Rule Based System for Modeling Diabetic Profile

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Abstract- The temporal database is represented using time stamps. A rule based temporal reasoning system is designed to work on medical temporal database. The temporal database stores the datarelated of the patients suffering from type 1 diabetes mellitus disease. The rule based system captures the blood glucose concentration of the diabetic patient and suggests the therapy based on clinical guidelines. In this paper we show the variation in BG concentration of the patient related to physical exercise.

Index Terms- temporal reasoning; temporal maintenance; temporal mediator; type 1 diabetes mellitus.

1. INTRODUCTION

The Rule Based Temporal Reasoning System (RBTRS) integrates the tasks of temporal reasoning and temporal maintenance. The system is designed for medical domain to model the blood glucose profile of the type 1 diabetic mellitus (T1DM) patient. The RBTRS consists of three modules: (i) Nutri-Diet module, (ii) Insulin-Glucose module and (iii) Diagnosis and Therapy Planner (DTP) module. The Insulin-Glucose module serves as the main function of reasoning system. The module exhibits the behavior of blood glucose and insulin in blood plasma. The design is based on open-loop insulin delivery strategy. The outputs obtained from Nutri-Diet module can be provided as inputs to Insulin-Glucose module. The various inputs provided to Insulin-Glucose module are net carbohydrate (CHO) intake, quantity of insulin induced exogenously and intensity of physical exercise along with patient's weight. Each of these inputs (clinical events) is associated with some various time-points along the 24hrs of time axis. Apart from these clinical events other inputs provided to the module are physical examination of patient (weight, gender and age) and quantitative parameters (fasting blood glucose value). The module forecasts the blood glucose concentration and the effect of carbohydrates (CHO) on blood glucose profile of a patient having T1DM. Further the module does predict temporal patterns by adopting a time series based temporal mining. The temporal patterns are based on various bands. In our model the safety band corresponds to normoglycemia range between 72 to $180\frac{mg}{dL}$. If the blood glucose level crosses the minimum value ($72\frac{mg}{dL}$) it will fall in lower band, while if it exceeds the maximum range ($180\frac{mg}{dL}$) it will fall in upper band. The blood glucose values falling under lower or upper bands represent the unconscious state of patient, while within safety band represents the normoglycemia range. The blood glucose curve crossing the barriers of safety band would depicts the unexpected behavior of blood glucose profile. To maintain the profile within the safety band the patient may modify dietary plan, quantity of insulin injection and exercise plan.

2. RULE BASED TEMPORAL REASONING SYSTEM (RBTRS)

The Insulin-Glucose module underlies the concept of Bergman minimal model [12] and the design will be based on open-loop insulin delivery techniques. To incorporate open-loop technique the RBTRS consists of various states defined over a period of 24hrs to regulate the profile of T1DM patient. The number of states adopted from dietary intake, insulin delivery and exercises are six, four and two respectively. For producing meal disturbance Fisher model [9] is adopted and one of its parameter is modified to create disturbance obtained from net CHO intake. The meal disturbance is defined over six states. The Fisher model is integrated with Bergman equations for predicting the blood glucose variation due to meal intake (external infusion of glucose). The insulin is delivered in the patient's body at four time-stamps in 24hrs and is defined as four states. Further the exercise model is incorporated in the existing design of Insulin-Glucose module for tighter glucose control, which is defined as two states. The exercise model is adopted from Roy et al. [1].

Figure 1 illustrates the reasoning system consisting of three modules. All the three modules are the part of reasoning system. The Nutri-Diet module acts as inputs while Diagnosis and Therapy Planner (DTP) module abstracts the blood glucose profile of the patient. The blood glucose profile is modeled using Insulin-Glucose module. The Nutri-Diet performs the tasks of data extraction and the extracted values are then passed to Insulin-Glucose for modeling the profile of T1DM patient [2, 13-21].

