SIMULATIONS OF A MODEL-BASED FUZZY CONTROL SYSTEM FOR GLYCEMIC CONTROL IN DIABETES

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Abstract: *This paper investigates a conventional fuzzy control algorithm to be used in a closed loop system that should return and keep the blood glucose concentration at normal values for diabetic patients. The controller design follows general guidelines in fuzzy control theory. Simulations are done using a model of glucose kinetics under the influence of insulin injection rates and exogenous glucose disturbance. The model is an extension to the well-known Bergman's minimal model by adding the carbohydrates absorption rate from Hovorka's model as the glucose disturbance input.*

Key words: *glycaemia control, fuzzy control of glucose concentration, Bergman minimal model, insulin to glucose model.*

1. Introduction

Several control algorithms for automatic blood glucose control in type 1 diabetes mellitus (T1DM) patients were tested over the years, in simulations or in live experiments. Detailed surveys of the most used algorithms in this subject during the latest 10 years are presented in [19], [20] and [14]. Also, very good summaries of the most important studies and results published in recent years are presented in [14] and [10], while the newest are presented in details in [6].

Two different approaches can be noted. The first is the model-based system design, which implies the use of a model to describe the glucose dynamics in various cases. The first example would be the modified Bergman minimal model [3], [8], for T1DM patients, which was intensively used in simulations [4]. Many studies presented solutions based on a model, and a good part of them stepped ahead towards testing the simulated control algorithms in live experiments.

The second approach focuses on system design methods and algorithms that use real data from live experiments and physicians' experience. Researchers argues that usually there is an important variability in physiological parameters from one patient to another and, even worse, for a single patient during a longer period of time. A blood glucose control system is intended to become a routine therapy solution and during 24 hours there are several influences over the parameters: having meals, doing exercises, night changes in metabolism, and others [18].

Physicians' experience and actions can be expressed with better relevance in an approximate logic. Treatment decisions are based on evaluating blood glucose levels in

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terms of "too low", "good" or "too high", and not on strict computations. This suggests that a fuzzy logic (FL) approach is worth to be investigated (at least). Another type of arguments for fuzzy logic control (FLC) comes from its theory: it is often mentioned that fuzzy control is less sensible to small variations of parameters and, if extended to an adaptive system, it can efficiently cope larger variations too.

On the other hand, fuzzy control theory doesn't offer strict design methods. In many cases, the controller's rule-base is set by following a set of design guidelines, handbook solutions or other examples that the engineer knows. Fewer solutions are obtained from recorded data or by translating expert's decisions into control rules. Hence, it seems that designing a fuzzy control system based on physicians' treatment actions and experience still has enough motivation.

Convincing studies presenting FLC systems for glycaemia control are significantly fewer than other control algorithms. The review published by Youssef et al. in 2009 [20] refers to the FLC as being promising, but largely clinically untested. Lunze et al. published a very good state-of-the-art article in 2013 [14] which do not even mention the FLC solution. One year later, Doyle et al. [10] present a summary of clinical trial protocols which shows the FLC as the less preferred solution.

However, encouraging studies and results were reported, even if most of them are simulations.

Campos-Delgado et al. [5] presented a two-loop FLC for long-time glycaemic control. Their solution uses two Mamdani-type fuzzy controllers (FC): one in the inner loop to adjust the quantities of injected insulin for three shots before meals, and one in the outer loop to adjust the maximum quantities to be provided to patient in a time-scale of days (as a supervisory support system). The system is mostly meant to incorporate medical knowledge about the treatment of T1DM, and not to offer a real control system in the most conventional meaning.

A simple solution for direct control of glycaemia is tested in [7], and compared to PID control. The input and output variables (glucose concentration, its rate of change and insulin dosage) are described by four terms each, and the rule base is based mostly on design guidelines.

Mauseth et al. [15] present a conventional table-based Mamdani-type FC which respects most guidelines in designing fuzzy controllers. They also introduce a personalization factor proportional to the patient's total daily dose of insulin. This is actually a scaling gain applied to the controller's output, which has strong influence on the system's performance.

These solutions are mostly designed based on control engineering experience, especially in fuzzy control theory. In opposite, Atlas, Nimri and their team [1], [16] proposed a system which applies the fuzzy logic theory to imitate lines of reasoning of diabetes caregivers, and so to focus on medical experience.

Finally, for the latest studies on glycaemic fuzzy control, please refer to the reviews in [17] and [6], while for an introduction in FLC theory, design guidelines and examples please refer to the book of Jantzen [12].

