



ON THE MATHEMATICAL MODEL FOR THE STUDY OF DIABETES IN TARKWA NSUAEM MUNICIPALITY

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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 and glucagon control blood glucose levels. The two most common forms of diabetes are due to either a diminished production of insulin (Type I diabetes), or diminished

response by the body to insulin (Type II 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. This paper explained how each hormone is activated and how it affects glucose levels in the blood. The model formulated in this project extends the one proposed by E. Ackerman (1969) to include three instead of two hormones concentrations. To be specific, this paper includes concentrations for glucose, glucagon and insulin.

KEYWORDS: Diabetes Mellitus, Body mass index, Blood sugar level, Frequent Urination.

INTRODUCTION

Diabetes Mellitus, commonly referred to as diabetes is a lifelong (chronic) disease that is rampant among overweight children from the age 10, overweight adults (who have BMI greater than 25, BMI simply means Body Mass Index: A key index for relating weight to height. BMI is a person's weight in kilograms (kg) divided by his or her height in meters squared. The National Institutes of Health (NIH) now defines normal weight, overweight, and obesity according to BMI rather than the traditional height/weight charts. Overweight is a

BMI of 27.3 or more for women and 27.8 or more for men. Obesity is a BMI of 30 or more for either sex (about 30 pounds overweight. A very muscular person might have a high BMI without health risks) and adults over age 45.

Diabetes mellitus is composed of heterogeneous group of disorders characterized by high blood sugar level (hyperglycemia). This disease is also characterized by polyuria, polydipsia and weight loss in spite of polyphagia, hyperglycemia and glucosuria. There are widespread biochemical abnormalities but the fundamental defects to which most of the abnormalities can be traced includes increase in liberation of glucose into the circulation from the liver and reduced entry of glucose into various peripheral tissue (Ayeni and Adewale, 2003; Derrick and Grossman, 1976; Ganongy, 1999).

A polypeptide hormone, insulin, is synthesized in the beta cells of the islets of Langerhans of the pancreas and is necessary for normal utilization of glucose by most cells in the body. In diabetic patients the normal ability of body cells to use glucose is inhibited due to the inability of a person's body to produce enough insulin, or because the cells in the body do not respond to the insulin that is produced in the body, or there is no insulin in the body at all. In response to this, the body produces symptoms of frequent urination (polyuria), increased hunger (polyphagia), increased thirst (polydipsia), weight loss and weakness (Wikipedia, 2012).

Diabetes affects millions of people worldwide with devastating human, social and economic impact (Watkins, 1993). Around 250 million people are estimated to be living with diabetes today and this number is expected to increase to over 380 million by 2025 (Hossain et al., 2007). The prevalence rate of diabetes has reached epidemic proportions and WHO predicts that people living in developing countries will be most affected in the 21st century. Currently, over 70% of the world's diabetic patients live in low and middle income countries. An estimated 285 million people, corresponding to 6.4% of the world's adult population live with diabetes in 2010. This number is expected to increase to 438 million by 2030, corresponding to 7.8% of the adult population. While the global prevalence of diabetes is 6.4% that of Africa is 3.8% which is expected to experience a relatively higher increase (Mehmood et al., 2011). The largest age group currently affected by diabetes is between 40-59 years. By 2030 this number is expected to move to the 60-79 age brackets with some 196 million cases. Non-communicable diseases, diabetes included, accounts for 60% of all deaths worldwide (IDF, 2011).

In Ghana, like many developing countries around the world, the erosion of traditional lifestyle and diet is largely causing diabetes. It is estimated that about 2.2 million Ghanaians are suffering from diabetes and a prevalence rate of 3.3% of the adult population (IDF, 2011). Diabetes Mellitus is one of the major causes of premature illness and death worldwide.

There are a lot of models of glucose and insulin dynamics which are aimed at assisting in the management of diabetes. This model extends the one proposed by Ackerman (1969) to include three instead of two hormones concentrations. In particular we include concentrations for glucose, glucagon and insulin. The model is based on a 3x3 system of non-homogenous ordinary differential equations.

History of Diabetes

Diabetes is one of the first diseases described with an Egyptian manuscript from 1500 BCE mentioning “too great emptying of the urine, (Ripoll, Brian C. and Leutholtz, Ignacio). The first described cases are believed to be of Type 1 diabetes. Indian physicians around the same time identified the disease and classified it as madhumeha or honey urine noting that the urine would attract ants. The term "diabetes" or "to pass through" was first used in 230 BCE by the Greek Apollonius of Memphis. The disease was rare during the time of the Roman Empire with Galen commenting that he had only seen two cases during his career. Type 1 and Type 2 diabetes were identified as separate conditions for the first time by the Indian physicians Sushruta and Charaka in 400-500 AD with Type 1 associated with youth and Type 2 with being overweight. The term "mellitus" or "from honey" was added by the British John Rolle in the late 1700s to separate the condition from diabetes insipidus which is also associated with frequent urination. While many measures were tried, effective treatment was not developed until the early part of the 20th century when the Canadians Frederick Banting and Charles Best developed insulin in 1921 and 1922. This was followed by the development of the long acting insulin NPH in the 1940s (Leonid Poretsky).

Signs and Symptoms

The classical symptoms of diabetes are polyuria (frequent urination), polydipsia (increased thirst) and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in Type I diabetes (Type I diabetes is partly inherited and then triggered by certain infections, with some evidence pointing at Coxsackie B4 virus. There is a genetic element in individual susceptibility to some of these triggers which has been traced to particular HLA genotypes (i.e., the genetic "self" identifiers relied upon by the immune system). However, even in those

who have inherited the susceptibility, Type I diabetes mellitus seems to require an environmental trigger) while in Type II diabetes (Type II diabetes is due primarily to lifestyle factors and genetics) they usually develop much more slowly and may be subtle or absent.

Prolonged high blood glucose can cause glucose absorption in the lens of the eye, which leads to changes in its shape, resulting in vision changes. Blurred vision is a common complaint leading to a diabetes diagnosis; Type I should always be suspected in cases of rapid vision change, whereas with Type II changes is generally more gradual, but should still be suspected.

A number of skin rashes can occur in diabetes that is collectively known as diabetic dermadromes.

Summarily Symptom checklist for Type I diabetes is.

- Exceptional thirst
- Dry mouth
- Frequent urination
- Loss of weight
- Weakness or fatigue
- Blurred vision

Having history of Type I diabetes in your family increases the chances of developing Type 1 diabetes.

Summarily Symptom checklist for Type II diabetes is:

- Blurred vision
- Cuts or sores take a long time to heal
- Itching skin or yeast infections
- Excessive thirst
- Dry mouth
- Frequent urination
- Leg pain

Diagnosis

Diabetes mellitus is characterized by recurrent or persistent hyperglycemia, and is diagnosed by demonstrating any one of the following as stated by (WHO, 1999)

- Fasting plasma glucose level ≥ 7.0 mmol/L (126 mg/dL).
- Plasma glucose ≥ 11.1 mmol/L (200 mg/dL) two hours after a 75 g oral glucose load as in a glucose tolerance test.
- Symptoms of hyperglycemia and casual plasma glucose ≥ 11.1 mmol/L (200 mg/dL).
- Glycated hemoglobin (Hb A1C) $\geq 6.5\%$. (Saydah SHet al., 2001).

A positive result, in the absence of unequivocal hyperglycemia, should be confirmed by a repeat of any of the above-listed methods on a different day. It is preferable to measure a fasting glucose level because of the ease of measurement and the considerable time commitment of formal glucose tolerance testing, which takes two hours to complete and offers no prognostic advantage over the fasting test (Saydah SHet al; 2001). According to the current definition, two fasting glucose measurements above 126 mg/dL (7.0 mmol/L) is considered diagnostic for diabetes mellitus.