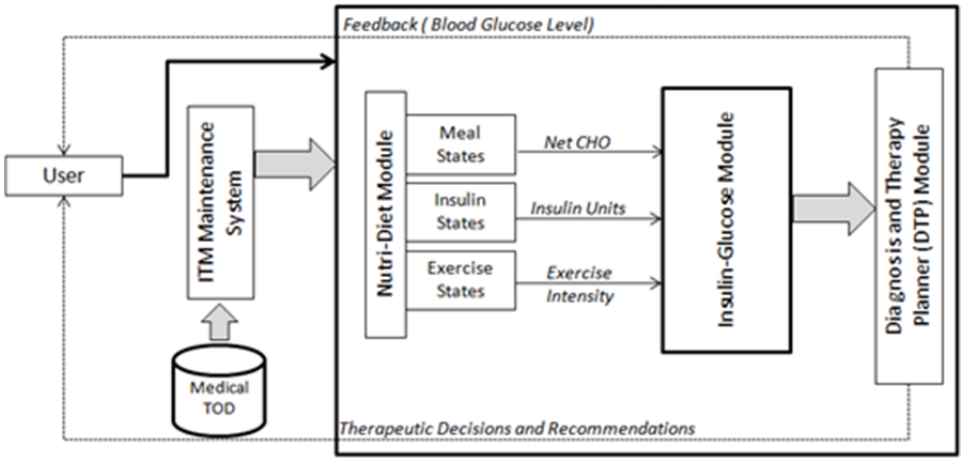

Figure 1: Rule Based Temporal Reasoning System(RBTRS)

3. RBTRS ARCHITECTURE

The Insulin-Glucose module utilizes Roy et al. [1] model for modeling exercise. Exercise plays an important role in the life of a diabetic person. The physical activity or exercise lowers the blood glucose at certain level as it burns the calories. For proper functioning of the body, it requires energy which is provided as calories. The number of calories present in any nutrient depends on how much energy it provides. The calories required by a person depend on age, weight, height, gender and physical activity level. The calories burned during an exercise depend on intensity and duration of exercise. The Table 1 illustrates the calories present in various nutrients [3].

Table 1: Calories content adapted from [3].

Nutrients	**Calories (per gram)**
Fat	9
Protein	4
Carbohydrates	4
Alcohol	7

The elevated exercise drops the plasma insulin level below the basal level [11]. This leads to increase of hepatic glucose production, due to energy uptake by working tissues [1]. The physical activity also amplifies glucose uptake rate [38]. As the duration and intensity of exercise increases, the hepatic glucose release also increases. The hepatic glucose release accomplishes from two processes: (i) glycogenolysis, and (ii) gluconeogenesis. Glycogenolysis is the production of glucose from liver stored glycogen, while in gluconeogenesis, glucose is produced from non-sugar carbon substrates. As the exercise duration passes this net hepatic glucose production does not fully compensate the glucose uptake rate by muscles [1]. Hence there is a decrease in blood glucose level and leads to hypoglycemia state [4, 6]. Liver glycogen decreases more quickly with increasing exercise intensity [1, 6]. During recovery period, after a short exercise the hepatic glucose production and glucose uptake rate by working muscles decreases to their basal level.

In Figure 3, if the exercise continues for a long period of time with the same intensity, the blood glucose level reduces below the basal value and the patient enters to hypoglycemia state.
The capacity of human body for physical activity is directly proportionate to maximum oxygen absorption [8]. The exercise intensity can be expressed as percentage of maximum rate of oxygen absorption (PVO_2^{max}). At basal level the average value of PVO_2^{max} is nearly 8% [1]. Ahlborg et al. [7] studied the behavior of PVO_2^{max} and predicted the fact that as the exercise starts the value of PVO_2^{max} reaches to a maximum level within 5-6 mins and will remains constants till exercise lasts. The Figure 6shows the behavior of PVO_2^{max}.

Roy et al. [18] defined the exercise model as follows. The rate of intensity of an exercise is given as:

$$\frac{d}{dt}PVO_2^{max}(t) = -0.8PVO_2^{max}(t) + 0.8u_{Ex}(t);\ PVO_2^{max}(0) = 0$$

$u_{Ex}(t)$, is the ultimate exercise intensity above basal level and takes input between 0-92%, for mid-to-moderate exercise.

