KWAME NKRUMAH UNIVERSITY OF SCIENCE AND TECHNOLOGY

MODELLING AN EQUATION FOR DETECTING DIABETES

BY

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DECLARATION

Candidate's Declaration

I hereby declare that this submission is the result of my own original work and that no part of it has been presented for another degree in this university or elsewhere.

Candidate's Signature: ..... Date: .....

Name: **Jacobs, Bernard Allotey**

Supervisor's Declaration

I hereby declare that the preparation and presentation of the thesis were supervised in accordance with the guidelines on the supervision of dissertation laid down by the Kwame Nkrumah University of Science and Technology.

Supervisor's Signature: ..... Date: .....

Name: **Dr. E. O. Frimpong**

Abstract

Diabetes is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in abnormally high blood sugar levels. Various hormones in our body such as insulin, growth hormone, glucagon control blood glucose levels, epinephrine best known as adrenaline, glucocorticoids and thyroxin. The two most common forms of diabetes are due to either a diminished production of insulin (Type 1 diabetes), or diminished response by the body to insulin (Type 2 and gestational diabetes). Both lead to hyperglycemia, which largely causes the acute signs of diabetes: excessive urine production, resulting compensatory thirst and increased fluid intake, blurred vision, unexplained weight loss, lethargy, and changes in energy metabolism. We will explain how the hormone, insulin is activated and how it affects glucose levels in blood. We present a mathematical model that determines diabetes in patients based in the results on the glucose intolerance test of 5 hours. The model is in line with the one proposed by E. Ackerman (1969). The model is based on a 2x2system of non-homogenous ordinary differential equations. A nonlinear least square method is used to determine the coefficient parameters of the system based on actual data from GTT. The simulations also provide an indicator similar to the one proposed by E. Ackerman (1969), to diagnose a diabetic condition.

Keywords: **Differential equation, diabetes, glucose, insulin.**

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DEDICATION

To my Oiada family in Cape Coast and in New Jersey

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Chapter one

Introduction

This chapter presents the background of the study, problem of the study, its objectives, the methodology, the justification and the organization of the study.

1.0 Background to the study

Barron's Accounting dictionary defines mathematical model as a Mathematical representation of reality that attempts to explain the behavior of some aspect of it. The mathematical model serves the following purposes:

(a) To find an optimal solution to a planning or decision problem.

(b) To answer a variety of what-if questions.

(c) To establish understandings of the relationships among the input data items within a model.

(4) To attempt to extrapolate past data to derive meaning.

Many everyday activities carried out without a thought are uses of mathematical models. Examples are a geographical map projection of a region of the earth onto a small plane surface which can be used for many purposes such as planning travel. Another simple activity is predicting the position of a vehicle from its initial position, direction and speed of travel, using the equation that distance travelled is the product of time and speed.

Differential Equation is a mathematical concept that perfectly explains mathematical modeling. Britannica Concise Encyclopedia defines Differential Equation as the Mathematical statement that contains one or more derivatives. It states a relationship involving the rates of change of continuously changing quantities modeled by functions. Differential equations are very common in physics, engineering, and all fields that involve quantitative study of change. They are used whenever a rate of change is known but the process giving rise to it is not. The solution of a differential equation is generally a function whose derivatives satisfy the equation. Differential equations arise in many areas of science and technology, specifically whenever a deterministic relation involving some continuously varying quantities (modeled by functions) and their rates of change in space and/or time (expressed as derivatives) is known or postulated. Many mathematicians and biologists have used differential equations to model diseases and epidemics such as the model of lake pollution, bacteria growth, enzyme kinetics and many more. This thesis seeks to model the test for detecting diabetes. One area of modeling that involves the interaction of two separate variables is called compartment models.

Compartment models are often used to describe transport of material in biological systems. A compartment model contains a number of compartments, each containing well mixed material. Compartments exchange material with each other following certain rules. Material can either flow from one compartment to another, it can be added from the outside through a source, or it can be removed through a drain. Most compartment models have more than one compartment and equations for such a model are obtained by describing a conservation law for each compartment. A compartment model could represent an ecological system where the material could be energy, the compartments could represent different species of animals and plants, and the flow between compartments could account for uptake and loss of food (or energy).

Compartment models also arise in physiology, where the material could be oxygen that is transported with the blood between different organs (compartments) in the body. In this project the materials are glucose and insulin and the compartment is the blood.

Diabetes is a worldwide concern now and many developed countries are making it their national concern in fighting it. Some developing countries are making an attempt to fight it. Ghana is no exception as the rate of diabetes cases are increasing tremendously. Many individuals have little or no knowledge about the disease and the extent of damage it can cause both to the individual and the nation as a whole. Diabetes is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in abnormally high blood sugar levels. Various hormones in our body such as insulin, growth hormone, and glucagon control blood glucose levels, epinephrine best known as adrenaline, glucocorticoids and thyroxin. Diabetes is a disease that is characterized by excessive glucose in the blood stream. Currently, there is an epidemic of diabetes that has resulted from unhealthy lifestyles, which are dramatically different from how humans survived many years ago when food was difficult to find. There are two forms of diabetes, Type 1, often called juvenile diabetes, and Type 2, often referred to as adult onset diabetes (which now occurs in children as young as 5). Type 1 diabetes, is an autoimmune disease, and represents only 10% of all cases of diabetes. Type 1 diabetes is a hereditary disease, which occurs in about 4-20 per 100,000 people with peak occurrence around 14 years of age (Cooke et al, 2008).

How does glucose metabolism work? We ingest food to obtain energy to sustain our bodies. The carbohydrates in the food are broken down into simple sugars, which are absorbed into the blood. This raises the concentration of glucose in the blood, where cells can access it for metabolism into energy. However, when glucose levels get too high, then pressures (osmotic?) increase that can cause problems in the tissues. For normal subjects, the rise in glucose concentration causes the β-cells in the pancreas to release insulin into the

blood (along with a number of other hormones). Insulin affects glucose concentration in several ways, including the facilitation of glucose transport across cell membranes, especially in skeletal muscles, and conversion of glucose to glycogen in the liver, which provides a good storage of glucose for future consumption. Thus, increasing the concentration of insulin results in blood glucose concentration decreasing. This negative feedback system helps the body tightly regulate glucose levels to maintain a balance. There are other significant hormones that are involved in the regulation of blood glucose.

In response to high energy demands, epinephrine (adrenalin) is released to break down the glycogen and produce glucose. This hormone works opposite insulin to increase blood glucose.

The glucocorticoids help metabolize carbohydrates, especially in the liver, and also help increase blood glucose concentrations. Growth hormone can block the effects of insulin by reducing the liver uptake of glucose and decrease muscle sensitivity to insulin. There are many other hormones that regulate glucose levels in the blood, creating a complex regulatory system that is crucial to maintenance of blood glucose for energy to all cells in the body.

Type 1 diabetes occurs when someone who is genetically predisposed to the disease incurs some unknown environmental assault that initiates the auto-immune system to attack their own β-cells. When the β-cells are destroyed, they boost the immune system to further attack more β-cells, leaving the body without the ability to produce insulin. This severely limits its ability to regulate glucose and results in the onset of diabetes. Because of the immune response, the body cannot regenerate new β-cells nor can transplants succeed. Figure 1.1 Illustrate the interaction between glucose and insulin. Figure 1.2 is simplified version of the glucose – insulin interaction.

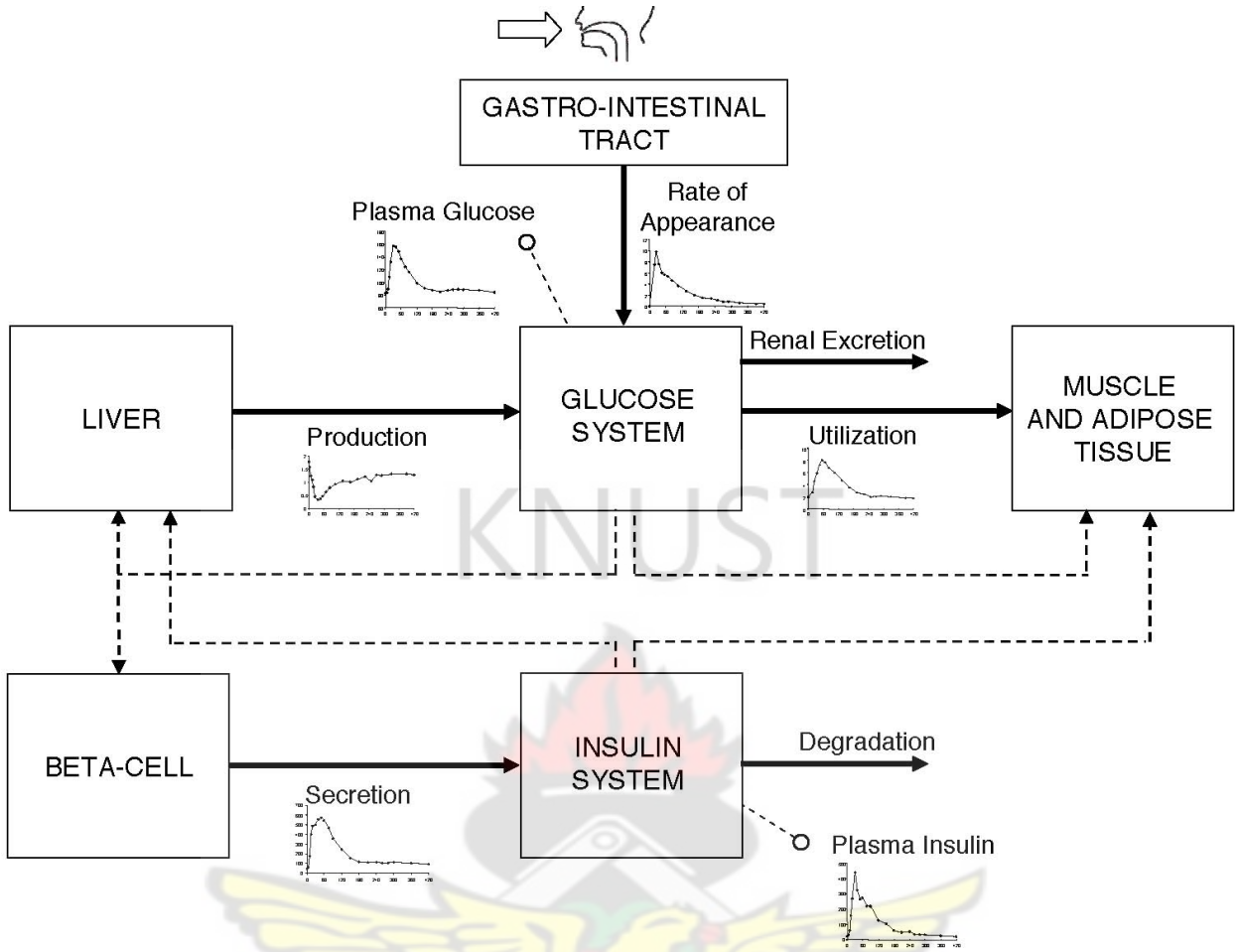


Fig. 1.1 Interaction between glucose and insulin

Normally, blood glucose levels are tightly controlled by insulin. The rise in blood sugar level normally signals special cells in the pancreas, called beta cells, to release the right amount of insulin to normalize the glucose level in the blood and lower it to the normal level. The glucose-insulin system inside a normal human body is shown in Figure 1.2, while Figure 1.3 shows the glucose-insulin system inside a diabetic patient. Typically, the normal range of the glucose level in a normal individual should fall between 3.9 – 7.7 millimole/liter, (mmol/l), or in metric system 70 – 140 milligram/deciliter, (mg/dl) [11, 12]. The conversion factor between mmol/l and mg/dl is given by the following 1 millimole/liter = 18.18 milligram/deciliter.

