On The Use of Robust Servo Control in Diabetes Under Intensive Care

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Abstract: The robust servo control of a model-based biomedical application, namely the glucose-insulin control of diabetes patients under intensive care, is presented in the paper. The synthesis and analysis is based on a modified two compartment Bergman model and realized with a two degree of freedom controller structure permitting to assure insulin tracking. The augmented $\Delta - P - K$ structure is described with the necessary weighting functions. A non-conservative complex μ-synthesis method is applied. Using the controller, not only the robust stability is met under multiplicative uncertainty, but also the nominal performance i.e. the disturbance rejection is fulfilled. Food (sugar) intake is considered as disturbance. Closed loop simulation results are edged for optimizing the insulin amount.

Keywords: diabetes mellitus, glucose-insulin control, robust control, multiplicative uncertainty, μ-synthesis method

1 Introduction

Nowadays health experts refer to diabetes mellitus as the disease of the future. The newest statistics of the World Health Organization (WHO) shows that 4% of the adult society of the world suffers from diabetes mellitus, and this value could increase to 5,4% by the year 2025. 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.

The maintenance of the glucose level in a diabetic patient under intensive care is currently an actively researched topic in the field of Biomedical Engineering. Van den Berghe have shown, [1], that tight glucose control can reduce the Intensive Care Unit (ICU) patient mortality by 45% if the glucose level is kept less than 6.1

mmol/l for a cardiac care population. It was shown, the automated control algorithms, capable to tight regulation of glucose intolerant ICU patients, would reduce mortality, as well the current burden on ICU medical resources and time.

To design an appropriate control, an adequate model is necessary. In the last 50 years, a variety of models for the interaction between glucose and insulin have been suggested such as [2], [3], [4], [5], [6] and strategies have been designed and applied to the problem by [7], [8], [9], [10], [11], [12], [13].

However, the simplest model proved to be the minimal model of Bergman, [2], but its shortcoming is its big sensitive to variance in the parameters. Henceforward, the plasma insulin concentration must be known as a function of time. Therefore, extensions of this minimal model have been proposed by [3], [14], [15], [16], trying to capture the changes in patient dynamics of the glucose-insulin interaction, particularly in respect to insulin sensitivity.

The authors have been focused on the optimization of the amount of insulin under exogenous disturbance and mismatch. A modified version of Bergman's minimal model [10], [17], was used and it was tried to take parameter variance into account by robust control strategies applying complex parameter uncertainty. In the literature the H_∞ control proposed by [18] and H_2/H_∞ control, [19], has been already elaborated. The paper proposes the complex μ-synthesis in order to restructure the uncertainties for robustness and performance purposes.

Therefore, the paper is structured to give firstly a brief description of the model and the control strategy used and then it presents the simulation results made for the non-linear system with the linear controller in case of food (sugar) intake and comparing them with previous results.

2 Minimal Model-based Human Glucose-insulin System

To simulate the insulin-glucose interaction in human body the following two-compartment model was employed:

$$\begin{aligned} \dot{x}_1(t) &= p_1 x_1(t) + p_2 h(t) \\ \dot{x}_2(t) &= (p_3 - x_1(t)) x_2(t) + i(t) + p_4 \end{aligned} \tag{1}$$

where the parameters have been identified, [20]:

$$\begin{aligned} p_1 &= -0.021151 \\ p_2 &= 0.092551 \\ p_3 &= -0.014188 \\ p_4 &= 0.077947 \end{aligned} \tag{2}$$

The terms $h(t)$ and $i(t)$ are the exogenous glucose [g/100ml] and insulin inlets [μU/ml], $x_1(t)$ and $x_2(t)$ stand for the concentration of glucose in the plasma and for the concentration of the insulin remote from plasma. In our case $x_1(t)$ and $x_2(t)$ represent both the states and the output of the system, as the dynamical performances of the measurement and actuator devices are considerably faster than the system itself.

