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Blood Glucose-Insulin Regulation and Management System Using MATLAB/SIMULINK

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***Abstract*-Biomedical signal processing has exponentially been expanding and demanding area for research and subsequent applications in its respective quarters. Exploration on diabetes is one of the main segments of this area which is being addressed for the decades. One of the main functions of the pancreas is to regulate glucose concentration in blood through release of the enzyme insulin. Some theoretical analysis of the control of blood glucose level in diabetic individuals is undertaken using a simple mathematical model of the dynamics of glucose and insulin interaction in the blood system developed by Stolwijk and Hardy dynamic model [1]. This paper is focused to envisage the regulation and management of the concentration of glucose and insulin in the blood of a diabetic. The model was modified by adding a term for exogenous insulin infusion. Using this model, a closed-loop feed back system which regulates and manages the blood glucose-insulin has been designed, implemented and analyzed using Matlab/Simulink. This system imitates as an artificial pancreas on day-to-day basis. A time-consuming and tedious series of diabetes experiments was carried out and results were analyzed on the basis of medical parameters. The obtained results showed significant regulation and management of the glucose-insulin delivery in the blood. Hence, we are reasonably confident of having contribution in the subject area.**

***Keywords*-**Insulin; pancreas; glucose-insulin, closed-loop control; Matlab/Simulation; diabetes, diabetic

1. INTRODUCTION

Diabetes mellitus is a metabolic disorder in which insulin, a kind of hormone which promotes the uptake of glucose into cells, cannot properly perform its role. People with diabetes cannot produce enough insulin that is required to convert sugar, starches and other food into energy needed for daily life. Diabetes Mellitus is so far an incurable disease affecting million of people worldwide. Approximately 177 million people have diabetes, and this number is expected to increase to 300 million by the year 2025 [1].Scientists are focusing on developing a manifold of new techniques and feasible instrumentation to offer wearable solutions and improve the life of patients. The patient is totally dependent on an external source of insulin to be infused at an appropriate rate to maintain blood glucose level. The blood glucose level should be controlled within the range of 60-120mg/dl .

Diabetics are at increased risks for developing chronic complications such as heart attacks, strokes, kidney failure, blindness and amputations. The majority of diabetic population is classified as Type-I or Type-II. The former is insulin dependent which accounts for 5-10% of the diabetic population whereas the latter is a non-insulin dependent diabetes mellitus, which accounts for 90-95% for the diabetic population [1].

For patients with diabetes especially for Type-I, insulin-dependent diabetes, tight control of glucose level is essential. Regulating blood glucose concentration using the insulin infusion device is important for these patients, because they have deficiency of insulin production by pancreas that prevents appropriate metabolism of glucose. Many patients, who take insulin infusion in their diabetes therapy, inject insulin with needles and syringes that deliver insulin just under the skin, so that the functions of the pancreas are replaced by some external devices. An external insulin pump is an electro-medical device that delivers insulin through narrow and flexible plastic tubing that ends with a needle inserted just under the skin near the abdomen. The pump releases doses of insulin at meals and during the periods when blood glucose is too high based on measured values of glucose sensors [1].

A patient's glucose concentration may change dynamically depending mostly on his /her physical activities and nutrition, and therefore, the amount of insulin needed varies from time to time. A number of diseases may occur, possibly resulting in life-threatening health conditions if the supply of insulin is not in time or not correctly dosed or fails for some reasons. For example, sustained hyperglycemia (blood glucose exceeding 120 mg/dL) may lead to most of the long-term complications associated with diabetes, such as nephropathy and retinopathy.

The current medical treatments suggest three to four daily glucose measurements and an equivalent amount of subcutaneous insulin injections. This method is not only inconvenient and painful but also unreliable due to the approximation involved in the amount and type of insulin delivered. Fortunately, a significant amount of research is being carried out to overcome the shortcomings of the current medical practice in which signal processing being dominating field of Electrical Engineering has contributed noticeably.

