LPV Modeling of Type 1 Diabetes Mellitus

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Abstract: The paper investigates the possibility of modeling the highly nonlinear and very complex Sorensen model, [1], of Type 1 diabetic patients using the polytopic LPV modeling possibility. It is illustrated that the LPV model is working correctly only in the considered polytope region, but inside it is approximating well the nonlinear model.

Keywords: diabetes mellitus, glucose-insulin control, polytope region, LPV control

1 Introduction

Nowadays health experts refer to diabetes mellitus as the disease of the future. According to the statistics of the World Health Organization (WHO) an increase of the adult diabetes population from 4% (in 2000, meaning 171 million people) to 5.4% (366 million worldwide) is predicted by the year 2030, [2].

From engineering point of view, the treatment of diabetes mellitus can be represented by an outer control loop, to replace the partially or totally deficient blood-glucose-control system of the human body. However, the blood-glucose control is a diffcult problem to be solved. One of the main reasons is that patients are extremely diverse in their dynamics and in addition their characteristics are time-varying. Due to the inexistence of an outer control loop, patients are regulating their glucose level manually. Based on the measured glucose levels (obtained from extracted blood samples), they decide on their own what is the necessary insulin dosage to be injected. Although, this process is supervised by doctors (diabetologists), mishandled situations often appear. Hyper- (deviation over the basal glucose level) and hypoglycemia (deviation under the basal glucose level) are both dangerous cases, but on short term the latter is more dangerous, leading for example to coma.

To design an appropriate control, an adequate model is necessary. In the last 50 years several models appeared. The mostly used and also the simplest one proved to be the minimal model of Bergman, [3], [4], but its shortcoming is its big sensitivity to variance in the parameters. Therefore, extensions of this minimal model have been proposed [5], [6], [7], [8], trying to capture the changes in patient dynamics of the glucose-insulin interaction, particularly with respect to insulin sensitivity, or even the mixed meal characteristics, [9]. Other more general models appeared, [10], but the most complicated and detailed one proved to be the model of Sorensen, [1].

Due to its comlexity, only few researchers have investigated the modeling and control of the Sorensen model. Mostly linear robust H_∞ and MPC control methods appeared, [11], [12]. In this paper, the authors have been investigating the LPV modeling possibility, which deals directly with the non-linear properties of the Sorensen model.

2 The Sorensen Model for Type I Diabetic Patients

The glucose-insulin system of the human body used in this work is based on Sorensen model modified by [11]. Its compartmental representation is given by Figure 1. The eight equations for the glucose part are given below:

$$\dot{G}_B^C = \left(G_H^C - G_B^C\right)\frac{q_B}{v_B^C} - \left(G_B^C - G_B^T\right)\frac{v_B^T}{T_B v_B^C} \tag{1}$$

$$\dot{G}_B^T = \left(G_B^C - G_B^T\right)\frac{1}{T_B} - \frac{\Gamma_{BU}}{v_B^T} \tag{2}$$

$$\dot{G}_H^C = \left(G_B^C q_B + G_L^C q_L + G_K^C q_K + G_P^C q_P - G_H^C q_H - \Gamma_{RBCU}\right)\frac{1}{v_H^C} \tag{3}$$

$$\dot{G}_S^C = \left(G_H^C - G_S^C\right)\frac{q_S}{v_S^C} + \frac{\Gamma_{meal}}{v_S^C} - \frac{\Gamma_{SU}}{v_S^C} \tag{4}$$

$$\dot{G}_L^C = \left(G_H^C q_A + G_S^C q_S - G_L^C q_L\right)\frac{1}{v_L^C} + \frac{\Gamma_{HGP}}{v_L^C} - \frac{\Gamma_{HGU}}{v_L^C} \tag{5}$$

$$\dot{G}_K^C = \left(G_H^C - G_K^C\right)\frac{q_K}{v_K^C} - \frac{\Gamma_{KE}}{v_K^C} \tag{6}$$