2. A Model of the Insulin to Glucose System, with Meal Glucose Disturbance

Probably the most used model to describe the effect of insulin injection rate and glucose disturbance input on the blood glucose concentration is the modified Bergman's minimal model. In its initial form, the model described the kinetics of glucose and insulin concentrations in blood during the intravenous glucose tolerance test [3]. A few years later, Cobelli et al. [8] adapted the model to describe the kinetics

of glucose concentration under the effects of exogenous insulin and glucose rates, with application in glycaemic control. Over the years, the modification of Bergman's model for T1DM patients became known as the "minimal model".

The model is a compartment-based 3-rd order nonlinear one, depicted as follows:

$$\frac{dG(t)}{dt} = -\left[p_1 + X(t)\right]G(t) + p_1 G_b + ad(t),$$

$$\frac{dX(t)}{dt} = -p_2 X(t) + p_3 I(t), \tag{1}$$

$$\frac{dI(t)}{dt} = -nI(t) + bu(t).$$

All notations are described in Table 1 (Detailed descriptions of each are presented in [9] and other values than those used in this paper are listed in [13]).

The input variables are the exogenous insulin rate, $u(t)$, and the disturbance glucose absorption, $d(t)$, while the output is the blood glucose concentration, $G(t)$.

The conversion factors a and b allow input variables to be described as flows (in terms of [mg/min] and [mU/min], rather than [mg/min/dL], respectively [mU/min/L] as would be require in the equations). Note that, by using these factors, the units would be in consistency with clinical convention of insulin delivery rate prescription.

The variables and parameters of the model　　　Table 1

Notation	Description (see also [9])	Unit	Values
$G(t)$	blood glucose concentration at time t [min]	mg/dL	-
$I(t)$	blood insulin concentration at time t [min]	mU/L	-
$X(t)$	a variable defining the effect on the insulin-excitable tissues at time t [min] (proportional to the insulin concentration in a "remote" compartment)	1/min	-
$d(t)$	disturbance input of glucose at time t [min]	mg/min	-
$U(t)$	exogenous insulin deliver rate at time t [min]	mU/min	-
G_b	subject's basal glucose concentration in blood	mg/dL	81
P_1	the insulin-independent rate of tissue glucose uptake (i.e. glucose effectiveness)	1/min	0
P_2	the active insulin decrease rate (decrease of uptake)	1/min	0.025
P_3	insulin-dependent increase of tissue glucose uptake	L/(mU×min×min)	$13×10^{-6}$
n	decay rate of blood insulin	1/min	0.0926
V	the assumed distribution volume of the insulin [14], which in some studies is considered the total blood volume [2]	L	12
a	glucose input conversion factor	1/L	0.0083
b	insulin input conversion factor	1/L	0.0833
D_g	the quantity of carbohydrates (CHO) in the meal	mg	50,000
A_g	CHO bioavailability - a factor describing how much of the meal's CHO is absorbed in the blood	unitless	0.8
$t_{g,max}$	the approximate time delay from the start of the meal when CHO absorption is at the maximum	min	40

In the example presented in [2], both factors depend on the total blood volume, *V*, and based on the units we considered, they should be $a = 0.1/V$ and $b = 1/V$.

The "remote" compartment in the model refers to the glucose uptake activity in the insulin-excitable tissues (as the liver and peripheral cells). The reason for this compartment is that the glucose uptake depends on the insulin concentration at "effector site", $X(t)$, not directly on the insulin concentration in the total blood volume, $I(t)$. The variable has more meaning in compartment-based modelling, than in a medical context.

The glucose disturbance input may refer to the injection of glucose in intravenous glucose tolerance tests [3], [14], or to the glucose increase due to carbohydrates absorption after a meal [2]. Based on these, two simulation scenarios can be set:

A) The patient has an initial high concentration of glucose, G_0. The control objectives are: to reduce the glucose concentration to its basal value, G_b, in less than 3 hours, and to avoid any overshoot (which in medical terms means hypoglycaemia).

B) Initially, the patient has a safe glucose concentration, $G_0 = G_b$, and he has a meal with 50 g CHO. The control objectives are to return to a normal value (under 160 mg/dL for T1DM patients) in less than 90 minutes, and also to avoid the overshoot.

To run more credible simulations with meal glucose disturbance, we considered an extension to the minimal model by including a sub-model to describe the glucose absorption after having a meal. This is presented by Hovorka et al. in [11],

and consists in the following non-linear Equation (notations are also described in Table 1):

$$d(t) = \frac{D_g A_g t \exp(-t/t_{g,\max})}{t^2_{g,\max}} . \qquad (2)$$

The time variation of the disturbance input according to this model is depicted in Figure 3a and the accumulation of glucose caused by this disturbance is in Figure 3b.