The manipulated Bergman equations adopted from Roy et al. [18] can be defined as:

$$\frac{d}{dt}I(t) = -nI(t) - I_e(t) + p_5u_1(t)$$

$$\frac{d}{dt}X(t) = -p_2X(t) + p_3[I(t) - I_b]$$

$$\frac{d}{dt}G(t) = -p_1[G(t) - G_b] - p_4X(t)G(t) + \frac{W}{Vol_G}\left[G_{prod}(t) - G_{gly}(t)\right]$$

$$-\frac{W}{Vol_G}G_{up}(t) + \frac{u_2(t)}{Vol_G}$$

$$\frac{d}{dt}G_{prod}(t) = a_1PVO_2^{max}(t) - a_2G_{prod}(t)$$

$$\frac{d}{dt}G_{up}(t) = a_3PVO_2^{max}(t) - a_4G_{up}(t)$$

$$\frac{d}{dt}I_e(t) = a_5PVO_2^{max}(t) - a_6I_e(t)$$

Here, $I_e(t)(\frac{\mu U}{ml-min})$ is the rate of insulin removal from circulatory system, $G_{up}(t)(\frac{mg}{kg-min})$ is the rate of glucose uptake rate, $G_{prod}(t)(\frac{mg}{kg-min})$ is hepatic glucose production induced by exercise, $G_{gly}(t)(\frac{mg}{kg-min})$ is decline of glycogenolysis rate during prolonged exercise due to depletion of liver glycogen store, $W(kg)$ is weight of the person.

In Figure 2, the blood glucose values are plotted for rest and exercise for a short duration of 60 minutes. One can easily predict the fact that there is a remarkable lowering of blood sugar level during exercise or physical activity.

Table 2: Parameter values adapted from [18].

Parameter	Value	Unit
a_1	0.00158	$\frac{mg}{kg.min^2}$
a_2	0.056	min^{-1}
a_3	0.00195	$\frac{mg}{kg.min^2}$
a_4	0.0485	min^{-1}
a_5	0.00125	$\frac{\mu U}{mL.min}$
a_6	0.075	min^{-1}

From Figure 4, initially the hepatic glucose release (from glycogenolysis and gluconeogenesis) increase with the duration of exercise, but if the exercise lasts for the long time it decreases with time duration.

From Figure 5, as the exercise continues the glucose uptake rate of working muscle is more in comparison to hepatic glucose release, hence results to lowering of blood sugar level.

From Figure 6, the intensity of exercise can be directly measured from maximum absorption of oxygen as during exercise the body utilizes oxygen to break glucose from glycogenolysis for the production of energy. The maximum oxygen is absorbed within 5-6 mins and the absorption will remain constant till the exercise last.

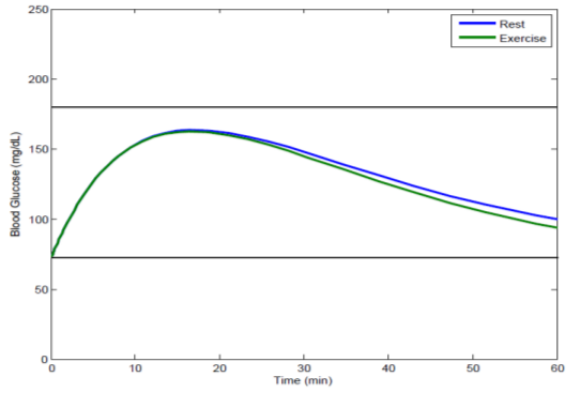

Figure 2: Variation in blood glucose level during rest and exercise of a diabetic patient, modeled by integrating Roy et al. [1] exercise model with the Bergman minimal model [12]. The result shows that adopting a physical exercise significantly lowers the blood glucose level and hence reduces the risk of hyperglycemia state.

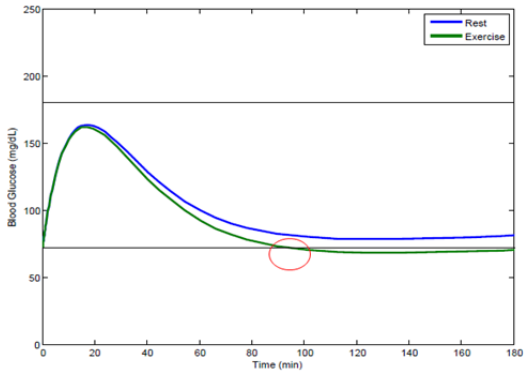

Figure 3: If the exercise performed by diabetic patient prolongs for a long time would significantly lowers the blood glucose value and results to hypoglycemia state.

The literature related to Insulin-Glucose Module is already published in the research paper entitled "Temporal reasoning with time oriented medical database using models based on insulin-glucose metabolism".