People with fasting glucose levels from 100 to 125 mg/dL (5.6 to 6.9 mmol/L) are considered to have impaired fasting glucose. Patients with plasma glucose at or above 140 mg/dL (7.8 mmol/L), but not over 200 mg/dL (11.1 mmol/L), two hours after a 75 g oral glucose load are considered to have impaired glucose tolerance. Of these two pre-diabetic states, the latter in particular is a major risk factor for progression to full-blown diabetes mellitus as well as cardiovascular disease. (SantaguidaPL et al.; 2008)

Glycated hemoglobin is better than fasting glucose for determining risks of cardiovascular disease and death from any cause. (Selvin E, et al; 2010)

Table 1: Diabetes diagnostic criteria.

Condition	2hour glucose	Fasting glucose	HbA _{1c}
	mmol/l(mg/dl)	mmol/l(mg/dl)	%
Normal	<7.8 (<140)	<6.1 (<110)	<6.0
Impaired fasting glycaemia	<7.8 (<140)	$\geq 6.1(\geq 110)$ & $<7.0(<126)$	6.0-6.4
Impaired glucose tolerance	$\geq 7.8 (\geq 140)$	<7.0 (<126)	6.0-6.4
Diabetes mellitus	$\geq 11.1 (\geq 200)$	$\geq 7.0 (\geq 126)$	≥ 6.5

(World Health Organization. www.who.int. 2006. Retrieved 2011-02-20) and Vijan, S.

Management of Diabetes

Diabetes mellitus cannot be cured except in very specific situations. Management concentrates on keeping blood sugar levels as close to normal ("euglycemia") as possible,

without causing hypoglycemia. This can usually be accomplished with diet, exercise, and use of appropriate medications (insulin in the case of Type I diabetes, oral medications as well as possibly insulin in Type II diabetes).

Patient education, understanding, and participation is vital since the complications of diabetes are far less common and less severe in people who have well-managed blood sugar levels. (Nathan DM et al; 2005). The goal of treatment is an HbA1C level of 6.5%, but should not be lower than that, and may be set higher (National Institute for Health and Clinical Excellence 2008). Attention is also paid to other health problems that may accelerate the deleterious effects of diabetes. These include smoking, elevated cholesterol levels, obesity, high blood pressure, and lack of regular exercise (National Institute for Health and Clinical Excellence 2008).

Medications

Oral medications (Anti-diabetic medication)

Metformin is generally recommended as a first line treatment for Type II diabetes as there is a good evidence that it decreases mortality (Ripsin, CM et al.; 2009). Routine use of aspirin however has not been found to improve outcomes in uncomplicated diabetes (Pignone M. et al.; 2010).

Insulin (*Insulin therapy*)

Type I diabetes is typically treated with a combination of regular NPH insulin, or synthetic insulin analogs. When insulin is used in Type II diabetes, a long-acting formulation is usually added initially, while continuing oral medications (Ripsin, CM et al.; 2009). Doses of insulin are then increased to effect (Ripsin, CM et al.; 2009).

Types of Diabetes

There are three (3) major types of diabetes. Type I or Insulin Dependent Diabetes Mellitus (IDDM) is caused by destruction of the beta cells and the resulting lack of insulin secretion. Type II or Non-Insulin Dependent Diabetes mellitus (NIDDM) ,which is the more common form, is caused by decreased tissue sensitivity to the effects of insulin, so that larger amounts of insulin are required to produce a normal effect. There is also Gestational Diabetes Mellitus (GDM) which is a form of diabetes consisting of high blood glucose levels during pregnancies.

Type I Diabetes

In this type of diabetes, the beta cells are progressively destroyed and therefore secrete little or no insulin. It is caused by an auto-immune reaction where the body's defense system attacks the insulin producing cells in the pancreas. In autoimmune disease, such as Type I diabetes, the immune system mistakenly produces antibodies and inflammatory cells that attack and cause damage to patients' own body tissues. In Type I diabetes patients, the beta cells of the pancreas, which are responsible for insulin production, are attacked by the misdirected immune system. It is believed that the development of abnormal antibodies in Type I diabetic patients is genetically inherited. The reasons why this occurs is not fully understood. This attack may be provoked by certain viral infections and or environmental toxins which trigger abnormal antibody responses that cause damage to the pancreas cells where insulin is made. These antibodies can be measured in majority of patients, and may help determine which individual is at risk for developing type diabetes.

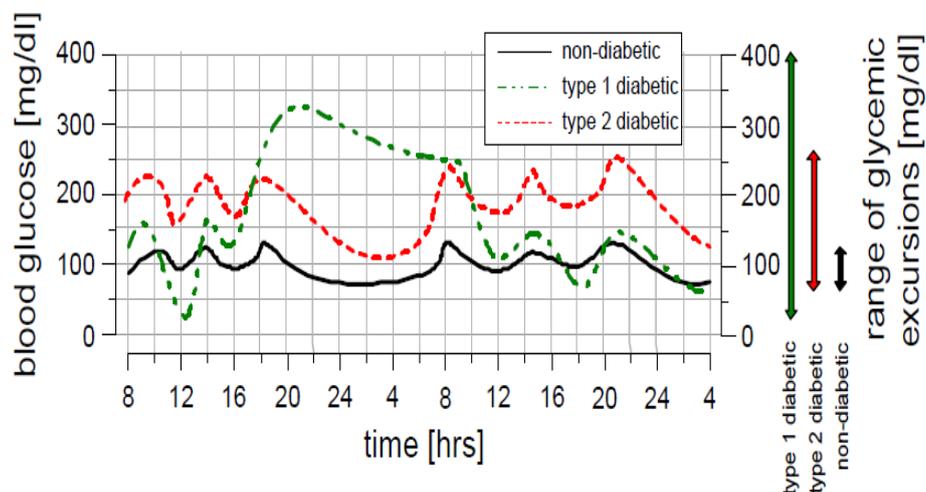


Fig. 1 Typical variations in plasma glucose concentrations in patients with Type 1 and Type 2 diabetes versus non-diabetic individuals over a two day period

Type I diabetes used to be called juvenile onset diabetes because it is usually diagnosed in people under the age of 20 even though it can affect people of any age (Stuart, 1996). Type I diabetes accounts for 10% known cases of diabetes. People with this form of diabetes need injections of insulin every day in order to control the levels of glucose in their blood. If people with this type of diabetes do not have access to insulin, they will die.

Type II Diabetes

Type II diabetes used to be called adult-onset diabetes because it's diagnosis usually occur after the age of 40 but can occur earlier, especially in high diabetes prevalence populations and accounts for at least 90% of all cases of diabetes. It is characterized by insulin resistance which may be combined with relatively reduced insulin secretion, either of which may be present at the time that diabetes become clinically manifest. Type II diabetes usually can remain undetected for many years and the diagnosis is often made from associated complications or incidentally through an abnormal blood or urine glucose test. It is often, but not always, associated with obesity, which itself can cause insulin resistance and can lead to high blood glucose levels.

A major feature of Type II diabetes is a lack of sensitivity to insulin by the cells in the body, especially the fat and muscle cells. In addition to the problem of increased insulin resistance is the defective and suboptimal nature of the insulin secreted by the pancreas which is as result of a steady decline in the production insulin by beta cells which worsens glucose control in persons with Type II diabetes. The liver in these patients continues to produce glucose despite high blood glucose levels.

Even though it is said that Type II diabetes mostly occurs in individuals over the age of 40, and the incidence increases with age, there are alarming number of patients with Type II diabetes who are in their teen age. Most of these cases are as a direct result of poor eating habits, higher body weight and lack of exercises.

