Mathematical Model of Glucose-Insulin Metabolism in Type 1 Diabetes Including Digestion and Absorption of Carbohydrates

Claudia Cecilia Yamamoto Noguchi *, Eiko Furutani * , and Shoichiro Sumi **

Abstract: The authors propose a mathematical model of glucose-insulin metabolism in type 1 diabetes based on Bergman and Shimoda insulin models, which are adjusted to represent diabetic state and improve the accuracy of subcutaneous insulin absorption, respectively. The authors also propose a model of digestion and absorption from carbohydrates based on the glycemic index (GI) of foods and carbohydrate bioavailability concepts that provide a glucose-equivalent representation of the impact of carbohydrates on blood glucose levels. Comparison with clinical data demonstrates that the proposed model is able to represent postprandial blood glucose excursion for carbohydrates with varying GI values.

Key Words: glucose-insulin metabolism, mathematical model, type 1 diabetes, glycemic index, carbohydrate bioavailability.

1. Introduction

In the human body, blood glucose levels are directly affected by food. In particular, carbohydrate is the only macronutrient that is converted directly into glucose in the bloodstream and absorption in the stomach and small intestine, from which glucose is finally absorbed into the bloodstream for its uptake and utilization. Glucose uptake requires a precise amount of insulin—a hormone produced by pancreatic β-cells—which is secreted according to glucose appearance such that homeostasis is constantly maintained throughout the day, regardless of the carbohydrate amount taken during meals. Impairment of glucose homeostasis results in blood glucose levels constantly over normoglycemia, which is diagnosed as diabetes mellitus and classified into several types depending on the pathogenesis. Specifically, type 1 diabetes (T1D) is caused by the immune system mistakenly triggering β-cell apoptosis. The resulting cessation of endogenous insulin secretion leads to hyperglycemia and eventual life-threatening conditions in the medium and long term. To prevent such outcome, T1D patients undergo a life-long intensive insulin therapy that consists of invasive blood glucose measurements, carbohydrate counting and insulin dose calculation previous to every meal or snack intake on a daily basis.

Both the physical and emotional burden of diabetes treatment, and the consequent negative impact on the quality of life of T1D patients have encouraged research on closed-loop blood glucose control systems for decades [1],[2]. Among the different types of control algorithms utilized for blood glucose control purposes, model predictive control is arguably the most promising due to its ability to deal with long delays and system constraints, and thus model error—or lack thereof—is a determinant factor for the performance of the control strategy. Several mathematical models of glucose-insulin kinetics have been developed to date [3]–[6], with varying levels of detail and complexity. Nevertheless, current closed-loop blood glucose control systems have a performance below satisfactory, particularly during postprandial state where blood glucose levels achieved during experiments in T1D patients [7] are no different from current open-loop (traditional insulin injection previous to each meal) treatment. Even though some studies offer interesting approaches such as glucose estimation [8] and insulin optimization methods [9] for postprandial state, we acknowledge that an adequate mathematical representation of carbohydrate intake, i.e., the disturbance input of the control system, has been particularly overlooked.

In the present study, the authors propose a mathematical model of glucose-insulin metabolism in T1D that includes the impact of carbohydrates on blood glucose levels. The proposed model is based on Bergman minimal model [10], which is originally a model of glucose-insulin metabolism in nondiabetics that is extended to T1D state, and Shimoda insulin kinetic model [11] wherein the authors consider a readjustment of parameters for a more accurate representation of subcutaneous insulin infusion. The authors also propose a model of carbohydrate absorption and gastric emptying that represents the effect of carbohydrates on blood glucose levels, whose parameters are based on the glycemic index (GI) of foods [12], an increasingly popular concept that estimates carbohydrate absorption in vivo as a single value; and carbohydrate bioavailability [13], which quantifies glucose release from carbohydrates in vitro and provides a more detailed classification based on their biochemical properties. Although these two approaches have been developed and perfected independently from one another, the proposed model unifies them for the sake of thoroughness in the representation of carbohydrate digestion and absorption. Additionally, we consider a first-order delay to represent delayed gastric emptying specifically in T1D patients, which occurs in over half of these patients [14]. Considering the above, the validity of the proposed model is demonstrated by direct comparison with pertinent clinical data as presented in this study.
The authors first give a general description in section 2, and thence describe carbohydrate digestion and absorption, subcutaneous insulin and glucose-insulin metabolism subsystems of the proposed model in sections 3, 4 and 5, respectively. In section 6 we present simulation results, from which we derive some discussion and conclusion in sections 7 and 8.