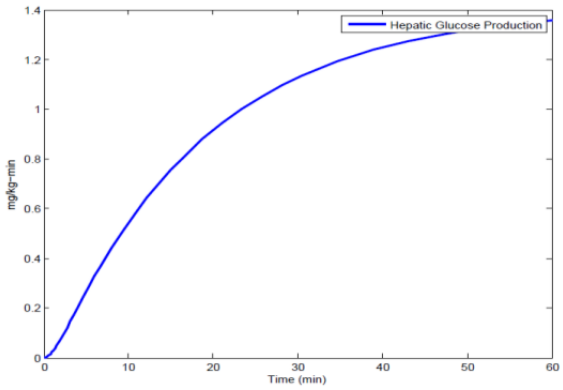

Figure 4: Hepatic glucose production.

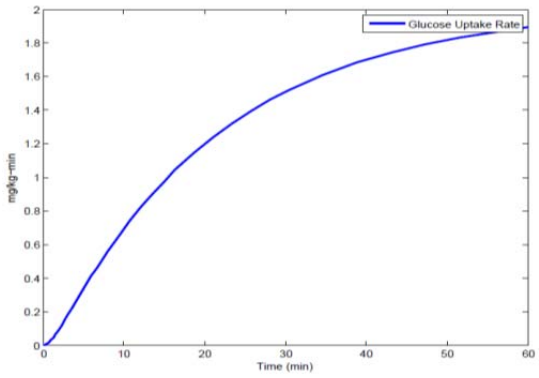

Figure 5: Glucose uptake rate.

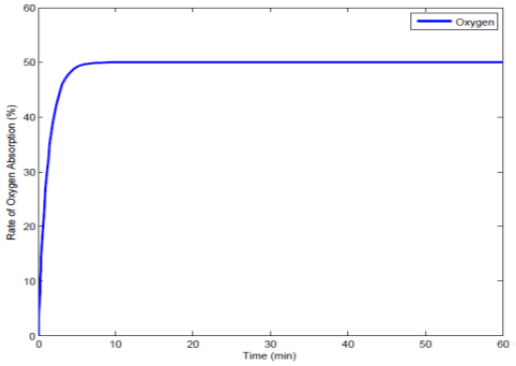

Figure 6: Rate of oxygen absorption.

4. SIMULATION

The Nutri-Diet module defines two states for the exercise subsystem. The Insulin-Glucose module implements the exercise subsystem, using an exercise model developed by Roy et al. [1]. The exercise model is integrated by Bergman minimal model for forecasting the effect of physical exercise on blood glucose concentration (Algorithm 2). By integrating exercise model with the minimal model one could have tighter control on blood glucose levels. In 24hrs of patient's blood glucose profile, the exercises are performed at two time-stamps: morning exercise and evening exercise. The morning exercise is performed before Breakfast, while the evening exercise is performed between Snacks-2 and Dinner. The result shows that there is an overall reduction of blood glucose level due to exercise. The range for intensity of exercise has been defined between 0 to 100%. The value 0% denotes patient is at rest (no exercise), while 100% denotes the exercise with maximum intensity.

From Figure 4, the morning and evening exercise is performed with intensities 70 and 50 respectively with a person's weight 70kg. There is a reduction in blood sugar level in the entire patient's blood glucose profile.

In Figure 5, three blood glucose profiles are plotted by varying exercise intensities as 10, 50 and 100%, making weight constant to 70kg. The result shows that as the intensity of exercise increase there is a drop in blood glucose level. An exercise with high intensity may drop the plasma blood glucose below the basal level and may cause loss of consciousness.

In Figure 6, three blood glucose profiles are plotted by varying weight of person as 40, 80 and 120kg, making exercise intensity constant to 50%. The result shows that, a person with more weight will have more drops in the blood glucose in comparison to person with less weight. This is because a person with more weight will absorb more oxygen. Hence the chances of hypoglycemia episodes are more prominent in case of person having more weight during long exercise with high intensity.

Algorithm 1: This algorithm integrates the exercise model with Bergman's minimal model.

Step 1: [Inputs the values for exercise state.]
UEXB := *input*('Exercise Intensity Before Breakfast:')
W := *input*('Weight:') %Weight of a person (kg)

Step 2: [Inputs the values for meal state and insulin state.]
CB := *input*('Breakfast:')
uB := *input*('Insulin Intake During Breakfast:')

Step 3: [Forecast the value of basal blood glucose level.]
G_ssB := *input*('Basal Blood Glucose Level (mg/dL)')

Step 4: [Initialize other exercise states.]
Set GPRO_state := 0 %Basal value for hepatic glucose production (mg/kg.min)
Set GUP_state := 0 %Basal value for glucose uptake rate (mg/kg.min)
Set IE_state := 0 %Basal value for Insulin removal from circulatory system %(mU/L.min)
Set O_state := 0 %Basal value for physical activity expressed as percentage of %maximum oxygen consumption (ml/kg.min)

Step 5: [Solve the procedure for time t=0 to 150 mins by utilizing *ode15s()* MATLAB function.]
Call the procedure **blood_glucoseBE**

Algorithm 2: blood_glucoseBE.