3. The Fuzzy Control Algorithm

The fuzzy controller used here is a Mamdani proportional-derivative (PD) type (see the diagram in Figure 1), having the control error and its derivative as the input variables and the insulin rate to be delivered as the output. Note that negative values for the insulin deliver rates are not possible, so the controller's output is limited to zero to avoid simulation errors.

The scaling gains for the input variables are not analysed in this paper ($g_e = g_{ce} = 1$) as they have a smaller influence on the control performances. However, to obtain a faster reaction to large error values, the scaling gain of the output variable was set to $g_u = 2$. This value could be personalized as in [15]. Further research on finding the optimal value is still to be done.

The control error is defined as:

$$e(t) = -[G_r(t) - G(t)] = G(t) - G_b ,$$

with $G_r(t)$ being the reference value of glucose concentration at time *t*, which in our case is set to be constant and equal to
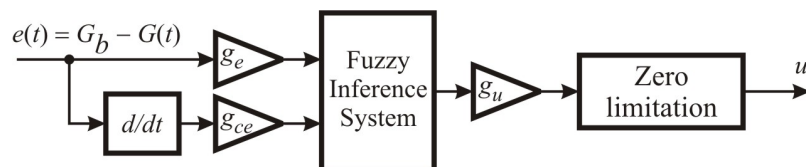

Fig. 1. *The fuzzy controller diagram*

The numerical rule-base of the fuzzy controller   Table 2

		change in error		
		$ce_1 = -0.5$	$ce_2 = 0$	$ce_3 = 0.5$
Error	$e_1 = 0$	0.1	0	0
	$e_2 = 40$	0.2	0.1	0
	$e_3 = 80$	0.3	0.2	0.1
	$e_4 = 120$	0.5	0.4	0.3
	$e_5 = 160$	0.7	0.6	0.3
	$e_6 = 200$	0.9	0.8	0.6
	$e_7 = 240$	1	1	0.8

the basal value of glucose concentration in blood:

$$G_r(t) = G_b.$$

The fuzzy inference mechanism is a Mamdani numerical table-based one [12], with the rules described in Table 2. At each iteration of the control algorithm the insulin dose is calculated as a weighted average of u_{ij} values in rule-table:

$$u(t) = \sum_{i=1}^{I} \sum_{j=1}^{J} w_{ij} u_{ij}, \qquad (3)$$

with the weights w_{ij} being inversely proportional to the "distance" between the $(e_i; ce_j)$ point and the currently measured pair $(e(t)); ce(t))$:

$$w_{ij} = 1 - \frac{(e_{i+1} - e_i)(ce_{j+1} - ce_j)}{(e(t) - e_i)(ce(t) - ce_j)}.$$

When the values of error and change in error are $e(t) = e_i$ or $ce(t) = ce_j$ (for any j), then the weights are calculated as:

$$w_{ij} = 1 - \frac{(ce_{j+1} - ce_j)}{(ce(t) - ce_j)},$$

or respectively as:

$$w_{ij} = 1 - \frac{(e_{i+1} - e_i)}{(e(t) - e_i)}.$$

When $e(t) = e_i$ and $ce(t) = ce_j$ the fuzzy controller's output is $u(t) = u_{ij}$.

4. Simulations Results and Discussion

To evaluate the controller's performance, a Matlab-Simulink model and the Matlab's Fuzzy Logic Toolbox were used. The two situations mentioned in previous section (A and B) were simulated. The results are depicted in Figures 2 and 3. For the B case, the glucose accumulation in blood due to the carbohydrates absorption for a diabetic patient is depicted in Figure 4.

In order to have a more realistic control, it was considered that the imaginary insulin deliver device adjusts the dosage every 5 minutes (Note the shapes of insulin dosage in Figures 2b and 3b.).