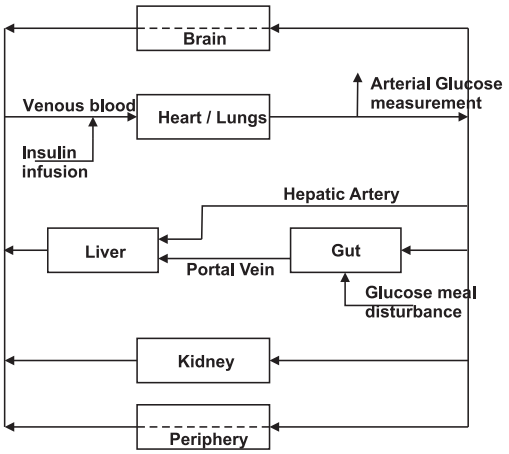

Figure 1
Compartmental representation of the Sorensen model, [11]

$$\dot{G}_P^C = \left(G_H^C - G_P^C\right)\frac{q_P}{v_P^C} + \left(G_P^T - G_P^C\right)\frac{v_P^T}{T_P^G v_P^C} \tag{7}$$

$$\dot{G}_P^T = \left(G_P^C - G_P^T\right)\frac{1}{T_P^G} - \frac{\Gamma_{PGU}}{v_P^T} \tag{8}$$

The seven insulin equations are:

$$\dot{I}_B^C = \left(I_H^C - I_B^C\right)\frac{Q_B}{V_B^C} \tag{9}$$

$$\dot{I}_H^C = \left(I_B^C Q_B + I_L^C Q_L + I_K^C Q_K + I_P^C Q_P - I_H^C Q_H + \Gamma_{IVI}\right)\frac{1}{V_H^C} \tag{10}$$

$$\dot{I}_S^C = \left(I_H^C - I_S^C\right)\frac{Q_S}{V_S^C} \tag{11}$$

$$\dot{I}_L^C = \left(I_H^C Q_A + I_S^C Q_S - I_L^C Q_L\right)\frac{1}{V_L^C} + \frac{\Gamma_{PIR}}{V_L^C} - \frac{\Gamma_{LC}}{V_L^C} \tag{12}$$

$$\dot{I}_K^C = \left(I_H^C - I_K^C\right)\frac{Q_K}{V_K^C} - \frac{\Gamma_{KC}}{V_K^C} \tag{13}$$

$$\dot{I}_P^C = \left(I_H^C - I_P^C\right)\frac{Q_P}{V_P^C} - \left(I_P^C - I_P^T\right)\frac{V_P^T}{T_P^I V_P^C} \tag{14}$$

$$\dot{I}_P^T = \left(I_P^C - I_P^T\right)\frac{1}{T_P^I} + \frac{\Gamma_{SIA}}{V_P^T} - \frac{\Gamma_{PC}}{V_P^T} \tag{15}$$

The other four equations which are composing the remaining states of the Sorensen model are the glucagon and three additional (undimensional) variables:

$$\dot{N} = \left(\Gamma_{PNR} - N\right)\frac{F_{PNC}}{V_N} \tag{16}$$

$$\dot{A}_{IHGP} = \frac{1}{25}\left[1.2088 - 1.138\tanh\left(1.669\frac{I_L^C}{21.43} - 0.8885\right) - A_{IHGP}\right] \tag{17}$$

$$\dot{A}_{NHGP} = \frac{1}{65}\left[\frac{2.7\tanh\left(0.388N\right) - 1}{2} - A_{NHGP}\right] \tag{18}$$

$$\dot{A}_{IHGU} = \frac{1}{25}\left[2\tanh\left(0.549\frac{I_L^C}{21.43}\right) - A_{IHGU}\right] \tag{19}$$

It can be observed, that in the different equations the Γ_i parameter appears, which corresponds for the different metabolic sinks:

$$\Gamma_{BU} = 70 \tag{20}$$

$$\Gamma_{RBCU} = 10 \tag{21}$$

$$\Gamma_{SU} = 20 \tag{22}$$

$$\Gamma_{HGP} = 155A_{IHGP}\left[2.7\tanh(0.388N) - A_{NHGP}\right]\cdot\left[1.425 - 1.406\tanh\left\{0.6199\left(\frac{G_L^C}{101} - 0.4969\right)\right\}\right] \tag{23}$$

$$\Gamma_{HGU} = 20A_{IHGP}\left[5.6648 + 5.6589\tanh\left\{2.4375\left(\frac{G_L^C}{101} - 1.48\right)\right\}\right] \tag{24}$$