While there is a strong genetic component to developing Type II diabetes, there are other risk factors, notable among them is obesity. There is a direct relationship between the degree of obesity and the risk of developing Type II diabetes and this hold true in both adults and children. It is estimated that that the chance to develop diabetes double for every 20% increase over desirable body weight.

Table 2: Comparison of Type I and Type II Diabetes.

Feature	Type I Diabetes	Type II Diabetes
Usual age of onset	Under 20 years	Over 40 years
Development of symptoms	Rapid	Slow
Percentage diabetic population	About 10%	About 90%
Development of ketoacidosis	Common	Rare
Association with obesity	Rare	Common
Beta cells of islets	Destroyed	Not destroyed

(at onset of disease)		
Insulin secretion	Decreased	Normal/increased
Autoantibodies to islet cells	Present	Absent
Body habitus	Thin or normal	Obese
Treatment	Insulin injection	Diet; oral simulation of insulin secretion

(Source: Stuart, 1996)

Gestational Diabetes Mellitus

Diabetes can occur temporarily during pregnancy and when it happens, it is called gestational diabetes mellitus. Significant hormonal changes during pregnancy can lead to blood sugar elevation in genetically predisposed individuals. Gestational diabetes mellitus (GDM) resembles type II diabetes in several respects, involving a combination of relatively inadequate insulin secretion and responsiveness. It occurs in about 2%–5% of all pregnancies worldwide and it usually resolves once the baby is born. However 20%–50% of affected women develop type II diabetes later in life, especially in women who required insulin during pregnancy and those who remain overweight after their delivery. Gestational diabetes is fully treatable but requires careful medical supervision throughout the pregnancy (Mathur 2012).

The Existing Mathematical Models on the Study of Diabetes Mellitus

While modeling has been accepted in cardiovascular and respiratory control (Topor *et al.*, 2004; Guyton, 1963), the acceptance of models to describe blood glucose regulation was more controversial. Early models were based upon differential equation representations of the dynamic relationships between glucose and insulin, and varied from extremely simple (Bolie, 1963) to extremely complex (Srinivasan *et al.*, 1970). However, the impact of modeling on the diagnosis and treatment of diabetes mellitus was limited. One reason for the lack of acceptance was the unfamiliarity of many endocrinologists with the process of using mathematical or computer representations to describe closed-loop feedback systems. Additional problems arose from the inherently non-linear nature of the function of the organs that play prominent roles in regulation of the blood glucose. The literature dealing with mathematical modeling for diabetes is in abundance these days. During the last decades, a variety of models have been devoted to different aspects of diabetes, including glucose and insulin dynamics, management and complications prevention, cost and cost-effectiveness of strategies and epidemiology of diabetes in general. Several reviews are published regularly on mathematical models used for specific aspects of diabetes (Boutayeb and Chetouani,

2006). Below is a list of mathematical models that are used in the diagnosis and treatment of diabetes.

The Minimal Model

The minimal model, which was presented by Bergman *et al.* (1981), is one of the oldest mathematical models and perhaps the most commonly used control relevant model for the interpretation of the glucose and insulin plasma concentrations because of its simplicity, both as a clinical tool and as an approach to understanding the composite effects of insulin secretion and insulin sensitivity on glucose tolerance and risk for Type II diabetes mellitus. The original assumption of the model have led to an understanding of the kinetics of insulin *in vivo*, as well as the relative importance of beta cell compensatory failure in the origination and development of diabetes. The minimal model is based on the closed loop relationship between glucose insulin secretion and insulin action (picture below) where the ‘tank’ represents blood glucose in extracellular fluid with the level of glucose indicated by the height of the fluid in the tank. The level of glucose is the balance between the rate of glucose production (flux from liver) and the rate of glucose utilization (drainage from tank). After meals the level of glucose increases evoking an insulin secretion response. Insulin crosses the endothelial barrier (represented by the wavy line) which increases glucose uptake by muscle and eventually suppresses lipolysis from adipose tissue, which in turns reduces liver glucose production. To make the model simple, only the extrapancreatic tissues are presented (indicated by the dotted arrow), including the net glucose utilization (Bergman, 2002).

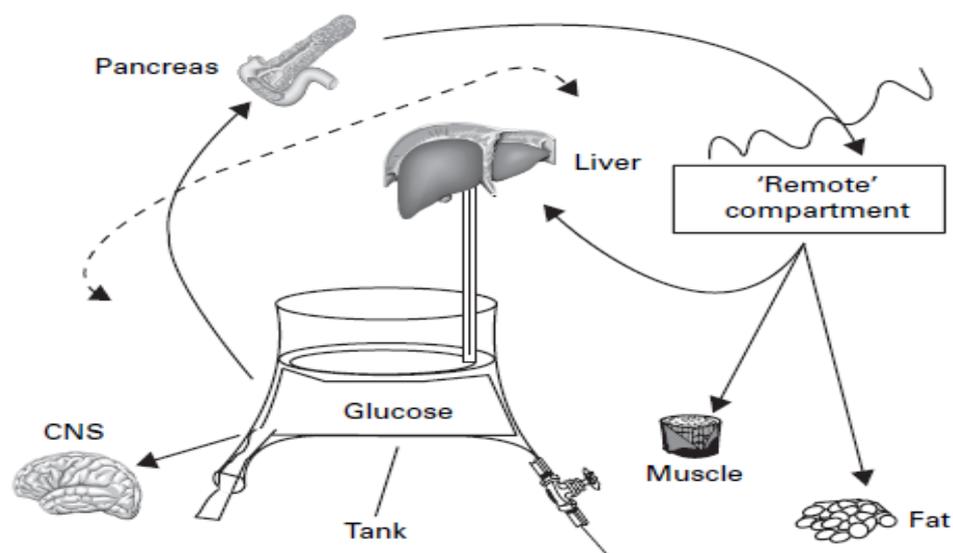


Fig. 2 Closed-loop relationship between glucose insulin secretion and insulin action

The minimal model is composed of two parts: the first consists of two differential equations and describes the glucose plasma concentration time-course treating insulin plasma concentration as a known forcing function; the second consists of a single equation and describes the time course of plasma insulin concentration treating glucose plasma concentration as a known forcing function (De Gaetano, 2000). The physiological factors that determine the restoration of plasma glucose after injection is represented by the first equation. S_G and $X(t)$ are the effect of glucose and effect of insulin in the interstitial compartment respectively with $X(t)$ acting synergistically with glucose to return the glycaemia to basal levels. The second equation represents the flux of insulin from plasma into the interstitial compartment where it acts (Bergman et. al, 1979). The equations used to represent the two subsystems (compartments) to represent glucose insulin dynamics are given below.

$$(1) \quad \frac{dG(t)}{dt} = -[p_1 + X(t)]G(t) + p_1G_b, \quad G(0) = p_0$$

$$(2) \quad \frac{dX(t)}{dt} = -p_2X(t) + p_3[I(t) - I_b], \quad X(0) = 0$$

$$(3) \quad \frac{dI(t)}{dt} = p_4[G(t) - p_5] - p_6[I(t) - I_b], \quad I(0) = p_7 + I_b$$

where

$G(t)$ [mg/dl] is the blood glucose concentration at time t [min];

$I(t)$ [μ UI/ml] is the blood insulin concentration;

$X(t)$ [min^{-1}] is an auxiliary function representing insulin-excitabile tissue glucose uptake activity, proportional to insulin concentration in a "distant" compartment;

G_b [mg/dl] is the subject's baseline glycemia;

I_b [μ UI/ml] is the subject's baseline insulinemia;

p_0 [mg/dl] is the theoretical glycemia at time 0 after the instantaneous glucose bolus;

p_1 [min^{-1}] is the glucose "mass action" rate constant, i.e. the insulin-independent rate constant of tissue glucose uptake, "glucose effectiveness";

p_2 [min^{-1}] is the rate constant expressing the spontaneous decrease of tissue glucose uptake ability;

p_3 [min^{-2} (μ UI/ml) $^{-1}$] is the insulin-dependent increase in tissue glucose uptake ability, per unit of insulin concentration excess over baseline insulin ;

p4 $[(\mu\text{UI/ml}) (\text{mg/dl})^{-1} \text{min}^{-1}]$ is the rate of pancreatic release of insulin after the bolus, per minute and per mg/dl of glucose concentration above the "target" glycemia;

p5 $[\text{mg/dl}]$ is the pancreatic "target glycemia";

p6 $[\text{min}^{-1}]$ is the first order decay rate constant for Insulin in plasma;

p7 $[\mu\text{UI/ml}]$ is the theoretical plasma insulin concentration at time 0, above basal insulinemia, immediately after the glucose bolus.

