoid traditional discrete diabetes mellitus treatment. Fuzzy - Genetic Algorithms controller was designed to deal with this plant through continuous insulin injection pump with choosing suitable membership functions as inputs and outputs for the proposed system in terms of keeping desired steady state plasma glucose level (0.81 mg/ml) against to exogenous glucose input. So a significant response of blood glucose-insulin regulation and management obtained.

ملخص

مرض السكري هو واحد من أهم الأمراض الرئيسية التي يتم تناوله في الأبحاث العلمية منذ عقود وذلك لخطورة هذا المرض إذا لم يتم التعامل معه بالشكل السليم، حيث أن البنكرياس هو العضو المسئول عن تنظيم تركيز السكر في الدم من خلال إفراز انزيم الانسولين . و داء السكري هو مرض مزمن غالباً ما تسببة عوامل وراثية أو نقص في إفراز انزيم الأنسولين أو عدم فعالية الأنسولين المنتج من البنكرياس، هذه الأسباب تؤدي الي زيادة تركيز مستوى السكر في الدم (BGL) مما يلحق الضرر بالعديد من أجهزة الجسم المختلفة وبخاصة الأوعية الدموية والأعصاب. كثير من الباحثين يعملون في هذا المجال من أجل تحسين طرق علاج مرض السكري ويستخدمون لهذا الغرض نماذج رياضية تعبر عن مستوى السكر والأنسولين في الدم. و في هذه الرسالة سوف أستخدم نموذج رياضي بسيط يحاكي آلية تفاعل الجلوكوز والأنسولين في الدم، قام بوضع هذا النموذج الرياضي الباحثين Stolwijk and Hardy ومن خلال إستخدام هذا النموذج، وإستخدام نظام التغذية الراجعة تم تصميم حلقة تحكم مغلقة لتنظيم مستوى السكر في الدم، وإضافة على هذا النموذج الرياضي ومن خلال هذة الرسالة سوف أقوم بإضافة مضخة انسولين لضخ الأنسولين اللازم بشكل مستمر الى الدم عبر الجلد وسوف نتحكم بها من خلال برنامج تحكم. تم تنفيذ هذة الرسالة بإستخدام أحد انواع التحكم وهو التحكم الضبابي Control Fuzzy Logic وتحليل هذا البرنامج بإستخدام MATLAB / SIMULINK . وتم إستخدام Mamdani-type fuzzy logic controller وهو أحد أنواع التحكم المنطقي الضبابي للتحكم في حقن الانسولين بناءاً على الخبرة والمعرفة في عملية تنظيم مستوى السكر في الدم (BGL) وسوف يتم تطبيق هذا المشروع أو المتحكم على نموذج رياضي يحاكي عمل البنكرياس الطبيعي مع فارق وجود خلل أو قصور في عمل هذا البنكرياس لإيجاد حالة مرضية من النوع الأول (TIDM) لمرضي السكر اللذين تتم معالجتهم عن طريق حقن الأنسولين. وأخيرا سوف أستخدم Fuzzy - Genetic Algorithm controller لإختيار المدخل الأفضل الى نظام التحكم.

قال تعالي:

وَيَسْأَلُوْنَكَ عَنِ الرُّوْحِ قُلِ الرُّوْحُ مِنْ أَمْرِ رَبِّيْ وَمَا أُوْتِيْتُمْ مِنَ الْعِلْمِ إِلاَّ قَلِيْلاً

صدق الله العظيم

[الاسراء:85]

Dedication

I dedicate my dissertation work to my family especially for the spirit of my father and my mother who their encouragement words ring in my ears and push me for tenacity. A special feeling of gratitude to my wife who have never left my side. I also dedicate this dissertation to my friends who have supported me throughout my work. I will always appreciate all they have done. Last and not least I dedicate this work to my wonderful sons Amr and Yousif. Both of you have been my best cheerleaders.

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At the beginning, I would like to thank ALLAH who helped me to accomplish this thesis and everyone who made this thesis possible and helped me all along the way with their support, expertise and friendship.

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Finally, I want to thank my family for their unconditional love and unlimited support.

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List of Abbreviations

BGL	Blood glucose level
FLC	Fuzzy logic control
BG	Blood glucose
GA	Genetic Algorithm
WHO	World Health Organization
IDF	International Diabetes Federation
T1DM	Type 1 diabetic mellitus
PID	Proportional-integral-derivative controller
IDDM	Insulin dependent diabetes mellitus
NIDDM	Non-insulin dependent diabetes mellitus
FPG	Fasting plasma glucose test
FL	Fuzzy Logic
MF	Membership function
FLS	Fuzzy logic system
C-O-A	Centre-of-Area
C-O-G	Centre of gravity
C-O-M	Centre-of-Maximum
M-O-M	Mean-of-Maximum
AI	Artificial Intelligence

Chapter 1

Introduction

Chapter 1
Introduction

1.1 Overview

Diabetes mellitus is a chronic disease of blood glucose-insulin regulatory system which resulting from pancreas failure in keeping the concentration of blood glucose between the ranges of 70-110 mg/dl (0.7–1.1 mg/ml). World Health Organization (WHO) estimates that 347 million people throughout the world Having diabetes and the diabetes is expected to be one of main leading cause of death in 2030 (Soylu, S., Danisman, K., Sacu, I., & Alci, M., WHO Diabetes, 2013). Diabetes consider one of the main segments of biomedical signal processing researches. Regulating and maintaining blood glucose level is the basic function of pancreas through insulin secretion. Blood glucose level is affected by food intake, digestion rate, exercise etc. After meals the BGL increases. Pancreas beta cells are stimulated to secrete insulin. The insulin secreted by pancreas inhibits the glucose concentration excessively. The blood glucose regulation is succeeded by glucose consumption of muscle cells or convert glucose to glycogen molecules which stored in liver and muscle cells. The other hand, in order to avoid excessively decreasing of BGL where there are no meals or during sleep, the alpha cells of the pancreas secrete glucagon. This interaction of insulin and glucagon regulates the BGL in the body (Thomas, B., Riverside, C., Stephen, A., & Pomona, C., 2001, Dua, P., Doyle, F, & Pistikopoulos, E., 2006).

For a healthy person, the regulation of blood glucose concentrations can be described by the simplified mechanism illustrated in figure 1.1, blood glucose concentrations are kept in balance around normal rang mainly 70-100 mg/dl due to insulin and glucagon hormones effects. These hormones insulin and glucagon are produced by beta- and alpha-cells of pancreas, respectively. If blood glucose level increases, for instance because of a meal, insulin release is stimulated. This insulin mediates the uptake of glucose from the blood to be stocked in the liver and muscles in the form of glycogen, thus reducing BG concentrations to a normal level. On the other hand if blood glucose concentration is low, glucagon is released by the pancreas. Glucagon stimulates the release of the stored glycogen from the liver and muscles to the

bloodstream, thus increasing BG concentration. This explanation is, of course, an oversimplification as the exact mechanisms are more complex and involve several hormones and external influences. Nevertheless, it is widely admitted that insulin and glucagon are the most significant actors in glucoregulation. Diabetes appears if this equilibriums disrupted and BG concentration cannot be lowered in an effective way anymore.

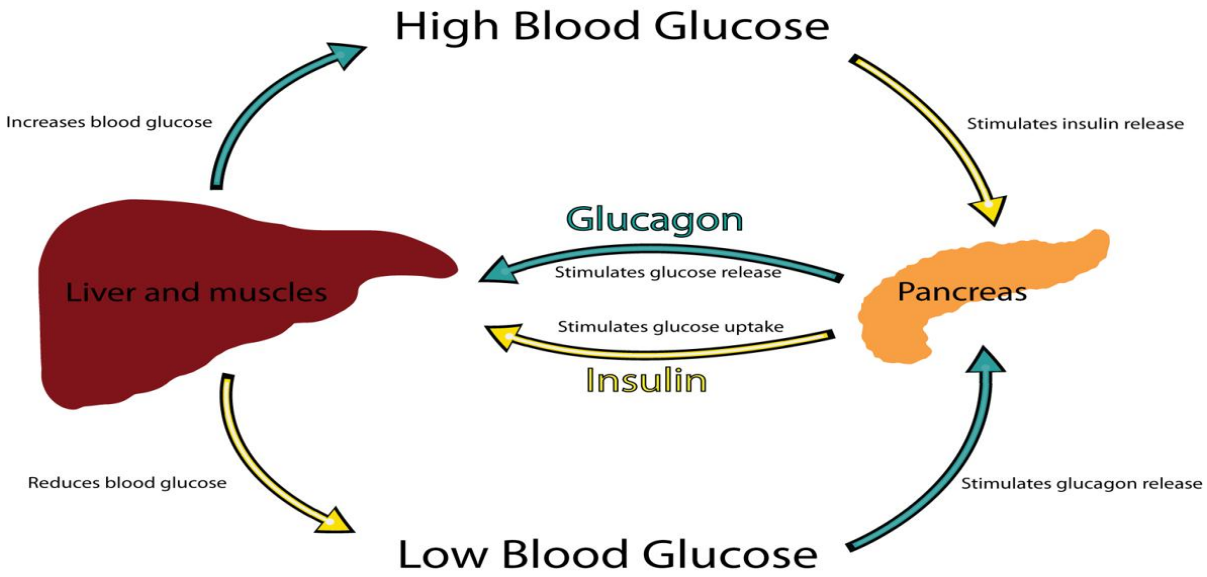


Figure (1.1): BG regulation mechanism in a healthy person.

Type -1 and Type-2 diabetes are two types of diabetes disease. Type - 1 diabetes caused as a result of beta cells which destructed by immune system. Type - 1 diabetes is more common in children and adolescents. On the other hand, more than 90 percent of diabetes patients are type II diabetes. In type - II diabetes, the insulin produced by the pancreas does not function properly well due to the resistance against insulin. The complications resulting from diabetes are; neuropathy, blindness, nephropathy, and other long term vascular complications (Cobelli, C., Dalla, C., Sparacino, G., Magni, L., De Nicolao, G., & Kovatchev, B., 2009). Low insulin producing as a result of pancreas deficiency leading to, high BGL in which we consider type I diabetics, those patients need external insulin to support and management glucose blood level. External insulin infused at an appropriate rate to keep normal ranges of BGL. Patients

need external insulin to support and management glucose blood level. External insulin infused at an appropriate rate to keep normal ranges of BGL.

The current method which used to measure BGL and also current medical treatment method to maintain and regulate blood glucose level is unsuitable and painful. Moreover it is difficult to give the patient the right amount and type of insulin.

Nowadays a lot of researches are being performed to overcome this deficiencies of the current medical treatments. In this study, I will focus on closed-loop control algorithms for insulin injections. Closed-loop control system includes BG sensor, mechanical pump and controller. To maintain BGL in a normal range the measured blood glucose data from glucose sensor should be transmitted to a control system which determines the required insulin injection rate. Then by mechanical pump the desired insulin amount could be delivered to the system. To maintain the BGL in normal ranges, the closed-loop system is more trustworthy since it simulates the normal pancreas behaviour very closely as shown in Figure 1.2.

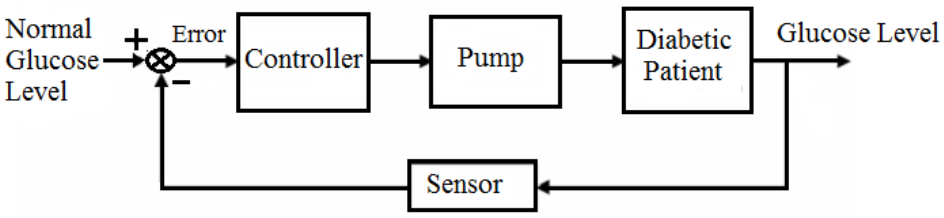


Figure (1.2): Closed-loop control of diabetic patient

1.2 Motivation

The incidence of both types of diabetes, especially type 2, increases at an alarming rate on a global scale. In year 2000, WHO estimated 171 million to be affected. International Diabetes Federation (IDF) estimated the number to 366 million (of which 183 million are undiagnosed), (International Diabetes Federation, 2012), already exceeding the 2030 forecast from WHO in 2000. By 2030, the expected number exceeds 500 million in IDF's recent analysis (International Diabetes Federation, 2012).

In 2012, more than 371 million people (International Diabetes Foundation 2011). This enormous, and constantly increasing prevalence generates global health care expenditures estimated around 470 billion USD in 2011 and expected to rise to be 600 billion USD by 2030. Also the complications from either very low glucose values,

hypoglycaemia, which may lead to coma, acute seizure and death. On the other hand very high blood glucose level concentrations, hyperglycaemia, which, over a longer time period may lead to include heart disease, vascular disease , blindness, stroke, nerve damage, kidney disease, and amputation. These long complication terms reduced expected life, increasing disability and society health costs. So all these figures highlight the primordial importance of research in diabetes prevention and care and essential needed to build a control system to improve the control system for these patients and to cut back the grow thing rate of monetary and physiological costs of this disease.

1.3 State of the Problem

1.3.1 Closed Problem

Diabetic people suffer from metabolic disorder in which insulin cannot properly perform its role. Diabetic patients cannot produce enough insulin which is needed to convert glucose into needed daily life energy. Scientists are focusing their efforts to develop new techniques and feasible instrumentation to offer wearable solutions and improve the life of patients. So all insulin dependent patients are need an external source of insulin to be infused at a suitable rate to maintain blood glucose level. The blood glucose level should be controlled within normal range of 70-110mg/dl.

1.3.2 Current medical treatment

Daily, several measurements of BGL being done and external injection of equal amount of insulin subcutaneously are given in the current medical treatments, but this method is unsuitable and painful. Moreover, it is difficult to deliver the right amount and type of insulin.

1.3.3 Proposed Solutions

Many models have been proposed to reproduce the glucose-insulin dynamics, such a model offers a powerful tool for generating predictions and clinical decision in diabetes care. In (Soylu et al, 2013), these models are used to design and test the

designed control algorithm. Once the insulin delivery rate is controlled the blood glucose level has been controlled. So by using one of these models closed-loop feed-back system will be designed and analyzed in order to maintain and regulate blood glucose – insulin level, using Matlab/Simulink. A Mamdani type fuzzy logic controller used for exogenous insulin infusion.

1.4 Thesis Objective

Diabetes Mellitus patients especially with type 1 should check there blood glucose level continually, but actually they don't, they used to inject subcutaneous Insulin dose daily as a routine without previous information about the blood glucose level, although this patient may need more or less Insulin dose. Thus, it was necessary to think about a good control system to monitor the BGL and then regulate the Insulin injection into the blood to keep blood glucose within normal range.Building a hybrid control system to cut back the progression of the disease, give proper BGL monitoring and protect the patient from health situation deteriorating.

1.5 Contributions

This thesis proposes to improve the treatment of T1DM while addressing most of the aforementioned. In order to develop and contribute in automatic insulin delivery system working under various conditions, a mathematical blood glucose and insulin dynamics interaction model developed by Stolwijk and Hardy will be used. In this thesis I will modify this model by adding insulin pump and used it with closed-loop feed-back system to regulate and manage the blood glucose-insulin. This will be implemented and analysed using Matlab/Simulink. I will use Fuzzy & Fuzzy - Genetic Algorithm to find better solution for our problem.

1.6 Literature Review

In this study, I used closed-loop control system to maintain and regulate blood-glucose concentration. Closed-loop control system consist a glucose sensor, a controller and a mechanical pump. The measured blood glucose concentration by glucose sensor would be transmitted to a control system which determines the required injection rate of insulin to keep the blood glucose concentration in a normal range **(**Soylu et al, 2013).

In the control terminology, the diabetic patient is identified as a system. So as to study and analyse the effect of glucose and insulin regulation, a model of pancreatic function is required. So modified Stolwijk-Hardy glucose insulin interaction model is used Soylu et al, 2013). Modified model was derived by adding an exogenous insulin infusion pump.

In my study, a closed-loop system which utilizes modified Stolwijk-Hardy glucose insulin interaction model is considered. A Mamdani type fuzzy logic algorithm (FLC) controller was used for exogenous insulin infusion pump. Simulations are performed to assess control function in terms of keeping desired steady state plasma glucose level (70-110 mg/dL range) against to exogenous glucose input. The simulation results are shown and significant in terms of controlling blood glucose level. (Soylu et al, 2013).

Fuzzy logic control system allows capturing more valuable information about the behavior of the controlled system variable and it can be good guide that helps us to discover artificial pancreas. Furthermore, fuzzy logic controllers have shown relatively successful results comparing with the renowned classical controller. Fuzzy based controllers to maintain normal range of BGL were designed in (Li, C., & Hu, R., 2009).

The desired insulin amount could be delivered by a mechanical pump. The closed-loop system must be reliable and trustworthy since it simulates the normal pancreas behaviour very closely. (Ahmed, J., & Alvi, B., 2008).

In (Ahmed et al, 2008) the author try to create a appropriate visualization of blood glucose –insulin management for diabetic patients by using modified Stolwijk and Hardy dynamic model.

In (Li, C., & Hu, R., 2007) the author discusses the insulin infusing development technique for open-land closed loop method But in his study the author didn't mention to the controller type that used.

The steady state blood glucose concentration for any normal or diabetic’s person is determined by existing amount of insulin. So, insulin injection is required to lower the BGL in diabetics. The controller determines the amount of insulin infusion rate based on the measured glucose concentration. The exogenous insulin infusion, which is

mentioned above, is added to the model to keep under control the BGL in a tight range around the steady state BGL of normal adults. Many different algorithms have been proposed to control the BGL in diabetics through the usability of mathematical models .Some of these algorithms employ proportional-integral derivative. Classical control techniques are inadequate for controlling such systems. These techniques are unrealizable in practice and inapplicable to a real patient (Grant, P., 2007). So this complex control problem could be solved by the help of fuzzy logic.

In (American Diabetes Association, 1996) the use of intravenous route discussed for insulin delivery to insulin-dependent diabetic patients. In this study, both the two control algorithms of insulin injections are discussed. In open-loop predetermined amount of insulin deliver to the patient and the amount of insulin is based on the insulin curve of the normal pancreas secretion. The purpose of the control system is to make the blood glucose level stability using closed-loop method. The closed-loop system method is a new and reliable direction, and it can maintain human blood glucose ideally.

1.7 Thesis Outline

Thesis outline as follows:

- Chapter 2 Introduces a brief introduction of diabetes mellitus and diabetes care, studying the specific main functions of the pancreatic, the effect of glucose and insulin regulation**.**
- Chapter 3 introduces a brief introduction of fuzzy logic control.
- Chapter 4 introduces a brief introduction of genetic algorithm.
- Chapter 5 introduces modified Stolwijk-Hardy glucose insulin interaction model.
- Chapter 6 introduces application and result. Results are compared.
- Conclusion is drawn in chapter 7 and an outlook on possible future work is given.

Chapter 2

Diabetes Mellitus

Chapter 2

Diabetes Mellitus

2.1 Anatomy

2.1.1 Enzymes

Chemical reactions within living organisms are very important for life management. Such as food uptake nutrition reactions, cells water utilization through tissue, immune system reaction, pH level management, and blood salt - sugar concentration. Most of these reactions are carried out spontaneously, some of these reactions require catalyst for initiate or to carry out fast. These catalysts are mainly proteins called enzymes. The glucose regularly process affected by these enzymes as they decrease the energy which needed for biochemical reaction (Knudsen, I. S., 2013). These enzymes are hormones of glucagon and insulin. These hormones are responsible for the management and regulation of blood parameters levels. Insulin is responsible for keeping blood glucose concentration within normal range. On the contrary to insulin, the glucagon hormone which maintain and keeping blood glucose concentration from decreasing by converted the stored glycogen into glucose.

2.1.2 Pancreas

Pancreas is very important human organ which has an important and significant role in blood glucose-regulatory system which secreted insulin and glucagon hormones. **Figure 2.1** show the pancreas organ location.