$$\Gamma_{KE} = \begin{cases} 71 + 71\tanh\left[0.011\left(G_K^C - 460\right)\right] & ,if\ \ G_K^C < 460\,\frac{mg}{dl} \\ 0.872G_K^C - 300 & ,if\ \ G_K^C \geq 460\,\frac{mg}{dl} \end{cases} \tag{25}$$

$$\Gamma_{PGU} = \frac{35G_P^T}{86.81}\left[7.035 + 6.51623\tanh\left\{0.33827\left(\frac{I_P^T}{5.304} - 5.82113\right)\right\}\right] \tag{26}$$

$$\Gamma_{LC} = F_{LC}\left(I_H^C Q_A + I_S^C Q_S + \Gamma_{PIR}\right) \tag{27}$$

$$\Gamma_{PIR} = 0 \tag{28}$$

$$\Gamma_{KC} = F_{KC} I_K^C Q_K \tag{29}$$

$$\Gamma_{PC} = \frac{I_P^T}{\frac{1 - F_{PC}}{F_{PC}} \frac{1}{Q_P} - \frac{1}{T_P^I V_P^T}} \tag{30}$$

$$\Gamma_{PNR} = \left[1.3102 - 0.61016 \tanh\left\{ 1.0571 \left(\frac{I_H^C}{15.15} - 0.46981 \right) \right\} \right] \cdot$$

$$\cdot \left[2.9285 - 2.095 \tanh\left\{ 4.18 \left(\frac{G_H^C}{91.89} - 0.6191 \right) \right\} \right] \tag{31}$$

The values of the used constants can be seen in Table 1, [11].

Table 1
Parameter values for the Sorensen model, [11]

[dL]	[L]	[dL/min]	[L/min]	[L/min]	[min]
$v_B^C = 3.5$	$V_B^C = 0.265$	$q_B = 5.9$	$Q_B = 0.45$	$F_{PNC} = 0.91$	$T_B = 2.1$
$v_B^T = 4.5$	$V_H^C = 0.985$	$q_H = 43.7$	$Q_H = 3.12$	$F_{LC} = 0.4$	$T_P^G = 5.0$
$v_H^C = 13.8$	$V_S^C = 0.945$	$q_S = 10.1$	$Q_S = 0.72$	$F_{KC} = 0.3$	$T_P^I = 20$
$v_S^C = 11.2$	$V_L^C = 1.14$	$q_L = 12.6$	$Q_L = 0.9$	$F_{PC} = 0.15$	
$v_L^C = 25.1$	$V_K^C = 0.505$	$q_A = 2.5$	$Q_A = 0.18$		
$v_K^C = 6.6$	$V_P^C = 0.735$	$q_K = 10.1$	$Q_K = 0.72$		
$v_P^C = 10.4$	$V_P^T = 6.3$	$q_P = 15.1$	$Q_P = 1.05$		
$v_P^T = 67.4$	$V_N = 9.93$				

The notation of the indexes are:

- A - hepatic artery
- B - brain
- BU - brain uptake
- C - capillary space
- G - glucose
- H - heart and lungs

- HGP - hepatic glucose production
- HGU - hepatic glucose uptake
- I - insulin
- IHGP - insulin effect on HGP
- IHGU - insulin effect on HGU
- IVI - intravenous insulin infusion
- K - kidney
- KC - kidney clearance
- KE - kidney excretion
- L - liver
- LC - liver clearance
- N - glucagon
- NHGP - glucagon effect on HGP
- P – periphery (muscle / adipose tissue).
- PC - peripheral clearance
- PGU - peripheral glucose uptake
- PIR - pancreatic insulin release
- PNC - pancreatic glucagon clearance
- PNR - pancreatic glucagon release (normalized).
- RBCU - red blood cell uptake
- S – gut (stomach / intestine).
- SIA - insulin absorption into blood stream from subcutaneous depot
- SU - gut uptake
- T - tissue space

3 Linear Time Varying Systems

Linear Parameter Varying (LPV) system is a class of nonlinear system, where the parameter could be an arbitrary time varying, piecewise-continuous and vector valued function denoted by $\rho(t)$, defined on a compact set $\mathcal{P}$. In order to evaluate the system, the parameter trajectory is requested to be known either by measurement or by computation.