Therapeutic Modeling of Type I Diabetes

This model aids the continuous infusion of insulin based on individual's requirements in terms of the care of decay of sugar concentration in a prescribed time. For each individual depending on many personal factors like obesity, age, kidney functions etc., a prescription is made of the desirable curve of sugar concentration from its highest level to the desirable lowest level in a given period of time which takes away much guesswork of the amount of insulin given intermittently or continuously.

The model uses continuous subcutaneous insulin infusion therapy, (Pickup and Keen, 2002), to model the dynamics of glucose in type I diabetic patients. The effect of an external source of insulin release is model as a prescribed function of time on glucose levels. The model is then used to assess the optimal insulin release profile, and the threshold amount required to bring the level of glucose to within a normal physiological range. The model is given as follows (Nilam et. al,2006);

$$(1) \quad \frac{dG}{dt} = -XG + l_1(G_b - G)^+$$

$$(2) \quad \frac{dX}{dt} = -p_1X + p_2(I - I_b)$$

$$(3) \quad \frac{dI}{dt} = l_2(G - G_c)^+ f(t) - l_3(I - I_b)$$

where

G blood glucose concentration

X auxiliary function representing remote insulin action

I insulin plasma concentration

G_b base line value of glucose concentration in plasma

G_c glucose threshold concentration in plasma

- I_b baseline value of insulin concentration in plasma
 I_1 the insulin dependent rate of tissue glucose uptake
 I_2 scaling factor determining TDD of insulin
 I_3 the rate of decay for insulin in plasma
 p_1 the rate of spontaneous decrease of glucose uptake
 p_2 the rate of insulin-dependent increase in tissue glucose uptake due to insulin concentration excess over its baseline.

Optimal Input Model

A lot of models on glucose-insulin dynamics, using optimal control or partial differentiation have been introduced by different authors (Palerm, 2003; Cobelli and Thomaseth, 1985; Cobelli and Thomaseth, 1987; Cobelli and Thomaseth, 1988; Cobelli and Thomaseth, 1989; Lam et. al, 2002). Using the minimal model, Cobelli and Thomaseth (1987) discussed the optimal input design in a model of glucose kinetics and proposed the following model.

$$\frac{dx(t)}{dt} = A(p)x(t) + Bu(t)$$

$$y(t) = c(p)x(t)$$

$$z(t) = y(t) + e(t)$$

Mbah's Model

According to Mbah (1998), the mathematical model used for the study of insulin dependent diabetes mellitus subjects is given as

$$\frac{dx}{dt} = a_1 q e^{-k(t-t_0)} - a_2 xy - a_3 x \quad (1)$$

$$\frac{dy}{dt} = b_1 x - b_2 y + b_3 (\gamma t + \delta) \quad (2)$$

$$x(t_0) = x_0, \quad y(t_0) = y_0$$

Where x and y represents glucose and insulin respectively and $a_1, a_2, b_1, b_2,$ and b_3 are all constants which were determined experimentally.

MATERIALS AND METHODS

Study Area

The Tarkwa Nsuaem Municipality is one of the districts in the Western Region of Ghana and is located between Latitude $4^{\circ}00'N$ and $5^{\circ}04'N$ and Longitudes $10^{\circ}45'W$ and $10^{\circ}21'W$ and

has a total area of 2354 sq. km. The district covers 17 towns and has a total population of almost 250,000 at a growth rate of 2.97%.

The district is one of the richest in Ghana in terms of natural resources. Gold is its major natural resource. There is also a manganese mine at Nsuta a suburb of Tarkwa. Tarkwa Nsuaem Municipality can boast of many mining companies and mining support services and industrial laboratories. There are a lot of small scale mining companies and illegal mining operators (galamsey), operating in the area who employ a sizeable proportion of the unemployed youth.

For effective health delivery, the District is divided into 8 operational sub-districts. Each sub-district has at least one health facility with a number of private clinics and maternity homes, which supports the few public health facilities.

A baseline study conducted by the Center for Environmental Impact Assessment (CEIA), Ghana and Wassa Association of Communities Affected by Mining, WACAM in 2008 revealed that all the 117 rivers and streams in the Tarkwa Nsuaem Municipality are perceived to have been polluted by either mining companies and/or 'galamsey' operators and this perception was proven to be true by the Commission of Human Rights and Administrative Justice (CHRAJ) report of 2008. This is because indigence in the Municipality have since 2004 reported thousands of cases of skin diseases (keratosis) and Type II diabetes caused by the high intake of arsenic, which is a naturally occurring element in the earth's crust found alongside some gold ores such as arsenopyrite ores and which according to the United States Environmental Protection Agency (USEPA), is a class 'A' human cancer causing agent that affects the lung, liver, kidney, bladder and skin. Reported incidence of diabetes mellitus in the municipality from 2004 to 2006 shows an increased from 388 in 2004 to 441 in 2005 and then reduced to 369 in 2006. Records from the Health Directorate of the Tarkwa Nsuaem Municipal Assembly (TNMA) shows a sharply rise in diabetes cases from 939 in 2007 to 1,626 in 2008 to 2,857 in 2009 and then reduced to 1,610 in 2010.

MODEL FORMULATION

The human body needs to maintain its glucose concentration level within a narrow range of 70 -109mg/dl following an overnight fast. In the glucose regulatory system, elevated glucose concentration level incites the beta cells in the pancreas to secrete insulin which, as already known, helps to return the glucose concentration to normal levels. As the glucose

concentration level decreases, the secretion of insulin stops gradually. For a normal person, after an overnight fast, the basal plasma insulin is in the range of 5-10 μ U/ml. It can be wide as 10-40 μ U/ml during continuous enteral nutrition and as large as 30-150 μ U/ml during meal consumption when glucose concentration level is high (Li et al., 2006; Simon and Brandenberger, 2002). If the human pancreas does not release sufficient insulin or the insulin does not trigger cells to utilize the glucose in the plasma and inhibit hepatic glucose production, diabetes mellitus is likely to develop (Bergman et al., 2002).

Fasting Blood Sugar (FBS), or an Oral Glucose Tolerance Test (OGTT) better known as GTT can be used to determine whether a person has diabetes or not. The FBS is a fasting test, meaning that you can't eat for 8-10 hours before you have your blood drawn. Fasting blood glucose of 70 mg/dl to 100 mg/dl is normal. If your fasting blood glucose level comes between 100mg/dl and 125mg/dl then you are considered to have impaired fasting glucose or pre-diabetes. A fasting glucose over 125mg/dl indicates that you have diabetes. With the GTT a fasting blood glucose is usually taken first to establish a baseline level. Then you are given a 75 grams glucose drink. Two hours later another blood sample is drawn to check your glucose level. If your blood glucose is under 140 mg/dl then your glucose tolerance is considered normal. If it is 140 mg/dl to 200 mg/dl, then you have impaired glucose tolerance or pre-diabetes. If your glucose is over 200 mg/dl then a diagnosis of diabetes is made (Cruz Rosado, 2009).