2. Model Overview

The mathematical model in the present study is divided into three main subsystems (see Fig. 1). For an input $G_{\text{food}}(t)$, the carbohydrate metabolism subsystem gives a mathematical representation of the impact of carbohydrates on blood glucose levels. Different from previous models that consider only amount, the authors propose a model that includes both carbohydrate amount and absorption parameters to quantify the impact of carbohydrates on blood glucose levels expressed by $G_{\text{ext}}(t)$. The subcutaneous insulin subsystem represents insulin kinetics from subcutaneous insulin administration $u_\text{s}(t)$ to plasma insulin concentration $I(t)$. Although it is based on Shimoda insulin model [11], in this study we readjust parameters to obtain a more accurate model of subcutaneous insulin kinetics. From these two subsystems, i.e., the external glucose-equivalent from carbohydrates and plasma insulin from subcutaneous insulin administration, serve as inputs to the glucose-insulin metabolism subsystem, which is based on Bergman minimal model [10]. Since this model originally describes glucose and endogenous insulin metabolism in nondiabetics, we modify some parameters to obtain a model of T1D state with plasma glucose concentration $G(t)$ as the output of the model. In the following sections we provide further detail of each subsystem.

3. Carbohydrate Metabolism

Carbohydrate metabolism subsystem represents digestion and absorption of carbohydrates in the stomach and small intestines. As shown in Fig. 2, input $G_{\text{food}}(t)$ indicates food intake at instant $t$. For a given amount and food-specific GI and carbohydrate bioavailability input parameters, the glucose-equivalent amount is calculated with a glucose relative (GR) function and further divided into it rapidly (RAG) and slowly (SAG) available glucose for a total glucose-equivalent GlcEQ($t$), where GlcRAG($t$) and GlcSAG($t$) are the proportion of rapidly and slowly available glucose, respectively, and their sum is the total glucose-equivalent GlcEQ($t$). Lastly, a first-order delay is added to represent gastric emptying delay in T1D patients. In this way, the output $G_{\text{ext}}(t)$ of this subsystem is a glucose-equivalent of the carbohydrate-rich food ingested, which basically represents an equivalent glucose infusion that results in the same impact on blood glucose as the carbohydrate-rich food ingested.

Each part of the carbohydrate metabolism subsystem is detailed in the remaining of this section.
3.3 Model of RAG and SAG Absorption

In the proposed model, \( G_{RAG}(t) \) and \( G_{SAG}(t) \) represent RAG and SAG absorption as defined by the Englyst method. Their absorption dynamics are represented by critically-damped second-order delay systems (blocks RAG and SAG in Fig. 2) of the form

\[
\frac{dx_R(t)}{dt} = \begin{bmatrix} 0 & 1 \\ -\frac{1}{T_{RAG}^2} & -\frac{2}{T_{RAG}} \end{bmatrix} x_R(t) + \begin{bmatrix} 0 \\ \frac{K_{RAG}}{T_{RAG}^2} \end{bmatrix} \text{Glc}_{RAG}(t),
\]

\( G_{RAG}(t) = \begin{bmatrix} 1 & 0 \end{bmatrix} x_R(t) \) (5)

\[
\frac{dx_S(t)}{dt} = \begin{bmatrix} 0 & 1 \\ -\frac{1}{T_{SAG}^2} & -\frac{2}{T_{SAG}} \end{bmatrix} x_S(t) + \begin{bmatrix} 0 \\ \frac{K_{SAG}}{T_{SAG}^2} \end{bmatrix} \text{Glc}_{SAG}(t) + \tau_{SAG}.
\]

\( G_{SAG}(t) = \begin{bmatrix} 1 & 0 \end{bmatrix} x_S(t) \) (6)

with variables \( x_R(t) = [x_{RAG}(t) \ x_{RAG2}(t)]^T \) and \( x_S(t) = [x_{SAG}(t) \ x_{SAG2}(t)]^T \) for RAG and SAG respectively, gain \( K \) and time-constant \( T \) parameters have both subscripts RAG and SAG for clarity which, together with a constant delay \( \tau_{SAG} \) considered in \( G_{SAG}(t) \), are detailed in turn in the remaining of this subsection.