A formal definition of the parameter varying systems is given below.

Definition 1 For a compact $\mathcal{P} \subset \mathbf{R}^s$, the parameter variation set $F_{\mathcal{P}}$ denotes the set of all piecewise continuous function mapping $\mathbf{R}^+$ (time) into $\mathcal{P}$ with a finite number of discontinuities in any interval. The compact set $\mathcal{P} \subset \mathbf{R}^s$ along with the continuous functions A: $\mathbf{R}^s \to \mathbf{R}^{n\times n}$, B: $\mathbf{R}^s \to \mathbf{R}^{n\times n_u}$, C: $\mathbf{R}^s \to \mathbf{R}^{n_y \times n}$, D: $\mathbf{R}^s \to \mathbf{R}^{n_y \times n_u}$ represent an n^{th} order LPV system whose dynamics envolve as:

$$\begin{aligned} \dot{x}(t) &= A(\rho)x(t) + B(\rho)u(t) \\ y(t) &= C(\rho)x(t) + D(\rho)u(t) \end{aligned} \tag{32}$$

with $\rho(t) \in F_{\mathcal{P}}$, [13].

As a result, it can be seen that in the LPV model, by choosing the parameter variables, the system's nonlinearity can be hidden.

There are different descriptions of the LPV systems. In the affine description possibility, a part of the ρ(t) parameters are equal with the $x(t)$ states. However, due to the complexity of the Sorensen model, this representation is impossible to be done.

Polytopic representation could be another description of the LPV systems. In this case, the validity of the model is caught inside a polytope region and the model is built up by a linear combination of the linearized models derived in each polytope point, [14]:

$$\Sigma(t) \subset \{\Sigma_1,\ldots,\Sigma_2\} = \left\{ \sum_{i=1}^{j} \alpha_i \Sigma_i : \alpha_i \geq 0, \sum_{i=1}^{j} \alpha_i = 1 \right\} \tag{33}$$

where $\Sigma_i = \begin{bmatrix} A_i & B_i \\ C_i & D_i \end{bmatrix}$.

It is important to understand that the polyopic LPV model is valid only inside the polytopic region. During a simulation linear interpolation can be used, if necessary, [14].

4 LPV Modeling of the Sorensen Model

From the equations of the Sorensen model (as well as from Figure 1) one can observe, that the system has two inputs (Γ_{meal} meal disturbance and Γ_{IVI} the injected insulin amount) and one output, the capillary heart-lungs glucose concentration, G_H^C. However, we have considered an output for the insulin too, namely the peripheric insulin concentration in the capillaries, I_P^C.

During the process of choosing the polytopic points we have restricted to the physiological meanings. The first point was the normoglycaemic point (glucose concentration y $= G_H^C$ = 81.1 mg/dL and calculated insulin concentration was $I_{P\ init}^C$ = 26.6554 mU/L), while the other points were deflections from this point (given below in %):

- glucose concentrations: 25%, 50%, 75%, 100%, 150%, 200%;
- insulin concentrations: 0%, 25%, 50%, 100%, 150%, 200%.

The glucagon and the additional values were kept at their normoglycaemic value.

In the points of the so generated polytope region (36 points) we have determined one by one a linearized model and we have analyzed the stability, observability and controllability properties of them. We have concluded, that each system was stable, but the observabilty and controllability matrices did not have full rank (we have got 15 and 14 respectively).

Finally, we have simulated the so developed polytopic LPV system of the Sorensen model, and we have compared the results with [11].

For meal disturbance we have used the same six hour meal disturbance function of [15], filtered with an $\frac{1/60}{s+1/60}$ first order lag used by [11] (Figure 2), while the insulin input was considered zero.