It is very unlikely to have a device that could change the injection rate in a time range of seconds. In terms of control engineering, this behaviour is described as a zero-order hold element, and it also allows a reasonable sampling time. In both cases, the glucose concentration returned to its basal value in the expected time range, and without crossing this value.
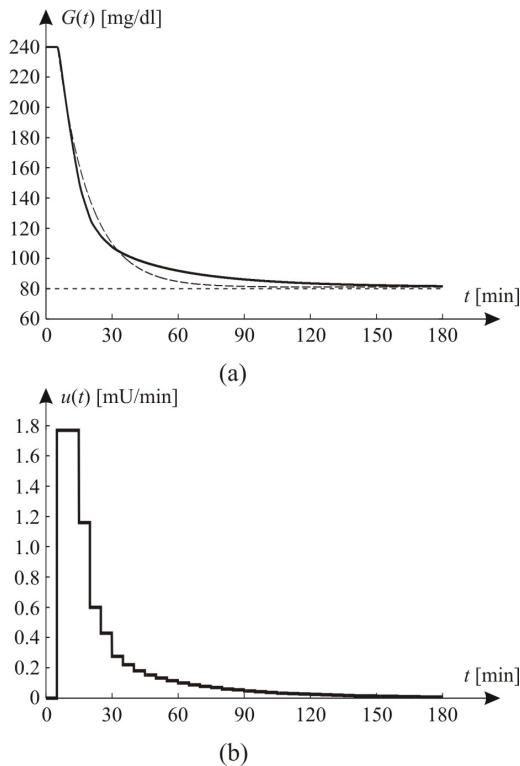
Fig. 2. *Glycemic control results: a) the blood glucose concentration in time from a high initial value to normal and b) the insulin injection rate (adjusted every 5 minutes) that produce this result*
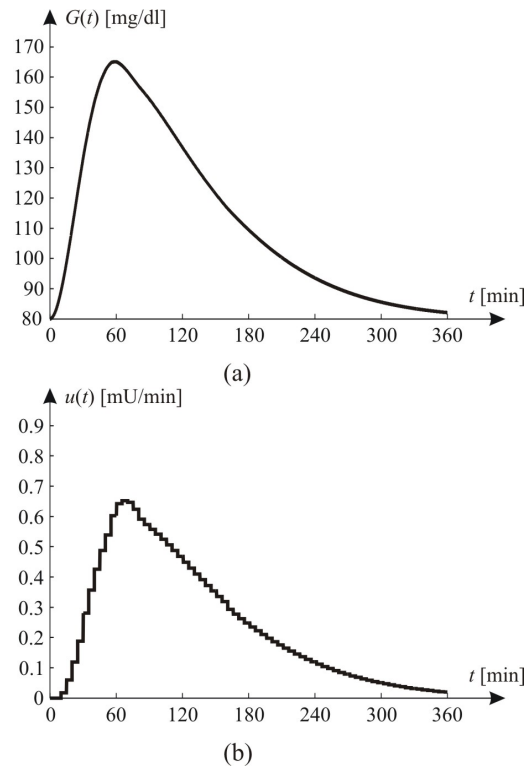
Fig. 3. *Glycaemia control results: a) the blood glucose concentration in time after having a meal with 50 g of carbohydrates, and b) the insulin injection rate (adjusted every 5 minutes) that produce this result*

5. Conclusions

When speaking about designing a system to control the blood glucose concentration ("artificial pancreas"), the caregivers' experience in T1DM treatment is the first to be considered. In most situations, their actions can be expresses in terms of fuzzy logic, which means that a fuzzy control algorithm gains enough motivation to be investigated. In fuzzy control theory, most applications follow a set of design guidelines that assures certain performance and an easy implementation.

In this paper, we proved the feasibility of using a fuzzy logic based simple solution to control the blood glucose concentration in the Bergman's minimal model.

The simulations of the system we presented suggest that fuzzy controller can assure control performances similar to those obtained by using more complex algorithms, as the intensively used model predictive control.

The controller assures a realistic return to normal values for the blood glucose concentration. More important, any overshoot value, which in this case means possible hypoglycaemia, was avoided.

The design procedure was quite easy and clear, and algorithm is easy to implement on any numerical device. The controller was obtained mainly from the experience in fuzzy control, but also following what it can be considered realistic results, as those described in today's literature.
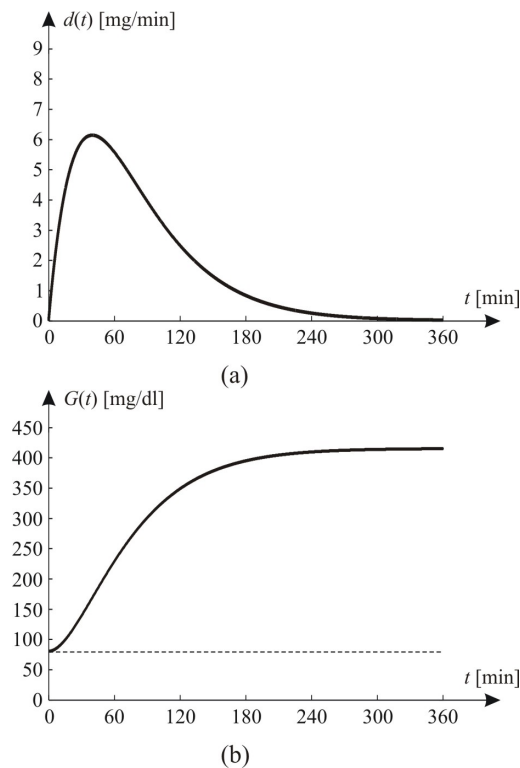
Fig. 4. *The glucose disturbance after having a meal: a) CHO absorption rate in time; b) the raise of glucose concentration for a T1DM patient from its initial value*

Acknowledgements

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