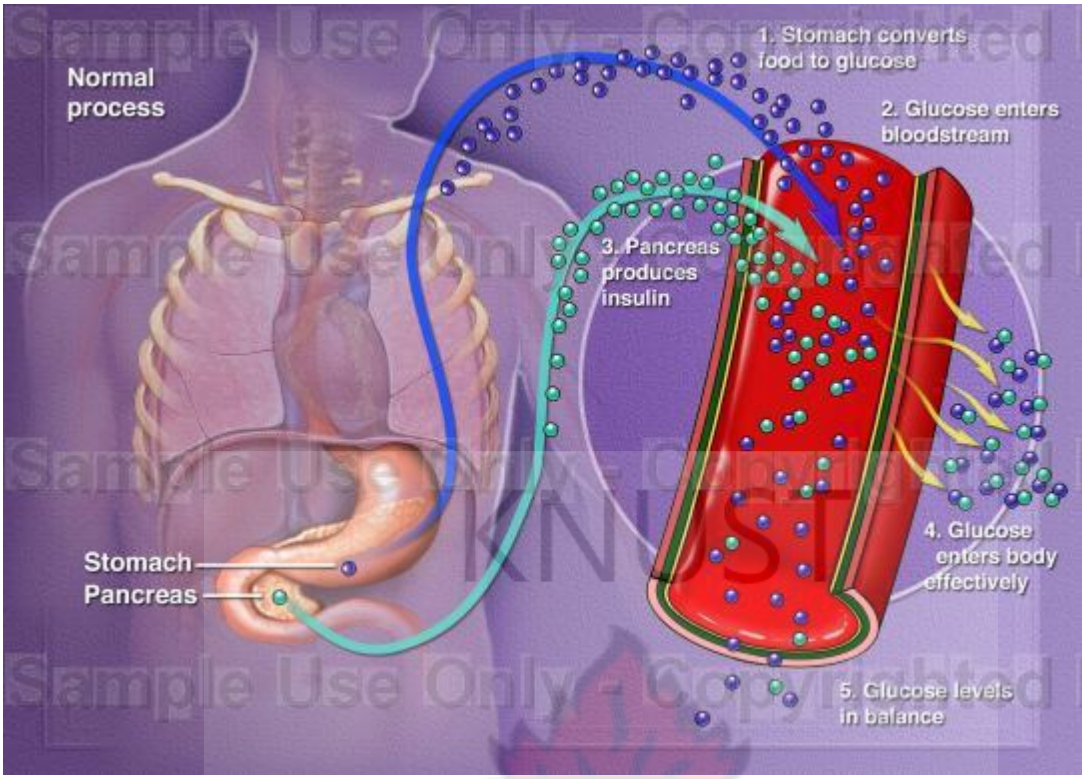


Figure 1.2 Glucose-insulin systems inside a normal human body

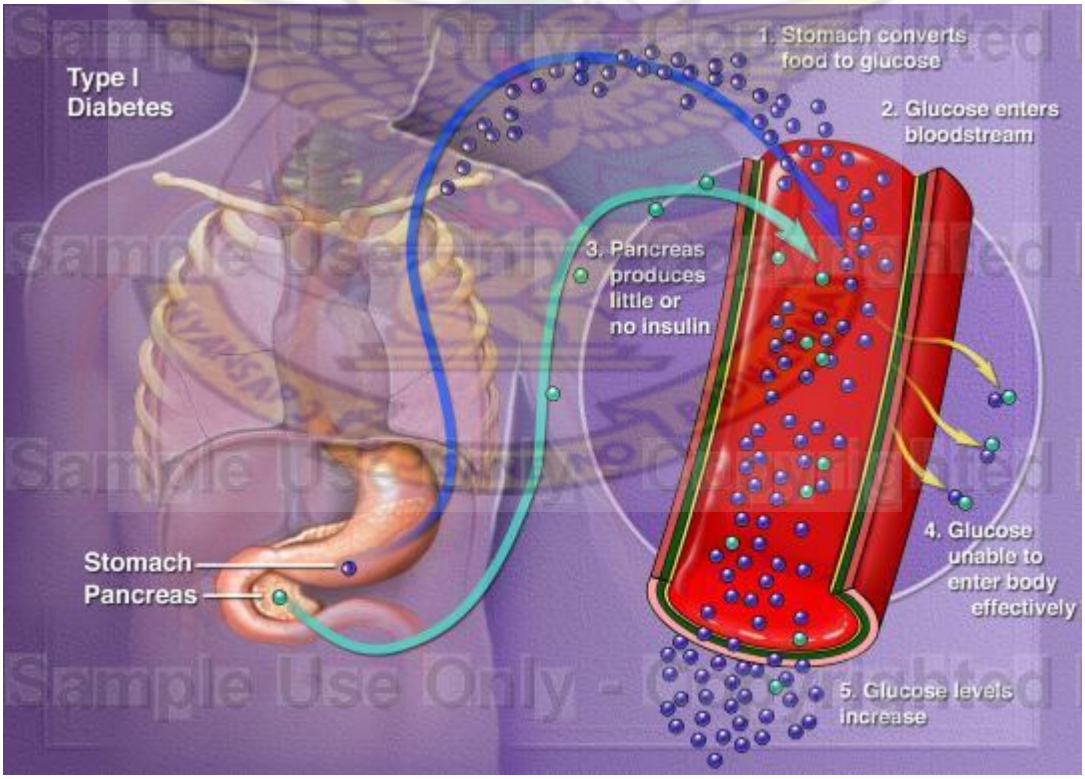


Figure 1.3 Glucose-insulin systems inside a diabetic patient body.

The normal range of blood glucose concentration should be maintained within narrow limits throughout the day. The average is 70–140 mg/dl, lower in the morning and higher after the meals.

Person's Category	Fasting State		Postprandial
	Glucose minimum value(mg/dl)	Glucose maximum value(mg/dl)	2-3 hours after eating (mg/dl)
Hypoglycemia	-	<59	<60
Early Hypoglycemia	60	79	60-70
Normal	80	100	<140
Early diabetes	101	126	140-200
Diabetic	<126	-	<200

Table 1.1 Blood glucose levels chart

For most normal persons, the glucose levels are between 80 mg/dl and 100 mg/dl in a fasting state that occurs when a person has not eaten or drunk anything for at least eight hours. Table 1.1 shows the glucose levels for different people categories with the minimum and maximum value of the glucose level for each category. After eating, the glucose level rises above the normal level and should fall back to the original starting point within two to three hours. If the glucose level does not fall, the person is classified as diabetic or at the early diabetes stage. However, the glucose level should not fall below 60 mg/dl as this is typically the symptom of hypoglycemia.

The classical symptoms of diabetes are increased hunger (Polyphagia), increased thirst (Polydipsia), and frequent urination (Polyuria) (Cooke et al, 2008). These symptoms tend to develop rapidly (weeks or months) in Type 1 diabetes. The frequent urination results from the poor water re-absorption in the kidney because of the osmotic imbalance of glucose in the blood. The dehydration from frequent and dilute urine causes the symptom of being thirsty. Other symptoms include blurred vision caused by glucose absorption in the lenses of the eyes, fatigue, weight loss, and poor wound healing. Type 1 diabetes may result is diabetic ketoacidosis, where the urine smells of acetone.

Diabetes increases the risk of heart disease, especially because of atherosclerosis from low insulin. Over time, diabetes can damage blood vessels and nerves, which increase the chance of foot injury and decrease the body's ability to fight infection. These problems can become sufficiently severe as to require amputations. The osmotic imbalances over time result is kidney damage (nephropathy) and nerve damage (neuropathy). The increased pressure in the eye or on the optic nerve can lead to blindness (retinopathy). Thus, diabetes when untreated has very serious consequences.

There are total of 25.8 million children and adults in the United States, and 8.3% of the populations have diabetes. Also, there is an estimated 79 million people who are classified as pre-diabetes patients in the United States. Worldwide there are about 346 million people who are diabetics. The number is expected to rise to about 438 million by year 2030. Diabetes is the seventh-leading cause of death worldwide. The condition and its complication cost an estimated $132 billion annually in the United State alone and about $376 billion worldwide, in terms of healthcare expenses and lost productivity (American Diabetes Association, 2011). Based on the death data, diabetes was a contributing cause of a total of 231,404 deaths in year 2007 in the United State only (National Institute of Health, 2011). The following statistics show the rate of heart disease and stroke due to diabetes (US news, 2006).

- In 2004, heart disease was noted on 68% of diabetes-related death certificates among people aged 65 years or older.
- In 2004, stroke was noted on 16% of diabetes-related death certificates among people aged 65 years or older.
- Adults with diabetes have heart disease death rates about two to four times higher than adults without diabetes.
- The risk for stroke is two to four times higher among people with diabetes

The onset of type 1 diabetes is most common in children or young adults and accounts for around 10% or less of the total number of people with diabetes. Type 2 diabetes accounts for almost all of the remaining cases of diabetes as the other forms are rare. Type 2 diabetes is a condition that predominantly affects middle-aged and older people but prevalence is increasing among children and young adults in countries with a high prevalence of obesity (WHO, 1980).

It is now commonly admitted that diabetes is sweeping the globe as a silent epidemic largely contributing to the growing burden of non-communicable diseases and mainly encouraged by decreasing levels of activity and increasing prevalence of obesity. The recent reports released by the World Health Organization and the International Diabetes Federation are alarming. In 2003, it was estimated that 194 million people were diabetic, representing a global prevalence exceeding 3% (5.1% for those aged 20 to 79) of the world population. The trend is increasing and the number is expected to reach 333 million (6.3%) by the year 2025. Moreover, for the first time, an estimation of 314 million (8.2%) is given for people in the pre-diabetic stage which constitutes a compartment from which at least one third will evolve to the diabetic stage after 10 years.

Diabetes prevalence studies in southern Ghana have recorded a steady increase. The earliest studies in the 1960s recorded 0.2% prevalence in a population of men in Ho (Ghana Medical Journal, 1964). Diabetes screening conducted by the Ghana Diabetes Association in the early 1990s suggested 2–3% prevalence in urban areas in southern Ghana; in the late 1990s a prevalence rate of 6.4% for diabetes and 10.7% for impaired glucose tolerance (IGT) was recorded in a community in Accra (Amoah et al, 2002). At Korle-Bu hospital, the percentage of medical admissions due to diabetes increased almost two-fold from 3.5 in the mid-1970s to 6.4% in the mid-1980s (Adubofuor et al, 1993).

The level of glucose inside the human being body changes significantly in response to food intake and other physiological and environment conditions. It is necessary to derive mathematics models to capture such dynamics for control design. Over the years, many mathematical models have been developed to describe the dynamic behavior of the human glucose-insulin system. Such models are highly nonlinear and usually very complex. The most commonly used and simplified model is the minimal model introduced by Bergman.