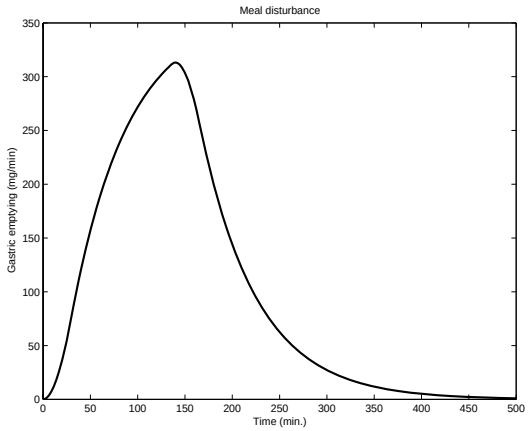

Figure 2
The glucose emptying function, [11]

Results are presented on Figure 3. It can be seen, that the LPV model is approximating with an acceptable error the nonlinear system. However, it can be also seen, that without an insulin injection the glucose concentration is going up to

an unacceptable value for a diabetic patient. It can be also seen, that for the considered polytope, the LPV system is stepping out from the phsiologically defined region.

Therefore we had to extend the polytope for the glucose concentration with other points too:

- glucose concentrations: 250%, 300%, 350%, 400%;

In this situation one can observe, that the LPV model remains inside the polytope region (Figure 4) and is correctly approximating the nonlinear model. Results are similar with those obtained by [11].

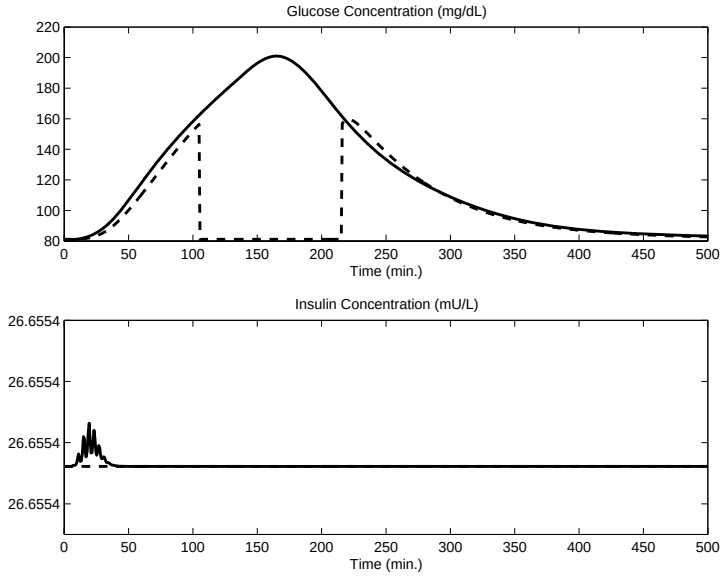

Figure 3
The simulation of the nonlinear Sorensen model (continuous) and the 36 points polytope region (dashed)

Conclusions

In this paper the polytopic LPV modelling possibility was investigated for the complex Sorensen model for Type 1 diabetic patients. It was illustrated that the LPV model is working only for the considered polytope region.

The constructed model approximated correctly the original nonlinear model. As a result in the future we will investigate the possibility of designing a robust LPV system for the Sorensen model.

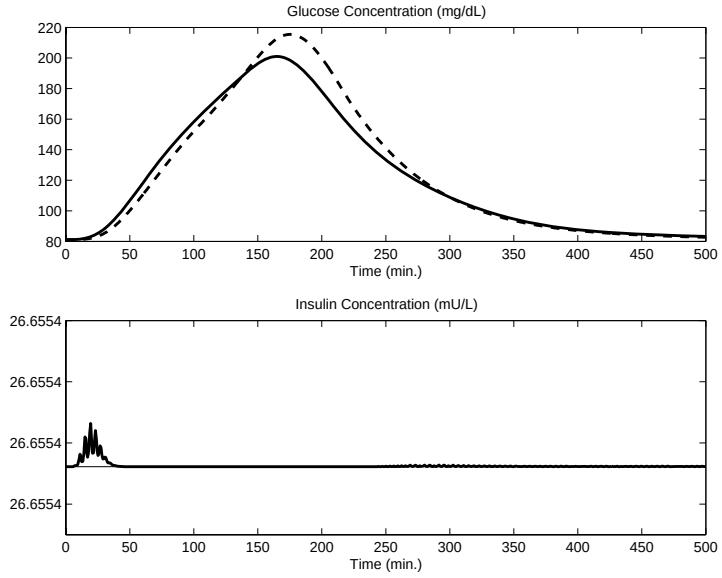

Figure 3
The simulation of the nonlinear Sorensen model (continuous) and the extended polytope region (dashed)

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