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Hyperglycemia is common in critically ill patients and is not limited to patients who are known to be diabetic. Several recent studies have established a correlation between tight glucose control and decreased preoperative morbidity and mortality in surgical and critically ill patients. Applying these findings to improve outcomes involves identifying patients at risk for hyperglycemia, monitoring blood glucose frequently, using an effective insulin infusion algorithm to control blood glucose within a narrow range, and adjusting insulin infusion rates in a timely and accurate manner. Adverse effects of hyperglycemia include dehydration, increased susceptibility to infection, and impaired wound healing. In fact, there are some data to suggest that aggressive glycemic management can help combat infection and several studies have showed a strong association between hospital mortality and glycemic levels. Whether the survival benefit is due to glycemic control or to insulin administration is still unresolved. The survival benefit of intensive insulin therapy is likely multifactorial and regardless of the mechanism, optimizing glycemic control with insulin infusions clearly appears to be beneficial [2].

A number of algorithms for controlling glucose levels with insulin infusions are currently in use throughout the world. Most of these protocols specify adjustments in insulin infusion rates based on hourly measurements of blood glucose with rescue administration of glucose for hypoglycemic episodes. The development of insulin injection programs has generally proceeded along two fronts: open-loop method and closed-loop method [3].

A. *Open Loop Method*

Open-loop systems deliver a predetermined amount of insulin to the patient and the amount of insulin is based on the insulin curve of the normal pancreas secretion. Open-loop control block diagram shown in Fig.1.

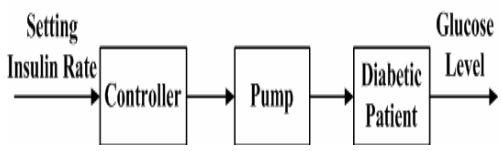

Fig. 1. Open-loop Control for Diabetics

B. *Closed Loop Method*

In the closed-loop control system, a glucose sensor is needed that can measure blood glucose level. This information then would be passed to a control system that would calculate the necessary insulin delivery rate to keep the blood glucose level in a stable range. Then a electro-medical device will deliver the desired amount of insulin. In general, the closed-loop method is more reliable in maintaining the level of blood glucose and also is close to the normal pancreas [4]. Fig.2 shows the block diagram of closed-loop control of diabetes patients.

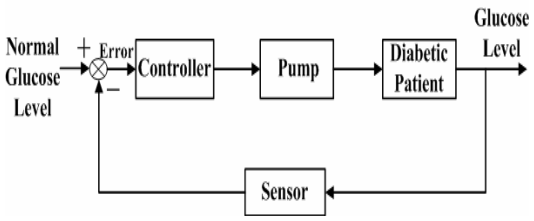

Fig. 2. Closed-loop System for Diabetics

For patients with diabetes especially for Type-1, insulin-dependent diabetes, tight control of glucose level is essential. Regulating blood glucose concentration using the insulin infusion device is important for these patients, because they have deficiency of insulin production by pancreas that prevents appropriate metabolism of glucose. Many patients, who take insulin infusion in their diabetes therapy, inject insulin with needles and syringes that deliver insulin just under the skin, so that the functions of the pancreas are replaced by some external devices. An external insulin pump is an electronic medical Device that delivers insulin through narrow and flexible plastic tubing that ends with a needle inserted just under the skin near the abdomen. The pump releases doses of insulin at meals and during the periods when blood glucose is too high based on measured values of glucose sensors [5].

To-date, the current method of therapy for diabetics is a series of 3~5 daily insulin injections with quantities of insulin based on 4~8 daily invasive glucose measurements. It is said that infusion of insulin is discretely controlled by users based on the feedback of several blood glucose measurements [5]. It is obvious that such treatment is lack of a reliable continuous monitoring, which may make glucose concentration out of permitted range because of control delay. In other words, this kind of therapy cannot restore metabolism to a state of a healthy patient, and wide glucose fluctuations continue to occur on many patients.

