

Temporal Reasoning with Time Oriented Medical Database using Models based on Insulin-Glucose Metabolism

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Abstract—In this paper, we will discuss the design of temporal reasoning system of Intelligent Temporal Mediator (ITM), which was developed to reasons with time-oriented medical database. The design of ITM reasoning system was based on open-loop insulin delivery technique and it utilizes various models of insulin-glucose metabolism. The designed ITM models the blood-glucose concentrations and provides therapeutic recommendations for the patient suffering from type 1 diabetes mellitus.

Keywords—temporal mediator; temporal maintenance; temporal reasoning; T1DM.

I. INTRODUCTION

It is almost impossible to represent or reasons with the medical data in the absence of time. Almost every medical data is associated with time dimension such as patient's physical examination, laboratory tests, patient monitoring, diagnosis, therapy planning and recommendations [1, 2, 3, 4, 5, 6]. The field of temporal data base is concerned with the collection of database on some time stamps. The time stamps may be time point or time interval, one is related to time instance while other is related to time duration. According to Shahar et al. [34] the research in the field of temporal database can be classified into two tasks one is temporal maintenance while other is temporal reasoning. The task of temporal maintenance is investigated by researchers of database community, often associated with management of time-oriented databases, while the task of temporal reasoning is related to intelligent analysis of time-oriented databases and is related to artificial intelligence. Shahar et al. [35] integrated the tasks of temporal maintenance and temporal reasoning through a temporal mediator. The temporal mediator will form a distinct middle layer making the user application independent of data resources [31].

This paper discuss the designing principles of temporal mediator called as intelligent temporal mediator (ITM) [7, 8], which integrates the tasks of temporal reasoning and temporal maintenance and was developed for modeling the insulin-glucose concentration of type 1 diabetic mellitus patient.

II. RESEARCH ISSUES OF INTELLIGENT TEMPORAL MEDIATOR

The designing methodology of ITM is the integration of two research directions. One is to perform the task of temporal reasoning based on patient time-oriented database (TOD) or temporal database, and other is to study the glucose-insulin metabolism of patient having type 1 diabetes mellitus (T1DM).

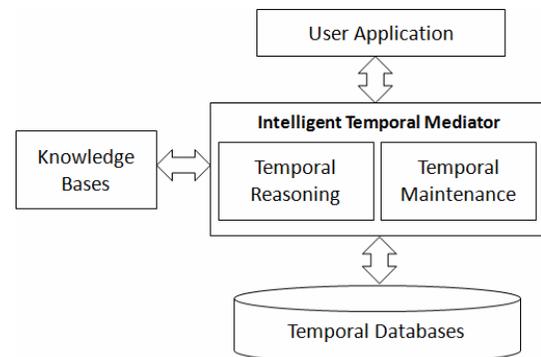


Fig. 1. Temporal mediator integrating the tasks of temporal reasoning and temporal maintenance, adapted from Shahar et al. [33].

A. Insulin Delivery Techniques

The artificial infusion of insulin in diabetic patient body can be accomplished in two ways: closed-loop, and open-loop.

1. *Closed-loop*: The closed-loop insulin infusion is an automated process controlled by computer algorithm. The closed-loop insulin delivery system acts as artificial pancreas, which senses plasma insulin concentration in the blood, calculates the amount of insulin needed by the body for maintaining normoglycemia level and finally delivers the correct amount of insulin [20]. The system is composed of glucose sensor, an insulin pump and control algorithm for regulating the insulin pump.

2. *Open-loop*: The open-loop methods of insulin delivery focus on a patient administering insulin to his or herself at different times of the day [29]. It is based on taking multiple injections using a combination of short and long acting insulin analogues supported by blood glucose self monitoring [17]. Normally the

patient has to take 3-4 injections daily for regulating the plasma glucose level in the blood. The physician suggests a diet chat for the patient and prescribes him the quantity and type of injections he has to take at various time intervals for maintaining normoglycemia levels.