Step 1: [Define states.]

```
Set I := x(1,1)          % Plasma Insulin Concentration (mU/L)
Set X := x(2,1)          % Plasma Insulin Concentration (mU/L) in remote
                         % compartment
Set G := x(3,1)          % Plasma Glucose Concentration (mg/dL)
Set GPRO := x(4,1)
Set GUP := x(5,1)
Set IE := x(6,1)
Set O := x(7,1)
```

Step 2: [Basal values of insulin concentration.]

```
Set Ib := 15             % mU/L
```

Step 3: [Meal disturbance from Fisher model.]

```
Set A := CB*0.36543
Set B := 0.05
D := A*exp(-B * t)
```

Step 4: [Parameters for type-1 diabetes mellitus.]

```
Set p1 := 0.068
Set p2 := 0.037
Set p3 := 0.000012
Set p4 := 1.0
Set p5 := 0.568
Set n := 0.142
Set a1 := 0.00158        %mg/kg.min
Set a2 := 0.056          %1/min
Set a3 := 0.00195        %mg/kg.min
Set a4 := 0.0485         %1/min
Set a5 := 0.00125        %μU/mL.min
Set a6 := 0.075          %1/min
Set VolG := 117          %Glucose distribution space (dL)
```

Step 5: [Integrating exercise model with minimal model equations.]

```
Odot := -0.8*O+0.8*UEXB          %Exercise level above basal
GPROdot := a1*O-a2*GPRO          %Hepatic glucose production
GUPdot := a3*O-a4*GUP            %Glucose uptake rate
IEdot := a5*O-a6*IE              %Insulin removal from circulatory system
Idot := p5*uB-n*IE               %Plasma insulin
Xdot :=  p3*(I-Ib)-p2*X          %Remote insulin compartment
Gdot := -p1*G-p4*X*G+p1*G_ssB+D+(W*GPRO)/VolG-(W*GUP)/VolG
                                 %Blood glucose during exercise
```

Step 6: Return

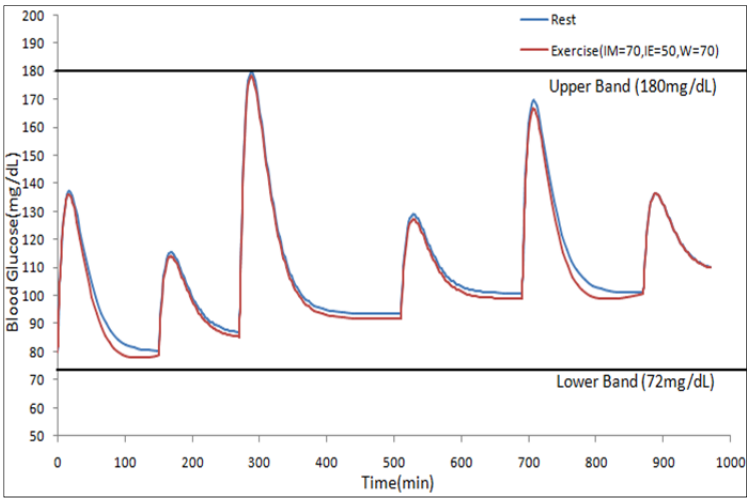

Figure 7: The blood glucose profile during rest and exercise. As discussed in Chapter 5 two states have been define for exercises. One is during morning and another is in evening. IM and IE represent the intensity of exercise during morning and evening respectively. W represents the weight of the person. The result shows that there is reduction in blood glucose level when the exercise is performed.