To represent RAG absorption, design specifications include (i) complete glucose absorption for an impulse food input between 0–20 min and (ii) area-under-the-curve of \( G_{RAG}(t) \) be equal to that of \( \text{Glc}_{RAG}(t) \) regardless of the amount and GI of the food ingested.

Regarding (i), we assume a small error margin such that 95% of RAG is absorbed within 20 min according to its definition, and thus we obtain \( T_{RAG} = 4.22 \text{ min} \). To satisfy (ii), we integrate \( G_{RAG}(t) \) and equal it to RAG amount, from which gain parameter \( K_{RAG} = \int \text{Glc}_{RAG}(t) dt \).

Likewise, design specifications for \( G_{SAG}(t) \) are (i) glucose absorption between 20–120 min and (ii) area-under-the-curve for \( G_{SAG}(t) \) be equal to that of \( \text{Glc}_{SAG} \). For simplicity in the calculations, we first consider the time span between 0–100 min to which we add a 20-min time delay to comply with the definition of SAG. Thus, for a 95% absorption between 0–100 min we obtain \( T_{SAG} = 21.1 \text{ min} \), and similarly obtain \( K_{SAG} = \int \text{Glc}_{SAG}(t) dt \). Having found SAG parameters, we add the aforementioned delay \( \tau_{SAG} = 20 \text{ min} \) to represent \( G_{SAG}(t) \) appropriately.

3.4 Gastric Emptying Delay in TID

Typical postprandial hyperglycemia in TID patients is usually accompanied with a delay in gastric emptying [17],[18], which extends to chronic gastroparesis in critical cases. We thus consider a first-order delay function as

\[
\frac{dG_{ext}(t)}{dt} = \frac{1}{\tau_{deg}} \left( G_{SAG}(t) - G_{ext}(t) \right),
\]

(7)

where \( G_{ext}(t) \) is the output of the carbohydrate metabolism sub-system, glucose-equivalent \( G_{SAG}(t) = G_{RAG}(t) + G_{SAG}(t) \) and \( \tau_{deg} \) is the food-specific time delay of carbohydrate digestion in T1D patients, whose food-specific values for the representative staple foods in this study are given in Table 1.

By definition, gastric emptying delay refers to the additional time required to pass from the stomach to the duodenum. Considering that glucose release occurs not only in the stomach but also in the small intestine, it might be as well included in the proposed model (Fig. 2) before or after RAG and SAG. Either case, a first-order delay does not alter the output of the sub-system and thus we include it at the end to maintain the clarity in the definition of RAG and SAG according to the Englyst method.

3.5 State-Space Representation

The carbohydrate metabolism subsystem is represented in state-space form as

\[
\dot{x}(t) = Ax(t) + Bu(t),
\]

\[
y(t) = Cx(t),
\]

(8)

where

\[
A = \begin{bmatrix} 0 & 1 & 0 & 0 & 0 \\ -T_{RAG}^{-2} & -2T_{RAG}^{-1} & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & -T_{SAG}^{-2} & -2T_{SAG}^{-1} & 0 \\ 1/\tau_{deg} & 0 & 1/\tau_{deg} & 0 & -1/\tau_{deg} \end{bmatrix},
\]

\[
B = \begin{bmatrix} 0 & 0 \\ K_{RAG}/T_{RAG}^2 & 0 \\ 0 & 0 \\ 0 & K_{SAG}/T_{SAG}^2 \\ 0 & 0 \end{bmatrix},
\]

\[
C = [0 \ 0 \ 0 \ 0 \ 1],
\]

with state and input variables

\[
x(t) = [x_{R}^T(t) \ x_{S}^T(t)]^T,
\]

\[
u(t) = \begin{bmatrix} \text{Glc}_{RAG}(t) \\ \text{Glc}_{SAG}(t) \end{bmatrix},
\]

(9)

where \( \tau_{SAG} = 20 \text{ min} \) is the delay of \( G_{SAG}(t) \) by design and \( \gamma(t) = G_{ext}(t) \) is the output of the carbohydrate metabolism sub-system.