The majority of mathematical models were devoted to the dynamics of glucose-insulin, including Intra Venous Glucose Tolerance Test (IVGTT), Oral Glucose Tolerance Test (OGTT) and Frequently Sampled Intra Venous Glucose Tolerance Test (FSIVGTT). So far, all the existing models were based on two variables only: glucose and insulin. The minimal model of glucose and insulin was formulated to be the easiest model with which to deal. This has been shown to be the simplest physiologically based representations that can respectively account for the observed glucose kinetics when the plasma insulin values are supplied and for the observed insulin kinetics when the plasma glucose values are supplied. The minimal model is capable of describing the dynamics of the diabetic patient.

1.1 Problem Statement

A recent study conducted by Diabetes Care in the United States was to estimate the prevalence of diabetes and the number of people of all ages with diabetes for years 2000 and 2030. According to their studies, Ghana has its diabetics age 25 years and above out of a sample size of 4733 (Sarah Wild et al, 2004). The rate at which diabetes is sweeping our middle aged group can affect our nation's manpower requirements. Apparently this disease is all over the nation affecting both the rich and the poor, young and old. Upon the many researches that had been on Ghana's diabetes, it points out that the disease is increasing at a fast rate and this has become a national issue.

1.2 Objectives

The goals of this study are

a. To model the interaction between glucose and insulin in the body.

1 b. To use the model to discuss a clinical test for the detection of various forms of diabetes.

c. To calculate the mean square error estimate of the solution

1.3 Methodology

Mathematical models will be derived from the interaction between glucose and insulin in the blood. The model will take the form as

$$\frac{dg}{dt} = F_1(g,h)$$
$$\frac{dh}{dt} = F_2(g,h)$$

where F_1 and F_2 are some functions, g is glucose, h is insulin and t is time.

Since the level of glucose inside the human being body changes significantly up or down based on the amount and the kind of food, it is a nonlinear model. One major key problem in nonlinear system identification is to estimate the unknown parameters. Estimating the unknown parameters of a mathematical model requires the input-output data and the class of model. The parameters estimation problem can be formulated as an optimization problem where the best model is the model that best fits the data according to the given criterion. The parameters are chosen or guessed so that the output of the model is the best match with respect to the experimental data. Nonlinear models require iterative methods that start with an initial guess of the unknown parameters. The iteration alters the current guess until the algorithm converges. Experimental data will be collected from a medical clinic or hospital that will be used to check the accuracy of the model. A MATLAB, a programmable software and Excel spreadsheet will be used in the estimation of the parameters.

1.4 Justification

This project is relevant because it helps bring to light the awareness of the disease called diabetes. Health services needs models of this nature to help educate the public on the disease, helping to remove the fear and panic of those infected and the confidence to those who wants test for it. Since a nations' growth is built on the people living in it if the people are strong and healthy it will guarantee a stronger nation as well.

1.5 Thesis Organization

The paper is made up of five chapters. Chapter one introduces the topic: model for detecting diabetes. It explains what a model is and what the disease diabetes is and why the need to model it. Chapter two gives an intensive review of some of the works done by other researchers on the same topic. Chapter three describes the methodology to be used in the model. Differential equation of course is a very useful concept for modeling and this chapter takes it further its usefulness. Chapter four lists out the data collected and how they are analyzed and finally the conclusion of the results is tied up in chapter five.

The next chapter is a review of other literatures in line with the topic at hand.

Chapter Two

Review of related concepts and research works

Chapter two explains some basic concepts and definitions that are used throughout the thesis. It also under list other research work done on diabetes (glucose – insulin interaction). These are researchers from across the globe looking into the same content but coming from different perspectives. Some describing the glucose – insulin interaction in the blood, the burden of diabetes on the society and its complications and others talks about some common foods that could be a risk factor for the development of type 2 diabetes.

2.0 Some basic definitions and concept

2.0.1. Diabetes and types of diabetes

Diabetes - is a syndrome of disordered metabolism, usually due to a combination of hereditary and environmental causes, resulting in abnormally high blood sugar levels. The two most common forms of diabetes are Type 1 diabetes and Type 2 diabetes which can be categorized as follows.

a. Type 1 diabetes is due to a diminished production of insulin, this is also called insulin-dependent diabetes or juvenile-type diabetes. The patient of type 1 diabetes is considered hypoglycemic.

b. Type 2 diabetes is caused by the decreased insulin production by the beta cells of the pancreas and an increased insulin resistance by the peripheral tissues. This causes hyperglycemia, or high blood glucose levels in the body. Therefore they are not insulin dependent but may require some exogenous form of insulin to help maintain normal blood glucose levels. Insulin is needed by the peripheral tissues to use the glucose in the body for energy. Without insulin the body is unable to use glucose causing body cells to starve and may result in complications in other parts of the body.

2.0.2 Forms of sugar

a. Dextrose is a name used in industry for pure, crystalline glucose sugar. It is produced by treatment of starch with the enzyme amylase or by putting starch in water mix with dilute hydrochloric acid.

b. Glucose is an end product of carbohydrate digestion. It plays an important role in the metabolism of any vertebrate since it is a source of energy for all tissues and organs. For each individual there is an optimal blood glucose concentration, and any excessive deviation from this optimal concentration leads to severe pathological conditions.

2.0.3 Types of hormone

a. Insulin is a hormone secreted by the (bête) β cells of the pancreas. After any meal of carbohydrate the G.I tract sends a signal to the pancreas to secrete more insulin. Without insulin the body cannot avail itself of all the energy it needs.

b. Glucagon is a hormone secreted by the (alpha) α cell of the pancreas. Any excess glucose is stored in the liver in the form of glycogen. In times of need this glycogen is converted into glucose. The hormone glucagon increases the rate of breakdown of glycogen into glucose.

c. Epinephrine (adrenalin) is a hormone secreted by the adrenal medulla. Epinephrine is part of an emergency mechanism to quickly increase the concentration of glucose in times of extreme hypoglycemia. Like glucagon, epinephrine increases the rate of breakdown of glycogen into glucose.

2.0.4 G.I. Tract - The **GI tract** refers to the **gastrointestinal tract** which includes everything from mouth to anus and is vital to processing food.

2.0.5 Nonlinear model is defined as an equation that is nonlinear or a combination of linear and nonlinear in terms of the dependent variable and its derivatives.

2.0.6 Nonlinear estimation is a process of fitting a mathematical model to experimental data to determine unknown parameters of that model

2.1 Related works

We discuss below research works undertaken by mathematicians, health organizations and others on diabetes and its related fields of study.

B. Kwach and his team presented a new mathematical model for Blood Glucose Regulatory System (BGRS) which include epinephrine as a third variable in the form $Y = AY$, and whose solution has been analyzed for equilibrium and stability to provide the blood glucose concentrations for diabetics and non-diabetics. They established that the final model is asymptotically stable compared to the existing models (B. Kwach et al, 2010)

Joseph M. Mahaffy from the University of British Columbia modeled type 1(Juvenile) diabetes in NOD mice. He deduced that diabetes mellitus results from the loss of β-cells, an auto - immune disease, the case where insulin production is severely reduced. It's a hereditary disease and the peak diagnosis occurs around age 14. He explains that 10% of diabetes cases are Type 1, while 90% are Type 2(where cells become insulin resistant, mostly in obese individual). (Joseph M. Mahaffy, 2006).

From the University of Puerto Rico, Yesenia Cruz Rosado also wrote a paper on mathematical model for detecting diabetes. He explains how the various hormones in our body; insulin, growth hormone and glucagon control blood glucose levels and how they are activated. He also presented a mathematical model that determines the diabetes in patients based in the results on the glucose tolerance test of 5 hours. His model extended from the one proposed by E. Ackerman which included three hormones instead of two (Yesenia Cruz Rosado, 2009).

F Stahl and R. Johansson worked on Diabetes mellitus modeling and short term prediction based on blood glucose measurement. Here an attempt is made to show how system identification and control may be used to estimate predictive quantitative models to be used in the design of optimal insulin regimens. The system was divided into three subsystems, the insulin subsystem, the glucose subsystem and the insulin-glucose interaction. The insulin subsystem aims to describe the absorption of injected insulin from the subcutaneous depots and the glucose subsystem the absorption of glucose from the gut following a meal.

Diabetes care in the United States under took a study to estimate the prevalence of diabetes and the number of people of all ages with diabetes for years 2000 and 2030. The prevalence of diabetes for all age groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. (Sarah Wild, et al, 2004).

A Boutayeb and others noted on the burden and complications of diabetes on the individual and the society as a whole. They observed three levels of estimating the cost of diabetes namely: (1) Cost directly related to the diagnosis and management of diabetes without complications. This includes the in-patient and out-patient care, means of treatment by insulin or tablets and the equipment of self control (blood and urine testing). (2) Costs generated by complications of diabetes. These are difficult to quantify because diabetes is linked to micro and macro vascular diseases such as heart disease, kidney failure, eye disease and amputation. Moreover, diabetes may add a cost of care by complicating other unrelated medical situations like infections, accidents and surgery. (3). Indirect costs correlated to the quality of life and the economic productivity which can be somehow estimated by the degree of disability (A Boutayeb, et al, 2004).

Diabetes is diagnosed if fasting blood glucose levels are higher than 126mg/dl on more than one occasion, if a random blood glucose level is higher than 200mg/dl along with symptoms, or if an oral glucose tolerance test indicates blood glucose levels are higher than 200mg/dl after two hours (Medline Plus, 2005).

Type 2 diabetes is the most common form of type 2 diabetes accounting for around 90% of all diabetics. Approximately 18.2 million people in the United States have diabetes, or about 6.3% of the population. An exact number is not available due to many people that are undiagnosed and living with type 2 diabetes. Approximately 13 million people are diagnosed with diabetes and approximately 5.2 million people are undiagnosed (American Diabetes Association, 2005).

There is not one single risk factor that causes an individual to develop type 2 diabetes, but it is having multiple risk factors that put an individual at risk. The risk factors for developing type- 2 diabetes are:

· Being overweight or obese.

· Having a history of type 2 diabetes in your family.

· Being African American, Latino, Native American, Asian American, or a Pacific Islander.

· Being an older adult.

· Having high triglyceride levels, or low levels of HDL cholesterol (the "good" cholesterol).

· Having a history of gestational diabetes or the first recognition of diabetes during pregnancy. (About, 2005)

Having type -2 diabetes not only causes high blood glucose levels but also it can cause complications in other parts of the body if not controlled. Complications of diabetes include:

· Retinopathy- disease of the retina in the eye, leading to blindness.

· Nephropathy- disease of the nephron of the kidney, leading to renal, or kidney, failure.

· Neuropathy- disease of the nerves.

· Hypertension- high blood pressure.

· Coronary artery disease- narrowing of the artery that supplies the heart.

· Peripheral vascular disease- narrowing of large blood vessels.

· Cerebrovascular disease- narrowing of the artery that supplies the brain.

· Hyperlipidemia- high lipid, or fat, levels in the blood. (U.S. Food and Drug Administration, 2005)

There are many signs or symptoms that one may have to indicate the presence of type 2 diabetes. Signs/symptoms of type -2 diabetes are:

· Polydipsia, or increased thirst.

· Polyphagia, or increased hunger.

· Hyperglycemia – an abnormally high concentration of sugar in the blood.

· Polyuria, or increased urination.

· Weight loss. (Mahan, 2004)

There are many common foods that Latinos eat on a day-to-day basis, which plays an important risk factor for the development of type 2 diabetes. Common foods are often high in fat, calories, or sodium and include; wheat, corn, beans, tortillas, high-fat organ meats, rice, sugar, lard, sausage, dried codfish, starchy tubers, salt, poultry, beef, and dairy (Lang, 1992).