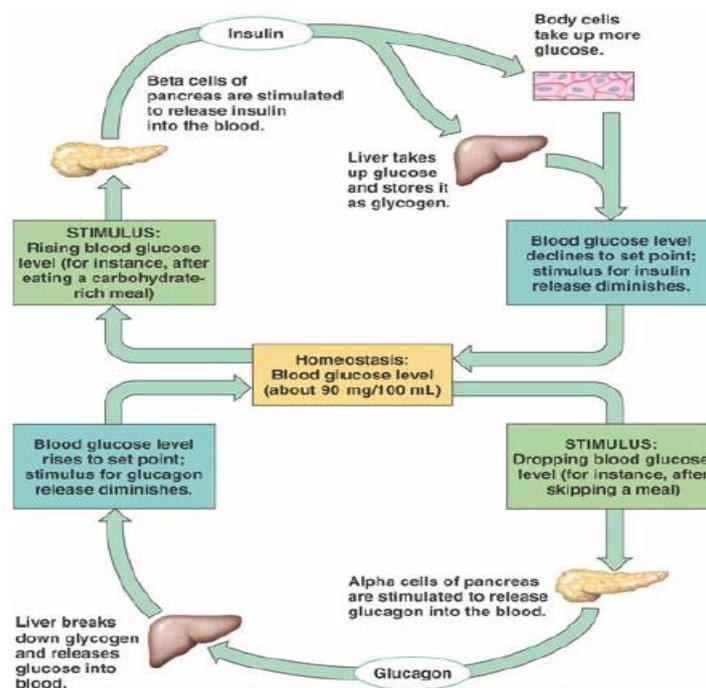


Fig. 3 Glucose Regulation from a Biological Perspective

The secretion of insulin in the glucose–insulin endocrine metabolic system occurs in an oscillatory manner over a range of 50–150 min and is usually referred to as ultradian oscillations (Simon and Brandenberger, 2002). Two noticeable time delays exist in this system. One is due to the electric action inside of β -cells upon glucose stimulation to release insulin, and physiological action that the glucose utilization correlates the so-called “remote insulin” which requires certain time for the newly synthesized insulin to cross the endothelial barrier (Li et al., 2006). The other represents the delayed effect of insulin on hepatic glucose production (Sturis et al., 1991; Tolic et al., 2000). Even though insulin regulates the liver in a direct fashion, however, its effect occurs within several minutes (Cherrington et al., 2002).

The model proposed serves to interpret the results of the Glucose Tolerance Test (GTT) on either normal or diabetes patients. Following the two time delay glucose-insulin regulatory system model presented by Li et al. (2006) glucose and insulin concentration at time $t \geq 0$ are represented by $X(t)$ and $Z(t)$ respectively and $Y(t)$ represents glucagon concentration in the blood.

$$\frac{dX(t)}{dt} = \text{glucose production} - \text{glucose utilization} \dots\dots\dots (1)$$

$$\frac{dY(t)}{dt} = \text{glucagon production} - \text{glucagon degradation} \dots\dots\dots (2)$$

$$\frac{dZ(t)}{dt} = \text{insulin production} - \text{insulin Clearance} \dots\dots\dots (3)$$

Insulin

Insulin can only be produced from beta cell secretion, mainly in response to the elevated glucose concentration. Although there are other secretagogues, e.g. free fatty acid and most amino acids, glucose is the most critical stimulus for insulin release (Li et al., 2006). Insulin is cleared by all insulin sensitive tissues. Insulin degradation is mediated primarily by the insulin receptor with a smaller contribution from non-specific processes. The liver and kidney are the primary sites of portal insulin degradation and peripheral insulin clearance, respectively. Insulin not cleared by liver and kidney is ultimately removed by other tissues, for examples, muscle and adipose cells. The insulin degradation is a regulated process involving insulin binding to its receptor, internalization, and degradation as in other tissues. The function of insulin clearance and degradation is to remove and inactivate circulating

insulin in order to control insulin action (Duckworth et al., 1998). According to Topp et al., (2000), the relationship of insulin degradation is proportional to insulin concentration.

Glucose

There are two sources for glucose production. Glucose is liberated from dietary carbohydrates such as starch or sucrose by hydrolysis within the small intestine, subsequently being absorbed into the blood. The most common ways of glucose infusion are through meal ingestion, oral glucose intake, continuous enteral nutrition, and constant glucose infusion (Sturis et al., 1991; Tolic et al., 2000)

The other source of glucose production is the liver. When the plasma glucose concentration level drops, the β -cells stop releasing insulin, but α -cells, also located in the Langerhans islets in the pancreas, start to release another hormone, glucagon. Glucagon exerts control over pivotal metabolic pathways in the liver and leads the liver to dispense glucose. Glucose utilization also consists of two parts, namely, insulin-independent utilization and insulin-dependent utilization. The insulin-independent glucose consumers are mainly the brain and nerve cells. The insulin-dependent glucose uptake is mostly due to muscles, fat cells and other tissues. These cells consume the glucose and convert it to energy.

Glucagon

Produced by the alpha cells in the pancreas, glucagon is released when the glucose level in the blood is low (hypoglycemia), causing the liver to convert stored glycogen into glucose and release it into the bloodstream. The control of glucagon production depends on the negative effects of plasma glucose and insulin concentration i.e. elevated concentrations of glucose and/or insulin result in reduced glucagon production.

By introducing two explicit time delays in the system where X is glucose, Y is glucagon and Z is insulin, the model now takes the form as follows;

$$\frac{dX(t)}{dt} = f_1(X(t), Y(t), Z(t)) + J(t) \quad (1)$$

$$\frac{dY(t)}{dt} = f_2(X(t), Y(t), Z(t)) \quad (2)$$

$$\frac{dZ(t)}{dt} = f_3(X(t), Y(t), Z(t)) + K(t) \quad (3)$$

where

$X(t)$ Blood glucose concentrations

$Y(t)$ Blood glucagon concentrations

$Z(t)$ Blood insulin concentrations

and $J(t)$, $K(t)$ denotes external rates of supplied glucose and insulin respectively and are assumed to be δ -functions, since an initial large quantity of glucose after a fast is given and the presence of initial insulin in the blood due to the secretion of glucagon into the blood during fast. It is also assumed that the body wants to maintain a homeostasis: (a metabolic equilibrium actively maintained by several complex biological mechanisms that operate via the autonomic nervous system to offset disrupting changes), for glucose concentration in the blood and hence $J(t)$ and $K(t)$ are acting like δ -functions, so they only affect the initial conditions and is effectively zero away from $t = 0$. If (X_0, Y_0, Z_0) represents the steady state or the equilibrium point of the system, then it is characterized by the equations.

$$f_1(X_0, Y_0, Z_0) = f_2(X_0, Y_0, Z_0) = f_3(X_0, Y_0, Z_0) = 0 \quad (4)$$

The homeostasis assumption means that we consider only a small perturbation or variations from the steady state or equilibrium point of the system. Thus the perturbation variables,

$$x(t) = X(t) - X_0; \quad y(t) = Y(t) - Y_0; \quad z(t) = Z(t) - Z_0 \quad (5)$$

where X_0 , Y_0 and Z_0 are the equilibrium values for blood glucose, glucagon and insulin concentrations respectively, and represents small variations from the optimal values.