4. Subcutaneous Insulin Absorption

The subcutaneous insulin absorption sub-system represents rapid-acting insulin kinetics from the subcutaneous depot to plasma insulin concentration. The proposed model is represented by Shimoda insulin model, which comprises the following three compartments
\[ \frac{dx_1(t)}{dt} = -k_{21} x_1(t) + u_x(t), \]  
\[ \frac{dx_2(t)}{dt} = k_{21} x_1(t) - (k_d + k_a) x_2(t), \]  
\[ \frac{dI(t)}{dt} = \frac{k_d}{V_d} x_2(t) - k_a I(t) + u_x(t), \]

where \( x_1(t) \) and \( x_2(t) \) are insulin mass at the subcutaneous depot and subcutaneous compartment proximal to plasma respectively, \( I(t) \) is plasma insulin concentration, \( V_d \) is plasma distribution volume, \( k_{21} \) is insulin diffusion parameter, \( k_d \) is insulin transition rate, \( k_a \) is degradation rate constant in subcutaneous tissue, \( k_e \) is degradation rate constant in plasma, and \( u_x(t) \) is subcutaneous insulin administration (bolus or continuous infusion). We provisionally include an intravenous insulin input \( u_x(t) \) in Eq. (12) for parameter identification purposes.

4.1 Considerations for Parameter Identification of the Proposed Model

Due to the crucial role of insulin as the actuator and the importance of its rigorous modeling for model-based blood glucose control systems, we strive for the most realistic representation of subcutaneous insulin administration of rapid-acting insulin. The validated parameters originally proposed by Shimoda et al. do not have an accurate representation of insulin kinetics when contrasted with clinical data. For the readjustment of model parameters, we include an alternative input \( u_x(t) \) in the plasma insulin compartment \( I \) of Shimoda model to represent intravenous insulin infusion. Besides Shimoda insulin model, the remote-insulin compartment \( X \) of Bergman minimal model—yet to be introduced in section 5—is also considered because of its representation of insulin pharmacodynamics. In this way, we reconsider the original parameters of the four compartments related to insulin absorption as detailed in the following subsection.

4.2 Parameter Identification

We rely on insulin time-action profile for parameter identification purposes, which provides a time-course of the glucose lowering effect of insulin. It essentially consists of a subcutaneous insulin dose administered at \( t = 0 \) and followed by a continuous glucose infusion rate (GIR) adjusted such that normoglycemia is maintained as long as the effect of insulin is active, similarly to the well-known euglycemic glucose clamp technique [19]. The resulting glucose-equivalent profile of the hypoglycemic effect of insulin reflects insulin pharmacodynamics, which is directly compared with compartment \( X \) in the proposed model. Therefore, we summarize the steps to validate the parameters of each compartment by relying on clinical data of GIR and insulin pharmacokinetics as follows.

1. Parameters of intravenous insulin effect: We set the parameters of compartments \( I \) and \( X \) to fit intravenous GIR data [20] for a standardized insulin dose at \( t = 0 \) in the intravenous input \( u_x(t) \). Figure 3 shows the comparison between intravenous insulin pharmacodynamics in the proposed model (—) and original parameters from Bergman model and Shimoda insulin model (- - -) for the aforementioned clinical data.

2. Parameters of subcutaneous insulin pharmacokinetics:

Having set parameters of compartment \( I \) and \( X \), we adjust subcutaneous insulin absorption parameters in compartments \( x_1 \) and \( x_2 \) to fit subcutaneous insulin pharmacokinetic from clinical data [21] from a standardized subcutaneous insulin bolus at \( t = 0 \) in the subcutaneous input \( u_x(t) \).

3. Verification: We authenticate the parameters previously determined by comparing the total subcutaneous insulin effect from compartments \( x_1 \) to \( X \) with the respective GIR data [22] for a standardized subcutaneous insulin bolus at \( t = 0 \) in the subcutaneous input \( u_x(t) \). Figure 4 shows that the proposed model in fact has an accurate representation of insulin (—) compared to the original parameters of Shimoda insulin model (- - -).

The parameters of the subcutaneous insulin subsystem obtained by the above procedure are presented in Table 2.

### Table 2 Proposed parameters of compartments \( X \) from Bergman model and Shimoda insulin model.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Bergman model</th>
<th>Shimoda model</th>
</tr>
</thead>
<tbody>
<tr>
<td>( p_2 )</td>
<td>( 8 \times 10^{-2} ) min(^{-1})</td>
<td>( 10 \times 10^{-6} ) L min(^{-1})</td>
</tr>
<tr>
<td>( k_{21} )</td>
<td>( 4.5 \times 10^{-2} ) min(^{-1})</td>
<td>( 2.0 \times 10^{-2} ) min(^{-1})</td>
</tr>
<tr>
<td>( k_c )</td>
<td>( 2.0 \times 10^{-2} ) min(^{-1})</td>
<td>( 2.1 \times 10^{-3} ) min(^{-1})</td>
</tr>
<tr>
<td>( V_d )</td>
<td>( 4.5 \times 10^{-2} ) L</td>
<td>( 4.5 \times 10^{-2} ) L</td>
</tr>
</tbody>
</table>

