An Algorithm of Regulation of Glucose-Insulin Concentration in the Blood

B. Selma, S. Chouraqui

Abstract—The pancreas is an elongated organ that extends across the abdomen, below the stomach. In addition, it secretes certain enzymes that aid in food digestion. The pancreas also manufactures hormones responsible for regulating blood glucose levels. In the present paper, we propose a mathematical model to study the homeostasis of glucose and insulin in healthy human, and a simulation of this model, which depicts the physiological events after a meal, will be represented in ordinary humans. The aim of this paper is to design an algorithm which regulates the level of glucose in the blood. The algorithm applied the concept of expert system for performing an algorithm control in the form of an "active" used to prescribe the rate of insulin infusion. By decomposing the system into subsystems, we have developed parametric models of each subsystem by using a forcing function strategy. The results showed a performance of the control system.

Keywords—Modeling, algorithm, regulation, glucose-insulin, blood, control system.

I. INTRODUCTION

THE glucose–insulin system offers one of the clearest and simplest methods of homeostatic control. The level of glucose in blood needs to be kept. It represents the principal metabolic substrate, and most tissues and organs, such as the brain, need glucose constantly, as an important source of energy. The low glucose concentrations give rise to diabetic malady.

In diabetic patients, hyperglycemia is characterized by high level of glucose. This malfunction is caused by: Pancreas that produces an inadequate dose of insulin; Liver and muscles do not respond well to face this insulin.

To design an appropriate control, an adequate model is necessary. In the last decades, several models appeared for type 1 diabetic patient [1]. The minimal model of Bergman [2] is the most commonly used for type 1 diabetics patients under intensive care. Three-state minimal model is extended from this model [3]. However, the simplicity of the model proved its disadvantage since, in its formulation, a lot of components of the glucose-insulin interaction were neglected.

Besides the Bergman model, other models appeared in the literature [4], [5], which were more general but more complicated. Sorensen-model is the most complex one proved to be the 19th order [4], which is based on the earlier model

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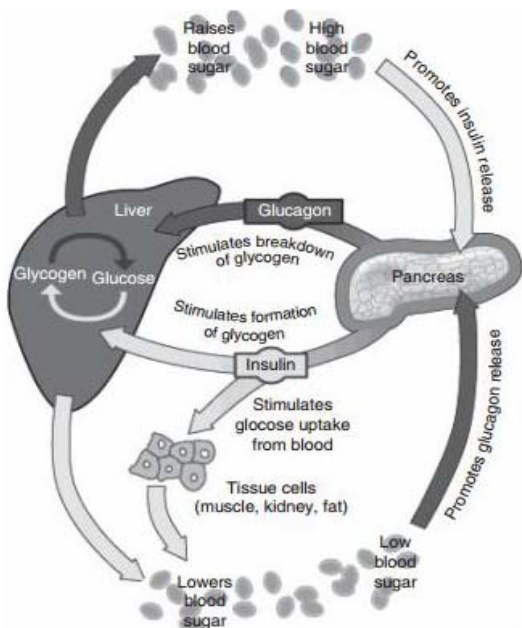
[5]. Even if the Sorensen-model describes the human blood glucose dynamics in a very exact way, it is rarely used in research problems due to its complexity.

For confronting many features of pathophysiology of diabetes, many simulation models have been proposed based on mathematical models [1]-[6]. Nonetheless, in these previous years, a novel knowledge has been acquired on glucose metabolism and its control by insulin amid a meal at the organ, tissue, and entire body level. This has been generally made possible by making use of multiple experiments and use of new technologies like NMR and PET [7], [8].

We model the glucose-insulin system by resorting to a subsystem forcing function strategy based on mathematical differential equations [9], which consider various interactions in the glucose–insulin regulatory system and reduce basic vulnerabilities in modeling the different unit processes. We develop a normal model for the ordinary subject.

In this paper, we develop a simulation model of the glucose-insulin regulation system in the ordinary human for describing the physiological events which occur during a standard mixed meal based on a mathematical model defined below, which studies the organism of human. This model is different from that of our preceding simulation models [10]-[12], which were mostly developed for describing a variety of intravenous glucose perturbations.

II. GLUCOSE AND INSULIN SUBSYSTEMS

Glucose in the blood should be maintained in a very narrow range. Blood glucose levels are checked by the cells in the pancreas. In the event that the blood glucose level drops significantly, the pancreas produces glucagon. This hormone signals the liver and muscle cells to change the stored glycogen back into glucose. So, other cells can use it for energy.