Expanding the general model to linear terms with these definitions yields the following perturbation model.

$$\frac{dx(t)}{dt} = \frac{\partial f_1(X_0, Y_0, Z_0)}{\partial x} x + \frac{\partial f_1(X_0, Y_0, Z_0)}{\partial y} y + \frac{\partial f_1(X_0, Y_0, Z_0)}{\partial z} z \quad (6)$$

$$\frac{dy(t)}{dt} = \frac{\partial f_2(X_0, Y_0, Z_0)}{\partial x} x + \frac{\partial f_2(X_0, Y_0, Z_0)}{\partial y} y + \frac{\partial f_2(X_0, Y_0, Z_0)}{\partial z} z \quad (7)$$

$$\frac{dz(t)}{dt} = \frac{\partial f_3(X_0, Y_0, Z_0)}{\partial x} x + \frac{\partial f_3(X_0, Y_0, Z_0)}{\partial y} y + \frac{\partial f_3(X_0, Y_0, Z_0)}{\partial z} z \quad (8)$$

where $x(t)$, $y(t)$ and $z(t)$ now represents the linearized perturbed variables.

The next step is to analyse the system by examining the partial derivatives of the functions f_1 , f_2 and f_3 with the understanding of the physiology of glucose, glucagon and insulin. An increase in glucose in the blood stimulates tissue uptake of glucose and glycogen storage in

the liver. Similarly, an increase in blood glucagon stimulates the liver to convert stored glycogen into glucose and release it into the bloodstream for the uptake by tissues whilst reducing the storage of glycogen in the liver. Also increases in insulin facilitate the uptake of glucose in the tissues and the liver. Hence

$$\frac{\partial f_1(X_0, Y_0, Z_0)}{\partial x} = -\alpha_1 < 0; \frac{\partial f_1(X_0, Y_0, Z_0)}{\partial y} = \beta_1 > 0; \frac{\partial f_1(X_0, Y_0, Z_0)}{\partial z} = -\gamma_1 < 0 \quad (9a)$$

In addition, increases in blood glucagon and glucose stimulate the release of insulin, while increases in insulin only results in increased metabolism of excess insulin. These physiological facts imply that

$$\frac{\partial f_2(X_0, Y_0, Z_0)}{\partial x} = -\alpha_2 < 0; \frac{\partial f_2(X_0, Y_0, Z_0)}{\partial y} = -\beta_2 < 0; \frac{\partial f_2(X_0, Y_0, Z_0)}{\partial z} = \gamma_2 > 0 \quad (9b)$$

$$\frac{\partial f_3(X_0, Y_0, Z_0)}{\partial x} = \alpha_3 > 0; \frac{\partial f_3(X_0, Y_0, Z_0)}{\partial y} = \beta_3 > 0; \frac{\partial f_3(X_0, Y_0, Z_0)}{\partial z} = -\gamma_3 \quad (9c)$$

Therefore the linearized system is given by

$$\frac{dx(t)}{dt} = -\alpha_1 x(t) + \beta_1 y(t) - \gamma_1 z(t) + J(t) \quad (10)$$

$$\frac{dy(t)}{dt} = -\alpha_2 x(t) - \beta_2 y(t) + \gamma_2 z(t) \quad (11)$$

$$\frac{dz(t)}{dt} = \alpha_3 x(t) + \beta_3 y(t) - \gamma_3 z(t) + K(t) \quad (12)$$

where all the constants $\alpha_i, \beta_i, \gamma_i$ are positive.

We find the equilibrium solution of Equations (10), (11), and (12) by calculating

$$\frac{dx(t)}{dt} = \frac{dy(t)}{dt} = \frac{dz(t)}{dt} = 0 \text{ simultaneously for } x(t), y(t) \text{ and } z(t).$$

Thus

$$-\alpha_1 x(t) + \beta_1 y(t) - \gamma_1 z(t) + J(t) = 0 \quad (13)$$

$$-\alpha_2 x(t) - \beta_2 y(t) + \gamma_2 z(t) = 0 \quad (14)$$

$$\alpha_3 x(t) + \beta_3 y(t) - \gamma_3 z(t) + K(t) = 0 \quad (15)$$

Hence there is a disease-free equilibrium $E_0 = (x_0, y_0, z_0) = (0, 0, 0)$ and an endemic equilibrium $\hat{E} = (\hat{X}, \hat{Y}, \hat{Z})$ where

$$\hat{X} = \frac{\beta_2\gamma_3J - \beta_2\gamma_1K + \gamma_2\gamma_3\beta_1 - \gamma_2\gamma_1\beta_3}{\gamma_3\alpha_2\beta_1 + \gamma_3\alpha_1\beta_2 - \gamma_1\alpha_2\beta_3 + \gamma_1\alpha_3\beta_2} \quad (16)$$

$$\hat{Y} = -\frac{\gamma_3\alpha_2J - \gamma_1\alpha_3\gamma_2 - \gamma_3\alpha_1\gamma_2 - \gamma_1\alpha_2K}{\gamma_3\alpha_2\beta_1 + \gamma_3\alpha_1\beta_2 - \gamma_1\alpha_2\beta_3 + \gamma_1\alpha_3\beta_2} \quad (17)$$

$$\hat{Z} = \frac{-\alpha_2\beta_3J + \beta_3\alpha_1\gamma_2 + \alpha_3\beta_2J + \alpha_3\gamma_2\beta_1 + \alpha_2\beta_1K + \alpha_1\beta_2K}{\gamma_3\alpha_2\beta_1 + \gamma_3\alpha_1\beta_2 - \gamma_1\alpha_2\beta_3 + \gamma_1\alpha_3\beta_2} \quad (18)$$

The basic task of the blood glucose regulatory system is to bring variations from the steady state (X_0, Y_0, Z_0) back to it in time. We therefore look for conditions on the coefficient matrix in equations (10), (11) and (12) that guarantee that the equilibrium point (X_0, Y_0, Z_0) has this stability property. This will be so if all the eigenvalues of the coefficient matrix in (10), (11) and (12) have negative real parts. A necessary condition for this is that the determinant of the Jacobian matrix, $J(E_0)$, be negative. This determinant is given by:

$$\begin{aligned} J(E_0) &= \begin{vmatrix} -\alpha_1 & \beta_1 & -\gamma_1 \\ -\alpha_2 & -\beta_2 & \gamma_2 \\ \alpha_3 & \beta_3 & -\gamma_3 \end{vmatrix} \\ &= -\alpha_1(\beta_2\gamma_3 - \beta_3\gamma_2) - \beta_1(\alpha_2\gamma_3 - \alpha_3\gamma_2) - \gamma_1(-\alpha_2\beta_3 + \alpha_3\beta_2) \\ J(E_0) &= -\alpha_1\beta_2\gamma_3 + \alpha_1\beta_3\gamma_2 - \alpha_2\beta_1\gamma_3 + \alpha_3\beta_1\gamma_2 + \alpha_2\beta_3\gamma_1 - \alpha_3\beta_2\gamma_1 \\ J(E_0) &= -(\alpha_1\beta_2\gamma_3 + \alpha_2\beta_1\gamma_3 + \alpha_3\beta_2\gamma_1) + \alpha_1\beta_3\gamma_2 + \alpha_3\beta_1\gamma_2 + \alpha_2\beta_3\gamma_1 \end{aligned} \quad (19)$$