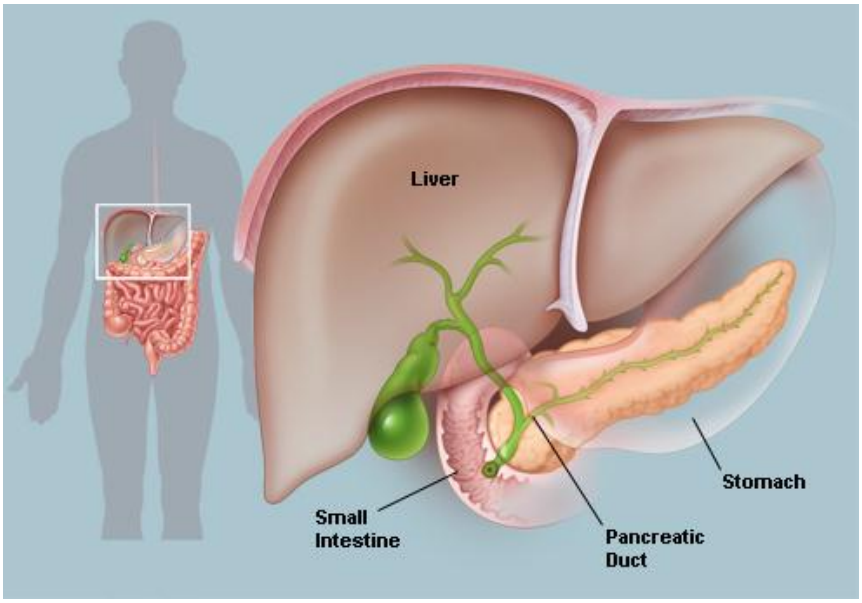


Figure (2.1): illustration and location of the pancreas.

Pancreas contribute in digestion process in small intestine, and consider an endocrine gland which secreting hormones insulin and glucagon. Pancreas consist of two tissue types, dark-staining cells related to the digestion process, and lighter-stained cell-clusters called the Islet of Langerhans (Knudsen, et al, 2013). The Islet of Langerhans are pancreatic regions. (Longnecker, D. S., 2014). There are five types of cells inject the secreted hormones into the blood stream. Such as a- cell type which secreted glucagon hormone and b-cell type that secreted insulin hormone.

2.2 Overview

At the interface between biological sciences and engineering disciplines can be found an interesting set of problems most easily classified as biosystems. Further subdivision of these systems yields problems addressing biomedical and biotechnical issues. Biomedical is related to medicine or the human patient, whereas the biotechnical issues deal with non-human organism. These biosystems offer a challenging set of modeling and regulation problems to the biological, medical and engineering communities. Biomedical problem of glucose regulation using different control strategies in diabetes patients is the focus of this study.

Diabetes mellitus disease consider public, global health problem and death leading cause of in many parts of the world **(**Soylu et al, 2013).

Design an automated closed-loop insulin delivery system is one of the approaches that attempts to find methods for diagnosing and treating diabetes disease, this automated closed-loop insulin delivery system can improve the blood glucose control in diabetic patients. This automated closed-loop insulin delivery system can mimic the activity of a normal pancreas and is capable of maintaining physiological BG levels for insulin-dependent diabetic patients. Such this artificial pancreas system can maintain glucose control without finger-stick blood glucose measurements, subcutaneous insulin injections, or hypo-glycemic/hyperglycemic events, thereby, dramatically improves the quality of life for an insulin-dependent diabetic patient. The artificial pancreas is a system of integrated devices containing only synthetic materials, which substitutes for a pancreas by sensing plasma glucose concentration, calculating the amount of needed insulin, and then delivering the correct amount of insulin. Such device is comprised of a glucose monitoring sensor, an insulin pump, and a controller

to regulate the pump to deliver the insulin in order to maintain nor-moglycemia in presence of sensor measurements. **Figure 2.2** shows a basic block diagram of this type of closed-loop control for the regulation of glucose levels. In this figure, a controller receives the difference between the glucose set point (desired BG) and the glucose reading, and uses this information to continuously adjust the rate of insulin delivery. (Chen, J., Cao, K., Sun, Y., Xiao, Y., & Su, X., 2008, Sasi, A. Y. B., & Elmalki, M. A., 2013).

The automated closed-loop insulin delivery system is similar to the healthy human pancreas, the research's aim is to design a device that functions as an artificial pancreas with good quality controller.

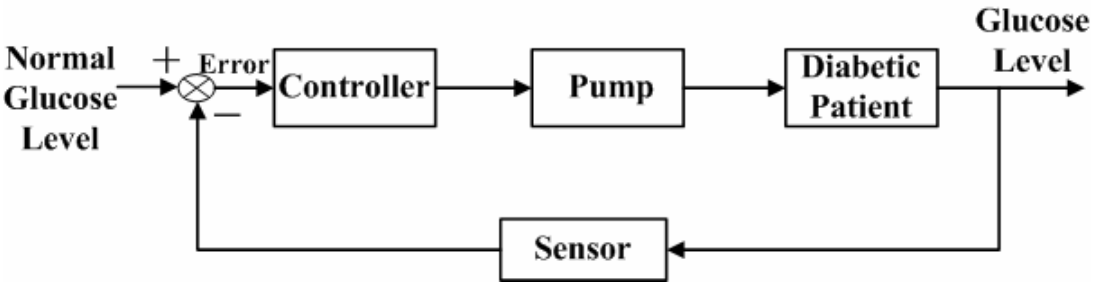


Figure (2.2): Block diagram of closed-loop insulin delivery system.

Pancreas is a human organ that present beside your stomach which secrete insulin hormone. Diabetic patient, pancreas either cannot uses the insulin in correct way, produce enough insulin, or both. This deficiency results in increased blood glucose concentration, which lead to damage many body systems, especially blood nerves and vessels. Insulin help glucose to enter the body's cells to be burned for energy. If the insulin not functioning properly well in the body, the glucose cannot enter the body cells. This causes increased in blood glucose concentrations, creating a condition of cells without fuel **(**Soylu et al, 2013).

Diabetes divided into two types, Type I & Type II. **Type I diabetes**, called insulin dependent diabetes mellitus (IDDM), and is usually diagnosed in children and teenagers. In Type I diabetic, blood glucose concentration rises beyond the normal range (70-110 mg/dl) due to pancreas insufficient insulin secretion from Langerhans beta cells. **Type II diabetes**, called non-insulin dependent diabetes mellitus (NIDDM), is usually diagnosed in adult-onset people and consider most common

form of diabetes. This form of diabetes usually begins with a condition in which fat, insulin resistance, muscle and liver cells do not use insulin properly.

2.3 Glucose and Insulin regulation system

Role of pancreas in healthy person is to regulate and maintain blood glucose levels, as **Figure 2.3** show. Blood glucose level is regulated with two paths. Firstly when the glucose levels falls due to physical activity (e.g. exercise), it stimulates α-cells of pancreas which turn signals the liver to deliver the stored glucose (glucagon) into the blood stream to regulate and maintain glucose concentration in the within normal range (70-100 mg/dl). Secondly, when the blood glucose level rises by meal intake, it stimulates the β-cells of pancreas to release insulin. Insulin acts as a funnel for glucose to enter cells, and glucose is taken up by cells to return to normoglycemic range. Malfunctioning of pancreas is the cause for diabetes. Due to that, glucose level goes beyond the normoglycemic range in diabetics. In such patients, monitoring the glucose level and administering insulin are vital. Present study is to develop closed loop devices (referred as artificial β-cells) to mimic the action of pancreas (Soylu et al, 2013).

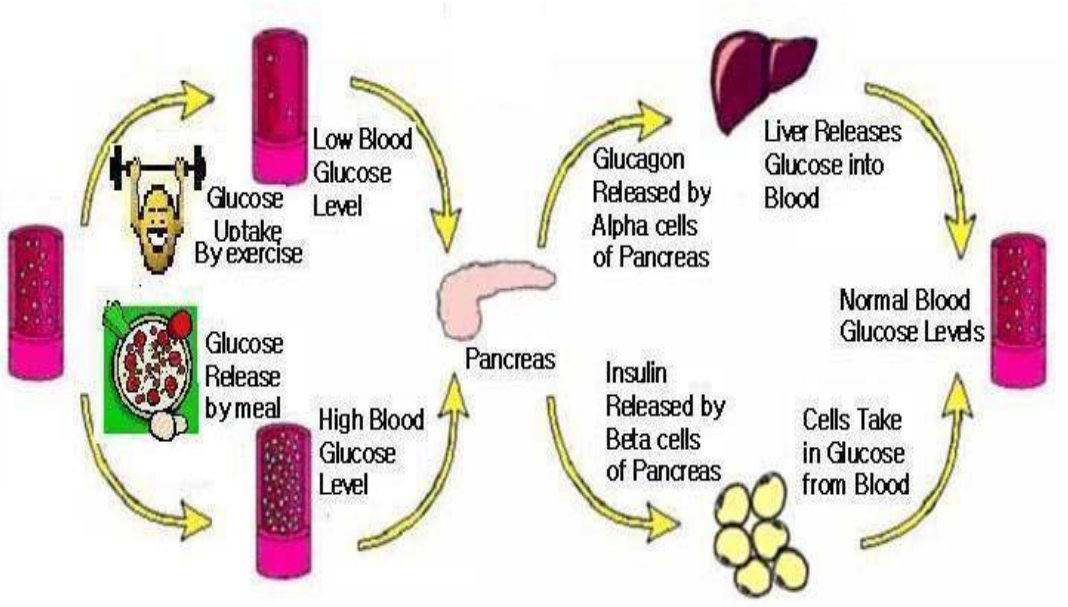


Figure (2.3): The glucose-insulin regulatory system

2.4 Diabetes Types

There are two common forms of diabetes: **type I and type II**

- **Type I**: Type I diabetes (formerly known as insulin-dependent) due to damage of Beta cells of pancreas which are consider the type I disease insulin occurred. As a result of insulin absence in blood because pancreas produce little or no insulin, so sugar in blood cannot get into the body's cells to be uses as energy. So diabetes patients type I must be injected by insulin to maintain and regulate their blood glucose concentration. Diabetic type I usually affects young people aged 20-30 years, but maybe occured at any age **(**Soylu et al, 2013).
- **Type II**: (formerly named non-insulin-dependent), in type II diabetes the pancreas produce insulin, but it maybe not enough or not work properly. This type sometimes can be controlled with a combination of certain diet, exercise and management of weight. However, sometime it is necessary to treatment through medications. Generally, people aged over 40 and overweight have the ability to affect by type II diabetes.

2.5 Causes of diabetes

Until this time the real reasons that causes diabetes are unknown, may these factors increase chance of getting diabetes (Joslin Diabetes Centre, 2013):

- Inherited factors or old history tendency
- Overweight
- Surgery or illness
- As a side effect of use some medications, such as steroid and blood pressure medications
- Injury to pancreas, such as infection, tumour and surgery
- Autoimmune disease
- Blood pressure disease
- Age, so the risk is increased with age
- Smoking
- Pregnancy

2.6 Diagnosed of diabetes

Fast plasma glucose test (FPG) is common way of diagnosing diabetes. FPG measures blood glucose level after fasting for 10 to 12 hours. The normal value of blood fasting glucose is between 70 and 110 mg/dl for normal people.

Main standard features of diabetic diagnoses are:

- Fasting blood glucose concentration is of 125 mg/dl or higher on two separate occasions; or
- Random blood glucose concentration is of 200 mg/dl or greater with common symptoms of diabetes, such as:
  - Increased thirst
  - Frequent number of urination
  - Increased the feeling of hunger
  - Fatigue
  - problem in vision
  - Weight losing
- On occasion, an oral glucose tolerance test may aid in the diagnosis of diabetes or an earlier abnormality that may become diabetes - called impaired glucose tolerance. HbA1c test, which measure the average percentage of glycated haemoglobin in blood. This test show the levels of blood sugar 2 to 3 months ago. It is good for giving idea for treatment plan. (Joslin Diabetes Centre, 2013).

2.7 Diabetes mellitus long - term complications

- **Eye disease** (**Retinopathy**): diabetic patients must regularly see an ophthalmologist for eye checking.
- **Kidney disease** (**Nephropathy**): Urine analysis yearly should be performed, regular blood pressure should be checked and keeping under 130/80 in adults to avoid nephropathy.
- **Nerve disease** (**Neuropathy**): diabetic patients are considered at high risk to have neuropathy, since they don't feel good their feet, the diabetic foot is the major

cause ulcer so that diabetic patients should check their feet daily for redness, or breakdown in skin tissue. [American Diabetes Association. A1C. Accessed (2013)].

2.8 Managing Diabetes

There is no cure for diabetes, but it can be treated and controlled. The goals of managing are:

1. To keep medication balance with food intake and activity.
2. Regulate blood lipid profile at normal ranges.
3. Control your blood pressure.

Other keys to managing your diabetes:

- Eating planning
- Regular exercises
- Take treatment on time
- Regular blood test and visit your doctor [American Diabetes Association. A1C. Accessed (2013)].

2.9 Insulin

Diabetes mellitus consider chronic disease which can be controlled by medical treatments and lifestyle adjustments. To prevent or minimize complications blood sugar levels must be under control. Insulin is an effective treatment for type 1 diabetes as it manage and maintain the blood glucose level to be normal, so insulin injection treatment compensates the lack of natural insulin. Insulin hormone secreted by pancreas that allows your body to use glucose from carbohydrates in the food for energy or to store glucose for future use. By insulin blood glucose level concentration maintain from getting too high (hyperglycemia) or too low (hypoglycemia). The cells in our body need glucose for energy. After meals the blood glucose level rises, beta cells in the pancreas are signaled to release insulin into our bloodstream. Insulin then attaches to and signals cells to absorb glucose from the bloodstream. Insulin considered a key which unlocks the cell to allow glucose to enter the cell and be used

for energy. If our body have more sugar than it needs, insulin enzyme help for storing the exceed sugar in our liver and releases it when needed, such as in between meals or during physical activity. If human body does not produce enough insulin or body cells are resistant to the effects of insulin, you may develop hyperglycemia (high blood glucose), which maybe cause long-term complications (Joslin Diabetes Centre, 2013).

2.9.1 Insulin Treatment for Diabetes

In diabetic patients type I insulin-producing cells of the pancreas (beta cells) are damaged or destroyed. So those patients need insulin injections to maintain blood glucose level and avoid complications from hyperglycemia.

In diabetic patients type II diabetic patients do not respond well or are resistant to insulin. They need insulin injections to maintain blood glucose level and to prevent long-term complications. Patients with type II diabetes may first be treated with oral medications with diet and exercise. This disease type is a progressive condition, the longer the patients have it, the more require insulin need to control and maintain blood glucose level.

2.9.2 Types of Insulin

- **Rapid-acting insulin**: approximately 15 minutes after injection it starts working and peaks at approximately 1 hour but continues to work for two to four hours. Usually it taken before a meal and in addition to a long-acting insulin.
- **Short-acting insulin:** approximately 30 minutes after injection it starts working and peaks at approximately 2 to 3 hours but will continue to work for three to six hours. This is usually given before a meal and in addition to a long-acting insulin.
- **Intermediate-acting insulin:** approximately 2 to 4 hours after injection It starts working and peaks approximately 4 to 12 hours later and continues to work for 12-18 hours. This is usually taken twice daily and in addition to short-acting or rapid insulin.

- **Long-acting insulin:** after several hours after injection it starts working and works for approximately 24 hours. Often used if necessary in combination with short-acting or rapid insulin (Joslin Diabetes Centre, 2013).

2.9.3 The role of insulin in the body

Good understanding of how insulin affects blood glucose can get better manage condition. Often insulin therapy is an important role of diabetes treatment. Understand the key role insulin plays in managing blood glucose. **Figure 2.4**, Show how insulin normally works in the body and what happens when you have diabetes

- **Regulate sugar in your bloodstream**, main function of insulin is to keep blood glucose concentration within a normal range. After meal, carbohydrates break down into glucose, so glucose level in blood is increased, so pancreas be simulated and produce insulin, which allows glucose to enter the tissues.
- **Storage of excess glucose for energy**. After meal glucose level in blood increased, so glucose is stored in the liver in form of glycogen. Between meals, when glucose levels are low, the liver releases glycogen into the bloodstream in the form of glucose. Such process keep and maintain blood glucose concentration (Joslin Diabetes Centre, 2013).

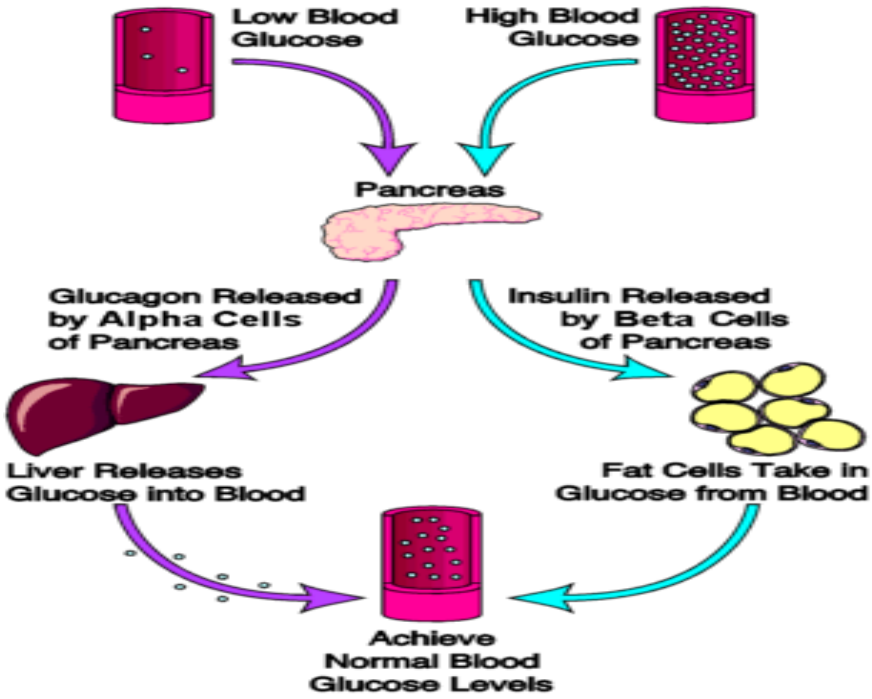


Figure (2.4): Insulin-glucagon feedback loop

2.9.4 The goals of insulin therapy

In type I diabetes, pancreas is unable to produce insulin, so insulin therapy needed. Insulin therapy is sometimes needed for type II diabetes and gestational diabetes when other therapies have failed to keep and maintain blood glucose concentration within normal range. Insulin therapy can prevent diabetes complications by helping keep blood glucose within normal range (Joslin Diabetes Centre, 2013).

2.9.5 Treatment plan

- **Type and amount of insulin**, many insulin types are available which vary in how long and quickly it can control blood glucose. Which types of insulin need and how much need, doctor will decide according to several factors? These include the type of diabetes have, and glucose levels.
- **Insulin delivery options**: insulin is infused or injected many times daily subcutaneously. The delivery way of insulin is choose among syringes, injection pens or an insulin pump that provides a continuous infusion of insulin subcutaneously.

2.9.6 Dose

To reach the optimal dose of insulin, the doctor will try sometime, so this process take certain time, so during this time it is important to check blood glucose concentration several times daily. Insulin dose often change according to changes in weight, meals, health conditions, activity level, and work can affect the amount of insulin needed to control blood glucose. Insulin treatment can be injected continuously by insulin pump that delivers insulin into the skin, a syringe and injection pen (subcutaneous injection). (Evers, I. M., de Valk, H. W., & Visser, G. H., 2004).

2.9.7 Factors affecting insulin action

- **Insulin dose**: insulin injected dose affected by the rate at which body absorbs it. For example, larger doses of insulin may be absorbed more slowly than a small dose. In case of insulin larger doses, the insulin may last longer or peak later than with

small doses. This could mean that blood glucose concentration is higher than expected within a few hours after meal but then becomes low.

- **Injection technique**: insulin injection angle and depth are important.
- **Site of injection**: changing of injection site usually recommend to minimize tissue irritation, also insulin is absorption rates are varying due to different body areas. Insulin injections before meal are absorbed fast, leading to high consumed of carbohydrates.
- **Subcutaneous blood flow**: insulin absorption affected by any factors that reduce blood flow rate to body's tissues. In contrast, insulin absorption increased by factors that increase skin temperature.
- **Time since opening the bottle**: insulin remains effective for up to one month after opened the bottle if it kept in refrigerator, the activity of intermediate or long-acting insulin begins to decrease after 30 days, so a problem can be occurred for patients who need small insulin doses. So new insulin bottle is advisable to be opened every 30 days, even if there is insulin left in the old bottle.
- **Individual factors**: the same dose of the same type of insulin may have different effects in different people with diabetes. So it is necessary to find the optimal dose and type for each (Joslin Diabetes Centre, 2013).

Chapter 3
Fuzzy logic Control

Chapter 3
Fuzzy Logic Control

3.1 Brief history of Fuzzy Logic control

Recently many applications of artificial intelligence techniques have been used to convert human experience into an understandable form by computers. Advanced control based on artificial intelligence techniques is called intelligent control. With fuzzy logic machines can be more intelligent enabling them to reason in a fuzzy manner like humans. Fuzzy logic, proposed by Lotfy Zadeh in 1965, emerged as a tool to deal with uncertain, imprecise, or qualitative decision-making problems. The controllers that consist of intelligent and conventional techniques are commonly used in the intelligent control of complex dynamic systems (Simoes, M. G., 2010).