When the levels of blood sugar rise, whether as a result of glycogen conversion, or from digestion of a meal, this increase in blood glucose signals the pancreas to produce insulin.

The insulin tells cells to take in glucose from the bloodstream. As the glucose moves into the cells, the blood glucose levels go down. Some cells use the glucose as energy. Other cells, such as in liver and muscles, store any excess glucose as a substance called glycogen. The body uses glycogen for fuel between meals.

Fig. 1 [13] shows how the insulin and glucagon regulate the concentration of glucose in the blood.

Fig. 1 Glucose regulation from a biological perspective, Courtesy of Campbell and Reese's Biology [13]

The homeostasis in a normal system is achieved by maintaining a blood glucose level of about 90 mg/100mL. This equilibrium is disturbed by a stimulus such as eating or skipping a meal. When we eat foods, the blood glucose level rises because sugar and carbohydrates are absorbed in the blood by the digestive system. As a result, blood glucose surpasses the set purpose of 90 mg/100 mL, also the β-cells of the pancreas release insulin in the blood. Insulin signals to the liver and body cells to take up glucose and to store it as glycogen. The blood glucose level decreases to the set point and the stimulus for insulin release diminishes as we return to homeostasis. After skipping a meal or poor nutrition, the blood glucose level drops because most of the glucose has been used from the past meal. As a result, blood glucose drops below the set point and the α-cells of the pancreas secrete glucagon in to the blood. Glucagon instructs the liver to convert glycogen to glucose. The blood glucose level rises to the set point and the stimulus for glucagon release diminishes, and we return, yet again, to homeostasis. This negative feedback loop of insulin-glucagon allows for precise regulation of the blood glucose.

III. Glucose Regulatory System Model

There are several models of regulating the level of glucose in the blood as in [14], [15]. Note that there are several tests to check if a person has diabetes type I, II or is not diabetic by comparing the glucose rate with that predicted by a complex model. Complete models, however exceptionally precise for regimen assessment, are in general inappropriate for real-time control, requiring anytime points of input to produce the insulin infusion profile. Also, they are not universal necessitating patient-specific data and identified glucose inputs. The object of this research is to create control schemes in the light of models that capture the fundamental dynamic system that do not require inaccessible data and are pertinent to a more extensive assortment of subjects. Basic models capture these important dynamic activities, giving a more appropriate establishment for real-time control design and analysis.
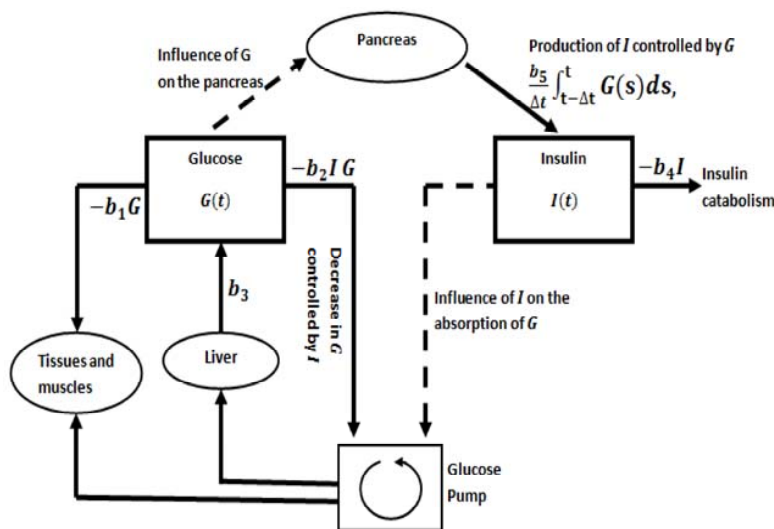

Fig. 2 Model of regulating glucose-insulin [9]

A. Mathematical Model

A model of regulating glucose-insulin [9] assumes that glucose controls the rate of insulin production in the pancreas, and insulin controls the absorption rate of the glucose by the liver and muscles. This model is illustrated in Fig. 2. The model scheme shown in Fig. 2 is associated with the following system of differential equations.

The notations are identical and the b_1 to b_5 coefficients are constants.

The equation for the rate of glucose is:

$$\frac{dG}{dt} = -b_1 G - b_2 IG + b_3 \qquad (1)$$

$b_1 G$: Loss of glucose to the tissues, $b_2 IG$: Loss of glucose by insulin, b_3 : Constant contribution of glucose from the liver.