5. Glucose-Insulin Metabolism in T1D

Glucose-insulin metabolism subsystem in the proposed model is based on glucose \( G \) and remote-insulin \( X \) compartments of Bergman minimal model as
\[ \frac{dG(t)}{dt} = -X(t)G(t) + p_1[G_0 - G(t)] + \frac{G_{ext}(t)}{V_1}, \quad (13) \]
\[ \frac{dX(t)}{dt} = -p_2X(t) + p_1I(t), \quad (14) \]

where \( G(t) \) is blood glucose concentration, \( V_1 \) is volume distribution space, \( p_1 \) is glucose mass action rate constant, \( G_0 \) is basal blood glucose level, \( X(t) \) is remote-insulin concentration proportional to glucose uptake rate, \( p_2 \) is rate of spontaneous decrease of tissue glucose uptake ability and \( p_1 \) is rate of insulin-dependent tissue glucose uptake ability. In particular, \( X(t) \) represents time of insulin binding, transport and glucose oxidation previous to its hypoglycemic effect on plasma glucose.

The authors propose the following changes to extend the minimal model to T1D state.

1. \( G_0 \) represents dynamic steady state, i.e., the match between glucose production and disappearance from the bloodstream provided no exogenous insulin effect. The exact value is determined by the residual \( \beta \)-cell function of the patient and hepatic glucose production in response to insulin deficiency, and is thus a patient-specific parameter. In the case of long-term T1D with complete \( \beta \)-cell apoptosis, \( G_0 \) value is several-fold that of normoglycemia.

2. \( p_1 \) refers to rate of endogenous glucose production (EGP) in the liver due to glycogenolysis/gluconeogenesis in T1D state. In the original minimal model [10], parameter \( p_1 \) specifies the rate towards total glucose balance between glucose uptake (in the liver and peripheral tissue) and secretion (EGP due to hypoglycemia). Nevertheless, changing the equilibrium point \( G_0 \) to hyperglycemic levels to represent T1D state implies a positive slope (EGP) in \( p_1[G_0 - G(t)] \) not only for hypoglycemic but also normo- and hyperglycemic blood glucose levels below \( G_0 \). In this way, \( p_1 \) can be interpreted exclusively as EGP rate under typical blood glucose excursion (including postprandial hyperglycemia) in T1D.

These two parameters and their physiological representation are in fact closely related. By changing the equilibrium point \( G_0 \), we make it possible to include the effect of glucose production \( p_1 \) without making modifications to the structure of the original minimal model. T1D is particularly characterized by an excessive hepatic glucose production [23] and other alterations in glucose-insulin metabolism such as the dawn phenomenon and Somogyi effect [24].

6. Simulation

This section presents simulation results of the proposed model in Matlab R2010b for four staple foods with GI values across the range to validate its accuracy by direct comparison with clinical data from a study by Mohammed et al. [25].

6.1 Simulation Settings

We set representative parameters of a T1D patient with \( G_0 = 300 \text{ mg/dL} \) (16.65 mmol/L), \( V_1 = 19.44 \text{ L} \), \( p_1 = 1 \times 10^{-3} \text{ min}^{-1} \) and insulin absorption parameters indicated in Table 2. Initial values for all simulations are set to \( x_i(0) = 0, x_2(0) = 0, I(0) = 0, X(0) = 0 \) and \( G(0) = 140 \text{ mg/dL} \) (7.78 mmol/L) to represent fasting conditions (no previous insulin administration) analogous to the aforementioned clinical study. Similarly, we represent food intake with an impulse at \( t = 0 \) in \( G_{food}(t) \) for 50 g of available carbohydrate (same for all foods) and carbohydrate absorption parameters as indicated in Table 1, along with an insulin bolus of \( a_i(0) = 10 \text{ IU} \), also constant for all foods, for a legitimate comparison with the aforementioned study.