Fuzzy Logic control system was used in many inventions and implementations disease diagnostic system, air conditioners, automatic gear system, washing machines, automobile engine, handling data, mobile robots, sorting, Information Systems, Pattern Recognition (Image Processing, Machine Vision), decision support, medical applications, traffic control systems.

3.2 Fuzzy Logic

Fuzzy logic control system based on analyzes analog input values into logical variables through mathematical system with continuous values between 0 and 1. Fuzzy Logic system is a method of reasoning in which resembles human reasoning. The approach of FL imitates human's decision making (Simoes, M. G., 2010).

Most common types of FLC

- Mamdani
- Tsukamoto

Implementation

- Fuzzy logic control can be implemented in systems with different sizes ranging from small micro-controllers to large and workstation-based control systems.

- It can be implemented in hardware, software, or a combination of both.

Why Fuzzy Logic?

FL is useful for practical and commercial purposes.

- It can control machines and consumer products.
- It may not give accurate reasoning, but acceptable reasoning.
- Fuzzy logic helps to deal with the uncertainty in engineering.

3.3 Fuzzy Sets

Fuzzy sets are represented by a membership function which defined on the universe of discourse. Where the universe of discourse is the space in which the fuzzy variables are defined. The membership function gives the degree, of membership within the set for any element of the universe of discourse. The membership function maps each elements of universe throw numerical values in the interval [0, 1]. The membership function value of zero means that the element is definitely not belong to the fuzzy set, while a value of unity means that the element fully belongs to the set. A grade of membership in between corresponds to the fuzzy membership to set (Simoes, M. G., 2010).

3.3.1 Crisp Logic

- True or false only.
    - Ahmed is a student (false)
    - Sport is healthy (true)
- Degree of truth is 0 or 1

3.3.2 Fuzzy Logic

– Degree of truth is between 0 and 1.
    - Ali is young (0.2 truth)
    - Air is hot (0.7 truth)

3.4 Fuzzy logic membership functions

Membership functions are a curve in which each input point in space defined how is it mapped to a membership value (or degree of membership) between 0

and 1. The input space is sometimes referred to as the universe of discourse. Membership functions allow to quantify linguistic term and represent a fuzzy set graphically. A membership function for a fuzzy *set A* on the universe of discourse X is defined as μA: X → [0, 1] (Simoes, M. G., 2010).

- X axis represents the universe of discourse.
- Y axis represents the degrees of membership in the [0, 1] interval.

There can be multiple membership functions applicable to fuzzify a numerical value. Simple membership functions are shown in the next figures.

1- **Triangular function**: **figure** 3.1 show triangular function which defined as lower limit **a**, upper limit **b**, and **m** value, where **a < m < b**.

$$\mu_A(x) = \begin{cases} 0, & x \le a \\ \frac{x-a}{m-a}, & a < x \le m \\ \frac{b-x}{b-m}, & m < x < b \\ 0, & x \ge b \end{cases}$$

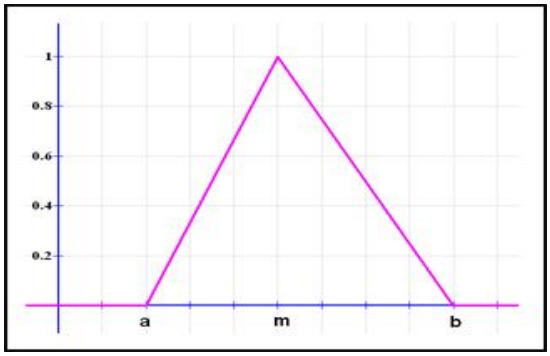


Figure (3.1): Triangular function

2- **Trapezoidal function**: **figure** 3.2 show trapezoidal function which defined as lower limit **a**, upper limit **d**, a lower support limit **b**, and an upper support limit **c**, where **a < b < c < d**.

$$\mu_A(x) = \begin{cases} 0, & (x < a) \text{ or } (x > d) \\ \frac{x-a}{b-a}, & a \le x \le b \\ 1, & b \le x \le c \\ \frac{d-x}{d-c}, & c \le x \le d \end{cases}$$

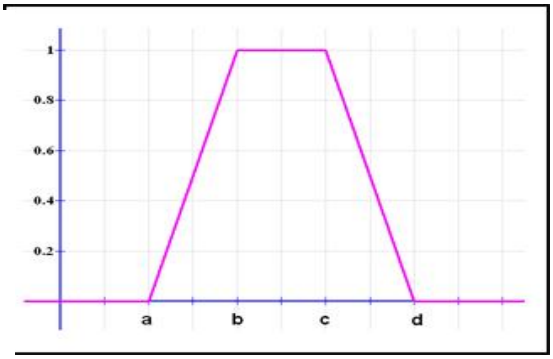
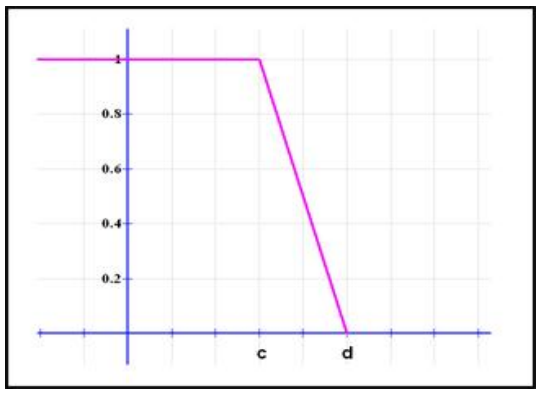


Figure (3.2): Trapezoidal function

Figure 3.3a and in **figure** 3.3b show special cases of a trapezoidal function, which are called R-functions and L-functions.

- R-functions: with parameters a = b = - ∞

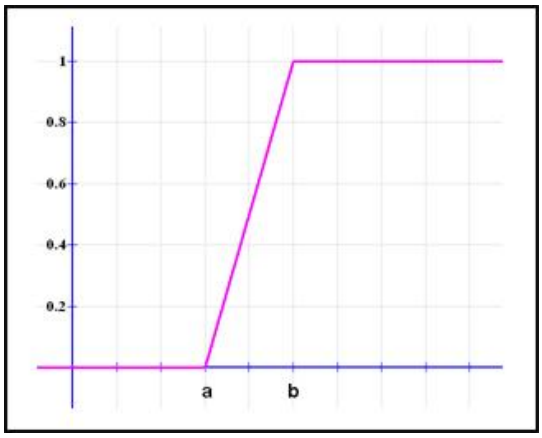
$$\mu_A(x) = \begin{cases} 0, & x > d \\ \frac{d-x}{d-c}, & c \le x \le d \\ 1, & x < c \end{cases}$$



(a)

- L-Functions: with parameters c = d = + ∞

$$\mu_A(x) = \begin{cases} 0, & x < a \\ \frac{x-a}{b-a}, & a \le x \le b \\ 1, & x > b \end{cases}$$



(b)

Figure (3.3): a) Trapezoidal R-functions and b) Trapezoidal L-Functions

3.5 Fuzzy logic system controller

- Fuzzy logic system (FLS) is nonlinear mapping of an input data set to a scalar output data, consists of main four parts: fuzzification, rules, inference engine and defuzzification (Simoes, M. G., 2010).

3.6 Algorithm of fuzzy logic system

- Define linguistic variables.
- Build fuzzy logic membership functions which define the values or meaning of the input and output terms that used in rules.
- Construct the rule base.
- Converted crisp input data to fuzzy values using membership functions.
- Evaluate the rules in rule base and combine the results of each rule (inference).
- Convert the output data to non-fuzzy values (defuzzification).

Fuzzy logic process:

- Crisp input data set converted to fuzzy set using fuzzy linguistic variables, fuzzy linguistic terms and membership functions. This step is known as fuzzification (Simoes, M. G., 2010).
- Inference process is create based on rules set.
- Output of fuzzy mapped to a crisp output using fuzzy membership functions, this step known as defuzzification step.

- **Linguistic Variables:** the input or output variables of the system whose values are words or sentences from a natural language, instead of numerical values. A linguistic variable is generally decomposed into a set of linguistic terms.
- **Fuzzification:** is the first step to apply a fuzzy inference system, most variables existing in the real world are crisp or classical variables, so these crisp variables both input and output needs to convert to fuzzy variables, and then apply fuzzy inference to process those data to obtain the desired output. Finally, in most cases, those fuzzy outputs need to be converted back to crisp variables to complete the desired control objectives. Generally, fuzzification involves two processes: derive the membership functions for input and output variables and represent them with linguistic variables (Simoes, M. G., 2010).
- **Fuzzy Rules:** Fuzzy rules considered as the knowledge of an expert in any related field of application. The fuzzy rule is represented by a sequence of the form IFTHEN, leading to algorithms describing what action or output should be taken in terms of the currently observed information of both input and feedback if a closed-loop control system is applied. The law to design or build a set of fuzzy rules is based

on a human being's knowledge or experience, which is dependent on each different actual application.

- **Defuzzification**: The result is a fuzzy value and should be defuzzified to obtain a crisp output. This is the purpose of the defuzzifier component of a FLS. Defuzzification process is performed according to the membership function of output variable (Simoes, M. G., 2010).

Chapter 4

Genetic Algorithms

Chapter 4

Genetic Algorithm

4.1 Brief history of Genetic Algorithm

Genetic algorithms consider one of the evolutionary computing, genetic algorithms are inspired by Darwin's theory about evolution. Genetic Algorithms were introduced to imitate many processes in natural evolution. Many biologists are astonished that life at high level complexity that observe could have evolved in the relatively short time suggested by the fossil record. GA idea is to use this evolution power to solve optimization problems. John Holland is considerd the father of genetic algorithm who invented it in the early 1970's (Internet Source).

4.2 What is Genetic Algorithms?

GAs consider a search algorithm method based on the evolutionary process of natural selection and genetics. GA consider an intelligent exploitation of a random search to solve optimization problems, random method of search and direct the search into area of better performance within the search space. Genetic algorithm implementation based on techniques of simulate processes in natural systems for evolution, especially those follow the principles first laid down by Charles Darwin of "survival of the fittest". Since in nature, competition among individuals for scanty resources results in the fittest individuals dominating over the weaker ones. Genetic algorithm simulate the survival of the fittest among generation individuals for solving problems. Each generation consists of a population of character strings that are analogous to the chromosome that see in DNA. Each individual consider a possible solution and point in the search space, then this individual go through a process of evolution (Internet Source).

Genetic algorithm based on the following foundations:

- **Individual** – All the possible solutions of the problem called individual, it can be in two forms:

- **Genotype:** particular set of genes called genotype

- **Phenotype:** genotype physical characteristic like smart, healthy and beautiful.

- Population - Group of all individuals
- Individuals in a population are compete for resources.
- Individuals which successful in each 'competition' will produce more offspring than poorly ones.
- Good individual's genes propagate throughout population, sometimes two good parents will produce offspring maybe consider better than either parent.
- Each successive generation will become more suited to their environment.

4.3 Why Genetic Algorithms?

Unlike older AI systems, do not break easily even if the inputs changed slightly, or in the presence of reasonable noise. Also, in searching a multi-modal state-space, large state-space, or N-dimensional surface, a genetic algorithm may offer significant benefits over more typical search of optimization techniques, so it is more strong and is better than conventional AI.

4.4 Biological Background

4.4.1 Chromosome

All living organisms consist of cells. In each cell there is the same set of chromosomes. The chromosomes consider as strings of DNA and serves as a model for the whole organism. A chromosome consist of genes, blocks of DNA. Each gene encodes a particular protein. Basically can be said, that each gene encodes a trait, for example color of eyes. Possible settings for a trait (e.g. blue, brown) are called alleles. In chromosome each gene has its own position. This position is called locus.

4.4.2 Reproduction

During reproduction, first occurs recombination (or crossover). The whole new chromosome form in some way from the parents genes. The new created offspring can then be mutated. Mutation process means a bit changed of the DNA elements.

This bit changes mainly caused by errors through copying genes from parents. Fitness process success of an organism measured by the organism success of its life.

4.5 Search Space

For solving any problem, usually should looking for good solution, which will be the best among others. Search space means all possible solutions in which the desired solution is. Any point in search space represent one feasible solution. Each feasible solution can be "marked" by its value or fitness for the problem. The looking solution consider one point or more among feasible solutions that is in the search space. Looking for better solution means looking for some extreme minimum or maximum in search space. Search space can be whole known by the time of solving a problem, but usually we know only a few points from it and we are generating other points as the process of finding solution continues.

4.6 Simple Genetic Algorithm

Any problem solving can be often expressed as looking for minimum or maximum of a function. This is exactly what the **figure 4.1** below shown here is.

4.7 Basic genetic algorithm outline

1. (Start) randomly generate population of n chromosomes which appropriate solutions.
2. (Fitness) the fitness function f(x) of each chromosome x in the population is evaluate.
3. (Population) the following steps will be repeatrd until the new population is complete

- (Selection) two parent chromosomes are selected from a population according to their fitness, so the better fitness, the bigger chance to be selected.
- (Crossover) process means the probability of parents to form a new offspring. If no crossover, offspring is exact copy of parents, so no good solution.

- (Mutation) process means probability to mutate new offspring with good characteristics.
- (Accepting) the good new offspring is placed in a new population

4. (Replace) new generated population is used for a further run of algorithm
5. (Test) If the new generated population is satisfied the end condition, stop, and return the best solution in current population
6. (Loop) Go to step 2

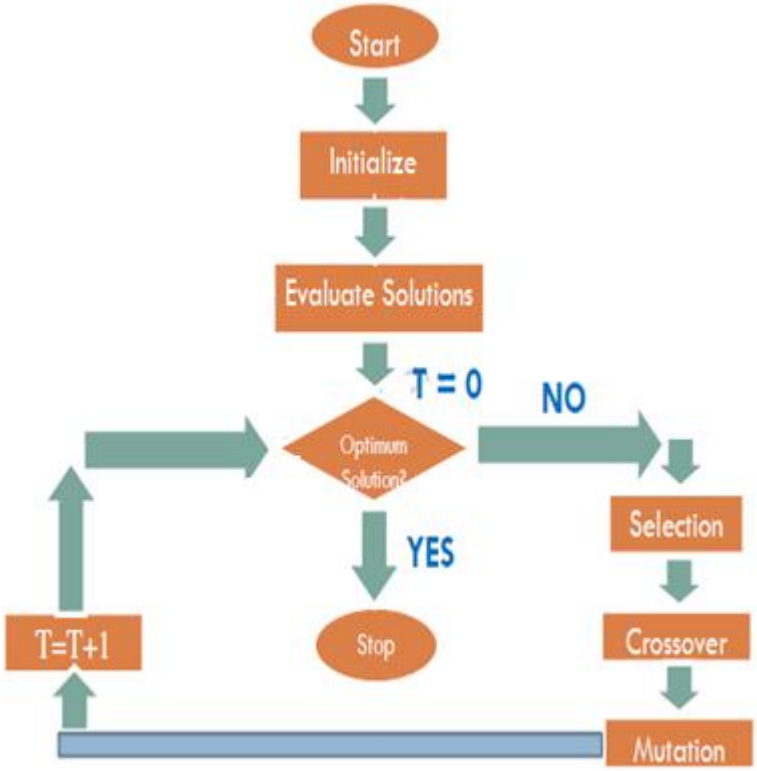


Figure (4.1): Simple Genetic Algorithms

4.8 Parameters of GA

4.8.1 Overview

Genetic algorithm performance is mainly affected by two processes, crossover process and mutation process.

4.8.2 Encoding of Chromosome

Through chromosome encoding process the solution is representing a solution in string form that conveys the important information, each gene in chromosome maintain and control the characteristic of the individual, like as in string each bit represents characteristic of the solution (Internet Source). In some way each chromosome should contain information about solution which it represents. Binary coded is the most common encoding method. Strings of chromosomes are consist of 0 and 1, each position in chromosome strings represents a particular characteristic of the problem.

Chromosome example:

Chromosome 1	1101100100110110
Chromosome 2	1101111000011110

Each chromosome has one binary string. Each string bit represent some characteristic of the solution. Or the whole string can represent a number, this has been used in the basic applet. There are many other ways of encoding such as, one can encode directly integer or real numbers, and sometimes it is useful to encode some permutations and so on. This depends mainly on the solved problem.

4.8.3 Crossover

If the encoding process will be used, crossover step must be done. Crossover process is create by choose genes from the parent chromosomes then creates a new offspring. This is done by choosing randomly certain crossover point and everything before this point still the same as the first parent and then let everything after this point copy from second parent (Internet Source).

Crossover types:

- One point : for the first parent a part is copied and the rest is taken in the same order as in the second parent
- Two point : for the first parent two parts are copied and the rest between is taken in the same order as in the second parent
- None: the new offspring is exact copy of the parents, means no crossover.

- One Point – Part Crossover for Example can then look like this:

Chromosome 1	11011/00100110110
Chromosome 2	11011/11000011110
Offspring 1	11011/11000011110
Offspring 2	11011/00100110110

4.8.4 Mutation

Just after the process of crossover is performed, mutation process take place, mutation process is done to prevent that all solutions in population to falling into local optimum solutions. In mutation the new offspring is changed randomly, that means choose few bits randomly and changed from 0 to 1 or from 1 to 0 in binary encoding. Mutation can then be following (Internet Source):

- Normal random : means few cities are chosen and exchanged
- Random, only improving: a few cities are randomly chosen and exchanged if they only improve solution.
- Systematic, only improving: systematically cities are chosen and exchanged only if they improve solution.
- Random improving : the same as "random, only improving", but before this is "normal random" mutation performed
- Systematic improving : the same as "systematic, only improving", but before this is "normal random" mutation performed
- None : no mutation

- Example of normal random mutation such as like this:

The original offspring 1	10011110000011110
The original offspring 2	10010001100000111
New mutated offspring 1	10011010000011110
New mutated offspring 2	10010011100000110

4.8.5 Crossover and Mutation Probability

Crossover probability often refer to crossover performed process, so there is no crossover when the new offspring is the same copy of the parents. When crossover occurred, new offspring created from chromosome parents' parts. When crossover probability is 100%, then all new offspring created by crossover. When crossover is 0%, then all new generations is exactly the same copies of chromosomes from old parents. Crossover process is needed to create new chromosomes with new good parts of old chromosomes in hope that new chromosomes will be better. Probability mutation refer to mutated chromosome parts. In case no mutation, the offspring is taken after crossover the same as parents without any change. In case of mutation, chromosome part is changed. In case 100% of mutation probability that's mean all chromosomes are changed, in case 0% mutation, nothing is changed. Mutation is made to prevent falling GA into local extreme, but it should not occur very often, because then GA will in fact change to random search (Internet Source).

4.8.6 Selection

As mentioned before about genetic algorithm that parent's crossover chromosomes are selected from population, these chromosomes are selected according to Darwin's evolution theory which says that the best chromosomes should survive and made new offspring. There are many methods for chromosomes selection such as rank, tournament selection, Boltzman selection, steady state selection and roulette wheel selection. Here are two familiar methods will be discussed ((Internet Source).

4.8.6.1 Roulette wheel selection

According to parent's fitness, the selection is done. The better the chromosomes are, the more chances to be selected they have. Consider a roulette wheel where all chromosomes in the population are placed in, every chromosome has its place area accordingly to its fitness function, such as like on the following picture (Internet Source)

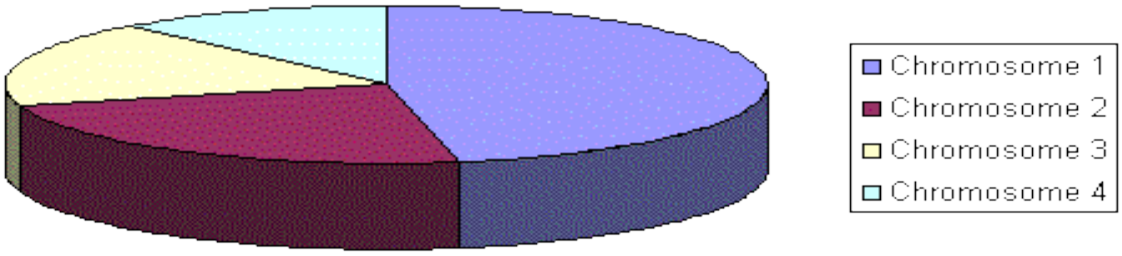


Figure (4.2): roulette wheel selection

In this method the chromosomes with high fitness are selected many times. This method can explain as:

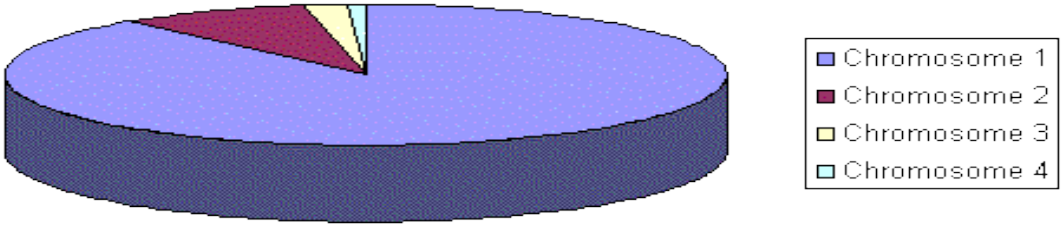
1. Sum: means sumation of all population chromosome fitness (sum S), for each population this step is performed only once.
2. Select: generate random number from interval (0, S) - r.
3. Loop: Go through the population and sum fitness from 0 - sum S. When the sum S is greater than r, stop and return the chromosome where you are.