It is quite difficult for a common man in India to use closed-loop technique for delivering insulin, as insulin pumps are expensive, costing thousands of dollars [36, 37]. Addition to this, annual expenses to operate a pump can be 1,500 USD or more [28]. According from Times of India newspaper [39], insulin pump has few buyers in India and the doctors in India say “Each pump costs as much as a small car”. The insulin pumps which are imported to India are sold for between 4,000 and 8,000 USD [39]. Above facts shows that in India it is quite difficult for each and every diabetic person to adopt closed-loop technique. Thus, the designed ITM will work on the principles of open-loop insulin delivery.

B. Models Based on Insulin-Glucose Concentrations

The models related to blood-insulin dynamics can be divided into three categories: (i) Strictly empirical, (ii) Semi-empirical, and (iii) Physiological based.

1. *Strictly empirical models:* These models are developed based on the input-output data without considering the fundamental properties (physiology) of the system [30, 25, 29,13].
2. *Semi empirical models:* These models consist of a minimum number of equations capturing the insulin glucose dynamics with a primary focus on emulating the data by considering only the necessary physiology [21, 32, 38, 14, 13, 11, 10, 26].
3. *Physiologically based models:* These models are more detailed and complex in terms of number of parameters and equations providing an in depth description of the physiology behind the various metabolic interactions taking place in the body [15, 27, 12].

III. MODELS UTILIZED IN THE DESIGN OF ITM

The design of ITM incorporates some of the models which are listed below [8, 9].

A. Bergman Model

This model was designed in 1970, by Bergman and co-workers [18, 19, 20, 21, 22, 23, 24] developed a minimal model of glucose and insulin plasma by conducting frequently-sampled intravenous glucose tolerance (FSIGT) tests on dogs and humans. In FSIGT test blood samples are taken during fasting following a single intravenous injection of glucose. The Bergman’s mathematical model consists of three compartments. The various compartments are $I(t)$, $X(t)$, and $G(t)$ called as plasma insulin $\left(\frac{\mu U}{ml}\right)$, remote insulin $\left(\frac{\mu U}{ml}\right)$, and

blood glucose $\left(\frac{mg}{dL}\right)$ compartments respectively. The model can be mathematically given as [18]:

$$\begin{aligned} \frac{dI(t)}{dt} &= -nI(t) + p_5 u_1(t), & I(0) &= I_b = \frac{p_4}{n} u_{1b} \\ \frac{dX(t)}{dt} &= -p_2 X(t) + p_3 [I(t) - I_b], & X(0) &= 0 \\ \frac{dG(t)}{dt} &= -p_1 G(t) - p_4 X(t) G(t) + p_1 G_b + \frac{u_2(t)}{Vol_G}, & G(0) &= G_b \end{aligned}$$

The parameter $u_1(t)$ denotes the rate at which insulin is induced exogenously. The induced insulin enters into the insulin compartment ($I(t)$), a portion of which enters into remote compartment. The inaccessible remote insulin ($X(t)$), actively takes part in promoting uptake of plasma glucose ($G(t)$) into the liver and peripheral tissues. The basal values of insulin and glucose concentrations are given by I_b and G_b .

The term u_{1b} $\left(\frac{mU}{min}\right)$ is the exogenous insulin infusion rate to maintain I_b , and $u_2(t)$ represents the external absorption of glucose through any diet.

B. Fisher Model

Fisher [16], defined the meal disturbance function $D(t)$, which represent the rate at which glucose enters the blood from intestinal absorption following a meal. The function $D(t)$ which perform desired behavior can be defined as [16]:

$$D(t) = B \exp(-kt), t \geq 0$$

If we take the values of $B = 0.5$ and $k = 0.05$, then there is rapid rise in blood glucose level to a maximum value within less than 30 mins and should fall at basal value after about 2-3 hours. The variable t is in minutes and $D(t)$ is $\frac{mg}{indL \cdot min}$.

C. Exercise Model

Roy et al. [1] defined the exercise model as follows. The rate of intensity of an exercise is given as [1]:

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

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

IV. ANALYSIS AND DESIGN OF INTELLIGENT TEMPORAL MEDIATOR

The fig. 2 depicts the schematic diagram of “Intelligent Temporal Mediator” (ITM) designed for medical domain. To support guidelines based therapy ITM integrates the tasks of

temporal reasoning and temporal maintenance. The system is designed to model the blood glucose profile of the patient suffering from type 1 diabetes mellitus (T1DM).