The equation for the rate of insulin:

$$\frac{dI}{dt} = -b_4 + \frac{b_5}{\Delta t} \int_{t-\Delta t}^{t} G(s)ds \qquad (2)$$

b_4 : Insulin catabolism (i.e. absorption), $\dfrac{b_5}{\Delta t} \displaystyle\int_{t-\Delta t}^{t} G(s)ds$: Insulin

production depending on the average value of glucose

$$\begin{cases} G(t) \equiv G_b & \forall t \in [-\Delta t, 0] \\ I(0) = I_b \end{cases} \qquad (3)$$

TABLE I
THE MODEL PROPERTIES

Known properties	Unknown properties
I_b, G_b: concentration of insulin and glucose at rest. b_1, b_2, …, b_5: constants. Δt: constant	G(t): glucose concentration in the blood. I(t): insulin concentration in the blood.

B. Algorithm Model

The algorithm model is then written:

Entry: the coefficients b_1, b_2, b_3, b_4, b_5 are constants;
System with Ib, Gb: concentration of insulin and glucose at rest and Δt: constant.
Test (G, G_b)
If** G < G_b **then
G causes
Glucose production by the liver
$G = G + b_3$
Loss of glucose by tissues
$G = G - b_1 G$
*--- **Total Equation** ---*
$$\frac{dG}{dt} = -b_1 G - b_2 IG + b_3$$
Otherwise
Insulin production by the pancreas
$$\frac{dI}{dt} = -b_4 + \frac{b_5}{\Delta t} \int_{t-\Delta t}^{t} G(s)ds$$
Absorption of insulin
$I = I - b_4 I$
Causes insulin pump glucose
Pump G glucose stores in the liver
$G = G - b_2 IG$
--- Total Equation---

$$\frac{dI}{dt} = -b_4 I + \frac{b_5}{\Delta t} \int_{t-\Delta t}^{t} G(s)ds$$

End if
End Tests
***Output:** A defined system by the obtained glucose.*

C. Model Prediction

There are models that allow us to determine the presence or absence of diabetes and their types. However, the resolution of this system does not allow better modeling that can be observed in patients. This slightly complex model leads to a model closer to reality. In this model, we have: A simulation is used as an example to illustrate the model. To evaluate the efficiency of the proposed model depends on virtually model-independent measurements of the various glucose and insulin fluxes happening during a meal [7], [16]. A time-delay model is used to describe the glucose–insulin regulatory system [17]. We will study a check-up of regulation glucose for 200 minutes. In a healthy person, before a meal, blood glucose is between 0.70 g/L and 0.90 g/L. During meals, food is digested and the glucose passes in the blood. The pancreas receives an increase in blood sugar and produces insulin that is discharged into the blood. This insulin participates very actively in glucose storage in the liver and muscles as glycogen. So, this glycogen constitutes a reserve.
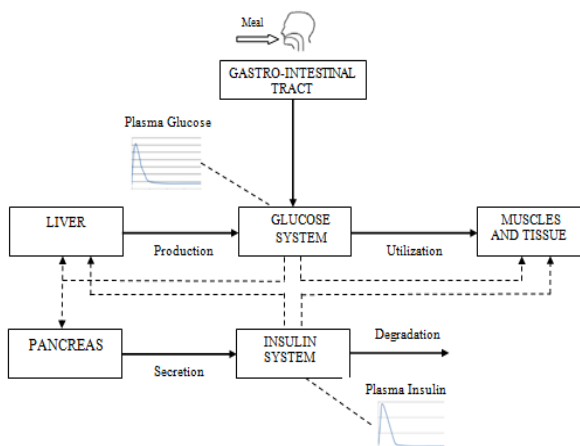