4.8.6.2- Rank Selection

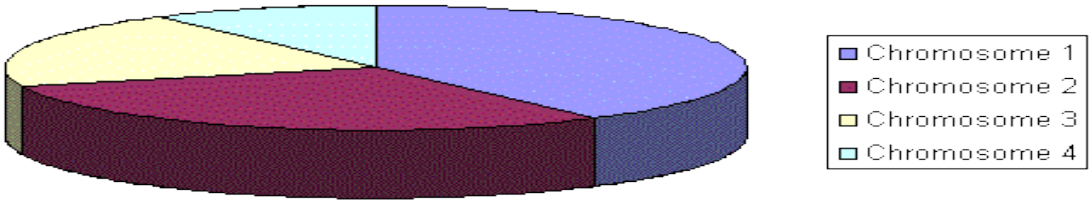
The previous selection type maybe have problems when there is very much fitnesses differs. For example, if the best chromosome fitness is 90% of all the roulette wheel then the other chromosomes will have very few chances to be selected.

Rank selection first ranks the population and then every chromosome receives fitness from this ranking. The worst will have fitness 1, second worst 2 etc. and the best will have fitness N (number of chromosomes in population).

In following picture we can see, how the situation changes after changing fitness to order number.



(a) Graph of fitnesses, situation before ranking



(b) Graph of fitnesses, situation after ranking

Figure (4.3): Rank Selection a) Graph of fitnesses, situation before ranking and b) Graph of fitnesses, situation after ranking

After this ranking all the chromosomes have a chance to be selected, but this method lead to slower convergence, because the best chromosomes do not differ so much from other ones (Simoes, M. G., 2010).

4.8.7 Fitness Functions

Fitness function responsible for performing evaluation and returning a positive integer number, or fitness value that says or reflects how optimal the solution is: the higher the number, the better the solution. Then fitness values are used in a process of natural selection to choose which solutions will continue on to the next generation, and which of them will not be used. It should be noted, however, that natural selection process does not merely choose the top x number of solutions, the solutions are chosen statistically such that it is more likely that a solution with a higher fitness value will be chosen, but it is not guaranteed. The users of genetic algorithms should be note that fitness function designing is the single most important aspect of using GAs to solve hard problems. There are two main reasons for this:

1. Most of a GA's runtime is spent in the fitness function. The fitness function has to be run once for each individual in the population. Furthermore, in each new generation, new individuals are constantly being generated and the fitness function has to be run for those to evaluate their fitness. Typically, a population would consist of hundreds, sometimes thousands, of individuals. It becomes readily apparent that efficient design of the fitness function can result in tremendous speed gains in overall runtime.

2. Individuals only adapt themselves to the fitness function. The purpose of the fitness function is to test the adaptability of each individual to the given problem. If, for any reason, the fitness function fails to test some corner case of the problem, then no chromosomes will evolve to take that corner case into account.

4.8.8 Elitism

During creating new population by crossover and mutation process, there is a big chance that the best chromosome will be lose. The first copies of the best chromosome or a few best chromosomes kept by elitism process to new population. The other rest chromosomes are done normally. This process increased the performance of GA, because it keep the best found solution of the problem from losing (Simoes, M. G., 2010).

4.8.9 Genetic Fuzzy Systems

Combining fuzzy systems with genetic algorithms is relatively easy once the process sequences are understood. Here in my study case I will use GA for tuning fuzzy sets of one of our system inputs to find optimal configurations of fuzzy sets. All we need is an appropriate coding, genetic operators, and a fitness measure. In our system, we have two input variables which are plasma glucose error and plasma glucose concentration derivative that defined the current value of glucose concentration level in blood and blood glucose concentration rate of change respectively; and one output variable, insulin infusion rate which defined the current delivery injected insulin to blood. (Ala Qumsieh, 2004).

4.8.10 Genetic algorithms applications

Genetic algorithms has been used for difficult problems, for machine learning and also for evolving simple programs. Advantage of GAs is in their parallelism. GA is travelling in a search space with more individuals and with genotype rather than phenotype, so they are less likely to get stuck in a local extreme like some other methods. They are also easy to implement. If there are some genetic algorithm, new

chromosome should have to be write for solving another problem. With the same encoding you just change the fitness function and it is all (Simoes, M. G., 2010).

GAs disadvantage is in their running computational time. It is consider slower method than other ones. Today this disadvantage consider less problem because the computers performance is improved and being fast.

Application problems solved using GA:

- Nonlinear dynamical systems - predicting, data analysis.
- Designing neural networks.
- Robot trajectory.
- Strategy planning.
- Finding shape of protein molecules.
- TSP and sequence scheduling.
- Creating images functions.

Chapter 5
Physiological Modeling of Diabetic

Chapter 5

Physiological Modeling of Diabetic

5.1 Overview

Model of a diabetic is very vital and important in testing control algorithm, because it is very complex and cost to test this control algorithm on a diabetic patient. Performance of the control algorithm in maintain and regulate levels of blood glucose for a diabetic is dependent on the accuracy of diabetic model. Mismatch in the model to patient dynamics is directly proportional to the designed controller performance degradation. So model development is a crucial step in designing the controller. As plasma glucose concentrations increased, the pancreas is stimulated to increase insulin secretion level in blood, which simulate tissues to increases the uptake of glucose in blood, so due to this step, glucose outflow from blood and interstitial fluid increased this leads to glucose concentration decreasing, which subsequently produces a reduction in insulin secretion (Michael C. K. Khoo-Physiological Control Systems_ Analysis, Simulation, and Estimation, 1999). The model that will introduce in this section was first proposed by (Stolwijk and Hardy in 1974). We assume the total volume of blood and interstitial fluids to be represented by a single large compartment (15L in a normal adult), and steady state glucose concentration of this model is G (in units of mg/dl). For this level of G to remain constant, the total inflow of glucose into the compartment must equal the total outflow from the compartment. A schematic representation in figure 5.1 showing the main processes that affect this balance. In normal conditions glucose inter blood by liver production and by gastrointestinal tract absorption. We assume this input flow rate to be QL (in mg/h). Glucose can be reduced in blood by three major ways through which are:

• When G rises up beyond a certain threshold (Θ), so kidneys excreted glucose at a rate proportional to the gradient between *G and* Θ:

$$\text{Renal Loss Rate} = \mu (G - \Theta), \quad G > \Theta \tag{5.1a}$$

$$= 0, \quad G \leq \Theta \tag{5.1b}$$

• Through diffusion property glucose leaves blood to enter tissues and cells. In some tissues, glucose utilization rate depends on extracellular-to-intracellular concentration

gradient (Michael C. K. Khoo-Physiological Control Systems_ Analysis, Simulation, and Estimation, 1999).

Usually intracellular concentration ignored. Thus, we have

$$\text{Tissue Utilization Rate (Insulin-independent)} = \lambda G \qquad (5.2)$$

• In certain types of cells, such as those in muscle and adipose tissue, insulin helps to stimulate this facilitated diffusion process. Therefore, the rate at which glucose is taken up by these cells is proportional to *x* as well as to the blood insulin concentration, *y:*

$$\text{Tissue Utilization Rate (Insulin-dependent)} = \nu G y$$

In the above equations, μ, λ, and ν are constant proportionality factors.

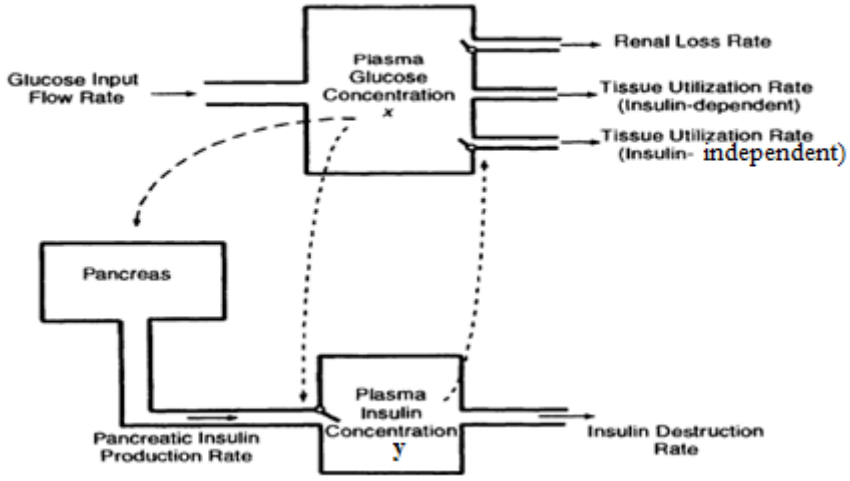


Figure (5.1): Schematic representation of glucose and insulin regulation.

Following blood glucose mass balance equations are obtained from the inflow and summation of the three outflows equations.

$$QL = \lambda G + \nu G y, \qquad G \le \Theta \qquad (5.3a)$$

$$= \lambda G + \nu G y + \mu (G - \Theta), \qquad G > \Theta \qquad (5.3b)$$

Note that in the above equation, a strong nonlinearity in the form of the product of G and y is introduced, along with the thresholding nonlinearity, which defines one regime above Θ and one below it. Also, the negative feedback in this control system

is clearly embedded in the characteristics described by Equations (5.3a) and (5.3b): since QL is a constant, an increase in G lead to decrease in y, and vice versa.

Blood insulin similar mass balance can be established. Insulin is produced by the pancreas at a rate dependent on the plasma glucose level. However, if G falls below a certain threshold (∅), insulin production ceases.

Thus, we have Insulin Production Rate = 0, $G \leq \emptyset$ (5.4a)

$= \beta (G - \emptyset)$, $G > \emptyset$ (5.4b)

Insulin is destroyed through a reaction involving the insulinase enzyme, at a rate proportional to its concentration in blood:

Insulin Destruction Rate = α y, (5.5)

Combining Equation (5.4) and Equation (5.5), we obtain the following equation relating the steady-state level of y to that of G:

$Y = 0$, $G \leq \emptyset$ (5.6a)

$= \frac{\beta}{\alpha}(G - \emptyset)$, $G > \emptyset$ (5.6b)

Where

Table 5.1. Model parameter description

Parameter	Description
G(t)	Instantaneous BGL error in mg/ml
I(t)	Instantaneous blood insulin level mU/ml
UG(t)	Exogenous glucose infusion in mg/h
UI(t)	Exogenous insulin infusion in mU/h
CG	Glucose capacitance in the extracellular space
CI	Insulin capacitance in the extracellular space
QG(t):	Glucose inflow into blood in mg/h
ƛ	Tissue usage rate of glucose that is independent of I(t)
v	Tissue usage rate of glucose that is dependent on I(t)
α	Insulin destruction rate
β	Insulin production rate by the pancreas
Θ	Threshold for renal discharge of glucose
∅	Threshold for pancreatic production of insulin
µ	Glucose excretion rate

Insulin to glucose response is basically linear. Steady state glucose and insulin concentration in blood under certain conditions can be predicted from this model by solving Equations (5.3) and (5.6) simultaneously. In **Figure 5.2a**, steady-state insulin concentration (in milliUnits per ml blood) is plotted against the steady-state blood glucose concentration (in mg per ml). The insulin response to glucose is shown as the bold curve, while the lighter curve reflects the glucose mass balance equation. These values of parameter are calculated according to normal adult person (Khoo, M. C., 2000), where $\Theta = 2.5$ mg ml^{-1}, $\mu = 7200$ ml h^{-1}, $\lambda = 2470$ ml h^{-1}, $v = 139000$ mU^{-1} h^{-1}, $\emptyset = 0.51$ mg ml^{-1}, β = mU.ml mg^{-1} h^{-1},

α =7600 ml h^{-1}, and QL = 8400 mg h^{-1}

Here the steady state points which yields from glucose – insulin curves intersection, such as N point, where glucose and insulin concentration is 0.81 mg ml^{-1} and 0.055 mU ml^{-1} respectively**.** (Khoo, M. C., 2000).

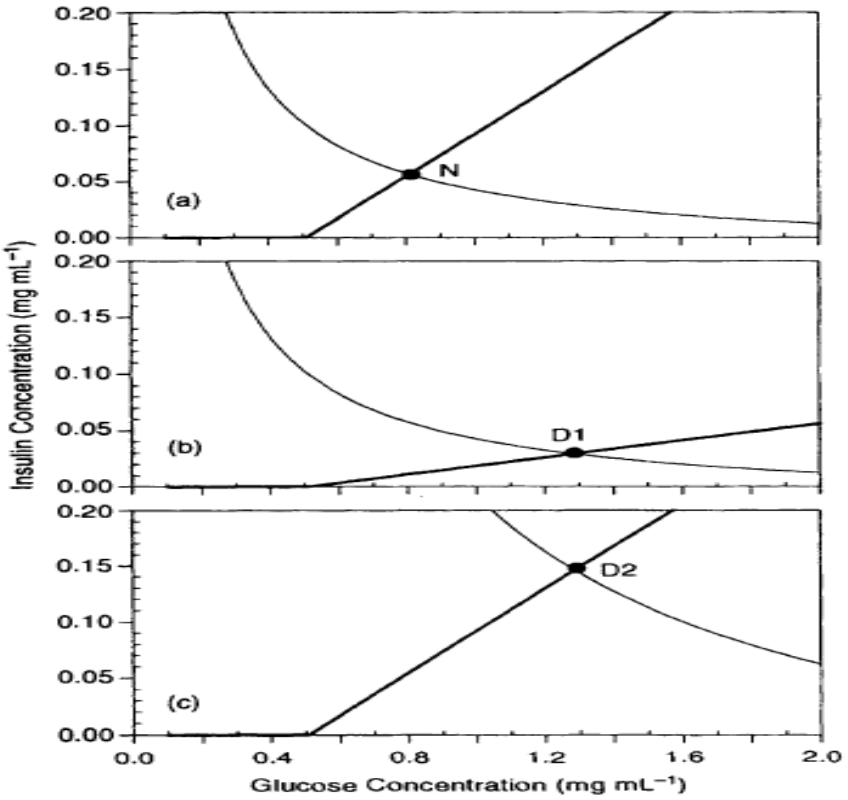


Figure (5.2): glucose – insulin regulation steady-state analysis, where (a) normal conditions; (b) Type-1 diabetes; and (c) Type-2 diabetes.

The Stolwijk and Hardy model will be used next to show glucose - insulin relation which increased due to diabetes. In Type-l or insulin-dependent diabetes, the main defect is in the inability of the islet cells in the pancreas to produce sufficient insulin. One form of disorder of pancreas to produce insulin (type I disease) begins in childhood and other form begins in adulthood. This condition of pancreas insulin producing can be done by reducing the sensitivity factor of the insulin response to glucose which is β, **Figure 5.2b** illustrate effect of reducing β to 20% of its normal value, so D1 new established point now at which blood glucose level increase of 1.28 mg ml^{-1} and insulin concentration decreased of 0.029 mU ml^{-1}. (Khoo, M. C., 2000). Type-2 diabetes is also referred to as non-insulin-dependent diabetes since, here, the pancreas may be making normal amounts of insulin. However, for unclear reasons, there is disorder in insulin ability to stimulate glucose uptake by tissues. We model this condition by changing the value of the parameter v, which is the constant that multiplies the product of G and y in the glucose mass balance equation. Insulin response to glucose may be remain normal or decrease. In **Figure 5.2c**, however, we have reduced v to 20% of its original value while leaving the insulin curve unchanged. The change in v produces a shift of the glucose curve away from the origin as well as a steepening in local slopes. The new equilibrium point is established at D2, where the glucose concentration is elevated to 1.29mg ml^{-1}. A somewhat counterintuitive result is that the steady-state insulin concentration now is actually almost three times higher than normal, at a level of 0.146 mU ml^{-1}: Thus, in this case, treatment with insulin clearly would not be useful. (Khoo, el at, 2000)

5.2 Mathematical Model

The diabetic patient in the control terminology is identified as a system. So as to study and analyze the effect of glucose and insulin regulation, a model of pancreatic function is required. As mentioned above a modified Stolwijk-Hardy glucose insulin interaction model will be used (JE Stolwijk, JD Hardy, 1974 & (Khoo, el at, 2000). This model was modified by adding mechanical pump infused exogenous insulin. Thus, the glucose dynamics are ruled by:

$$\mathbf{C_G}\frac{dG}{dt} = U_G + Q_G - \lambda G - vGI, \qquad G \leq \Theta$$

$$\mathbf{C_G}\frac{dG}{dt} = U_G + Q_G - \lambda G - vGI - \mu (G - \Theta), \qquad G > \Theta \tag{5.7}$$

The insulin dynamics are ruled by:

$$\mathbf{C_I}\frac{dI}{dt} = UI - \alpha I, \qquad G \leq \emptyset$$

$$\mathbf{C_I}\frac{dI}{dt} = U_I - \alpha I + \beta(G - \emptyset), \qquad G > \emptyset \tag{5.8}$$

Glucose inflow into the blood based on two ways, glucose produced from the liver or glucose absorbed from the gastrointestinal tract. Additively, as it can be shown from parameters above, coefficients are related to physiology and vary according to the condition of patient. The used parameter values are given in (Ahmed, J., & Alvi, B. A., 2008, & Khoo, el at, 2000). In this model, volume of plasma and fluids are (3l+12l, in healthy adult person). Normal value of glucose and insulin concentration in this model are 0.81 mg/ml and 0.055 mU/ml, respectively. In diabetic patients type-1 the main problem is inadequacy of beta cells to produce the necessary amount of insulin. This case situation is modeled by reducing the sensitivity of insulin response to glucose. From this modeling for type-1 diabetic patient, glucose and insulin concentrations can be found as 1.28 mg/ml and 0.029 mU/ml in the steady state, respectively (Khoo, el at, 2000).

Chapter 6

Simulations

Chapter 6

Simulations

6.1 Model Simulations

6.1.1 Simulation without exogenous insulin pump

Glucose infusion into the model is simulated through the use of a pulse generator block, which produces a rectangular wave. The period of the output waveform is set equal to the simulation time of 5 hours, with time step being 0.01 hour. The duty cycle is set to 5% so that glucose infusion occurs over a duration of 0.25 hour or 15 minutes, starting at t = 0.5 hours. The glucose infusion rate (amplitude of the rectangular wave) is set equal to100000 mg h^{-1}. (JE Stolwijk, JD Hardy, 1974 & (Khoo, el at, 2000). Using Matlab/Simulink, the glucose-insulin regulation model is examined and performed **without** exogenous insulin infusion UI (t). Simulink model is presented in **Figure (6.1a)** and **Figure (6.1b)** for normal person and diabetic person respectively (Khoo, el at, 2000). Control studies related to the exogenous insulin infusion UI (t) will take place in the next section of this thesis.