The nutrient content of Mexican's diet tends to be high in saturated fat, calories, and sodium. The nutrients are most likely to be inadequate in calcium, iron, vitamin A, folic acid, and vitamin C. The diet appears to be adequate in protein due to the high content of beans, eggs, fish, beef, poultry, and pork in their diet (Ohio State University, 2005).

The Puerto Rican diet is high in calcium and complex carbohydrates. Their diet is also high in incomplete proteins, such as, rice and beans. The younger generation in Puerto Rico has become more susceptible to the Americanization of their diet. The Puerto Rican diet has become Americanized since many foods are imported from the United States. This has led to their diet being high in pizza, hot dogs, fast foods, and processed foods (Ohio State University, 2005).

Recipe modification in a typical Latino meal is necessary to facilitate compliance with a type 2 diabetic's diet. Easiest modifications include incorporating more fruits and vegetables, lowering the consumption of egg yolks and full-fat cheeses, increasing fiber, and substituting polyunsaturated fats for lard and other saturated fats. To decrease the sodium content, other spices, garlic, and onions may be used (Hernandez, 1998).

There are many serious complications of type 2 diabetes if the blood glucose levels are not controlled. These complications include heart disease, renal failure, blindness, elevated cholesterol levels, circulatory problems, and neuropathy (Perrin, 1991).

Exercise is anything physical that gets your body moving. Physical activity can lower blood glucose levels, blood pressure, cholesterol, and weight. Physical activity also helps the peripheral tissues to recognize insulin; therefore decreasing insulin resistance and causing the insulin to work better (American Diabetes Association, 2005).

There are different types of exercise including aerobic and anaerobic. Aerobic exercise increases your heart and breathing rate, and works the muscles and it is often done over a period of time. Examples of aerobic exercise include running, walking, swimming, dancing, or riding a bike (American Diabetes Association, 2005).

Anaerobic exercise includes releasing short bursts of energy and then is followed by a period of rest. Examples of anaerobic exercise include push-ups, pull-ups, and lifting weights (Kids Health, 2005).

Nutrition is a key component in maintaining near normal blood glucose levels. Limiting calories and fat to achieve a 5-10% weight loss, consuming less salt and watching how many carbohydrates are eaten are all important in the nutritional management of type 2 diabetes (Mahan, 2004). It is important to control portion sizes, eat nutrient dense foods, and include a variety of foods that are unprocessed. Eating a variety of foods including fruits, vegetables, complex carbohydrates, non-fat dairy, lean meats, beans, poultry, and fish are all important in a healthy diet (American Diabetes Association, 2005).

There are many tools or suggestions that one can use when trying to maintain normal blood glucose levels. One tool is the "Rate Your Plate", which is a great tool to use when you are trying to control portion sizes. One-fourth of the plate should be filled with whole grains, one-forth should be protein, and half of the plate should be non-starchy vegetables. Other tools also include carbohydrate counters or exchange lists, which is when you count the carbohydrates or exchanges in each meal (American Diabetes Association, 2005).

If exogenous insulin is required, it may be taken when according to the exchanges eaten at each meal. This helps achieve better control. Suggestions for maintaining blood glucose and losing weight include activities count and reading food labels. Any activity that is done counts towards improving nutrition, health, and maintaining normal blood glucose levels. Examples include parking farther away, walking at the mall, taking the stairs versus the elevator, doing exercises in front of the television, or even walking around the house. Reading food labels is important because it will tell you what is in the product, how much is a serving size, and how many nutrients are in the product (American Diabetes Association, 2005).

Diabetes prevalence studies in southern Ghana have recorded a steady increase. The earliest studies in the 1960s recorded 0.2% prevalence in a population of men in Ho. Diabetes screening conducted by the Ghana Diabetes Association in the early 1990s suggested 2–3%

prevalence in urban areas in southern Ghana; in the late 1990s a prevalence rate of 6.4% for diabetes and 10.7% for impaired glucose tolerance (IGT) was recorded in a community in Accra. At Korle-Bu hospital, the percentage of medical admissions due to diabetes increased almost two-fold from 3.5 in the mid-1970s to 6.4% in the mid-1980s. (Ama De-Graft Aikins, 2007).

Diabetes mellitus can be classified into four principal types .This includes type 1 diabetes, type 2 diabetes, other specific types of diabetes, and gestational diabetes mellitus. The most common types of diabetes seen in Sub-Saharan Africa are type 2 and type 1 diabetes mellitus. Although type 1 diabetes is not caused by the adverse effects of lifestyle, as type 2 can be, the chronic complications of both type 1 and type 2 diabetes on the eyes, cardiovascular system, nerves, and kidneys are similar (WHO 1999).

Lynch and Bequette tested the glucose minimal model of Bergman to design a Model Predictive Control (MPC) to control the glucose level in a diabetic patient. The insulin secretion term ($\gamma*(g-h)*t$) of the differential equation of the minimal model was replaced by a constant term which makes the infusion of the insulin to be constant and independent of the glucose level.

Fisher used the glucose insulin minimal model of Bergman to design a semi-closed loop insulin infusion algorithm based on plasma glucose samplings taken over a three hours time span. The study concentrates on the glucose level and did not take into consideration some important factors such as free plasma insulin concentration and the rate at which insulin is produced as the level of glucose rises.

Furler modified the glucose insulin minimal model of Bergman by removing the insulin secretion and adding insulin antibodies to the model. The algorithm calculates the insulin infusion rate as a function of the measured plasma glucose concentration. The linear interpolation was used to find the insulin rate. The algorithm neglected some important

variations in insulin concentration and other model variables. Also, it took more than two hours to bring the glucose level to the neighborhood of the glucose basal level.

Chapter Three

Mathematical Model

In this chapter, we discuss compartment modeling, the model assumptions, formulation of the model, the general solution of the model and the estimate of the parameters.

3.0 Compartment modeling

Mixing model or compartmental model is concerned with the interaction of two or more quantities. This chapter deals with only two quantities glucose and insulin. The model leads to pairs of simultaneous differential equations for the two quantities and, because of the interaction, the equations are coupled. A systematic method of uncoupling and hence solving such equations involves eliminating one of the two quantities to give a second-order differential equation.

3.1 Model assumption

a) The model omits details of biochemistry involved and ignores the effect of other hormones.
b) It treats the bloodstream, moreover as if it were contained in a single compartment throughout which concentrations of glucose and insulin are uniform at each instant.
c) Provided there has been no recent digestion, glucose and insulin concentrations will be in equilibrium. We are interested in how the system responds to a change in that equilibrium.
d) It is also assumed that there is an external rate at which the blood glucose concentration is being increased.
e) We assume that the body wants to maintain a homeostasis for glucose concentrations in the blood.

f) A rise in the concentration of glucose in the bloodstream results in the liver absorbing more of the glucose, which it converts and stores as glycogen; a drop in the concentration of glucose reverses the process.

g) A rise in the concentration of glucose in the bloodstream stimulates the pancreas to produce insulin at a faster rate; a drop in the glucose concentration lowers the rate of insulin production.

h) A rise in the concentration of insulin in the bloodstream enables the glucose to pass more readily through the membranes of the cells in skeletal muscle, resulting in greater absorption of glucose from the bloodstream.

Homeostasis is defined as the tendency to maintain or maintenance of normal, internal stability in an organism by coordinated responses of the organ systems that automatically compensate for environmental changes.

3.2 Formulation of the model

Glucose, an end product of carbohydrate digestion is converted into energy in the cells of the body. A hormone secreted by the pancreas facilitates the absorption of glucose by cells other than those of the brain and nervous system. A delicate balance is normally maintained between the amounts of glucose and insulin in the bloodstream. If the insulin concentration is too low then too little glucose is absorbed from the bloodstream; the unabsorbed glucose is then lost in the urine along with other nutrients. If on the other hand, the insulin concentration is too high, then too much glucose is absorbed by cells other than those of the brain and nervous system; lack of glucose available to the cells of the brain then impairs its function. The main features that a model of the glucose-insulin regulation system must take into account are as follows.

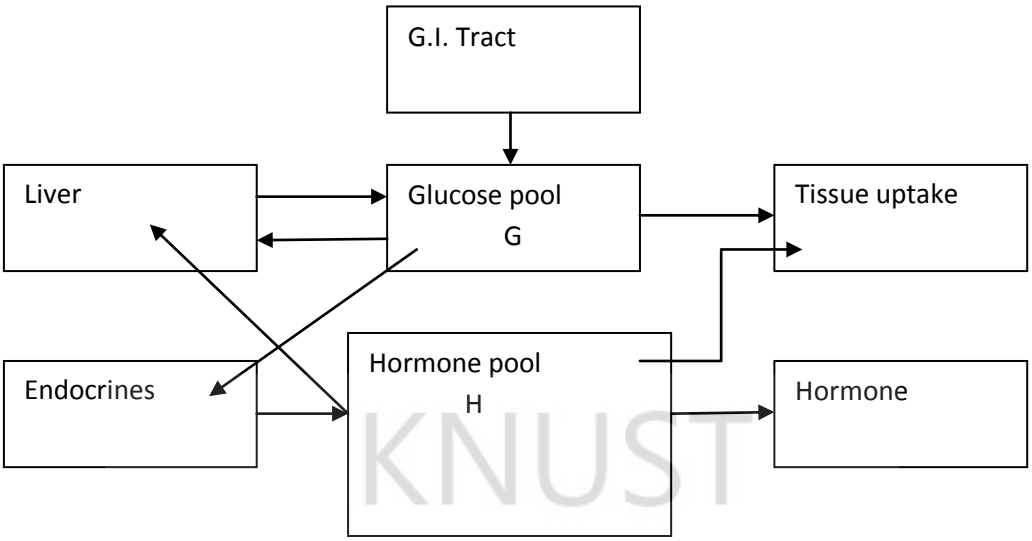


Figure 3.1 schematic figure of glucose-insulin pool

Referring to figure 3.1the following models can be deduced.

i. A rise in the concentration of glucose in the bloodstream results in the liver absorbing more of the glucose, which it converts and stores as glycogen; a drop in the concentration of glucose reverses the process.

$\frac{dg}{dt} = -ag$, where ***g*** represent glucose concentration***, t*** represent time and ***a***, a constant.

ii. A rise in the concentration of glucose in the bloodstream stimulates the pancreas to produce insulin at a faster rate; a drop in the glucose concentration lowers the rate of insulin production.

$\frac{dg}{dt} = -bh$, where ***h*** represent insulin concentration and ***b***, a constant.

iii. There is an external rate at which the blood glucose concentration is being increased.

$\frac{dg}{dt} = J(t)$

iv. A rise in the concentration of insulin in the bloodstream enables the glucose to pass more readily through the membranes of the cells in skeletal muscle, resulting in greater absorption of glucose from the bloodstream.

$\frac{dh}{dt} = cg$, where, ***c*** is a constant.

v. Insulin produced by the pancreas, is constantly being degraded by the liver.

$\frac{dh}{dt} = -dh$, where, ***d*** is a constant.