Therefore, it is urgent to design a continuous closed-loop control system for insulin infusion. The continuous control would be a great improvement in the daily treatment of diabetes, especially in some cases that medical persons are not presented or the patients have less knowledge about the disease. Such an automatic control will benefit patients and avoid some mistakes during injections and operations [5].

II. GLUCOSE-INSULIN REGULATION MODEL

In order to study the effects of glucose and insulin regulation in body we need a model of a pancreatic function. One of the main functions of the pancreas is to regulate the glucose concentration in the blood through release of the enzyme insulin. In a normal patient, insulin tightly regulates the metabolism of glucose. Diabetes patients suffer from a dysfunction of this process. The glucose-insulin regulation

model used is based on Stolwijk and Hardy's dynamic model [5]. The model was modified by adding a term for exogenous insulin infusion. Hence, the glucose dynamics are governed by following equations [5]. Therefore, our work is based on the research carried out by [1-5].

$$C_G \frac{dG}{dt} = U_G + Q_G - \lambda G - \nu GI, \qquad G \leq \theta \qquad \ldots\ldots(1)$$

$$C_G \frac{dG}{dt} = U_G + Q_G - \lambda G - \nu GI - \mu (G - \theta), \quad G > \theta,$$

$$C_I \frac{dI}{dt} = U_I - \alpha I \qquad G \leq \varphi \qquad \ldots\ldots (2)$$

$$C_I \frac{dI}{dt} = U_I - \alpha I + \beta (G - \varphi) \qquad G > \varphi$$

Where,

G = Instantaneous blood glucose level in mg/dl
I = Instantaneous blood insulin level mU/d
U_G = Exogenous glucose infusion in mg/h
U_I = Exogenous insulin infusion in mU/h
C_G = Glucose capacitance in the extra cellular space
C_I = Insulin capacitance in the extra cellular space
O_G = Glucose inflow into blood in mg/h

Λ = Tissue usage rate of glucose that is independent of I (t)
N = Tissue usage rate of glucose that is dependent on I (t)
A = Insulin destruction rate
B = Insulin production rate by the pancreas
Θ = Threshold for renal discharge of glucose
Φ = Threshold for pancreatic production of insulin
μ = Constant proportionality factor (gain)

Glucose inflow into the blood can be either through absorption from the gastrointestinal tract or through production from the liver. In addition, as seen from the parameter descriptions above, the coefficients have physiological significance, and also differ depending on the condition of the patient. Type-1 Diabetic Mellitus (DM) patients lack the capacity to produce adequate amounts of insulin, The glucose-insulation regulation model, which is described in equations (1) and (2) and comprises an internal feedback loop provided by the pancreas, can be thought of as a two-input and two-output dynamic system as shown in Fig.3

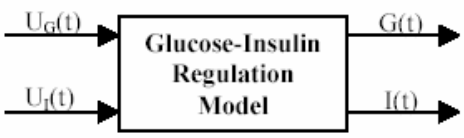

Fig. 3. Two-input Two-output pancreatic model

III. DESIGN PARAMETERS FOR PANCREATIC MODEL

The pancreatic model according to the dynamic equations (1) and (2) can effectively and efficiently be implemented in Matlab/Simulink with the help of parameters mentioned in Table 1. Accordingly, Plasma volume and interstitial fluid volume are represented in a single compartment (3L+12L, in the normal adult) with constant volume). The steady state concentration of glucose in this compartment is x (in mg/mL). Glucose enters through absorption from the Glucose-Insulin tract or through production from the liver at the flow rate of Q (G) t in (mg/h). Glucose leaves the extracellular volume to enter the cells to be metabolized and/or stored. In insulin independent tissue the rate of glucose utilization depends only on the extracellular to intracellular glucose gradient. The intracellular concentration is ignored Glucose uptake in insulin dependent tissue is facilitated by insulin concentration (y). Therefore, the rate of insulin dependent glucose utilization UI (t) is given as