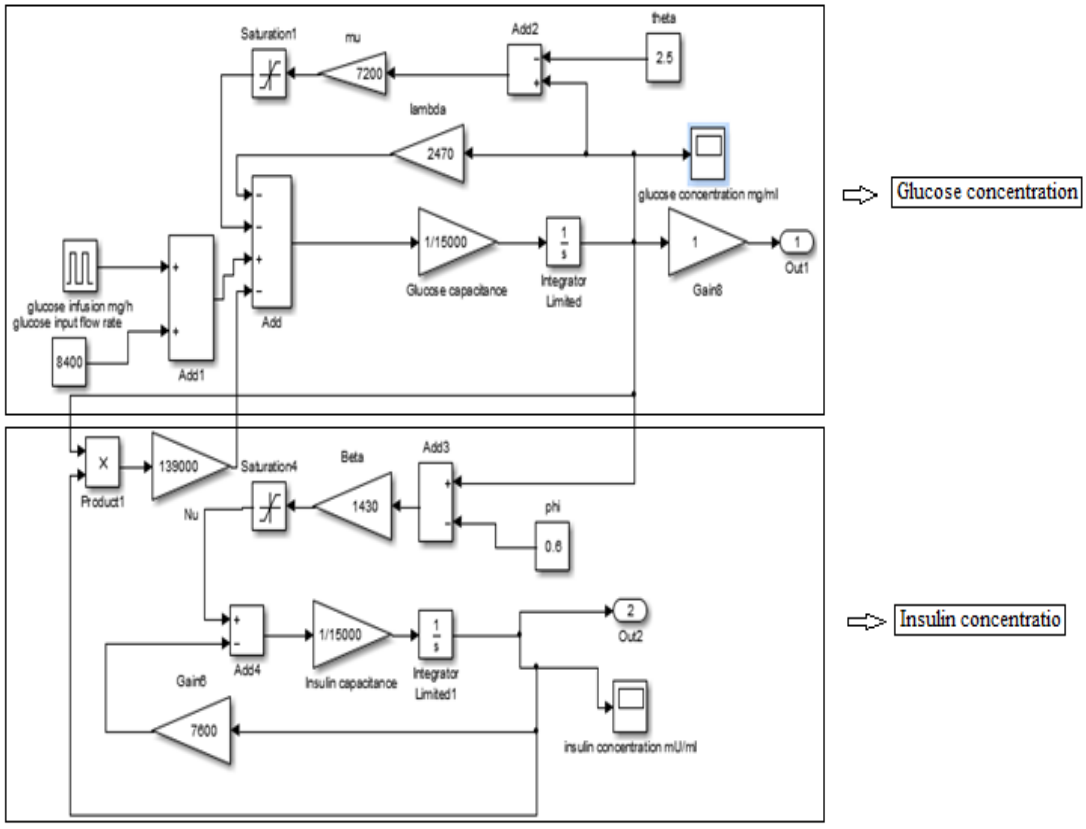


Figure (6.1a): Normal person glucose-insulin regulation model simulink

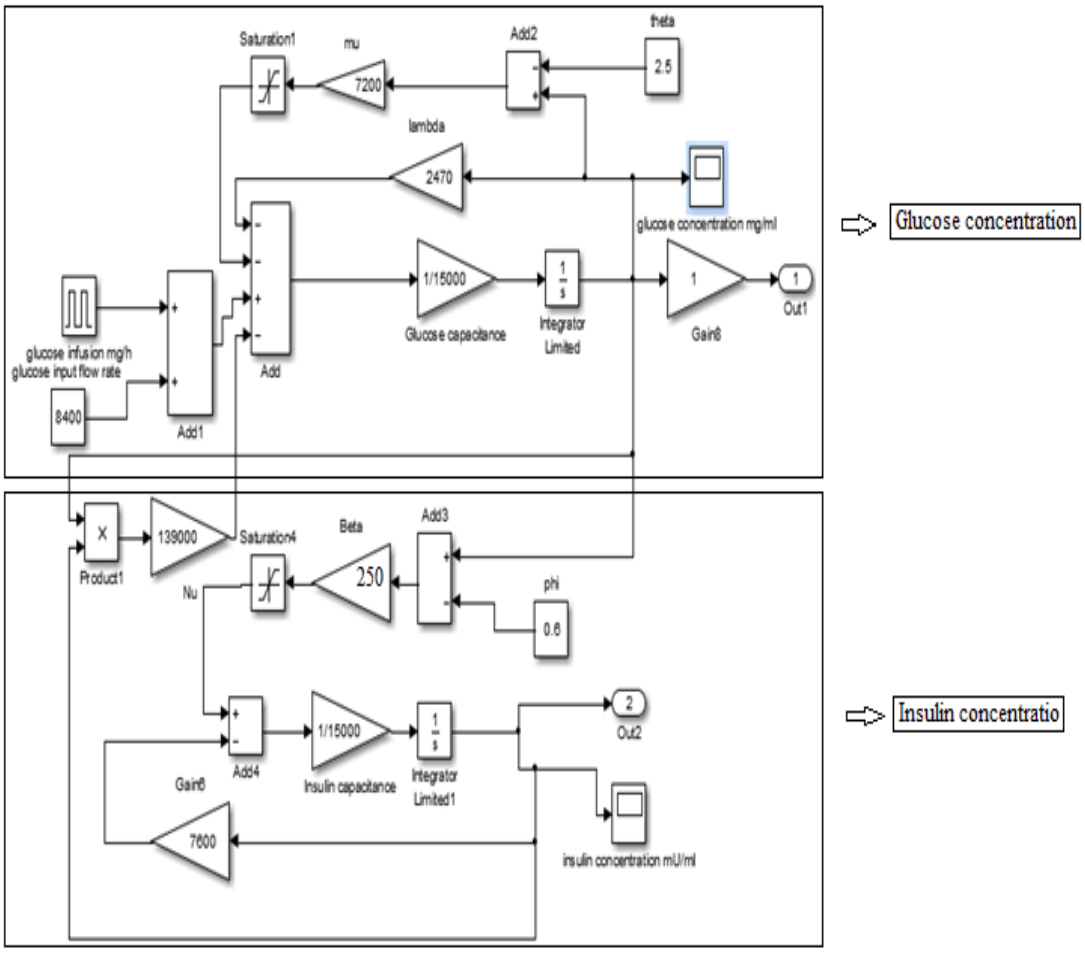


Figure (6.1b): Diabetic person glucose-insulin regulation model simulink

Examples of two simulation runs are displayed in **Figure 6.1**. The input waveform, blood glucose concentration and insulin concentration are shown in **Figure 6.2, Figure 6.3** and **Figure 6.4**, respectively. In the **Figure 6.3**, with glucose infusion which is considered as food intake it is observed that the abrupt rise in glucose concentration level. Then, after certain time the glucose concentration settles down to the steady state after. The secreted level of insulin is related to the BGL. It is shown in **Figure 6.4**. Two classes of subjects are examined here: the normal adult (solid curves) and the Type-1 diabetic (dashed curves).

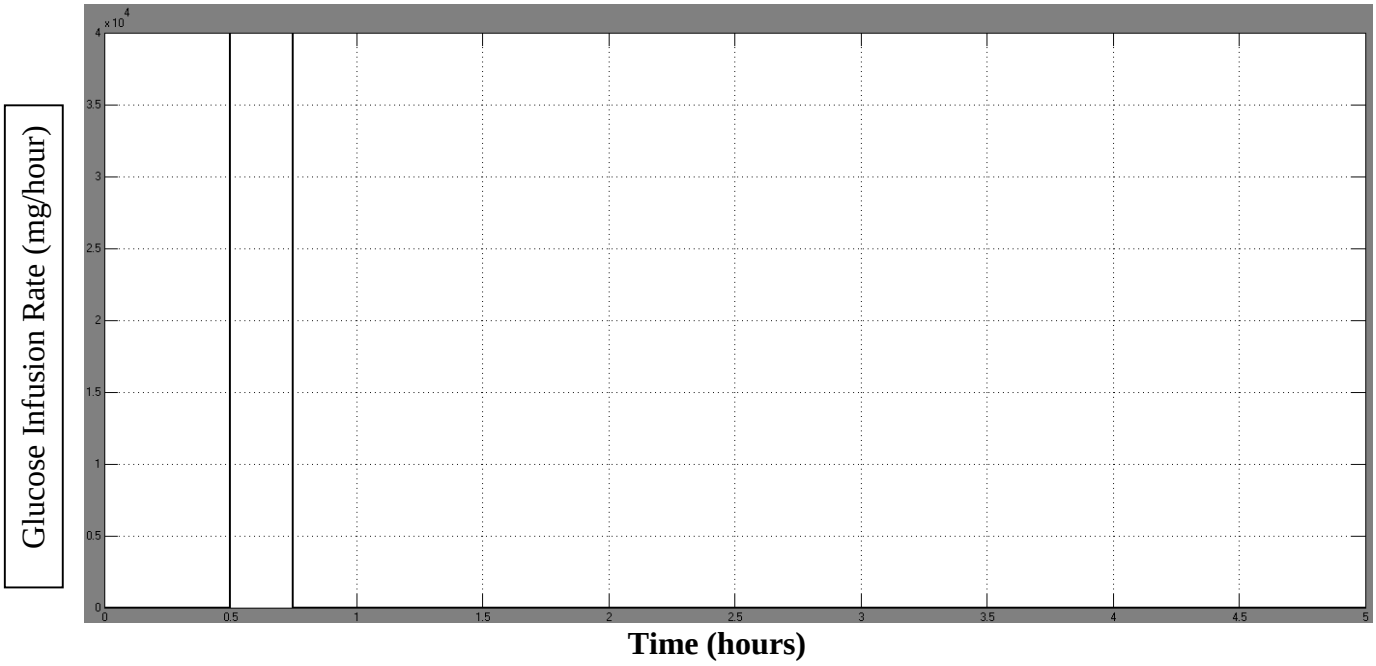


Figure (6.2): The input waveform

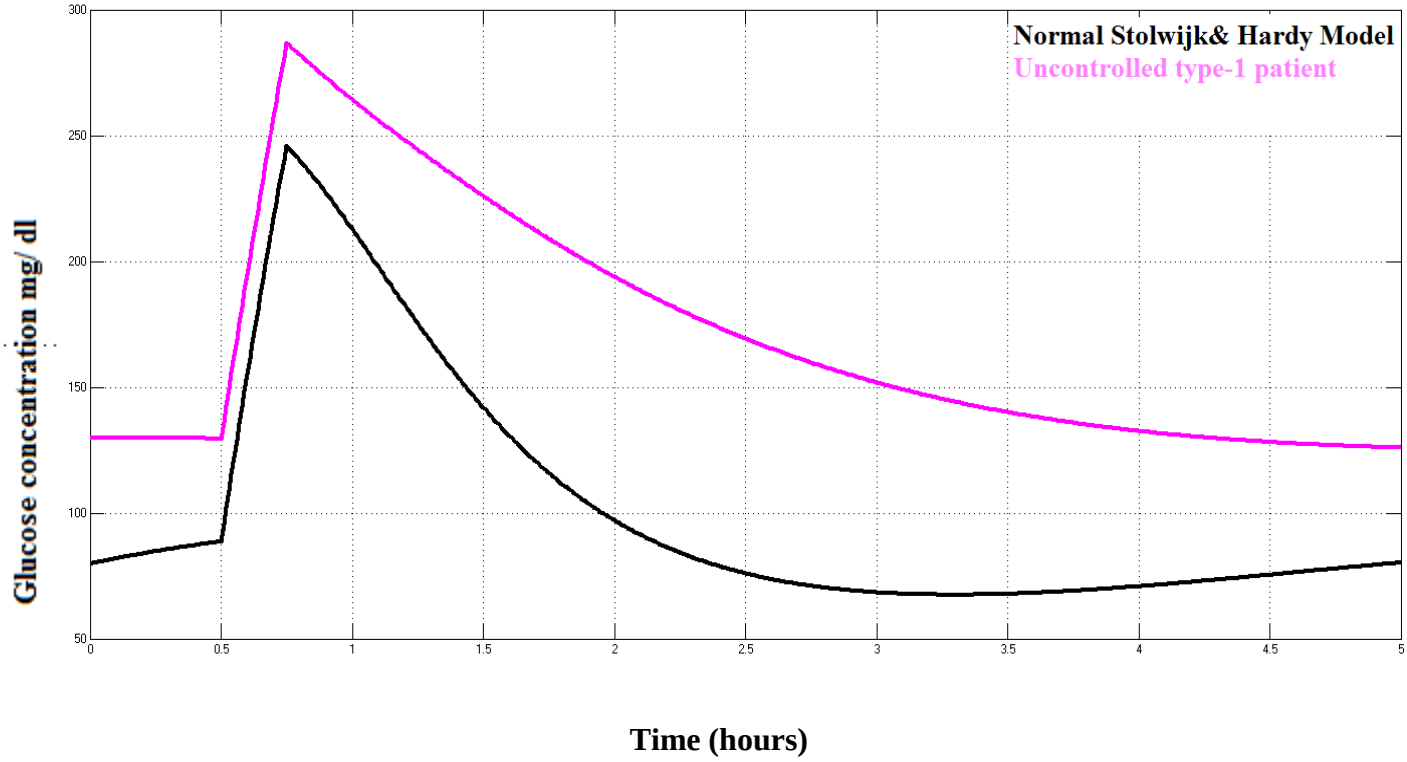


Figure (6.3): Glucose concentration

It can be obviously seen in **Figure 6.3**, the steady state BGL of type-1 diabetic patient is higher than normal person. Furthermore, for diabetic patient type-1, blood glucose and insulin levels reach steady state slower than normal subject.

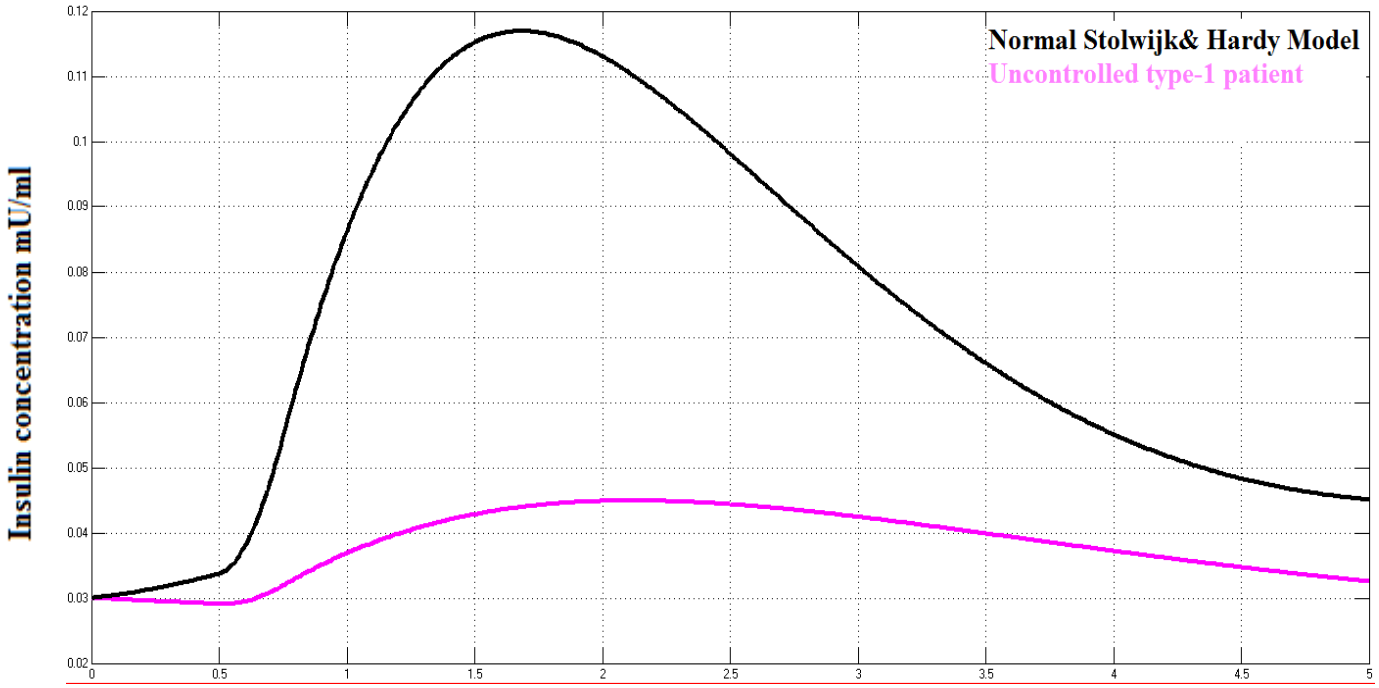


Figure (6.4): Insulin concentration

6.1.2 Simulation with exogenous insulin pump

The same model with all pervious conditions will be simulated this time with adding exogenous insulin pump (modified model) to control the BGL using Matlab/Simulink, the glucose-insulin regulation modified model is examined and performed **with** exogenous insulin infusion UI (t). Simulink model is presented in **Figure 6.5**

6.2 Control Studies

The steady state BGL in the person's blood for any normal person or diabetics is determined by existing amount of insulin. So, insulin injection is required to lower the BGL in diabetics. Therefore, the controller measured glucose concentration level then determines the insulin infusion rate that body need. The exogenous insulin infusion UI (t), which is mentioned above, is added to the model to keep under control the BGL in a tight range around the steady state BGL of normal adults.

Control of the BGL in diabetics have been proposed in many different algorithms through the usability of mathematical models. This complex control problem could

be solved by the help of fuzzy logic. Fuzzy logic allows capturing more valuable information about the behaviour of the controlled variable and it can be good guide that helps us to discover artificial pancreas. Furthermore, fuzzy logic controllers have shown relatively successful results comparing with the renowned classical controllers.

Fuzzy based controllers to maintain normal range of BGL were designed in (Li, C., & Hu, R., 2009). In the following paragraphs, design of the FLC controller is introduced.

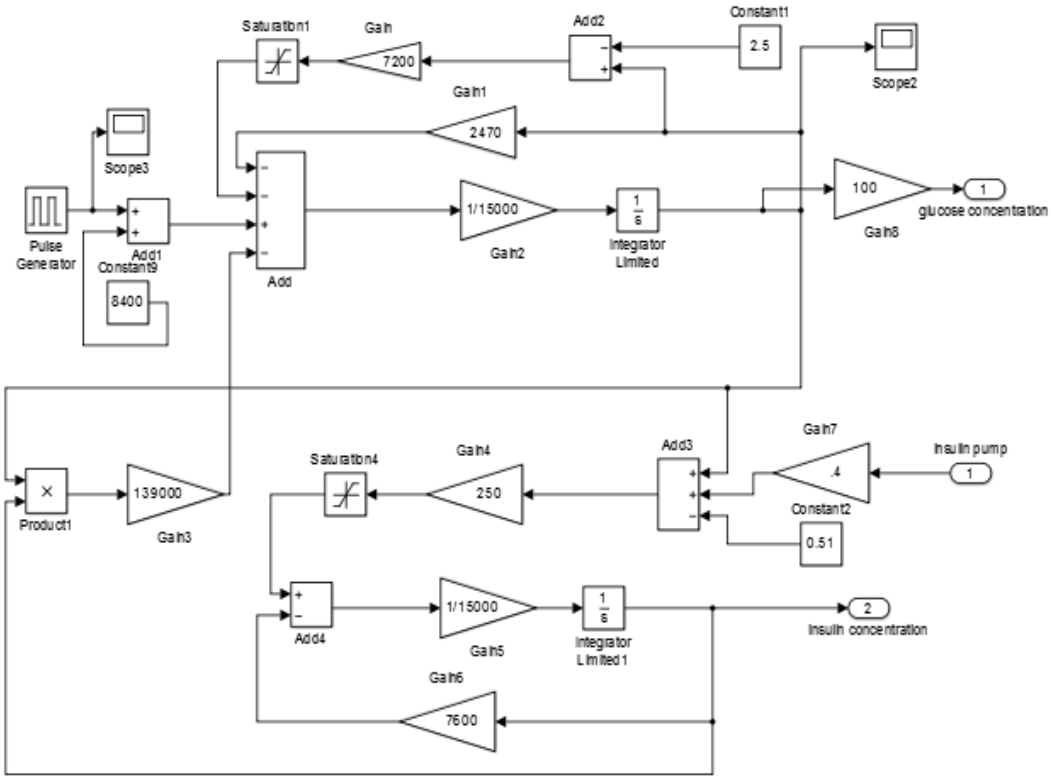


Figure (6.5): Simulink model of glucose-insulin regulation with Insulin infusion pump

6.3 Fuzzy Logic Controller (FLC) Design

Fuzzy control systems allow extremely precise control of insulin injection. Closed-loop feedback control system with the proposed FLC is shown in Figure 6.6.