The general model is written as

$$\begin{aligned} \frac{dG}{dt} &= f_1(G,H) + J(t), \\ \frac{dH}{dt} &= f_2(G,H). \end{aligned} \tag{3.01}$$

Where the $J(t)$ is the ingested source of glucose, f_1 and f_2 are functions of G and H. Generally they could be described as the concentration of glucose and insulin respectively. The homeostasis assumption means that we want to consider a local perturbation of the dynamical system away from equilibrium. Thus, we create the perturbation variables,

$g(t) = G(t) - G_o$ and $h(t) = H(t) - H_o$

Where G_o and H_o are the equilibrium values for blood glucose and insulin concentrations, respectively and G(t), H(t) are displacements of glucose and insulin from their respective basal values. Thus,

$f_1(G_o, H_o) = f_2(G_o, H_o) = 0$

The general model (1) is expanded to linear terms yielding the linearized perturbation model given by

$$\begin{aligned} \frac{dg}{dt} &= \frac{\delta f_1(G_o,H_o)}{dg} g + \frac{\delta f_1(G_o,H_o)}{dh} h, \\ \frac{dh}{dt} &= \frac{\delta f_2(G_o,H_o)}{dg} g + \frac{\delta f_2(G_o,H_o)}{dh} h, \end{aligned} \tag{3.02}$$

Where $g(t)$ and $h(t)$ now represent the linearized perturbed variables. By examining the partial derivative of equation (2) and simplifying we obtained

$$\frac{dg}{dt} = -ag - bh + J(t)$$
$$\frac{dh}{dt} = -ch + dg \qquad (3.03)$$

Where a, b, c and d are constants.

To determine how the solutions of the differential equation behave, one must have some information about the coefficients **a, b, c** and **d**. A particular useful fact is that each of ***a***, ***b***, ***c*** and ***d*** is positive.

3.3 Determining the signs of constants

From model component (i) it follows that $\frac{dg}{dt}$ is negative for $g > 0$ and $h = 0$, since the blood glucose concentration will be decreasing through tissue uptake of glucose and the storing of excess glucose in the liver in the form of glycogen. This in turn makes the constant **a** positive.

From model component (ii) it also follows that $\frac{dg}{dt}$ is negative since a positive value of h tends to decrease blood glucose level by facilitating tissue uptake of glucose and by increasing the rate at which glucose is converted to glycogen. This makes **b** a positive constant.

Model component (iv) depicts that $\frac{dh}{dt}$ must be positive since a positive value of g causes the endocrine glands to secrete those hormones which tend to increase **H**. This makes constant d positive also.

Finally model component (v) follows that $\frac{dh}{dt}$ must be negative since the concentration of hormones in the blood decreases through hormone metabolism. This leaves constant c to be positive.

3.4 Solution of the model

Equations (3.01) and (3.02) are two first – order differential equations for g and h. However, since only the concentration of glucose in the blood is measured it is likely that variable h is removed. This can be accomplished as follows:

Differentiating (1) with respect to t gives

$$\frac{d^2g}{dt^2} = -a\frac{dg}{dt} - b\frac{dh}{dt} + \frac{dJ(t)}{dt} \tag{3.04}$$

Substituting (2) into (3)

$$\frac{d^2g}{dt^2} = -a\frac{dg}{dt} - b(-ch + dg) + \frac{dJ(t)}{dt} \tag{3.05}$$

Rearranging (4) gives

$$\frac{d^2g}{dt^2} = -a\frac{dg}{dt} + c(bh) - bdg + \frac{dJ(t)}{dt} \tag{3.06}$$

From (1)

$$bh = -\frac{dg}{dt} - ag + J(t) \tag{3.07}$$

Substituting (6) into (5) gives

$$\frac{d^2g}{dt^2} = -a\frac{dg}{dt} + c\left(-\frac{dg}{dt} - ag + J(t)\right) - bdg + \frac{dJ(t)}{dt} \tag{3.08}$$

$$\frac{d^2g}{dt^2} + (a+c)\frac{dg}{dt} + (ac+bd)g = cJ(t) + \frac{dJ(t)}{dt} \tag{3.09}$$

Let

$$\alpha = (a+c)/2$$
$$\omega_o^2 = ac + bd$$
$$S(t) = cJ(t) + \frac{dJ(t)}{dt}$$

Equation (8) now becomes

$$\frac{d^2g}{dt^2} + 2\alpha\frac{dg}{dt} + \omega_o^2 g = S(t) \tag{3.10}$$

For the purpose of this study, let t=0 be the time at which the glucose load has been completely ingested, thus making S(t) = 0. Then, for t≥0, g(t) satisfies the linear second-order constant coefficient homogeneous equation

$$\frac{d^2g}{dt^2} + 2\alpha\frac{dg}{dt} + \omega_o^2 g = 0 \tag{3.11}$$

This model certainly conforms to reality in predicting that the blood glucose concentration tends to return eventually to its optimal/basal concentration after initial ingestion.

Let $g = Ae^{mt}$ be one of the solutions of equation (3.11)

$$\frac{dg}{dt} = Ame^{mt} \text{ and } \frac{d^2g}{dt^2} = Am^2e^{mt}$$

Substituting $g, \frac{dg}{dt} and \frac{d^2g}{dt^2}$ into equation (3.11)

$$Am^2e^{mt} + 2\alpha Ame^{mt} + \omega_o^2 Ae^{mt} = 0 \tag{3.12}$$

$$Ae^{mt}(m^2 + 2\alpha m + \omega_o^2) = 0 \tag{3.13}$$

$$Ae^{mt} \neq 0$$

Therefore $m^2 + 2\alpha m + \omega_o^2 = 0$ (3.14)

Equation (3.14) is the auxiliary equation of equation (3.12). Equation (3.14) is a quadratic equation which can be solved using the quadratic formula

$$m = -b \pm \sqrt{b^2 - 4ac} / 2a \quad (3.15)$$

Comparing the quadratic formula to equation (13)

$$a = 1 \quad b = 2\alpha \quad \text{And} \quad c = \omega_o^2 \quad (3.16)$$

Substituting (15) into (14)

$$m = \frac{-2\alpha \pm \sqrt{(2\alpha)^2 - 4(1.\omega_o^2)}}{2.1} = \frac{-2\alpha \pm \sqrt{4(\alpha^2 - \omega_o^2)}}{2} = -\alpha \pm \sqrt{\alpha^2 - \omega_o^2} \quad (3.17)$$

The solution of g(t) depends on the signs of $\alpha^2 - \omega_o^2$. This generates three cases of solution namely: Over damped- the case where $\alpha^2 - \omega_o^2$ is positive .Critically damped- the case where $\alpha^2 - \omega_o^2$ is negative and under damped- the case where $\alpha^2 - \omega_o^2$ is zero. Figure 3.2 shows all three cases of solution.

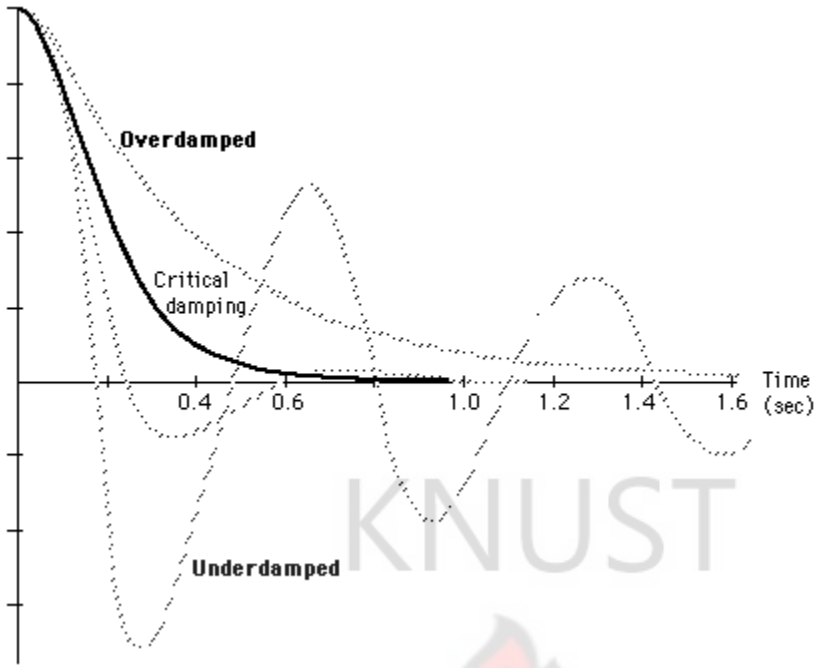


Figure 3.2 over damped, critically damped and under damped case solution curves.

3.4.1 Solution of the Over damped case

In this case $\alpha^2 - \omega_o^2 > 0$

Let $\alpha^2 - \omega_o^2 = \gamma$

Then $m = -\alpha \pm \gamma$ and $g(t) = Ae^{(-\alpha \pm \gamma)t}$

The solution of g (t) is

$$g(t) = e^{-\alpha t}(Ae^{\gamma t} + Be^{-\gamma t}) \tag{3.18}$$

3.4.2 Solution of critically damped case

$$\alpha^2 = \omega_o^2$$

In this case equation (3.11) has the general solution

$$g(t) = e^{-\alpha t}(A + Bt) \tag{3.19}$$

According to Ackerman et al the model for glucose and insulin interaction is similar to the case of the under damped because of the nature of glucose concentration in the body. It rises and falls with time.

3.4.3 Solution of the under damped case

Recalling the following equations:

$g = Ae^{mt}$ And $m = -\alpha \pm \sqrt{\alpha^2 - \omega_o^2}$

Since $\alpha^2 - \omega_o^2 < 0$ let $\alpha^2 - \omega_o^2 = \beta$ then $m = -\alpha \pm j\beta$

Substituting $m = -\alpha \pm j\beta$ into $g = Ae^{mt}$

$$g(t) = Ae^{(-\alpha \pm j\beta)t}$$

The solution of g (t) becomes

$$g(t) = Ae^{(-\alpha + j\beta)t} + Be^{(-\alpha - j\beta)t}$$

$$g(t) = Ae^{-\alpha t}.e^{j\beta t} + Be^{-\alpha t}.e^{-j\beta t}$$

$$g(t) = e^{-\alpha t}(Ae^{j\beta t} + Be^{-j\beta t}) \tag{3.20}$$

But $e^{j\beta t} = \cos\beta t + j\sin\beta t$ and

$$e^{-j\beta t} = \cos\beta t - j\sin\beta t \tag{3.21}$$

Substituting equation (3.21) into equation (3.20)

$$g(t) = e^{-\alpha t}\left[A(\cos\beta t + j\sin\beta t) + B(\cos\beta t - j\sin\beta t)\right]$$

$$g(t) = e^{-\alpha t}\left[(A+B)\cos\beta t + j(A-B)\sin\beta t\right]$$

(3.22)

Let $A+B=C$ and $A-B=D$

$$g(t) = e^{-\alpha t}\left[C\cos\beta t + jD\sin\beta t\right] \quad (3.23)$$

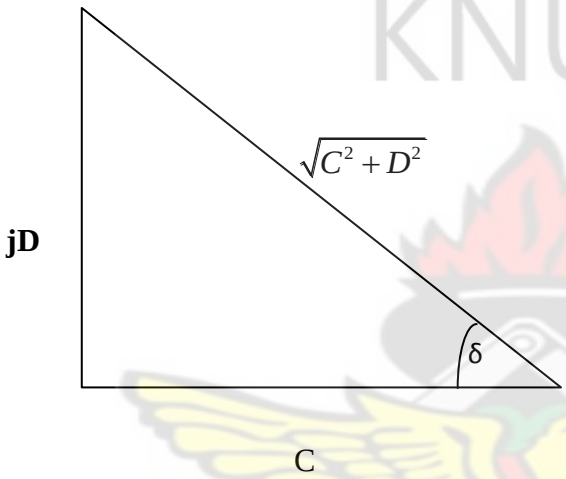


Figure 3.3 Right angle rule

From figure 3.3

$$\cos\delta = \frac{C}{\sqrt{C^2+D^2}}$$

$$C = \sqrt{C^2+D^2}\cos\delta$$

Let $\sqrt{C^2+D^2} = K$ then

The general solution for equation (10) now becomes

$$g(t) = Ke^{-\alpha t}\cos(\beta t - \delta)$$

Consequently,

$$g(t) = g_o + Ke^{-\alpha t}\cos(\beta t - \delta) \quad (3.24)$$

Where g_o , is the patient's blood glucose concentration before the glucose load is ingested. This is determined by measuring the patient's blood glucose concentration immediately upon arrival at the hospital. After which the patient is given an amount of glucose to take, then four additional measurements $g_1, g_2, g_3 and g_4$ of the patient's blood glucose concentration at times $t_1, t_2, t_3 and t_4$ are recorded. These measurements will be used to determine the unknowns; $K, \alpha, \beta and \delta$ from the four equations

$$g_j = g_o + Ke^{-\alpha tj}\cos(\beta t_j - \delta) \qquad j = 1,2,3,4. \qquad (3.25)$$

This solution has four unknown parameters to be fit to the data. The parameter represents g_o , the equilibrium blood sugar level, **α** measures the ability of the system to return to equilibrium state after being perturbed, and **β** gives a frequency response to perturbations. It is expected that measuring **α** should be the primary measure of whether someone was diabetic, as people with diabetes should not be able to return rapidly to normal equilibrium levels.