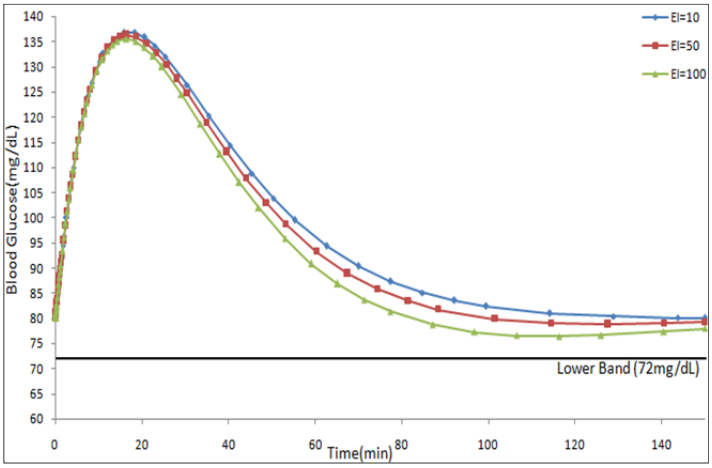

Figure 8: Change in blood glucose concentration with the variation in exercise intensities by keeping person's weight constant. The result shows that as the intensity of exercise increases there is a reduction in blood glucose concentration. EI represents exercise intensity.

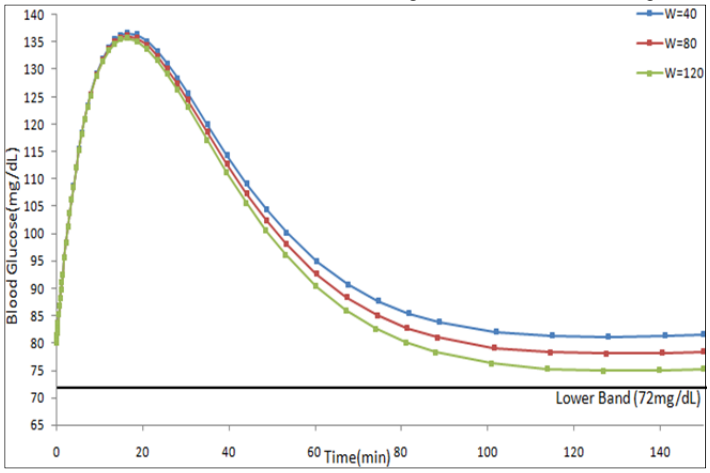

Figure 9: Change in blood glucose concentration with the variation in weight by keeping exercise intensity constant. The result shows that blood glucose concentration declines rapidly in weighted person in comparison to the person having less weight. W represents the weight of the person.

5. SUMMARY

The Insulin-Glucose module for modeling blood glucose and plasma insulin is developed in MATLAB for T1DM patients. The temporal reasoning tasks performed by Insulin-Glucose module is are forecasting. The various states which are defined in Nutri-Diet module for meal intakes, insulin infusions and exercise are implemented as subsystems of Insulin-Glucose module. The module utilizes the concept of time series based methodology and three bands range have been defined. The various bands are safety, lower and upper bands. The safety band corresponds to normoglycemia blood glucose level, while the other bands represent the unexpected trend in the blood glucose values. If the blood glucose level is less than $72\frac{mg}{dL}$ it will fall in lower band and results to hypoglycemia state which lead to comma. A severely high blood glucose level more than $180\frac{mg}{dL}$ would shift the blood glucose curve to upper band and results to hyperglycemia state which lead to heart failure. The section of blood glucose curve on a particular band range corresponds to a temporal pattern. These temporal patterns act as inputs to Diagnosis and Therapy Planner (DTP) module for performing the tasks of diagnosis, monitoring and therapy planning.

The module underlies its designing principles from Bergman minimal model [12] developed for closed-loop insulin infusion. The Bergman minimal model is successfully converted to open-loop from closed-loop, to meet the designing requirements of open-loop dynamics. One of the parameter of Fisher [9] meal model is modified and is integrated with Berman minimal model to create meal disturbance obtained from CHO (carbohydrates). The Fisher model acts as meal disturbance model which helps in external absorption of glucose through a diet and would results to rise in the blood glucose level.

The exogenous absorption of insulin is achieved by defining the four states during which the insulin is delivered to patient's body. The Insulin-Glucose module also incorporates the existing exercise model (Roy et al. [1]) for implementing exercise subsystem to have tighter blood glucose control, as exercise largely effects the blood glucose concentration of diabetic patient. The exercise subsystem is defined over two states one is during morning while another is in evening. The physical exercise reduces the blood glucose level and it depends on the type of exercise performed, duration and patient's weight. The meal disturbance subsystem, insulin delivery subsystem and exercise subsystem forms an integral part in designing the Insulin-Glucose module.

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