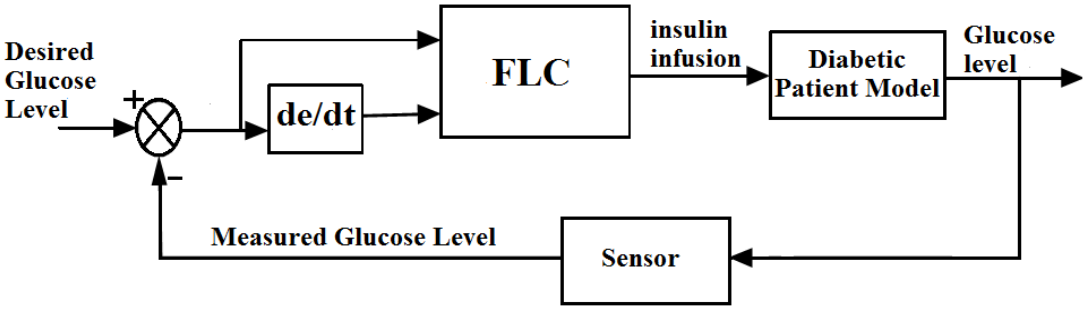


Figure (6.6): Fuzzy logic control block diagram

There are three main essential components for designing and implementing of artificial pancreas closed-loop, which are shown in **Figure 6.7**

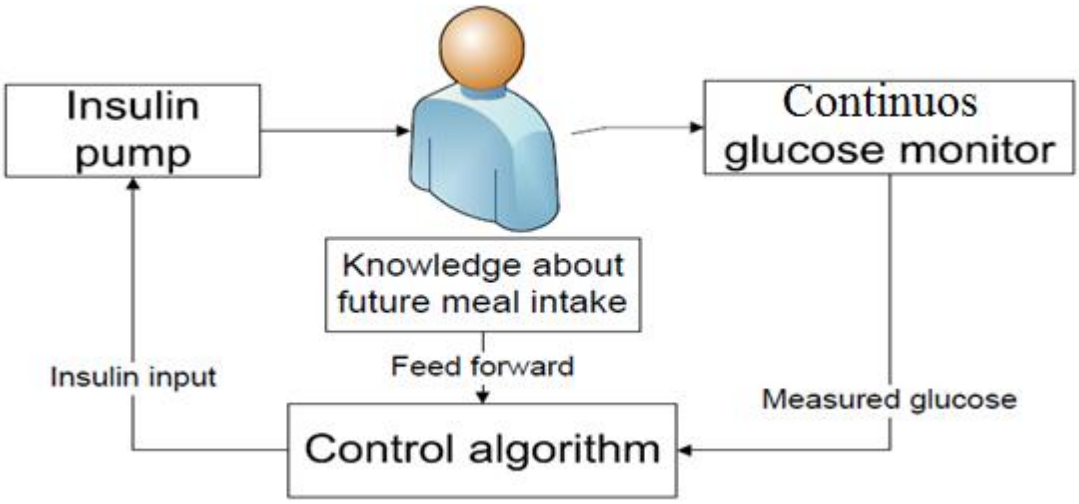


Figure (6.7): Illustration and Implementation of artificial pancreas closed-loop.

6.3.1 Mechanical insulin Pump

This mechanical pump provide continuous insulin infusion subcutaneous all the time as body needed. This injection way is safety and easy to infuse than intravenous way. (Takahashi, D., Xiao, Y., Hu, F., & Lewis, M., 2008).

Figure (6.8): Mechanical insulin pump with continuous glucose monitor

Mechanical insulin pump shown in **figure 6.8,** is externally connected and attached to the body in proper way, with its fitting connections, provided with insulin bottle for continuous insulin infused. The kit of needle and tube should be changed every 72 hours. This pump is programmed as doctor says to provide suitable dose of insulin continuously through 24 hours. The pump programmer should take in consideration that additional insulin dose should be after meals time, depend on food that will be eating. Although, this pump is suitable and easy to use, but it is not widespread because of its high cost.

A diabetes Pump Transfer Function

This pump is very helpful because it allows a smooth transition of blood-glucose levels, rather than a violent reaction to a large amount of insulin. The next equation is the much simplified final transfer function in the s-domain that represents the glucose in, insulin out system that is trying to be obtained. This is the transfer function of the individual beta cells in the pancreas.

$$T(s) = \frac{0.2}{s^2+0.2s+2} . \qquad (6.1)$$

6.3.2 Glucose Monitoring

- The sensors which used for glucose measurement are small devices in order to be inserted subcutaneous into the body tissue in.as this sensor connected in proper and correct way it can measure the blood glucose. (Takahashi, D., Xiao, Y., Hu, F., & Lewis, M., 2008). Main advantage of this subcutaneous sensor that it can give continuous blood glucose concentration monitoring. (Girardin, C. M., Huot, C., Gonthier, M., & Delvin, E., 2009).

• This continuous blood glucose measurement device need daily calibrated to be sure that its measurements are reliable.

• Blood glucose monitor sensor should be changed every 3 to 6 days.

• Device measurements accuracy are dependent on device calibration.

• Until this time these blood glucose detecting sensors are still very expensive.

6.3.3 Device algorithm control

Many control algorithm were designed to make the blood glucose closed loop is automatic one, so many decision rules for insulin injection into body according to blood glucose concentration measurements are needed. Several attempts have been made to design such a control algorithm using the theories of MPC, H-infinity, PID control and Fuzzy logic among others, here I will use a fuzzy control algorithm which is consider one of many attempts which are suitable to make automatic BGL. Some aspects of the human glucose regulation and today's available diabetes treatment equipment makes automatic control particularly challenging. These elements are identified as:

• Measurement time delay, as insulin is infused to the body, the program controller give suitable time delay for measurement, so that the injected insulin can take effect, this lead to correct blood glucose measurements.

• Input, continuous blood glucose monitor system model is designed with two inputs which are injected insulin and food intake, here injected insulin decrease blood glucose level and food intake increase blood glucose level, here only one input is controlled by algorithm, so when blood glucose is too low there is no any control algorithm action to avoid this problem which can lead to hypoglycaemia. As a solution for solving this problem glucagon injection was proposed (Ward, W. K., Engle, J.,

Duman, H. M., Bergstrom, C. P., Kim, S. F., & Federiuk, I. F., 2008), but until now it has not successfully.

• Safety, such like this system need more safety because it deal with human and it must be able to avoid fatal outcome problems.

6.4 Fuzzy Controller

With Mamdani-Fuzzy type the controller is structured, with two input and one output variables. The blood glucose error G (t) and its rate of change dG/dt are the input variables and the output variable is the exogenous insulin infusion rate. The characteristics of the input and output variables are given in table 2 and 3, respectively. The types of membership functions applied in the design are chosen triangular membership functions for simplicity. These membership functions were selected according with the fuzzy classification of the input and output variables. The inputs and output membership functions are shown in **figure 6.9** respectively.

Table 6.1 characteristics of input variables

Input variables	Interval	Membership Functions						
Glucose error G(t)	[-300 100] mg/dl	Negative Large	Negative Big	Negative Medium	Negative Small	Normal	Positive Small	Positive Big
Glucose error deviation dG/dt	[-20 20] mg/dl	Negative	Zero	Positive				

Table 6.2 characteristics of output variable

Output variables	Interval	Membership Functions						
Insulin Infusion U(t)	[-1 8] µU/mg	Negative Big	Negative Small	Zero	Positive Small	Positive medium	Positive Big	Positive Large

Variables fuzzy sets are determined as: Negative Large (NL), Negative Big (NB), Negative Medium (NM), Negative Small (NS) Normal (N), Positive Small (PS), Positive Medium (PM), Positive Big (PB), Positive Large (PL), Negative (NEG), Zero (Z), and Positive (POS).

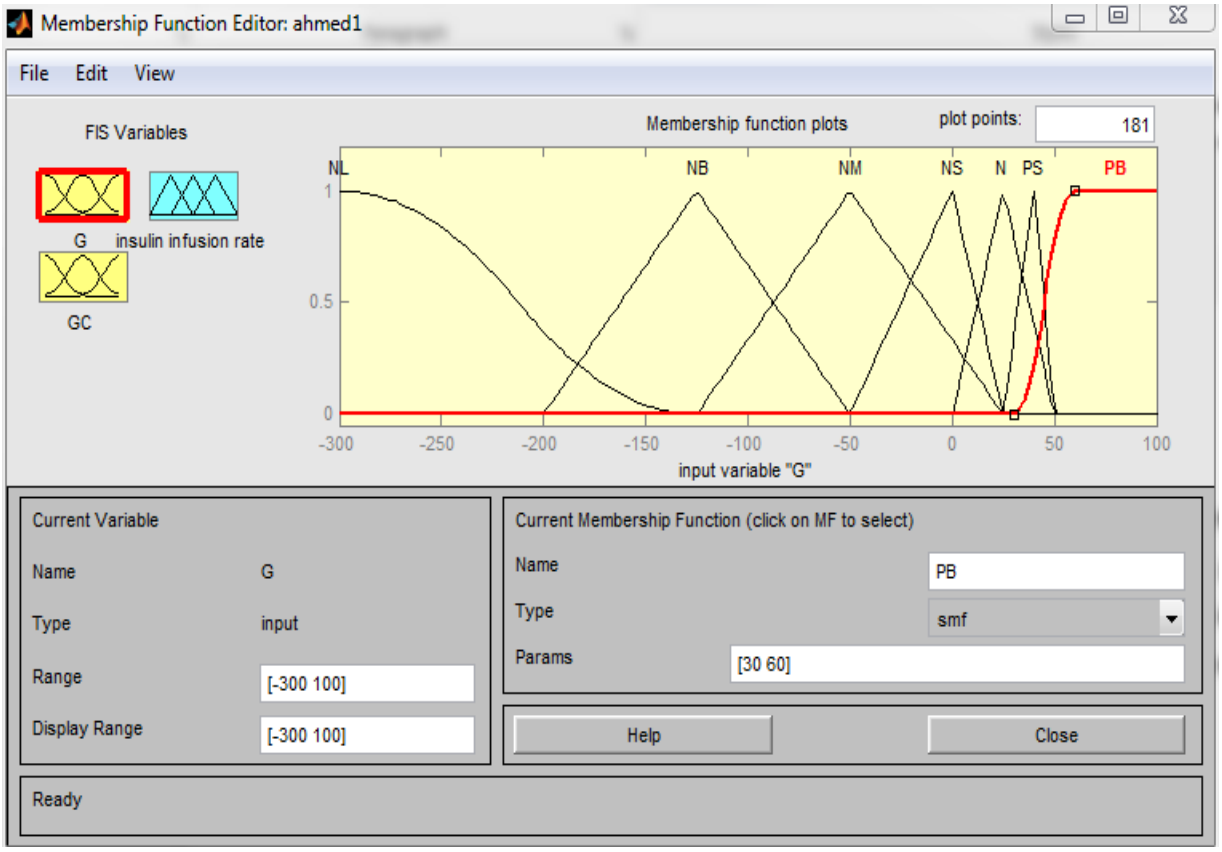


Figure (6.9a): glucose concentration (mg/dl)

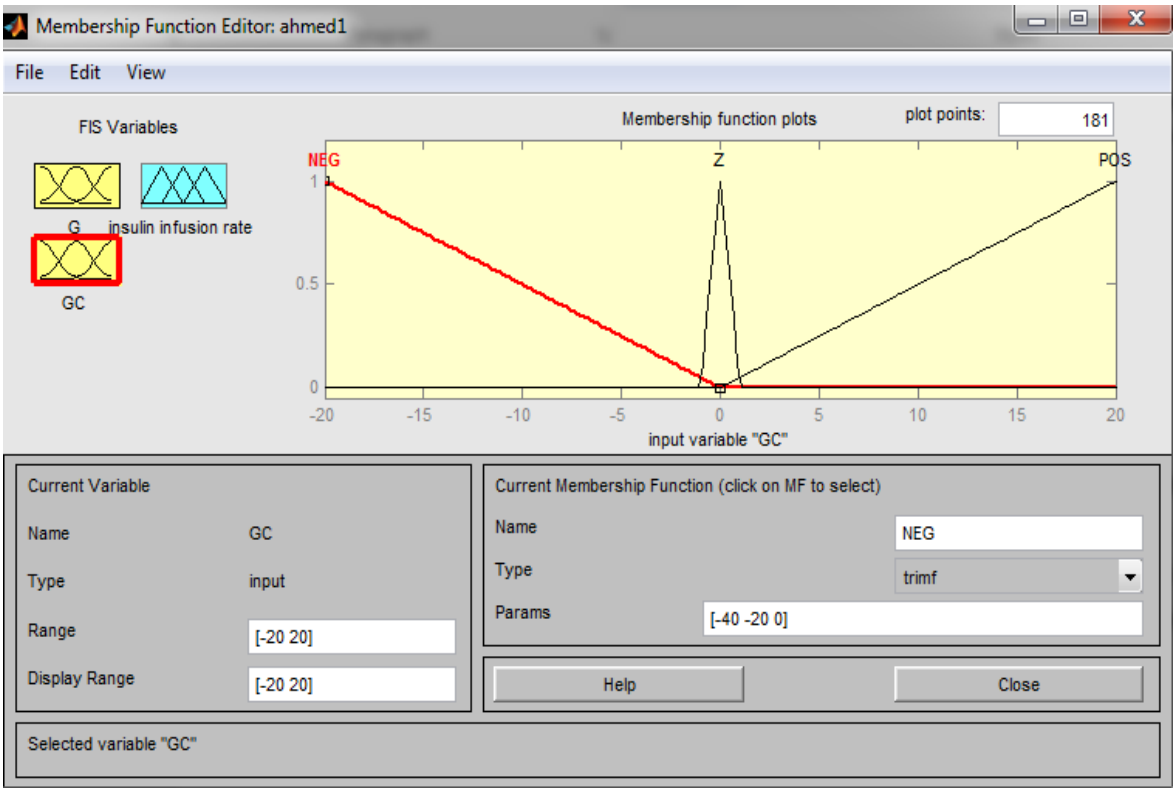


Figure (6.9b): glucose deviation (mg/dl)

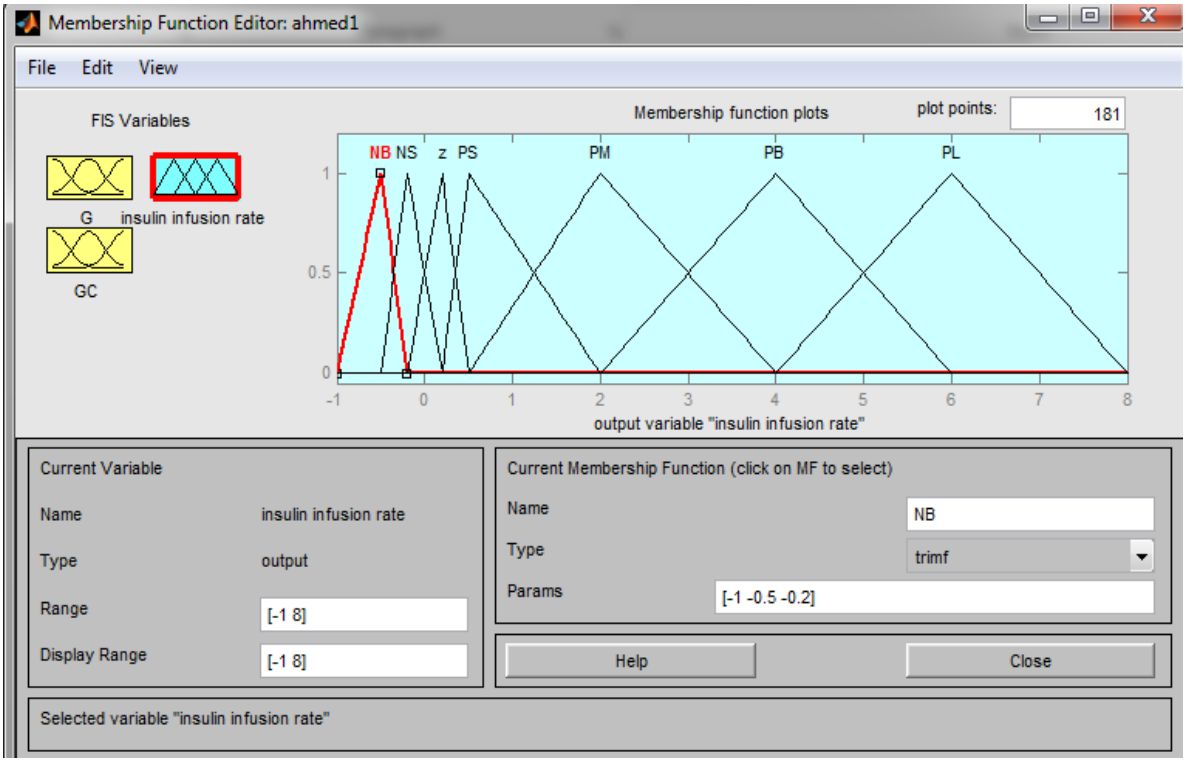


Figure (6.9c): insulin infusion rate (micro U/mg)

By the definition of the input and output fuzzy sets, a total of 21 IF-THEN rules were defined. These rules were of AND (minimum) type antecedent. The output (defuzzification method) is calculated by the CENTROID method. The linguistic rules are detailed in table 3.

Table 6.3 Fuzzy IF-THEN rules.

	Glucose error rate of change		
Glucose error	Negative	Zero	Positive
NL	PB	PB	PL
NB	PM	PM	PL
NM	PM	PM	PB
NS	Z	PS	PM
N	Z	Z	PS
PS	Z	Z	Z
PB	Z	Z	Z

The linguistic rules also can be written in another form as are detailed below:

- If (G is NL) and (GC is NEG) then (insulin infusion rate is PB) (1)
- If (G is NL) and (GC is Z) then (insulin infusion rate is PB) (1)

Fuzzy controller output surface using previous rules is shown in Figure **6.10**. It is obvious that inputs change with the output.

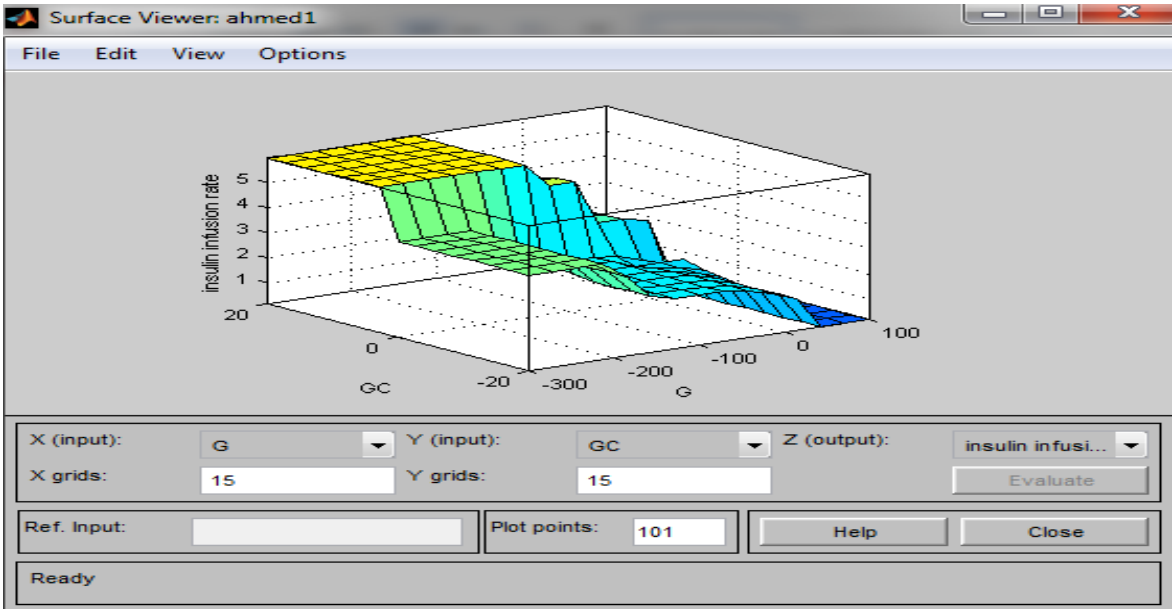
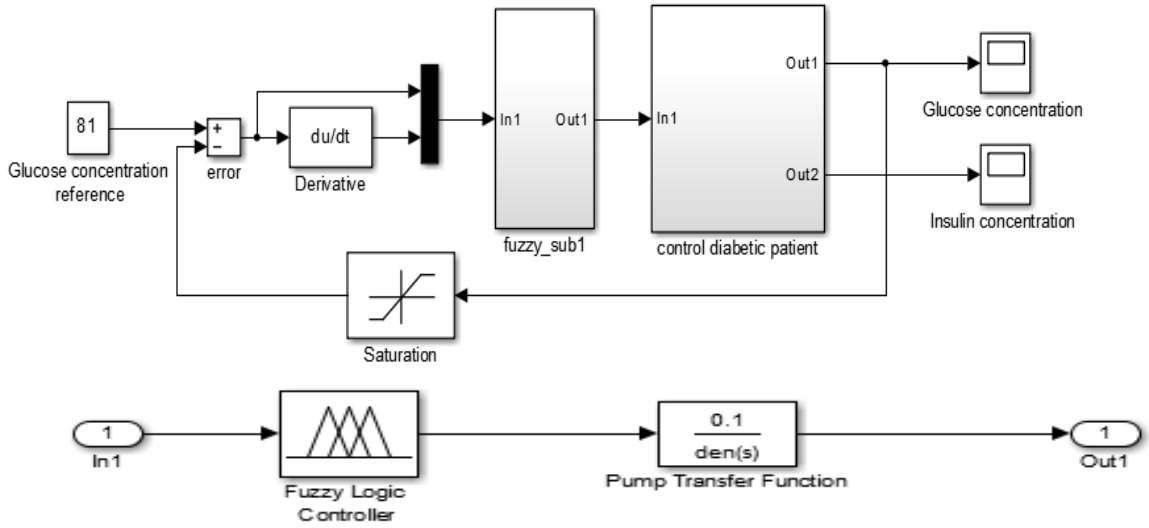


Figure (6.10): Control action surface.