These parameters can be determined by minimizing the least Square Error of the equation

$$E = \sum_{j=1}^{n}\left[g_j - g_o - Ke^{-\alpha tj}\cos(\beta t_j - \delta)\right]^2 \qquad (3.26)$$

3.5 Parameter Estimation

Parameter estimation is a common problem in many areas of process modeling. The goal is to determine values of model parameters that provide the best fit to measured data, generally based on some type of least squares or maximum likelihood criterion. Parameter estimation can be described as a method that is able to take control of a model running it as many times

as it needs while adjusting its parameters until the discrepancies between selected model outputs and a set of data or laboratory measurements are reduced to a minimum in the weighted least square sense.

3.5.1 Least Squares Parameter Estimation

The method of least squares assumes that the best-fit curve of a given set of data is the curve that has the minimal sum of the deviations squared (*least squares error*) from a given set of data. Assume a set of data given as, $(x_1, y_1), (x_2, y_2), (x_3, y_3), ..., (x_n, y_n)$, where the independent variable is x and the dependent variable is y. The curve $f(x)$ is the fitting curve that has the deviation or what is called the error d. The error d is basically the horizontal (or vertical) distance between the points and the fitted graph. The error d can be defined as the following

$$\begin{aligned} d_1 &= y_1 - f(x_1) \\ d_2 &= y_2 - f(x_2) \\ d_3 &= y_3 - f(x_3) \\ d_n &= y_n - f(x_n) \end{aligned} \tag{3.27}$$

As per the principle of the least square method, the best fitting curve has the following property

$$\prod = d_1^2 + d_2^2 + d_3^2 + ...d_n^2 = \sum_{i=1}^{n} d^2{}_i \tag{3.28}$$

Where the symbol Π represents the minimum least square error. Now substituting equation (3.27) into equation (3.28), we obtain

$$\prod = \sum_{i=1}^{n} [y_i - f(x_i)]^2 \tag{3.29}$$

When the function is the m-th degree polynomial form

$$f(x) = a_o + a_1 x + a_2 x^2 + a_3 x^3 + ...a_m x^m \tag{3.30}$$

the minimum Least Squares Error becomes

$$\prod = \sum_{i=1}^{n} [y_i - f(x_i)]^2 = \sum_{i=1}^{n} \left[y_i - (a_0 + a_1 x_i + a_2 x_i^2 + a_3 x_i^3 .... a_m x_i^m) \right]^2 \tag{3.31}$$

The unknown coefficients $a_0, a_1, a_2, a_3, ..., a_m$ can be estimated to yield a minimum least squares error.

3.5.2 Square Relative Error (SRE):

In general, the **R**elative **E**rror, (**RE**) indicates how good an estimate is, in relative to the true values. Although absolute errors are useful, they do not necessarily give an indication of the importance of an error. If the experimental value is denoted by g_{ex} and the estimated (or simulated) value is denoted by g_{est}, then the relative error is defined as

$$RE = \frac{g_{ex} - g_{est}}{g_{ex}}$$

And the **S**quare **R**elative **E**rror, (**SRE**) can be expressed as

$$SRE = \left(\frac{g_{ex_i} - g_{est_i}}{g_{ex_i}} \right)^2$$

When the data is sampled over a certain period of time, the **M**ean **S**quare **R**elative **E**rror (**MSRE**) can be used. The **MSRE** is defined as

$$MSRE = \frac{1}{n} \sum_{i=1}^{n} \left(\frac{g_{ex_i} - g_{est_i}}{g_{ex_i}} \right)^2, \; for$$

$$i = 1, 2, ..., n$$

Where g_{ex_i} is the experimental value at sample *i*, g_{est_i} is the estimated value at sample *i*, and where *n* is the number of samples of a data set.

Chapter four

Data Collection, Analysis and Results

This chapter has the data obtained and its analysis, a fitted data to a curve in order to determine the parameter values and the consequent error of deviation.

4.0 Data collection

Using the conversion 1millimole/liter = 18.18milligram/deciliter the gathered data was converted from millimole/liter to milligram/deciliter.

As can be seen in the subsequent tables' individuals whose data were collected was categorized into the following subjects.

Subject A: Is an individual with a normal glucose – insulin interaction.

Subject B: Is an individual with type 1 diabetes (hyperglycemic).

Subject C: Is an individual with a mild form of diabetes (pre-diabetic).

Table 4.1: Data on subject A

Time (hour)	Glucose Concentration (millimole/liter)	Glucose Concentration (milligram/deciliter)
0	**4.7**	**85.446**
1	**6.6**	**119.988**
2	**5.1**	**92.718**
3	**4.7**	**85.446**
4	**4.6**	**83.628**

Table 4.2: Data on subject B

Time (hour)	Glucose concentration (millimole/liter)	Glucose Concentration (milligram/deciliter)
0	**10.7**	**194.526**
1	**33.3**	**605.394**
2	**33.3**	**605.394**
3	**33.0**	**599.94**
4	**32.4**	**589.032**
5	**19.7**	**358.146**

This patient recorded a high glucose level in the first hour after which he was administered 10ml of insulin. The glucose level did not drop after the next hour upon given the insulin so a dosage of 5ml insulin was administered to him.

Table 4.3: Data on subject C

Time (hours)	Observed Glucose Conc.(mmol/liter)	Observed Glucose Conc.(mg/dl)
0	**5.50**	**100**
1	**12.10**	**220**
2	**9.62**	**175**
3	**5.50**	**100**
4	**4.67**	**85**
5	**4.95**	**90**

4.1 Data Analysis

The data in the tables are fit to the model equation $g(t) = g_o + Ke^{-\alpha t}\cos(\beta t - \delta)$

A least square best fit is performed using Excel. An inbuilt tool, Solver was used to minimize the Least square error in order to obtain the optimal values for $g_o, K, \alpha, \beta and \delta$ .A table of the best fitting parameters for each of the subjects and the least sum of square errors are shown below in table 4.1.1.

The tables are arranged in the following columns.

Column 1: Time

Column 2: Observed glucose concentration

Column 3: Predicted glucose concentration

Column 4: Square of the difference that is the square of the difference between the predicted value and the observed value.

Column 5: Square relative Error (SRE)

Column 6: Mean Square Relative Error (MSRE)

The tables also include the Mean Square Relative Error percentage and parameter estimates.

The following were used as the initial parameters.

4.1.1 Analysis of Subject A

G	**85.446**
K	**1**
α	**1**
β	**1**
δ	**1**

Table 4.1.1 Results of Subject A

Subject A- normal						
Time (hour)	**Observed Glucose Concentration (mg/dl)**	**Predicted Glucose Concentration (mg/dl)**	**difference squared**	**SRE**	**MSRE**	**MSRE%**
0	**85.446**	**85.43881971**	**5.15566E-05**	**7.062E-09**	**8.062E-06**	**0.00081**
1	**119.988**	**119.8739354**	**1.3010728E-02**	**9.037E-07**		
2	**92.718**	**92.75207858**	**1.16135E-03**	**1.351E-07**		
3	**85.446**	**85.01541599**	**1.85402593E-01**	**2.539E-05**		
4	**83.628**	**83.93945414**	**9.7003679E-02**	**1.387E-05**		

Sum of difference squared = 2.96629906E-01

Parameter estimates	
g	**83.94540986**
K	**287.7098641**
α	**1.743175135**
β	**0.789623301**
δ	**1.565605623**

Substituting these parameters into equation (3.25) gives

$$g(t) = 83.95 + 287.7e^{-1.74t}\cos(0.79t - 1.57) \tag{3.32}$$

Figure 4.1.1 shows the graph of time (horizontal axis) against glucose concentration (vertical axis) for table 4.1.1. On the graph the predicted points are shown in red whiles the observed points are shown in blue.

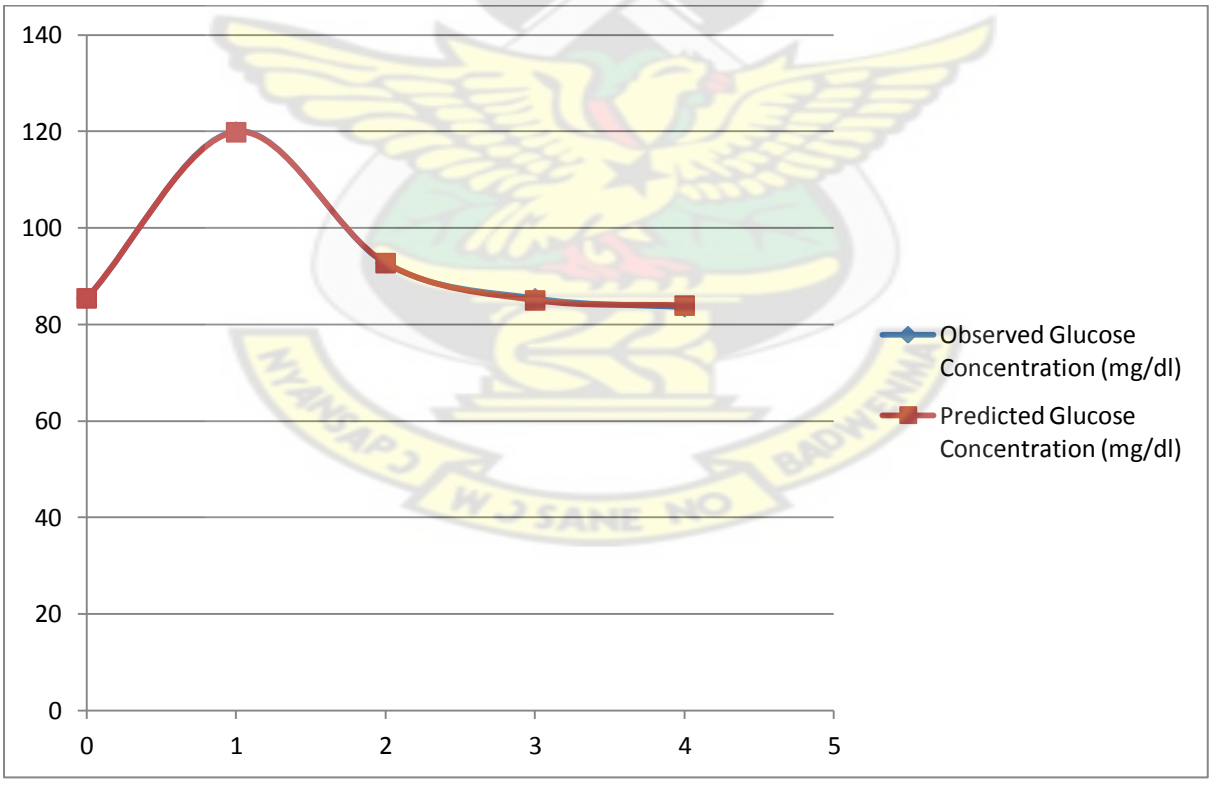


Figure 4.1.1 graph of subject A

Using the criterion set by Ackerman et al the natural period of the system can be calculated as follows;

From equation (3.32)

$$\omega_o = \sqrt{\beta^2 + \alpha^2} = \sqrt{0.789^2 + (-1.743)^2} = 1.913678$$

And $T_o = \frac{2\pi}{\omega_o} = \frac{2*\pi}{1.914} = 3.284$

Since $T_o < 4$ it implies that the person is normal.