It can be observe that if the values of β_3, γ_2 are very small with the rest of the coefficients fixed, then the determinant is negative. Therefore the limiting case of $\beta_3, \gamma_2 = 0$ is considered which reduces the coefficient in equations (10), (11) and (12) as follows:

$$\begin{aligned} J(E_0) &= \begin{vmatrix} -\alpha_1 & \beta_1 & -\gamma_1 \\ -\alpha_2 & -\beta_2 & 0 \\ \alpha_3 & 0 & -\gamma_3 \end{vmatrix} \\ &= -\alpha_1(\beta_2\gamma_3 - 0) - \beta_1(\alpha_2\gamma_3 - 0) - \gamma_1(0 + \alpha_3\beta_2) \\ J(E_0) &= -\alpha_1\beta_2\gamma_3 - \alpha_2\beta_1\gamma_3 - \alpha_3\beta_2\gamma_1 \\ &= -(\alpha_1\beta_2\gamma_3 + \alpha_2\beta_1\gamma_3 + \alpha_3\beta_2\gamma_1) \end{aligned}$$

The eigenvalues of the matrix J , can be determined by the roots of the characteristics equation $|J - \lambda I|$ where I is the identity matrix

$$\begin{vmatrix} -\alpha_1 - \lambda & \beta_1 & -\gamma_1 \\ -\alpha_2 & -\beta_2 - \lambda & 0 \\ \alpha_3 & 0 & -\gamma_3 - \lambda \end{vmatrix} = 0$$

$$-\gamma_3 - \lambda \begin{vmatrix} -\alpha_1 - \lambda & -\beta_1 \\ \alpha_2 & -\beta_2 - \lambda \end{vmatrix} = 0$$

Let A be $\begin{bmatrix} -\alpha_1 - \lambda & -\beta_1 \\ \alpha_2 & -\beta_2 - \lambda \end{bmatrix}$

Then all the eigenvalues of matrix $J(E_0)$, λ are negative if

- i. $\det(A) > 0$
- ii. $\text{Trace}(A) < 0$

Now

$$\det(A) = (\alpha_1 + \lambda)(\beta_2 + \lambda) + \alpha_2\beta_1$$

$$\text{Trace}(A) = -(\alpha_1 + \lambda) - (\beta_2 + \lambda)$$

Clearly it can be seen that both conditions have been fulfilled i.e. $\text{Trace}(A) < 0$ and $\det A > 0$ since all the coefficients α_1 , α_2 , β_1 , and β_2 are all positive.

The implication of the negativity of all the eigenvalues of the Jacobian is that disease – free equilibrium is stable.

To discuss the properties of the endemic equilibrium $\hat{E} = (\hat{X}, \hat{Y}, \hat{Z})$ we form an associated Jacobian matrix J^* and obtain the eigenvalues as usual from $|J^* - \lambda I| = 0$. The characteristic polynomial for this matrix is given by:

$$|J^* - \lambda I| = \begin{vmatrix} -\alpha_1 - \lambda & \beta_1 & -\gamma_1 \\ -\alpha_2 & -\beta_2 - \lambda & 0 \\ \alpha_3 & 0 & -\gamma_3 - \lambda \end{vmatrix} = 0$$

$$(-\alpha_1 - \lambda)[(-\beta_2 - \lambda)(-\gamma_3 - \lambda)] - \beta_1[-\alpha_2(-\gamma_3 - \lambda)] - \gamma_1[-\alpha_3(-\beta_2 - \lambda)] = 0$$

$$(-\alpha_1 - \lambda)(\beta_2\gamma_3 + \lambda\beta_2 + \lambda\gamma_3 + \lambda^2) - \beta_1[\alpha_2\gamma_3 + \lambda\alpha_2] - \gamma_1[\alpha_3\beta_2 + \alpha_3\lambda] = 0$$

$$\begin{aligned}
 & -\alpha_1\beta_2\gamma_3 - \lambda\alpha_1\beta_2 - \lambda\alpha_1\gamma_3 - \alpha_1\lambda^2 - \lambda\beta_2\gamma_3 - \lambda^2\beta_2 + \lambda^2\gamma_3 + \lambda^3 - \alpha_2\beta_1\gamma_3 - \lambda\alpha_2\beta_1 \\
 & \quad - \alpha_3\beta_2\gamma_1 \\
 & - \alpha_3\gamma_1\lambda = 0
 \end{aligned}$$

$$\begin{aligned}
 & \lambda^3 + (\alpha_1 + \beta_2 + \gamma_3)\lambda^2 + (\alpha_2\beta_1 + \alpha_1\beta_2 + \alpha_1\gamma_3 + \alpha_3\gamma_1 + \beta_2\gamma_3)\lambda \\
 & \quad + (\alpha_1\beta_2\gamma_3 + \alpha_2\beta_1\gamma_3 + \alpha_3\beta_2\gamma_1) = 0
 \end{aligned}$$

$$\therefore \rho(\lambda) = \lambda^3 + d_1\lambda^2 + d_2\lambda + d_3 = 0 \quad (14)$$

where

$$\begin{aligned}
 d_1 &= \alpha_1 + \beta_2 + \gamma_3, \\
 d_2 &= \alpha_2\beta_1 + \alpha_1\beta_2 + \alpha_1\gamma_3 + \alpha_3\gamma_1 + \beta_2\gamma_3, \quad d_3 \\
 &= \alpha_1\beta_2\gamma_3 + \alpha_2\beta_1\gamma_3 + \alpha_3\beta_2\gamma_1
 \end{aligned} \quad (15)$$

It can be observed that the characteristic equation only has positive coefficients which, from basic differential equations, imply that the solutions to λ are either three negative real roots; or one negative root and two complex conjugate roots with negative real parts. Thus, the endemic equilibrium could be stable, unstable, or saddle.

NUMERICAL SIMULATIONS AND DISCUSSION OF RESULTS

Numerical Simulations

The system is solved using a fourth order Runge-Kutta scheme. The parameter values that we used for the numerical simulations are shown in Table 4.1 with initial conditions: $X(0) = 118$, $Y(0) = 103$ and $Z(0) = 7$. There are a lot of mathematical models explaining the dynamics of blood insulin concentration and glucose concentration but few has been modeled with the three hormones; glucose, glucagon and insulin. Therefore we illustrate some numerical results for the model with these three hormones.

Table 4.1: Parameters values used for the numerical simulation

Parameter	Values	References
α_1	0.0251	Tada et. al
α_2	$7.074e^{-5}$	Assumed
α_3	0.0950	Tada et. al
β_1	0.015	Assumed
β_2	0.066	Tada et. al
β_3	0.033	Assumed
γ_1	0.0703	Tada et. al
γ_2	0.0236	Tada et. al
γ_3	0.0423	Tada et. al