Now after designed of fuzzy controller, I will connect it to closed loop system, then using Matlab simulation as shown in **figure 6.11**



fuzzy_sub1

Figure (6.11): fuzzy controller with diabetic patient model

Figure 6.12 show the blood glucose and insulin concentration as mentioned before for diabetic patient model before applying the fuzzy controller, **figure 6.12a** show that blood glucose concentration level at steady state is high nearly 140 mg/dl, after glucose or meal intake BGL increase to reach nearly 300 mg/dl and after that due to insulin weak production the BGL decrease but still high around 140 mg/dl.

F**igure 6.12b** show that blood insulin concentration level at steady state is low nearly 0.03 mU/dl, then due to glucose or meal intake the BGL is increase, so the insulin concentration tightly increase to reach nearly 0.05 mU/ml.

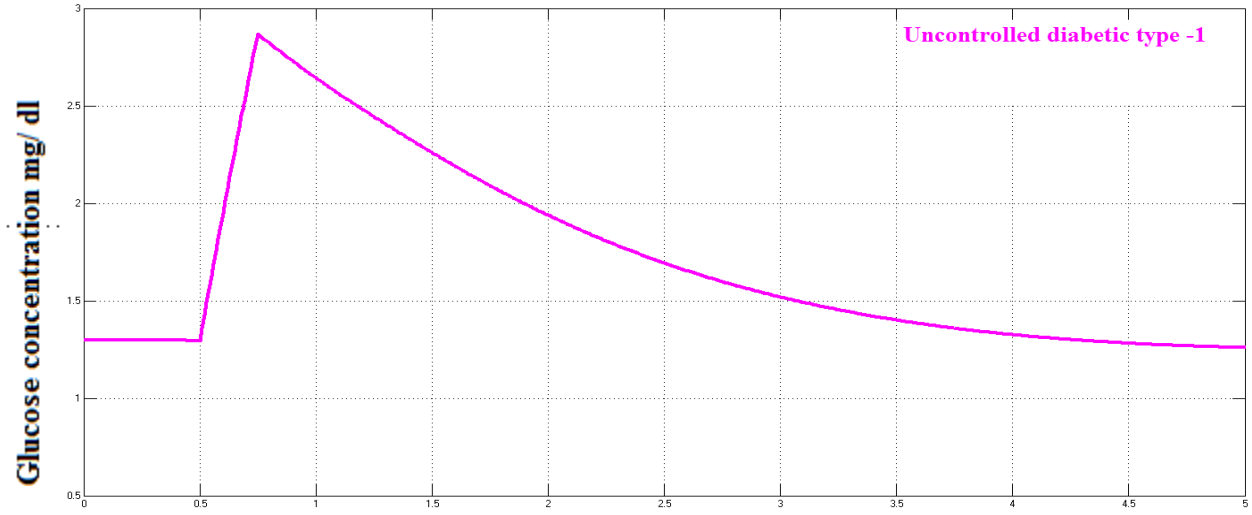


Figure (6.12a): Glucose concentration

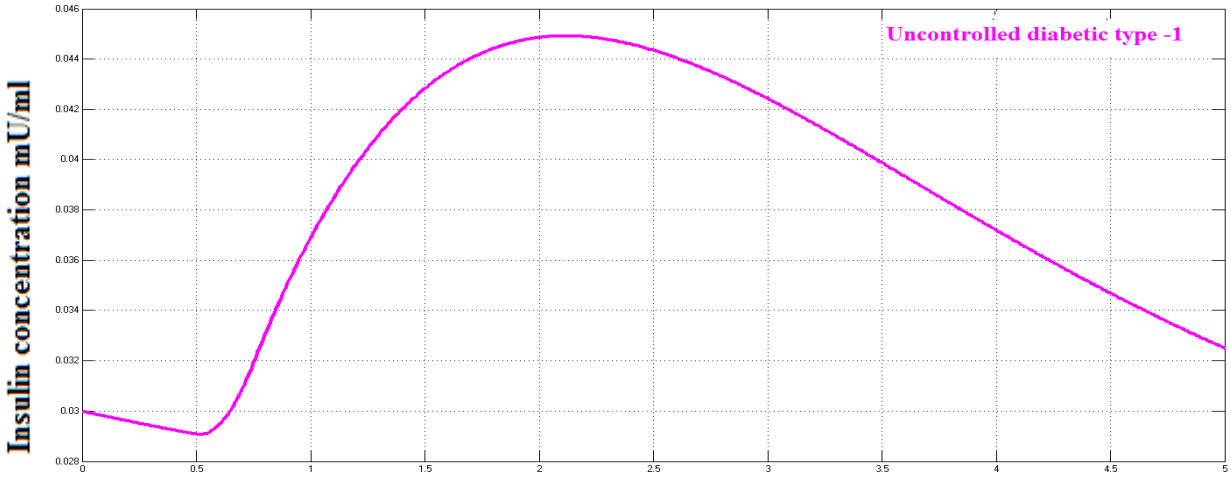


Figure (6.12b): Insulin concentration

The same diabetic patient model with all pervious conditions will be simulated this time with applying the fuzzy controller algorithm to control the BGL using Matlab/Simulink, as shown in the next **figure 6.13**

- Simulation results after applying fuzzy controller algorithm to our system are:

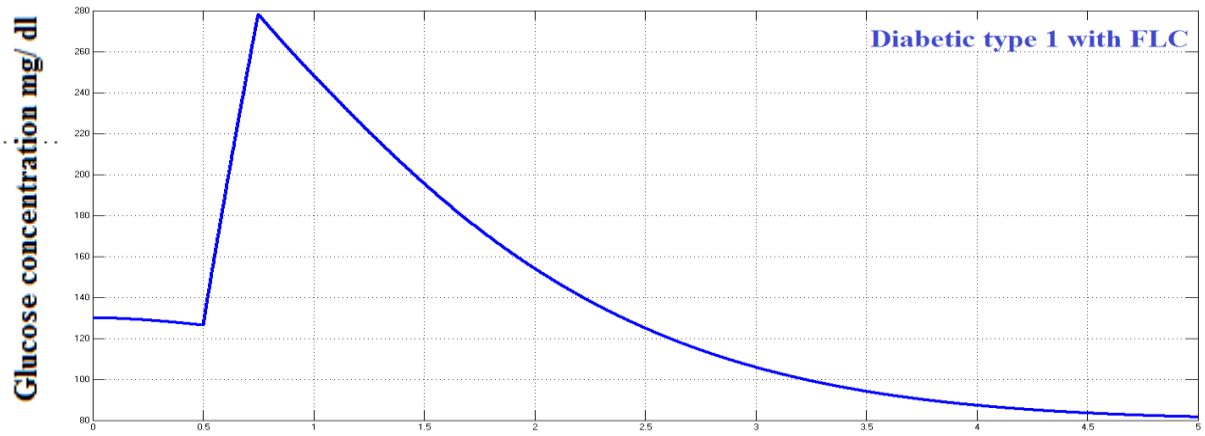


Figure (6.13a): Glucose concentration with FLC

Figure 6.13a show that blood glucose concentration level at steady state is high nearly around 140 mg/dl, after glucose or meal intake BGL increase to reach nearly 300 mg/dl and after that due to fuzzy algorithm BGL controller, BGL decrease to reach normal value 80 mg/dl.

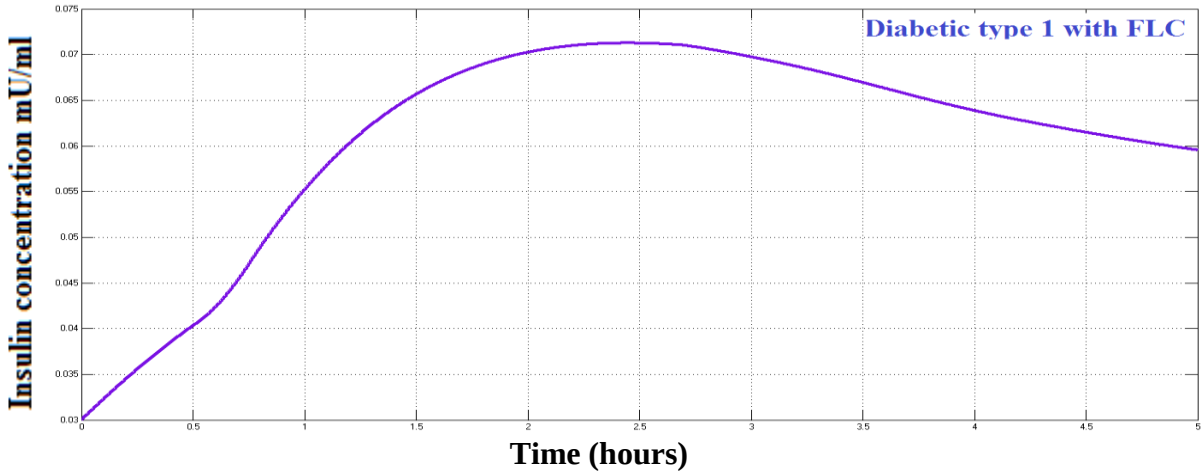


Figure (6.13b): Insulin concentration with FLC

Figure 6.13b show that blood insulin concentration level at steady state is low nearly 0.03 mU/dl, then due to glucose or meal intake the BGL is increase, so the insulin concentration increased in proper way due to use fuzzy algorithm BGL controller to reach nearly 0.09 mU/ml.

- Now a complete system for the blood glucose insulin regulation system illustrated as shown in **Figure 6.14** to give complete picture of the model simulation results, as shown in **figure 6.15**

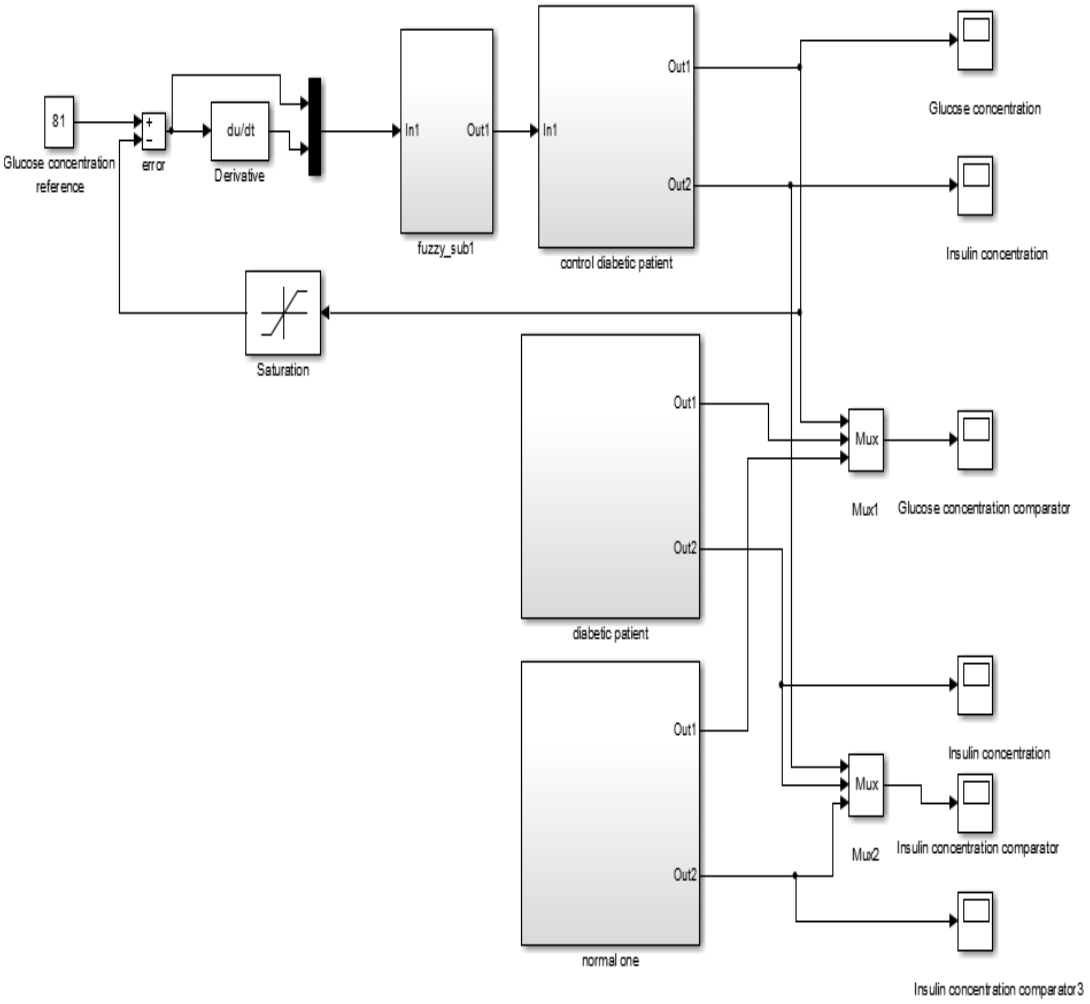


Figure (6.14): block diagram of the blood Glucose and Insulin regulation simulation for three case

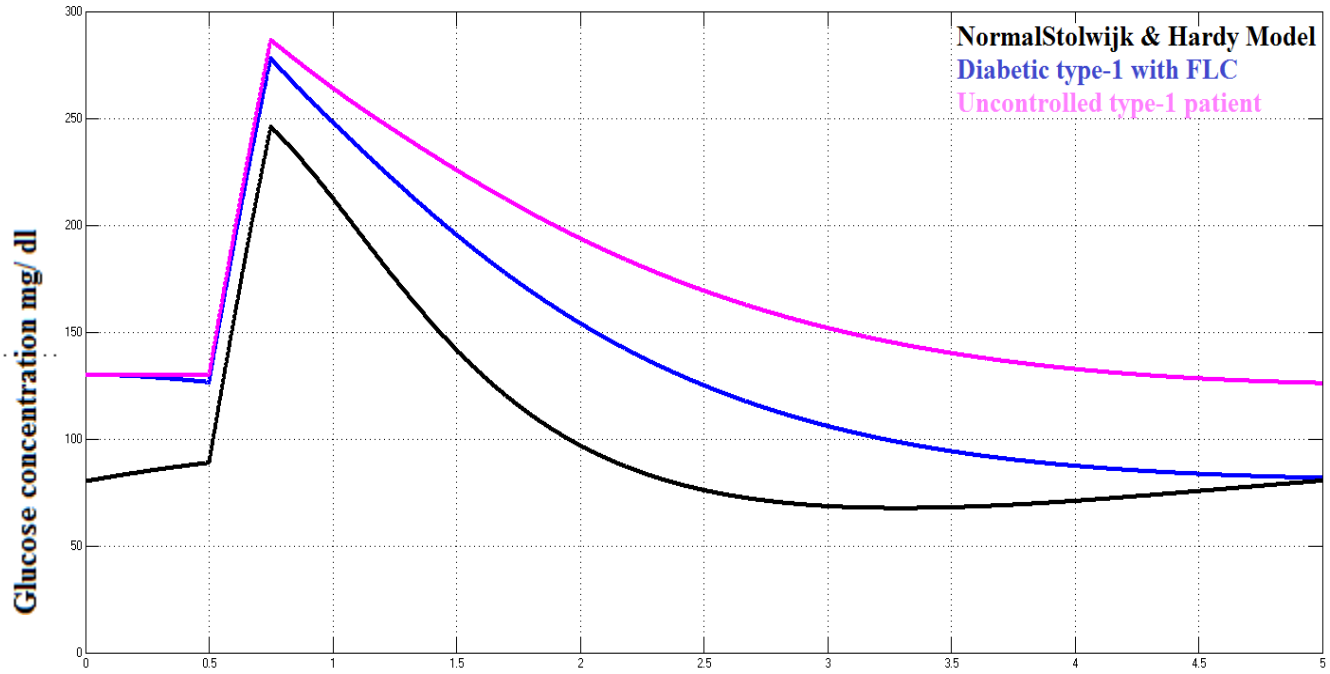


Figure (6.15a): Simulation of glucose concentration for three cases

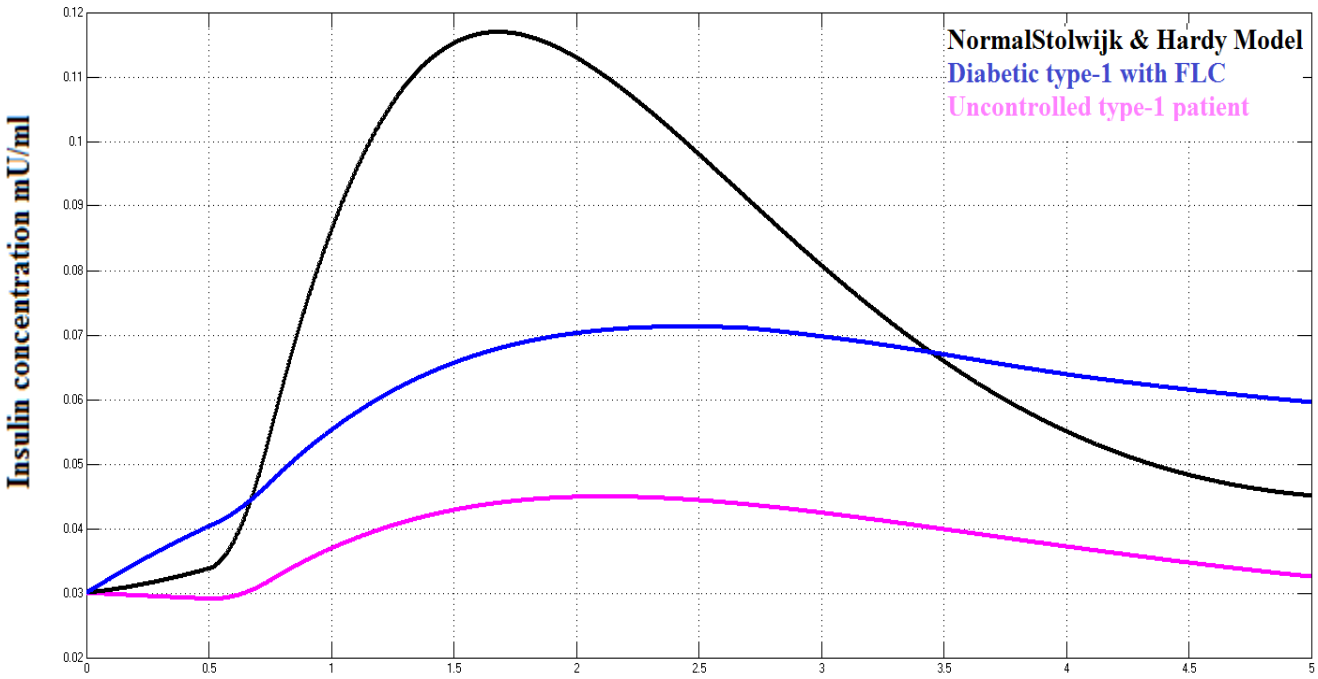


Figure (6.15b): Simulation of insulin concentration for three cases

By comparing the three results of the simulation, normal person, FL controlled type 1 diabetic patient and uncontrolled type 1 diabetic patient. It can be clearly seen that the Fuzzy controller gives more effective results in terms of the regulation of the blood glucose level, as shown in **figure 6.15a** and in **figure 6.15b**

6.5 Generating fuzzy systems using genetic algorithms for our model

The performance of a fuzzy logic controller depends on its control rules and membership functions. Hence, it is very important to adjust these parameters to the process to be controlled. A method is presented for tuning fuzzy control rules by genetic algorithms to make the fuzzy logic control systems behave as closely as possible to the operator or expert behaviour in a control process. The tuning method fits the membership functions of the fuzzy rules given by the experts with the inference system and the defuzzification strategy selected, obtaining high-performance membership functions by minimizing an error function defined using a set of evaluation input-output data.