4.1.2 Analysis on Subject B

Initial Parameters

g	**194.526**
K	**1**
α	**1**
β	**1**
δ	**1**

Table 4.1.2 Results of Subject B

Subject B - diabetes						
Time (hour)	Observed Glucose concentration (mg/dl)	Predicted Glucose Concentration (mg/dl)	Difference Squared	SRE	MSRE	MSRE%
0	194.526	194.5122614	0.00018875	4.9880E-09	0.053006	5.300573
1	605.394	551.5721503	2896.791507	7.9038E-03		
2	605.394	551.5721715	2896.789219	7.9038E-03		
3	599.94	551.5721715	2339.44683	6.4997E-03		
4	589.032	551.5721715	1403.238748	4.0443E-03		
5	358.146	551.5721715	37413.68384	2.9168E-01		

Sum of difference squared = 46949.95

Parameter Estimates	
g	551.5721715
K	786.2821511
α	17.40826645
β	0.910820217
δ	4.241014072

Substituting the parameters into equation (3.25)

$$g(t) = 551.57 + 786.28e^{-17.4t}\cos(0.91t - 4.24) \tag{3.33}$$

$$\omega_o = \sqrt{\beta^2 + \alpha^2} = \sqrt{0.9108^2 + (17.408)^2} = \mathbf{17.43207774}$$

$$T_o = \frac{2\pi}{\omega_o} = \frac{2*\pi}{17.432} = 0.36048$$

The value of T_o indicates that with subject B time is not an essence, the individual can maintain a high glucose level for a long period of time until insulin is injected to begin to reduce the glucose .

The figure below shows the graph of table 4.1.2.

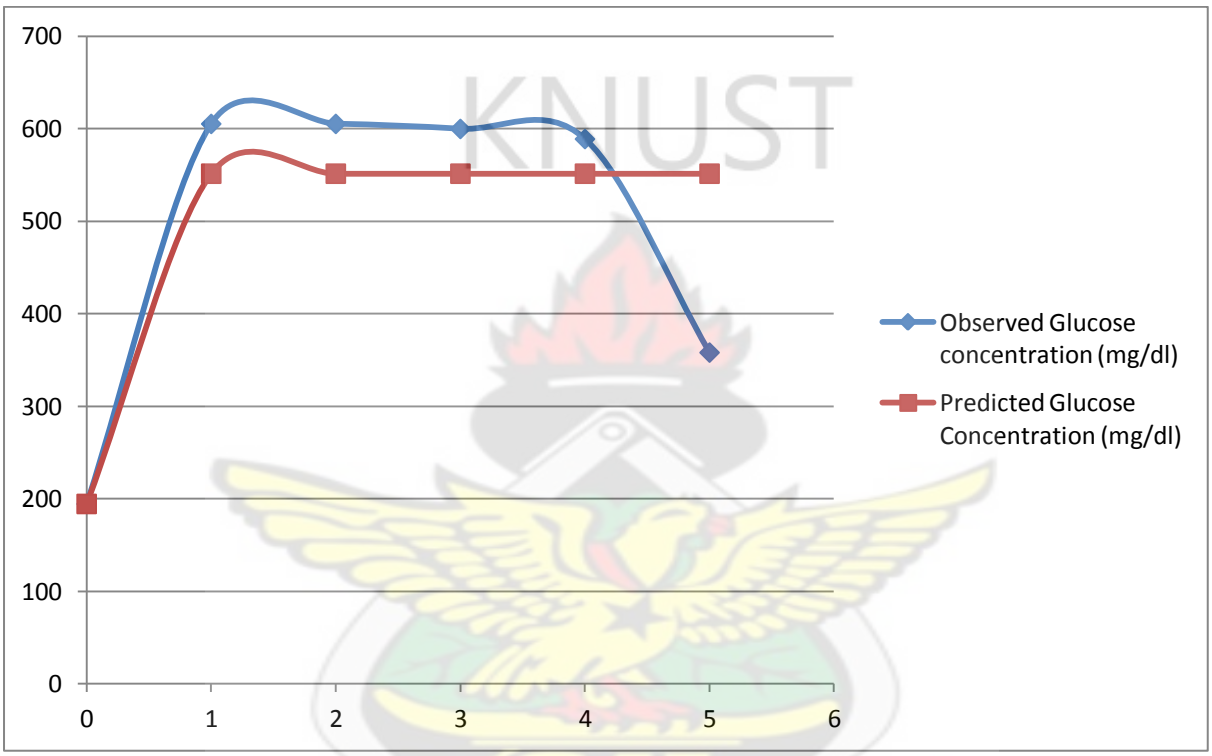


Figure 4.1.2 Graph of subject B

From the figure it is observed that the predicted points are the red and the observed points are the blue.

4.1.3 Analysis on Subject C

Initial parameters

g	**100**
K	**1**
α	**1**
β	**1**
δ	**1**

Table 4.1.3 Analysis on subject C

Subject C						
Time (hour)	Observed Glucose Concentration (mg/dl)	Predicted Glucose Concentration (mg/dl)	Difference squared	SRE	MSRE	MSRE%
0	100	99.79420264	0.042352553	4.2352E-06	0.000674	0.067391
1	220	220.8929173	0.797301314	1.6473E-05		
2	175	172.5304381	6.098736136	1.9914E-04		
3	100	103.7998814	14.43909902	1.4439E-03		
4	85	81.20734359	14.38424266	1.9908E-03		
5	90	91.77464209	3.149354537	3.8880E-04		

Sum of difference square = 38.91108622

Parameters	
g	104.8558461
K	230.5246798
α	0.538558627
β	1.062200113
δ	1.592755148

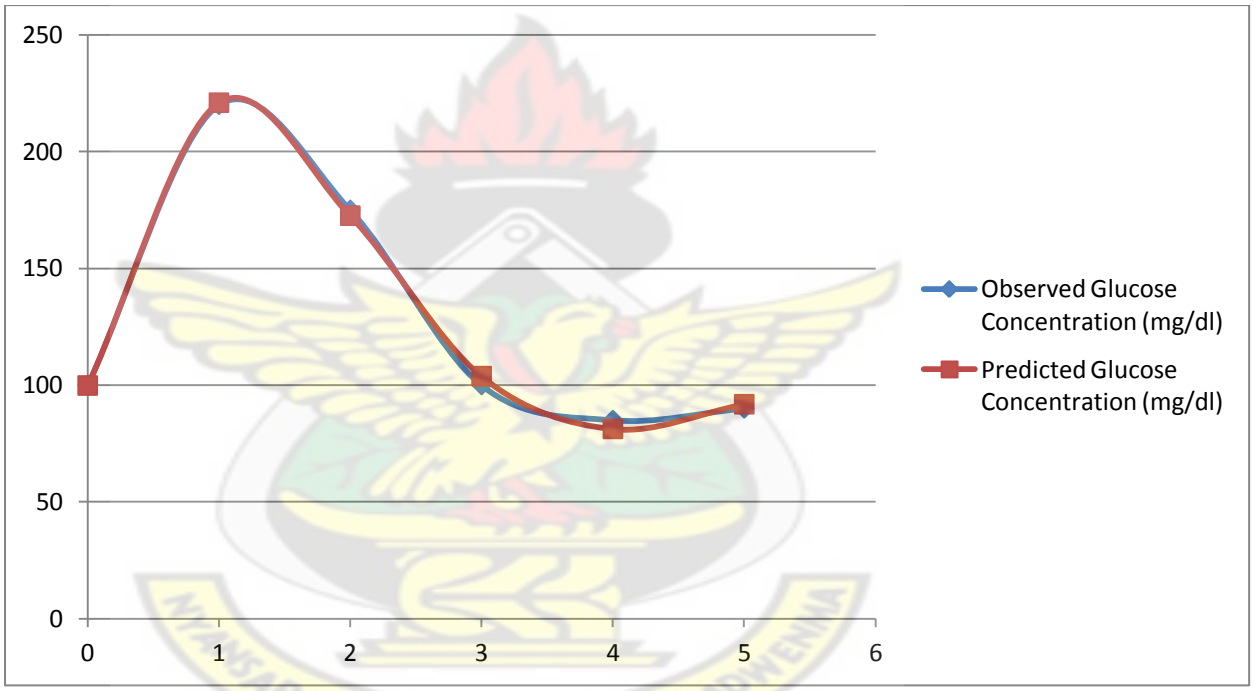


Figure 4.1.3 Graph of subject C

Figure 4.1.3 shows the graph of subject C. From the figure the predicted points are shown in red whiles the observed points are in blue.

By substituting the parameters into equation (3.25) the general solution becomes

$$g(t) = 104.86 + 230.5e^{-0.5t}\cos(1.06t - 1.59) \tag{3.34}$$

Also $\omega_o = \sqrt{0.538^2 + 1.06^2} = 1.191$ and $T_o = \frac{2\pi}{\omega_o} = \frac{2*\pi}{1.191} = 5.278$

Since $T_o > 4$ it implies that subject C is a diabetic.

4.2 Discussion of results

Comparing figures 4.1.1, 4.1.2 and 4.1.3 we noticed that figure 4.1.1 produced the best curve of fit. The predicted values fall exactly on the observed or measured values and this means that the values are good. It continues to make equation (3.32) the best model for detecting diabetes.

Figure 4.1.3 is the next best fit curve since the predicted values were just too close to the measured values. The natural period calculated for subject C shows that it is pre-diabetic that is a mild form of diabetes. Equation (3.34) of subject C also becomes a good model for detecting diabetes.

Figure 4.1.2 shows an advanced form of diabetes where the patients' blood glucose shown on the graph seems not to fall. This is called a hyperglycemic, a situation where the patient maintains a high level of glucose over a period of time unless is given insulin to help step down the glucose level.

Chapter five

Conclusion and Recommendation

The chapter summarizes all findings under conclusion, also the possible hindrances that might have affected the results of the model and the recommendations that will help in a future research regarding the subject at hand.