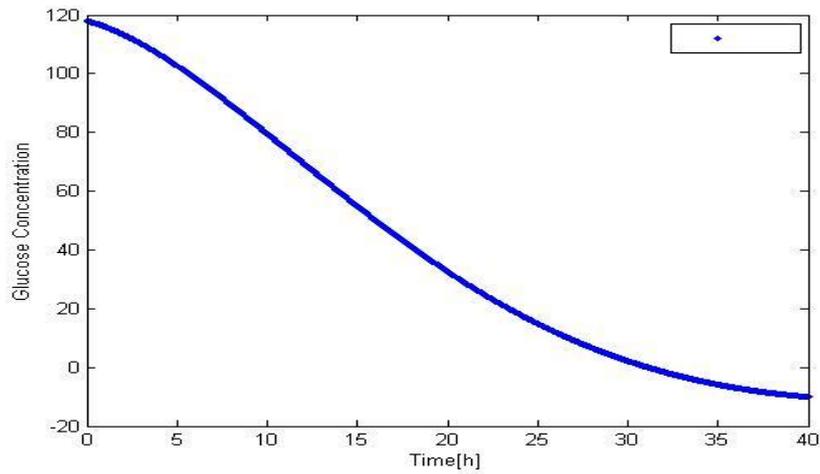


Fig. 4.1 The Dynamics of Glucose in a diabetic subject

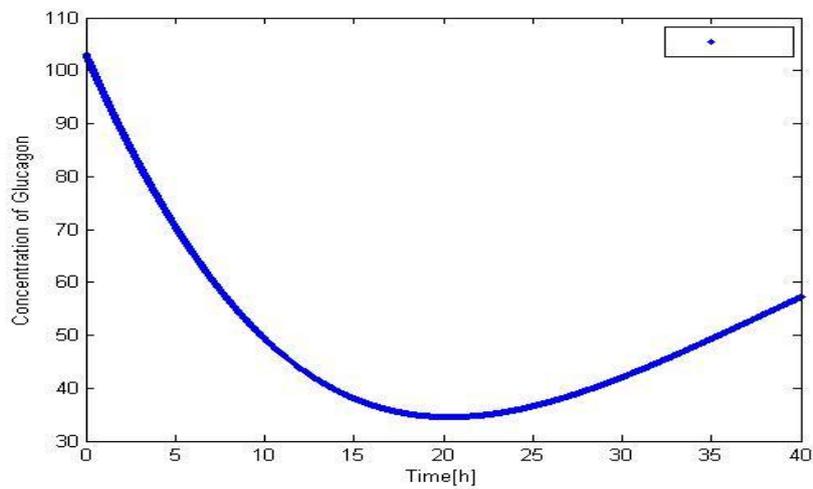


Fig. 4.2 Simulation of Blood Glucagon Concentration

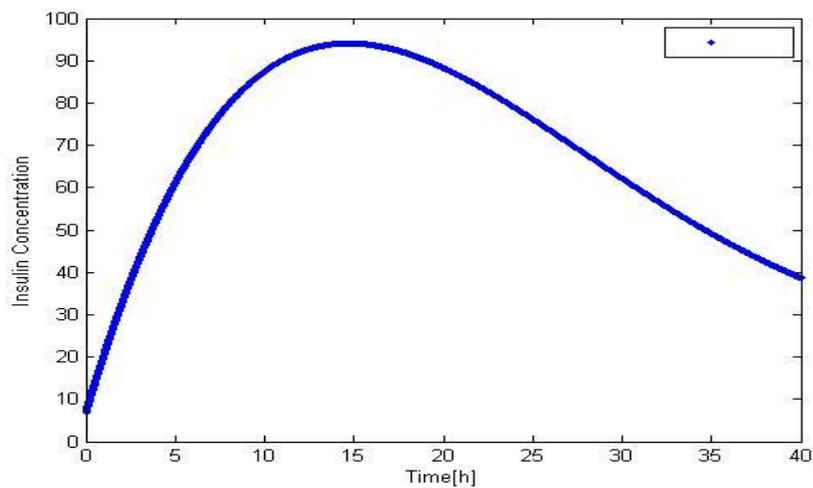


Fig. 4.3 Blood insulin Concentration

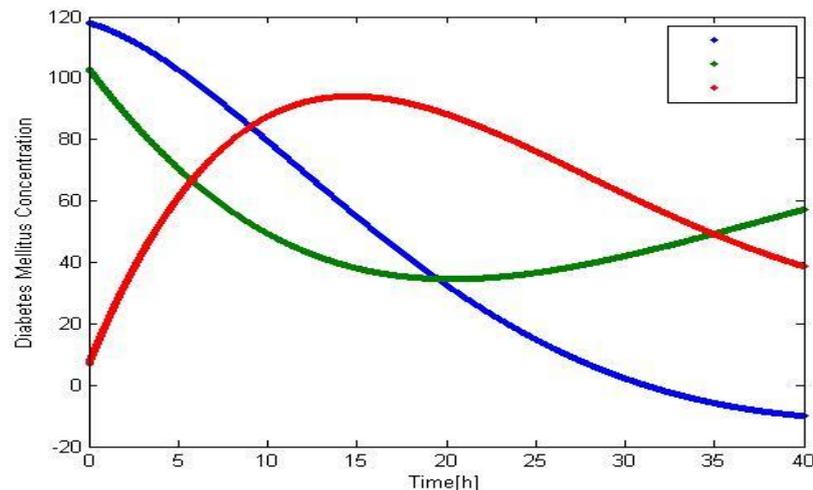


Fig. The Dynamics of Blood Glucose, Glucagon and Insulin in a Diabetic Subject

From figure 4.1 it can be observed that blood glucose levels rises and falls with time due to insulin secretion and action but in diabetic patients this level can be maintained at a very high level for a longer time. In figures 4.2 and 4.3 normal levels of blood glucagon and insulin can be observed. It can be shown that the system has three equilibrium points (i.e., steady-state solution), occurring at \hat{E} . The equilibrium can be shown to be stable, which indicates physiologically that, at least for modest deviations from the steady-state values, the system returns itself to equilibrium, as would be expected in a healthy individual; i.e., when the plasma concentration of one or more of the substances deviates from equilibrium, the system readjusts itself so as to drive the concentrations back to equilibrium. This behaviour is illustrated in Figure 4.3, where neither food nor insulin is given, while the initial values are taken to be $X(0) = 118$, $Y(0) = 103$ and $Z(0) = 7$ (i.e., glucose initially below equilibrium, insulin and glucagon at equilibrium). The graphs show that the glucose level very quickly returns to the equilibrium level, due to a combination of a short-term drop in the insulin level (by about 25%) and a rise in the glucagon level (of about 20%). This behaviour is expected because of the known effect of glucagon to raise glucose levels and of insulin to lower them.

DISCUSSION OF RESULTS

Several reasons for studying mathematical models of blood glucose regulation have been reviewed in this work. The parameters of the model formulated allows description of the blood glucose, plasma insulin and glucagon responses to a slow insulin infusion test. The appropriateness of the model need not imply its uniqueness. Other researchers are studying and comparing alternative ways of modeling and designing new experiments.

One may regard the simulations reported here as testing whether: (1) the simplified model is adequate to represent the responses of blood glucose and plasma insulin levels to both glucose and insulin infusion; or (2) more complex models are needed. As is the case for the oral glucose tolerance test, the simplified model is adequate to describe the gross features of the response and hence is a convenient conceptualization of the blood glucose regulatory system in normal and diabetic subjects. However, it also is apparent that more complex models are necessary to represent details such as the exact time of occurrence of the blood glucose nadir and the effect of physical activities on blood glucose levels.

CONCLUSION AND RECOMMENDATIONS

CONCLUSIONS

Diabetes is a slow killer with no known curable treatments. However, its complications can be reduced through proper awareness and timely treatment. Three major complications are related to blindness, kidney damage and heart attack. It is important to keep the blood glucose levels of patients under strict control for avoiding the complications. One of the difficulties with tight control of glucose levels in the blood is that such attempts may lead to hypoglycemia that creates much severe complications than an increased level of blood glucose. Researchers now look for alternative methods for diabetes treatment. The goal of this project is to give a mathematical model for the study and treatment of diabetes. It is my belief that diabetes is one of the highly demanding research topics of the new century and I want to encourage new researchers to take up the challenge.

Suggested Recommendations

To reduce the prevalence rate of diabetes in the Tarkwa Nsuaem Municipality and also avoid the dangerous complications associated with the disease, the following recommendations should be taken into consideration.

- Diabetes prevention must be a public health priority
- More research work should be carried on the sources of water in the municipality as it is believed to be one of the causes of increase in diabetes cases in the municipality
- Improve coordination of community based diabetes prevention and management services, including patient self-management.
- Ensure ready access to guidelines, protocols, decision aids and service directories for diabetes service providers and consumers.
- Ensure ready availability of new technology for diabetes.

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