6.6 New fuzzy controller implementation using GA

Here in my thesis work genetic algorithm will be used to reach near optimized membership function, and fitness function which used is sum of the error. Genetic algorithm matlab code is used to fittest the membership function range, this code is divided into two codes main code which responsible for performing the GA steps such as generate new population, selection, crossover and mutation. The second one is responsible for testing the new population to determine fitness function and find the best fitness value, here in our system the fuzzy controller have two inputs and one output, the first input which is glucose error consist of seven membership one of these membership is S membership function, five are triangular memberships and one is Z, the second input consist of three triangular memberships. Here in our GA code I will let the second input which is change of glucose error (derivative) and the output which consist of seven triangular memberships function are fixed and test the first input membership range or shape by GA to get best results. In triangular membership function there are three parameters that can be modified to change its range or shape, centre, right edge and left edge where in Z and S membership functions there are two

parameters, top edge and left or right edge. The first input have 19 edges I will consider 16 edges of them as variable and the other four are fixed. The fitness function that will be used is integral absolute error values.

There are many parameters effect the control process of our system like as the shape or the range of inputs and output memberships of fuzzy controller. These parameters can be tuned to give near optimal results. GA is used to reach near optimized shape of these fuzzy memberships'.

The new input membership's function of glucose which is the first input which optimized by genetic algorithm is shown in figure 6.16.

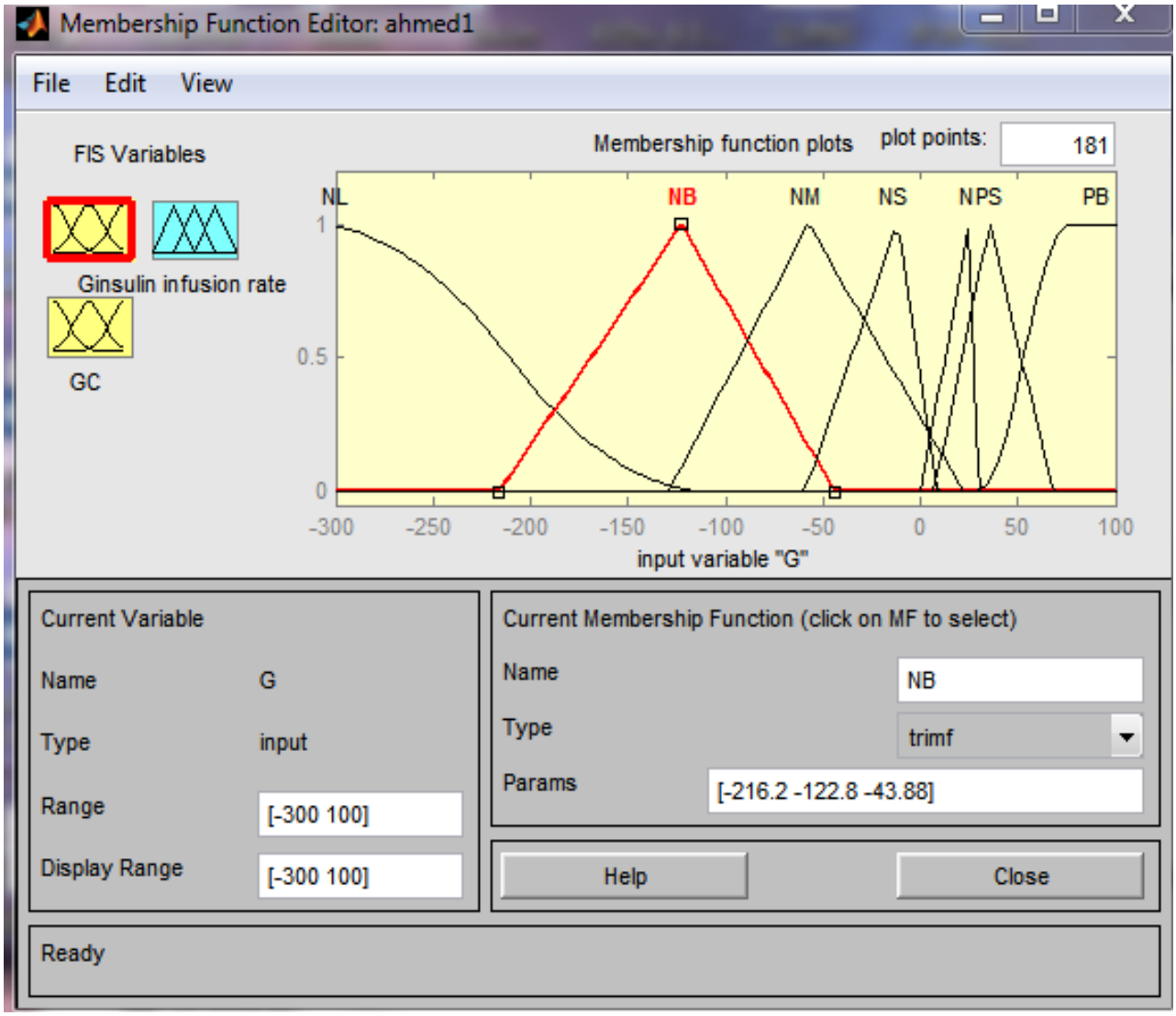


Figure (6.16): Glucose input membership's function using genetic algorithm

Where the new glucose error parameters with Fuzzy – Genetic Algorithm are:

'NL': [-314.6823 -106.9550]

'NB': [-216.2463 -122.7517 -43.8807]

'NM': [-129.1642 -57.3314 22.0870]

'NS': [-59.4428 -12.0235 9.0274]

'N': [0 25 30]

'PS': [6.7986 35.5230 68.0450]

'PB': [27.7126 78.0841]

While the glucose error parameters with fuzzy logic controller are:

'NL': [-300 -125]

'NB': [-200 -125 -50]

'NM': [-125 -50 25]

'NS': [-50 0 25]

'N': [0 25 50]

'PS': [25 40 50]

'PB': [30 60]

So it is clear that there is change in glucose error input parameters range, these new parameters were tested and simulated by Matlab/Simulink. These new parameters give improve in results as will show in next section.

6.7 Experimental results

The results of experimental show that genetic algorithm method has good performance as shown in the next glucose concentration error figures:

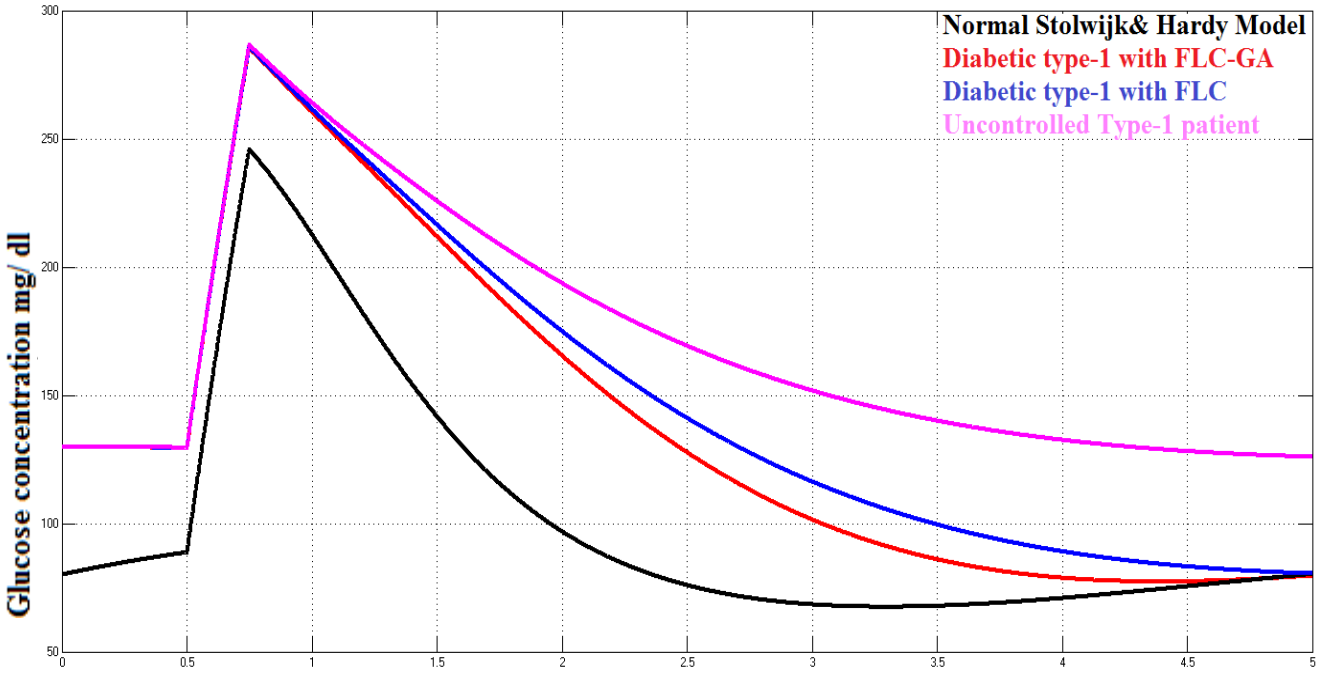


Figure (6.17a): Simulation of glucose concentration for the four cases

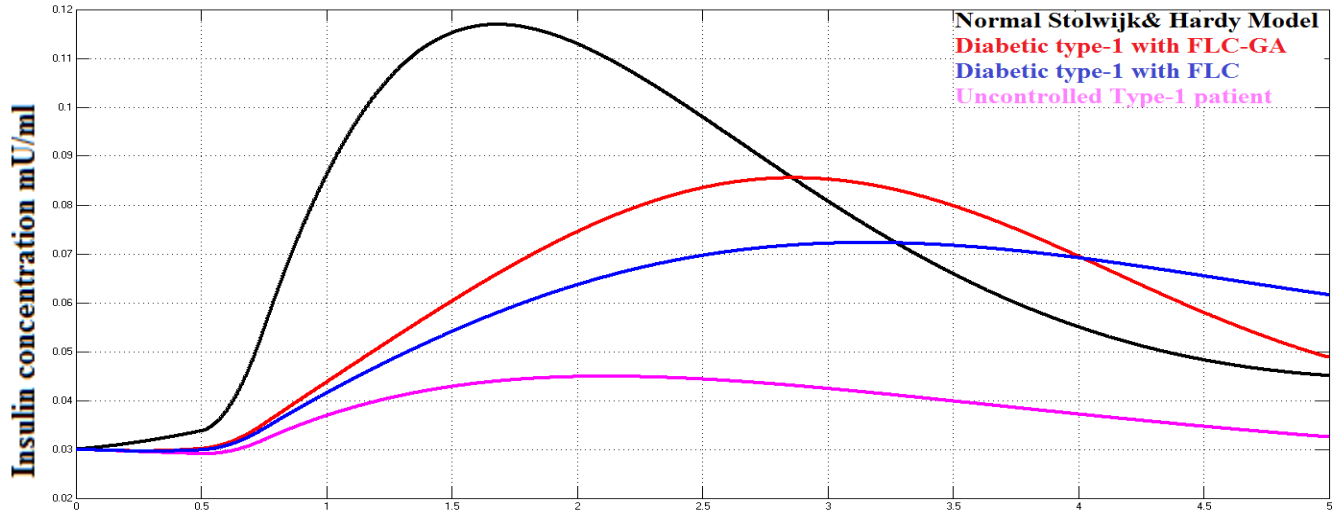


Figure (6.17b): Simulation of insulin concentration for the four cases

By comparing the results of the simulation for four cases, normal person, FL controlled type 1 diabetic patient, FLC with GA and Uncontrolled type 1 diabetic patient. It is observed that Fuzzy controller with GA gives more effective results in terms of the regulation of the blood glucose level, as shown in **figure 6.17a** and in **figure 6.17b.**

Chapter 7
Conclusion

Chapter 7

Conclusion

7.1 Conclusion

In this thesis, the closed-loop control of pancreatic model is designed, conducted and analyzed with the aid of Matlab/Simulink for the management of the glucose-insulin regulation. The closed-loop control techniques are firstly evaluated to the Stolwijk-Hardy glucose-insulin model. This model was cmodified by adding robust insulin to improve the treatment of T1DM. This control system is designed, implemented using fuzzy controller & fuzzy - genetic algorithm, and then tested using Simulink of Matlab program.

By comparing the results of the simulation for four cases (Normal person, FL controlled type 1 diabetic patient, FLC with GA and Uncontrolled type 1 diabetic patient) it can be clearly seen that the Fuzzy controller with GA gives more effective results in terms of the regulation of the blood glucose level and also the Fuzzy-GA controller comes into prominence in terms of settling time and steady state error.

So with aid of insulin pump and control algorithm that developed for regulation of glucose – insulin blood concentration, life quality of type-1 diabetes patient's is improved.

7.2 Future work

Monitoring of blood glucose concentration is still important factor in performance improvement of glucose – insulin regulation system, so hopefully this system can be developed, be more better and getting more robust

Control algorithm that developed for the regulation of blood glucose concentration must be improved to be able to prevent from Hypoglycemia

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Appendix A GA Matlab Programs

1- Genetic Algorithm main Program Matlab Code

```
clc
clear
global aaa e_abs yout timef  rin set_p
Ts=0.001;
ahmed1=readfis('ahmed1');
open_system('fuzzy_Glucose');
MAXGEN = 2;%100; % maximum Number of generations
NVAR = 16; % Generation gap, how many new individuals are
created
GGAP = .5; % Generation gap, how many new individuals are
created
PRECI = 10; % Binary representation precision
NIND = 10; % No. of individuals per subpopulations
% First, a field descriptor is set up
FieldD = [rep([PRECI],[1, NVAR]); rep([-20;20],[1, NVAR]);...
rep([1; 0; 1 ;1], [1, NVAR])];
% The population is then initialised
FieldD;
BsJ=0;
E = crtbp(NIND, NVAR*PRECI);
% Initial population is evaluated
for  kg=1:1:MAXGEN
     time(kg)=kg;
       Kfuzzy=bs2rv(E,FieldD);

    for s=1:1:NIND
         %****** Step 1 : Evaluate BestJ ******
        Kfuzzyi=Kfuzzy(s,:);

        [Kfuzzyi,BsJ]=mychap5_2f4(Kfuzzyi,BsJ);

        BsJi(s)=BsJ;
    end
    [OderJi,IndexJi]=sort(BsJi);
    BestJ(kg)=OderJi(1);
    BJ=BestJ(kg);
    Ji=BsJi+1e-10;

    fi=1./Ji;

    [Oderfi,Indexfi]=sort(fi);          %Arranging fi small to
bigger
    Bestfi=Oderfi(NIND);            % Let Bestfi=max(fi)
    BestS=E(Indexfi(NIND),:);       % Let BestS=E(m), m is the
Indexfi belong to max(fi)

    kg
    BJ
    BestS;

    %****** Step 2 : Select and Reproduct Operation******
    fi_sum=sum(fi);
```

```
    fi_Size=(Oderfi/fi_sum)*NIND;

    fi_S=floor(fi_Size);        %Selecting Bigger fi value
    kk=1;
    for i=1:1:NIND
        for j=1:1:fi_S(i)        %Select and Reproduce
            TempE(kk,:)=E(Indexfi(i),:);
            kk=kk+1;              %kk is used to reproduce
        end
    end
    %************ Step 3 : Crossover Operation ************
    pc=0.99;
    n=ceil(160*rand);
    for i=1:2:(NIND-1)
        temp=rand;
        if pc>temp                  %Crossover Condition
            for j=n:1:160
                TempE(i,j)=E(i+1,j);
                TempE(i+1,j)=E(i,j);
            end
        end
    end
    TempE(NIND,:)=BestS;
    E=TempE;
    %************ Step 4: Mutation Operation **************
    %pm=0.001;
    pm=0.001-[1:1:NIND]*(0.001)/NIND; %Bigger fi, smaller pm
    %pm=0.0;    %No mutation
    %pm=0.1;    %Big mutation

    for i=1:1:NIND
        for j=1:1:3*PRECI
            temp=rand;
            if pm(i)>temp               %Mutation Condition
                if TempE(i,j)==0
                    TempE(i,j)=1;
                else
                    TempE(i,j)=0;
                end
            end
        end
    end
    %Guarantee TempE(Size,:) belong to the best individual
    TempE(NIND,:)=BestS;
    E=TempE;
end
Bestfi
BestS
Kfuzzybest=bs2rv(BestS,FieldD);
[Kfuzzyi,BsJ]=mychap5_2f4(Kfuzzybest,BsJ);
Kfuzzyi
Best_J=BestJ(MAXGEN)
figure(2);
%plot(time,BestJ);
xlabel('Times');ylabel('Best J');
 figure(3);
% plot (timef, set_p,'r',timef, yout,'b');
% xlabel('Time(s)');ylabel('rin,yout');
```

2- Fuzzy Genetic Algorithm Matlab Code Simulation Program

```
function [Kfuzzyi,BsJ]=fuzzy_gaf(Kfuzzyi,BsJ)
global rin aaa e_abs yout timef  set_p



%-------------------------------------------------------------------
------
a=newfis('ahmed1');
    a=addvar(a,'input','G',[-300,100]); % parameter g
    a=addmf(a,'input',1,'NL','zmf',[-300-Kfuzzyi(1),-125-
Kfuzzyi(2)]);
    a=addmf(a,'input',1,'NB','trimf',[-200-Kfuzzyi(3),-125-
Kfuzzyi(4),-50-Kfuzzyi(5)]);
    a=addmf(a,'input',1,'NM','trimf',[-125-Kfuzzyi(6),-50-
Kfuzzyi(7),25-Kfuzzyi(8)]);
    a=addmf(a,'input',1,'NS','trimf',[-50-Kfuzzyi(9),0-
Kfuzzyi(10),25-Kfuzzyi(11)]);
    a=addmf(a,'input',1,'N','trimf',[0,25,30]);
    a=addmf(a,'input',1,'PS','trimf',[25-Kfuzzyi(12),40-
Kfuzzyi(13),50-Kfuzzyi(14)]);
    a=addmf(a,'input',1,'PB','smf',[30-Kfuzzyi(15),60-Kfuzzyi(16)]);



    a=addvar(a,'input','GC',[-40,40]); % parameter gc
    a=addmf(a,'input',2,'NEG','trimf',[-40,-20,0]);
    a=addmf(a,'input',2,'Z','trimf',[-1,0,1]);
    a=addmf(a,'input',2,'pos','trimf',[0,20,40]);

    a=addvar(a,'output','insulin infusion rate',[-10,80]); %
parameter insulin
    a=addmf(a,'output',1,'NB','trimf',[-10,-5,-2]);
    a=addmf(a,'output',1,'NS','trimf',[-5,-2,2]);
    a=addmf(a,'output',1,'z','trimf',[-2,2,5]);
    a=addmf(a,'output',1,'PS','trimf',[2,5,20]);
    a=addmf(a,'output',1,'PM','trimf',[5,20,40]);
    a=addmf(a,'output',1,'PB','trimf',[20,40,60]);
    a=addmf(a,'output',1,'PL','trimf',[40,60,80]);

    %
**********************************************************************
**
    rulelist=[ 1 1 6 1 1;
        1 2 6 1 1;
        1 3 7 1 1;

        2 1 5 1 1;
        2 2 5 1 1;
        2 3 7 1 1;

        3 1 5 1 1;
        3 2 5 1 1;
```

```
        3 3 6 1 1;

        4 1 3 1 1;
        4 2 4 1 1;
        4 3 5 1 1;

        5 1 3 1 1;
        5 2 3 1 1;
        5 3 4 1 1;

        6 1 3 1 1;
        6 2 3 1 1;
        6 3 3 1 1;

        7 1 3 1 1;
        7 2 3 1 1;
        7 3 3 1 1];

a=addrule(a,rulelist);
%showrule(a)                          % Show fuzzy rule base

a=setfis(a,'DefuzzMethod','centroid');  % Defuzzy
writefis(a,'ahmed1');                 % save to fuzzy file "fuzzf.fis"
which can be
% simulated with fuzzy tool
ahmed1=readfis('ahmed1');
ahmed1.input(1,1).mf(1,1)
    ahmed1.input(1,1).mf(1,2)
    ahmed1.input(1,1).mf(1,3)
    ahmed1.input(1,1).mf(1,4)
    ahmed1.input(1,1).mf(1,5)
    ahmed1.input(1,1).mf(1,6)
    ahmed1.input(1,1).mf(1,7)

[t,x,y]=sim('fuzzy_Glucose');
clear t;
clear x;
clear y;
BsJ=0;
%------------------------
  figure(1);
  hold on
 % plot(timef,set_p,'r',timef,yout,'b');
  % xlabel('Time(s)');ylabel('rin,yout');
  hold off
 %-------------------------------------
ts=0.001;
  for k=1:1:5001
     % timef(k)=k*ts;
     % Ji(k)=(e_abs.time(k)*e_abs.signals.values(k))
    Ji(k)=(0.5*e_abs.signals.values(k));
     BsJ=BsJ+Ji(k);
  end
  BsJ

end
```