6.2 Simulation Results

To demonstrate the accuracy of the proposed model, we compare simulation results with clinical data from in T1D patients, which consists of the postprandial response to staple foods with varying GI despite the same amount (50 g) and insulin bolus (10 IU). Similarly to the aforementioned study, carbohydrate input in our model is simulated with \( G_{food}(0) = 50 \text{ g} \) and carbohydrate absorption parameters for each staple food as given in Table 1. Postprandial glycemic excursion from the proposed model and their respective clinical data are shown in Fig. 5, where the accuracy for pearled barley (···) and spaghetti (―), i.e., low and medium GI foods respectively, is evident. The impact of high GI foods, i.e., instant potato (·), white bread (―), on blood glucose levels is also consistent with clinical data, although the proposed model evidences a difference of approximately 40 mg/dL during late postprandial state.

7. Discussion

This study proposes a model of glucose-insulin metabolism in T1D that includes the effect of carbohydrate intake on blood glucose levels. To the best of our knowledge, this is the first model of carbohydrate metabolism that considers not only amount but also carbohydrate composition as given by the GI of foods and carbohydrate bioavailability concepts. Previous models of carbohydrate absorption and gastric emptying such as the well-known Lehmann model [26] are dependent on the amount ingested exclusively. However, it has been demonstrated that the glycemic response can be inasmuch as 4-fold for the same amount of carbohydrates [12] depending on the GI value. The proposed model of carbohydrate metabolism provides an authentic representation of the impact of carbohydrates on postprandial glycemia with four additional parameters (GI, RAG, SAG and \( t_{deb} \)) besides amount.

The in vitro methodology utilized by the Englyst method has been criticized for being potentially misleading [27] since it only quantifies carbohydrate breakdown in the gut. In contrast to this, the in vivo GI method includes several other physiological factors that affect stomach emptying and thus provides the
total impact of carbohydrates on postprandial glyemia. We relied on both concepts for the development of the carbohydrate metabolism subsystem because, on one hand, a mathematical model of carbohydrates with the GI value as the only parameter of carbohydrate absorption is insufficient and, on the other hand, values estimated by the Englyst method are only an in vitro replication of carbohydrate breakdown in the stomach and small intestine. In this way, by considering both concepts we can build a model that is not only accurate but also physiologically meaningful.

Gastric emptying delay \( \tau_{dg} \) in Table 1 was adjusted, although arbitrarily, according to the GI value because of their strong linear relationship [28]. The authors suspect that values of \( \tau_{dg} \) in the proposed model include not only food properties but also additional delays during carbohydrate absorption process. One of them might precisely be related to the inaccuracy of the proposed model to represent the impact of high GI foods during late postprandial state, where it starts to diverge after 180 min. Such difference might be explained by the existence of an upper limit in gastric emptying rate during hyperglycemia [29], perhaps a physiological reaction to prevent further increase in blood glucose levels. Considering that only high GI foods cause postprandial hyperglycemia in T1D patients, we contemplate the eventual addition of a saturation function to \( G_{RAG}(t) \) to increase the accuracy of the proposed model.

Previous closed-loop systems seemingly successful in controlling blood glucose levels have published results based on mathematical models with unrealistic insulin kinetics [30]. This urged our study to strive for a more realistic representation considering the use of the proposed model in eventual studies of blood glucose control algorithms. In this study, we propose a simple three-step method to validate parameters of subcutaneous insulin absorption provided clinical data of subcutaneous insulin pharmacokinetics and insulin time-action profile (GIR) of intravenous and subcutaneous insulin. It should be noted that the clinical data utilized in the present study is limited to that of lispro insulin, which is one type of rapid-acting insulin formulations. Previous studies [31],[32] indicate that alternative rapid-acting insulin formulations are akin to lispro, and thus the proposed model is equally valid. Still, parameters of the subcutaneous insulin submodel can be readjusted following the method proposed in the present study and the pertinent clinical data.

The simplicity of the minimal model makes it arguably the most used mathematical model of glucose-insulin kinetics to date. The authors intended to avoid major modifications to the original proposal, and still represent TID state with physiological meaningfulness. The authors achieved this by redefining the physiological interpretation of parameters \( p_1 \) and \( G_0 \) and their respective values for TID state. Moreover, by separating glucose uptake and production we can represent abnormal hepatic EGP in these patients [33], especially in those with poor glycemic control [34].

8. Conclusion

This study proposed a model of glucose-insulin metabolism in T1D with a novel mathematical representation of carbohydrate metabolism. Even though the current proposal is based on minimal models of glucose-insulin kinetics and subcutaneous insulin absorption, it has a considerable degree of accuracy to represent postprandial state for different types of carbohydrate-rich foods, which was confirmed by simulation results and validated with clinical data.

References


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