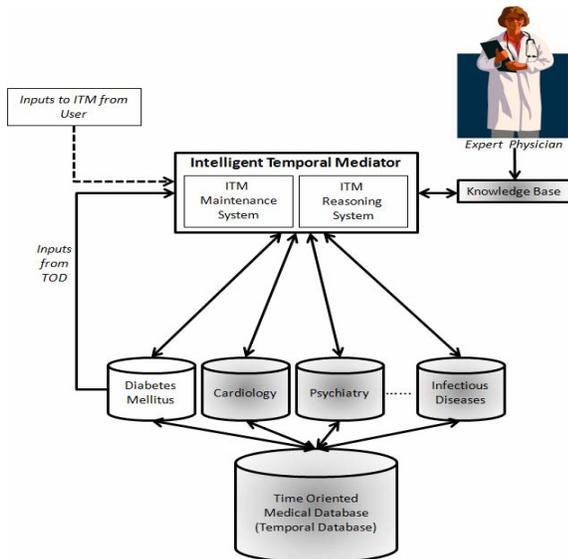


Fig. 2. Intelligent temporal mediator designed to work on time-oriented medical database related to type 1 diabetes mellitus (T1DM).

A. ITM Reasoning System

The ITM reasoning system performs the tasks of inference on time-oriented medical data. The reasoning system performs the task of temporal abstraction for creating interpretations of time-stamped data in terms of higher-level concepts and patterns that hold over time intervals. The temporal patterns are based on value of blood glucose concentrations on some time-intervals. The temporal pattern accounts for hypo and hyper blood glucose episodes. The diagnosis is based on blood glucose temporal patterns along the time line of 24 hours. The monitoring task is related to therapy plan execution of the patient. To achieve the open-loop insulin delivery techniques the system has been divided into various states. The various states defined are six, four and two for meal intake, insulin delivery and physical activity respectively. The various inputs are provided to the systems at various time-stamps related to meal intake, quantity of injections and exercise intensity with duration. The concentrations of blood glucose and plasma insulin are modeled with the help of Bergman equations [18]. The Fisher [16] model was modified for creating meal disturbance based on net carbohydrates (CHO) intake and is incorporated in the equations of Bergman model. The effect of exercise on the profile of T1DM is modeled using exercise model developed by Roy et al. [1].

B. ITM Maintenance System

Temporal maintenance is related with the effective storage and retrieval of data based on some time-stamps. The ITM maintenance system accepts (from TOD) or collects (input to ITM from user on certain time-stamps) following data of diabetic patient: physical examination of patient (weight, sex and age), quantitative parameter (fasting blood glucose value), and several events (insulin administration, meals, and physical

exercise). The maintenance system has limited use in our context, so we are providing the data through “Inputs to ITM” interface (fig. 2).

V. MODULES OF ITM REASONING SYSTEM

The ITM reasoning system consists of three modules: (i) Nutri-Diet module, (ii) Insulin-Glucose module, and (iii) Diagnosis and Therapy planner (DTP) module.

A. Nutri-Diet Module

The module accepts various inputs from maintenance system such as mixed meal intakes, quantity of insulin induced and types of exercise performed. These inputs are provided at various time-stamps defined over states. The inputs are then processed and the output is provided to Insulin-Glucose module. From the mixed meal intake of patient at various time-points, the Nutri-Diet module calculates the net contents of carbohydrates (CHO), fats, saturated fats, and cholesterol present in the food. Here we are going to model only the effect of net CHO on the patient’s blood glucose profile. Net CHO means the quantity of CHO that affects the glycemic level of blood sugar. If a person takes 100gms of CHO, it doesn’t mean all the 100gms will raise the blood sugar level. The amount of CHO that will raise the blood sugar level is known as Net CHO.

The Nutri-Diet module also calculates the intensity of exercise performed by the patient, this intensity value in turn acts an input to the Insulin-Glucose module. The intensity percentage is calculated from the type of exercise adopted by the patient. The exercise is suggested by the physician depending on the blood glucose profile of the diabetic patient and it varies from person to person.