Fig. 3 Scheme of the glucose–insulin control system

After the meal, the glucose remains below 1.5 g /L. Low insulin manufacturing persists to allow the entry of glucose in all cells of the body. Therefore, these consume glucose which is in the blood. That glucose does not descend below 0.70 g/L. During this intermediate time between meals, muscle ensures that its energy needs by consuming its own glycogen.
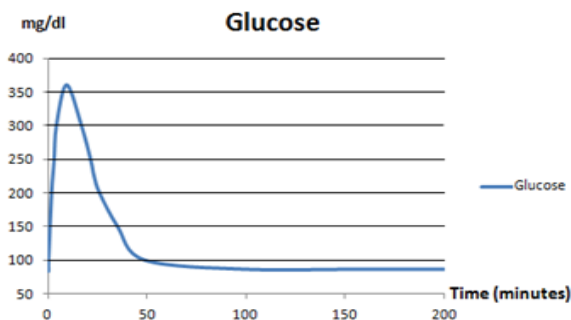
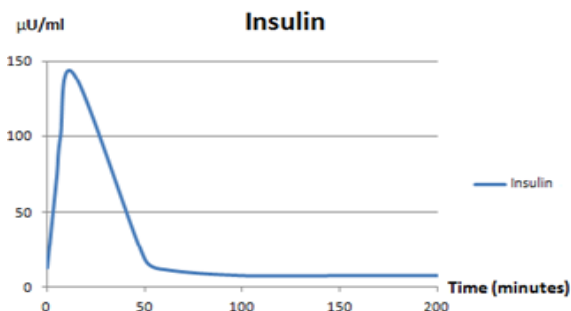Fig. 4 Regulating the glucose update rate by insulin control

Fig. 5 Regulating the insulin production rate by the presence of glucose

IV. DISCUSSION AND CONCLUSION

A new model of the glucose-insulin regulatory system has been presented. Basing on quantitating physiological events after a meal is of obvious importance because this operation is used in everyday life. The post-prandial state has also been intensively investigated recently, which allows taking advantage of all new quantitative knowledge that has become available.

The model is based on a mathematical model which is an approximation to the real one, describing the different processes that have been identified using a forcing function strategy. This is the principal novelty of the proposed model, which depends on virtually model-independent measurements of the various glucose and insulin fluxes happening during a meal [7], [16]. The glucose-insulin system is, absolutely, extremely intricate and the sole accessibility of plasma glucose and insulin concentrations does not enable us to fabricate a dependable simulation model which requires a system of differential equations of first order to solve this operation, because a good description of plasma glucose and insulin concentrations can be obtained with various descriptions of the underlying fluxes in the system, similar meal glucose rate of appearance, hepatic glucose production, and glucose utilization, with structural errors in some unit process models repaying those in others. Alternately, the accessibility of glucose and insulin fluxes permits us, by utilizing a forcing function strategy, to improve particular dependable parametric models of every unit process.

From a dynamical perspective, the pancreas and tissues frame an incorporated system with feedback regulations to be attractive to have a model specifically defining the entire system. This could be fitted in a one pass to both glucose and insulin data, instead of part the model into two subsystems and fitting independently everyone. In fact, for a model fitting simultaneously the two arms of the control mechanism, the error variance would be a more appropriate expression of the effective applicability of the assumptions underlying both subsystems to the experimental situation. We perceive the coherent fitting of the whole dynamical model to the whole set of perceptions. By devising the two subsystems, we may evaluate the coefficients for one segment, by optimally fitting the corresponding data, which are not the ones which would produce an ideal guess to the entire set data if the collaboration between the two subsystems was permitted. The last outcome is that, by devising the system, we get an impression of accomplishment in light of the fact that our model pretended to be known without error; however, we are in fact precluding an inward coherency check. So, we may affirm that the (global) system works in some way (i.e. with a few parameters) which may be distinct from the best estimate to the real one. It might certainly occur (like in finding a value for b_5 lesser than the value for G_b) that the system cannot work at all with the assessed parameter values.

Examination results in reassuring observations: the model is very close to reality. There are models which determine quickly if the person is diabetic or not and what type without accurate data.

According to the input data and the obtained control results, the model developed is very close to reality. It is therefore a good model for regulating glucose in the blood.

In conclusion, we have proposed a physiologically model of the glucose-insulin concentration system during meals. The modeling approach is novel and has taken advantage of a unique meal data in normal human in which relevant glucose and insulin fluxes during a meal were available.

The set model in this article is slightly complex in its formulation as it indicates the presence of an integral in one or two expressions of the system. This suggests that the presence of glucose regulates the rate of insulin production which controls the rate of glucose uptake. Although experimentally the phenomenon is not as described, the proposed model is simple and seems to be closer to reality. We note that in the model that was used in this example is the system of differential equations of first order. In addition, there are other models such as the model made by Sorenson [4] which has nearly 19 equations to solve. Although it is accurate, it is too long in its resolution. A physical process can be modeled in more than one manner. The important thing is to identify clearly the assumptions and the use of the model that reproduces the most important processes while neglecting those which are the least. In engineering, as in all sciences, there is no mathematical model that can explain everything. The quality of any model is based on assumptions and its judicious application.

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