$$UI(t) = \nu y$$

Insulin is produced at a rate dependent on plasma glucose levels. However if x falls below a certain threshold insulin secretion ceases. Insulin is removed from the plasma involving the insulinase enzyme at a rate proportional to its concentration in blood. The steady state concentration for insulin (y) is given as

$$Y = 0 \quad , \quad X = \varphi$$
$$Y = \alpha (X - \varphi) \quad , X > \varphi$$

The steady state level of glucose and insulin in the blood under a given set of conditions can be predicted from solving these equations simultaneously. Further, the following parameter values are used for pancreatic model.

Table 1: Parameters for Pancreatic Model

Parameters	Values
G(t)	2.5 mg/mL
μ	7200 mL/h
λ	2470 mL/h
ν	139000 l/(mUh)
φ	0.51mg/mL
β	1430mUmL/(mgh)
α	7600mL/h
Q_G (t)	8400mg/h

Based on the parameters shown in Table 1, glucose-insulin or pancreatic model, Figure 4, is designed; implemented and analyzed using Matlab/Simulink Release 14. The model exhibits the pancreatic functionality by adopting the closed-loop feedback system approach.

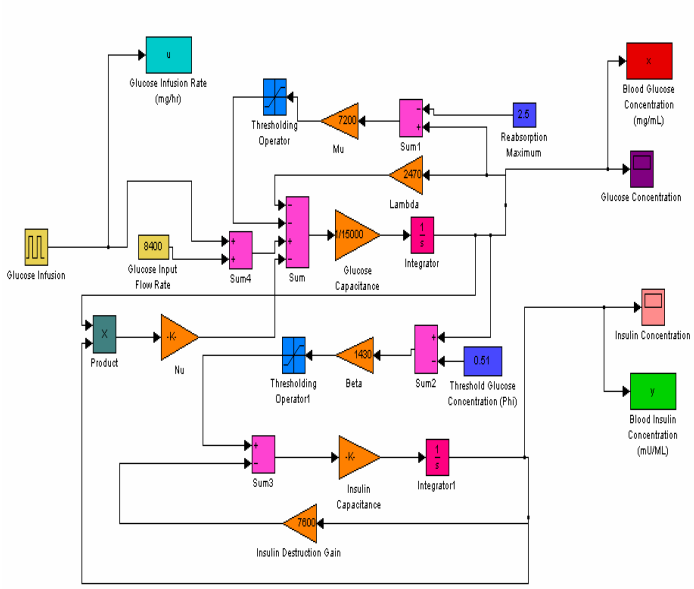

Fig. 4. Simulink Model of glucose-insulin regulation control system

IV. RESULTS AND DISCUSSION

Matlab/Simulink is used to simulate the pancreatic model by using the parameters stated in Table 1. Each block has been implemented with meticulous approach and various signals are employed for the purpose of glucose-insulin representation. Subsequent to the successful implementation of the model, Fig. 4, an exhaustive series of experiments was carried out for the insulin versus glucose level.

Fig. 5 demonstrates the blood glucose concentration in mg/dl against time interval which is taken into minutes to match the practical approach of the diabetic. The graph clearly shows the abrupt rise of glucose level and then coming to steady state after certain period of time. On the contrary, Fig. 6 demonstrates the infusion of level of insulin in mU/ML against time interval. It is to be pointed out that, the release of level of insulin is according to the level of glucose level thereby regulating and managing the amount of insulin to be required by a diabetic on different time intervals. Further, the precision and accuracy of the regulation and management is overwhelmingly dependent on the parameters described in Table 1. Therefore, to achieve the results demonstrated over here, truly, needed well concentrated and specific selection of Simulink blocks and various signals for the faithful and successful achievement of the proposed model

In this closed-loop system, the demonstrated results have taken into account the different modes of glucose level like fasting or random because it really plays a very important role in the management of insulin for diabetic.