B. Insulin-Glucose Module

This module serves as the main function of ITM reasoning system. This module exhibits the behavior of blood glucose and insulin in blood plasma. It is programmed in MATLAB R2008b version 7.7.0.471. The blood glucose profile of the patient is modeled using time series technique known as band ranges. The blood glucose profile of the patient is plotted across these band ranges (fig. 3). The blood glucose level may exist among three states defined as safety, lower, and upper band. The safety band corresponds to normal blood sugar level while other bands depict the unconsciousness state of T1DM patient.

If the person is having blood glucose level between $72 \frac{mg}{dL}$ and $180 \frac{mg}{dL}$ it would fall in safety band. A point (x_i, y_i) would fall in safety band if, $\alpha \leq y_i \leq \beta$, for $0 \leq i \leq n$. where α and β are the minimum and maximum blood glucose values. In our case, we are assuming value for α is $72 \frac{mg}{dL}$ and for β is $180 \frac{mg}{dL}$. A severely low blood sugar level may lead to unconsciousness. A point (x_i, y_i) would fall in lower band if, $y_i < \alpha$, for $0 \leq i \leq n$. The simulator can be used to simulate the situation where patient takes his insulin, but rushes off to work without having breakfast. In such a situation he may be running a significant

risk of hypoglycemia in the midmorning. A severely high blood sugar may results in various symptoms like breathlessness. A point (x_i, y_i) would fall upper band if, $y_i > \beta$, for $0 \leq i \leq n$.

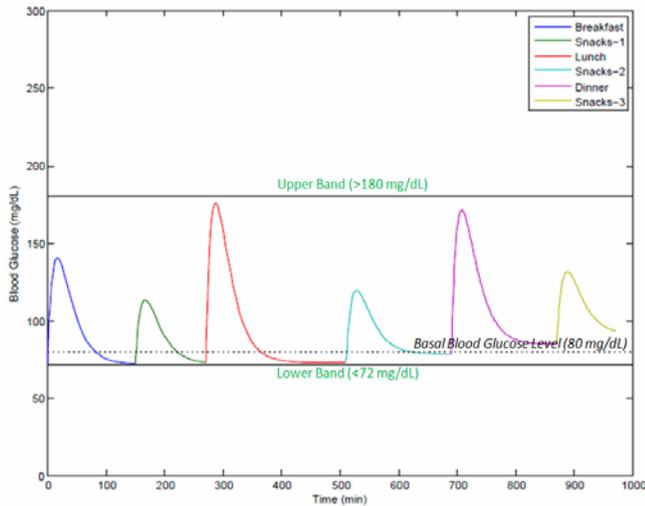


Fig. 3. The blood glucose concentration plotted across various bands range. The different color of the curve represents the various meal sates.

C. Diagnosis and Therapy Planner

The interval based temporal abstraction obtained by Insulin-Glucose module is passed to the Diagnosis and Therapy Planner (DTP) module for performing monitoring and diagnosis tasks related to temporal reasoning based on patient's blood glucose level. The 24 hrs blood glucose profile of patients can be modeled as set of blood glucose temporal patterns. The temporal patterns can be classified into two categories: (i) hyperglycemia episodes and (ii) hypoglycemia episodes. The DTP module functions in two ways: (i) Diagnosis and (ii) Therapy planning. The data related to patient has been collected and stored. This data can be processed into useful information, which helps in decision making. The decision making process helps in diagnosis or assessment regarding the blood glucose profile of the patient. After successful diagnosis therapy planning has been conducted.

VI. CONCLUSION

In this paper we discussed the design of intelligent temporal mediator (ITM). The ITM was designed on the underlying concept of open-loop insulin delivery for planning and diagnosis of patient suffering from type 1 diabetes mellitus. The implementation of ITM involves various models of glucose-insulin metabolism. The ITM performs the tasks of temporal reasoning based on blood glucose episodes encountered in the profile of the patient. The maintenance system of ITM collects the data related to patient on some time-stamps or it can also accepts data from patient's time-oriented database. The ITM is highly desirable in modeling the blood glucose profile of type 1 diabetic patient.

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