5.0 Conclusion

In this thesis a model for detecting diabetes Mellitus in the blood was derived given by the equation (3.24). Data were collected on patients from the Central Regional Hospital and the Nonlinear Least Squares Method were used to estimate the unknown parameters of the differential equations that describe the glucose-insulin dynamics with the help of Excel spreadsheet inbuilt optimization tool called solver. The simulation diagram of the proposed mathematical model with the estimated parameters was constructed. The error between the simulated data and the experimental data was calculated to be very small in subject A and subject C. The case with subject B indicate that our model described above can only be used to diagnose mild diabetes or pre-diabetes, since it was assumed throughout that the deviation of g of G from its optimal value G_o is small. Very large deviations of G from G_o usually indicate severe diabetes or diabetes insipidus, which is a disorder of the posterior lobe of the pituitary gland (Ackerman et al, 1969).

5.1 Recommendation

It is worth noting that the model developed in this study only considered an internal rate at which blood glucose concentration is being increased. Future research may take into account an external rate at which blood glucose concentration is being increased. Variables such as epinephrine and glucagon should be included as separate variables in future models describing glucose-insulin dynamics. Evidence indicates that levels of epinephrine may rise

dramatically during the recovery phase of the GTT response, when glucose levels have been lowered below fasting levels. I recommend this work to the various health services in the country to aid in the detection of the disease at an early stage.

Appendices

Excel operation on Subject A

Initial Table

Time (hour)	Observed Glucose Concentration (mg/dl)
0	85.446
1	119.988
2	92.718
3	85.446
4	83.628
Parameters	
g	85.446
K	1
α	1
β	1
δ	1

Calculating the predicted Glucose values

Time (hour)	Observed Glucose Conc.(mg/dl)	Predicted Glucose Conc.(mg/dl)
0	85.446	=B21+B22*EXP(-B23*A14)*COS(B*A14-B25)
1	119.988	85.81387944
2	92.718	85.51912197
3	85.446	85.42528127
4	83.628	85.42786765
Parameters	Initial values	
g	85.446	
K	1	
α	1	
β	1	
δ	1	

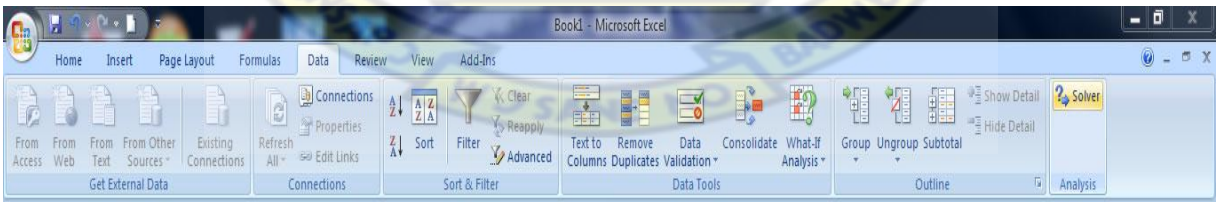
Calculating the difference squared

Time (hour)	Observed Glucose Conc.(mg/dl)	Predicted Glucose Conc.(mg/dl)	Difference Squared		
0	85.446	=B21+B22*EXP(-B23*A14)*COS(B*A14-B25)	=(C14-B14)^2		
1	119.988	85.81387944	1167.870516		
2	92.718	85.51912197	51.82384495		
3	85.446	85.42528127	0.000429266		
4	83.628	85.42786765	3.239523575		
		Sum of Difference	= 1223.22624		
Parameters					

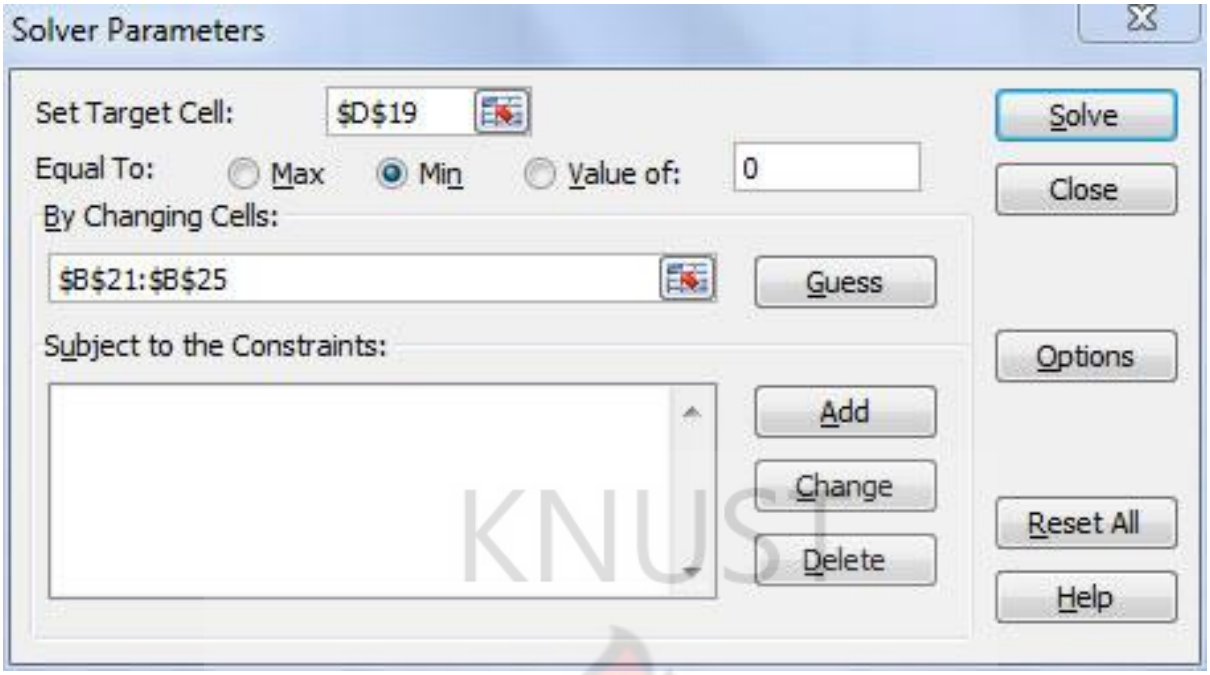
g	**85.446**				
K	**1**				
α	**1**				
β	**1**				
δ	**1**				

Using the in built optimization tool, the Solver

The solver tool is found in the main tool bar under the DATA tool. It is located at the far right side of the toolbar DATA.



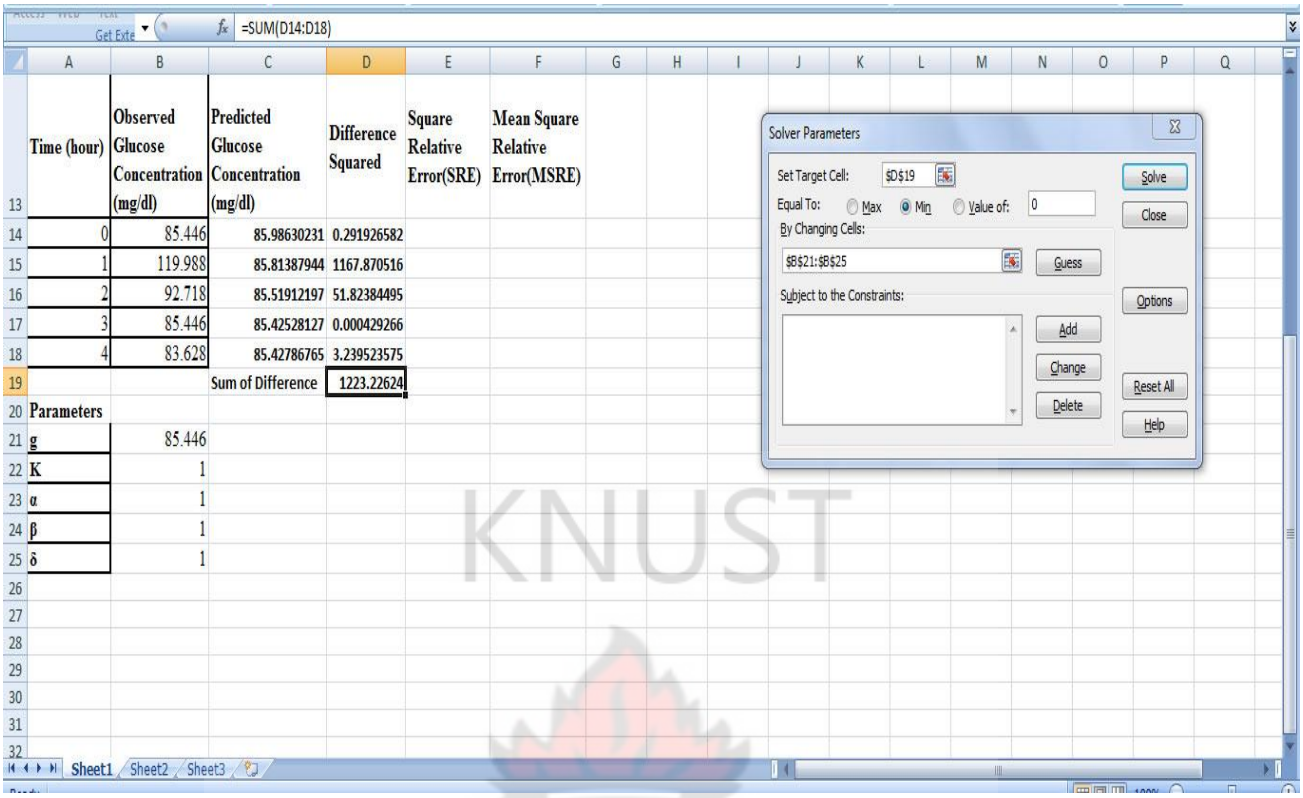
The solver dialogue box appears as below



Here the target cell is D19 which is the **sum of the difference squared.**

Now since we seek to minimize the target cell we set the **Equal To** to **Min**

Under the **By Changing Cells** option cells **B21 to B25** are selected which represent the parameters.



After which we click **solve** and **ok.**

The final results is shown below.

Time (hour)	Observed Glucose Concentration (mg/dl)	Predicted Glucose Concentration (mg/dl)	Difference Squared
0	85.446	85.43881971	5.15566E-05
1	119.988	119.8739354	0.013010728
2	92.718	92.75207858	0.00116135
3	85.446	85.01541599	0.185402593
4	83.628	83.93945414	0.097003679
		Sum of Difference =	0.296629906
Parameters			
g	83.94540986		
K	287.7098641		
α	1.743175135		
β	0.789623301		
δ	1.565605623		

Time (hour)	Observed Glucose Concentration (mg/dl)	Predicted Glucose Concentration (mg/dl)	difference squared		SRE	MSRE	MSRE%
0	85.446	85.43881971	5.15566E-05		7.062E-09	8.062E-06	0.00081
1	119.988	119.8739354	0.013010728		9.037E-07		
2	92.718	92.75207858	0.00116135		1.351E-07		
3	85.446	85.01541599	0.185402593		2.539E-05		
4	83.628	83.93945414	0.097003679		1.387E-05		
					4.031E-05		
		sum of diff^2	0.296629906				
Parameters							
g	83.94540986						
K	287.7098641						
α	1.743175135						
β	0.789623301						
δ	1.565605623						

Further the **Square Relative Error (SRE)** and **the Mean Square Relative Error (MSRE)** were also calculated.

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