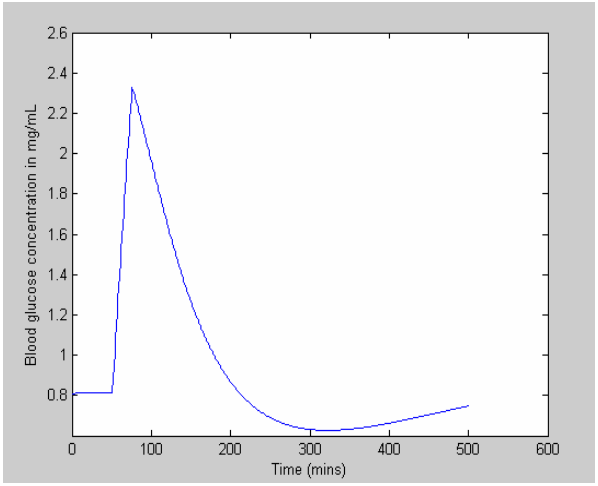

Fig. 5. Blood Glucose Concentration (X)

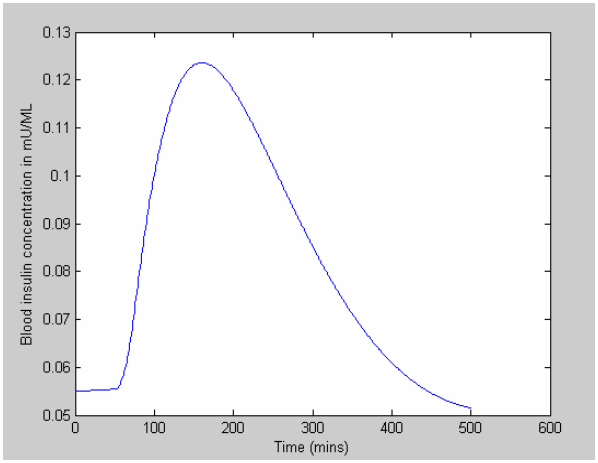

Fig. 6. Blood Insulin concentration

From the above simulated model we see how a natural pancreas model can be imitated as an artificial pancreatic model by using Simulink. As the blood-glucose becomes unstable the pancreas secretes insulin to regulate and control the blood glucose to its stable and controllable point. We observe that, as the blood-glucose concentration 'x' approaches to its peak value the pancreas secretes insulin accordingly and when blood-glucose level is at its peak the insulin concentration secreted by pancreas is also at its peak level which shows a proportional relation between glucose and insulin in the body. As soon as the blood-glucose level

approaches to stability or controllable state the pancreas secretion becomes slow till it comes to stable state in the body.

V. CONCLUSION

A closed-loop pancreatic model for the regulation and management of glucose-insulin has been designed, implemented and analyzed by using dynamic equation parameters for the diabetics. The model is simulated with the help of Matlab/Simulink and performed variety of experiments over the period of last one year. The analysis based on the results obtained on the proposed model show significant regulation and management of the glucose-insulin by exhibiting notable proportion of parameters. Though various aspects of the diabetic are catered for in the implementation and subsequent exercise of results, nevertheless, we understand that it is so demanding and absorbing area for research that the work could substantially be carried forward in following directions as a future work:

1. Improvement of the mathematical model of insulin-curve
2. Enhancement of efficiency and reliability of sensor in closed-loop system
3. Biological compatibility of sensor, electro-medical device and diabetic
4. Finally, the model needs to be transformed on efficient and high speed hardware.

VI. ACKNOWLEDGEMENT

We sincerely acknowledge the research of authors [1-5], who undoubtedly served the human being by carrying out their research in this area and, as a result, we also attempted to take this piece of work from their contribution.

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