This modified, minimal model has been set for Type I diabetes patients under intensive care. The identified parameters cover only a relatively small part of these patients, so the previously designed controllers were true only for this set without the robustness of the controller. However, the obtained results, [10], [19], [21] encouraged the authors to extend the model with the use of robust controller. Therefore, robust techniques give the possibility to wider the parameter interval by supposing uncertain system.

Firstly, the nonlinear system was linearized in the vicinity of steady state, [21]. The obtained linear model is:

$$\begin{aligned} \dot{x} &= \begin{pmatrix} p_1 & 0 \\ \dfrac{p_4}{p_3} & p_3 \end{pmatrix} x + \begin{pmatrix} p_2 & 0 \\ 0 & 1 \end{pmatrix} u \\ y &= \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix} x + \begin{pmatrix} 0 & 0 \\ 0 & 0 \end{pmatrix} u \end{aligned} \qquad (3)$$

where $x(t)$ represents the state, $u(t)$ and $y(t)$ are the input and output relative variables. The linear system proved to be fully controllable and observable.

3 Robust Servo Control Design Using Complex μ Synthesis

In this section, the applied control theory is briefly summarized, in respect to the explanation of weights and structures. The nonlinear plant, described in the previous section could be linearized at an equilibrium point in order to create a nominal plant to linear μ synthesis. Both the linear and the nonlinear description suppose to have two inputs. One of them is the control input, the other is assumed to be disturbance for instant. The control input is the insulin inlet, the measured quantities are the insulin and glucose concentrations. The aim of the robust control under model mismatch is the disturbance rejection on insulin, the tracking of a predefined insulin reference, if needed. During the synthesis, one takes the input saturation into account, and the controller will be applied to the nonlinear plant with noise corrupted measurements. The robust two degree of freedom controller is realized by μ synthesis.

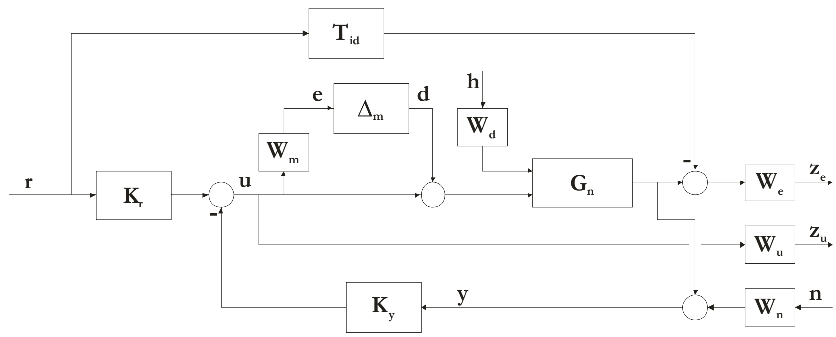

Figure 1
Augmented closed loop interconnection

Linear H_∞, respectively μ control syntheses are promising methods on the palette of the robust control systems. These postmodern techniques date back to around two decades [22]. Progressively it gains ground by the more and more powerful computational soft- and hardware, [23], [24]. One of the biggest advantages of these methodologies (beyond the well defined mathematical backgrounds) might be the robustness itself. Robustness against model mismatches, against disturbances. For robust control synthesis, let us consider the augmented system drawn in the Figure 1.

Consider the closed-loop system which includes the feedback structure of the model G_n and controller K, and elements associated with the uncertainty models and performance objectives. In the diagram, r is the reference, u is the control input, y is the output, n is the measurement noise, and z_e is the deviation of the output from the required one. The structure of the controller K may be partitioned into two parts: $K = [K_r\ K_y]$, where K_y is the feedback part of the controller and K_r is the pre-filter part.

Model based control systems use the mathematical abstraction of the actual plant to be controlled. However, vast identification techniques can be found in the literature, perfect fitting of the model-real plant does not exist. Therefore, the model (or nominal plant) always contains neglected dynamics of the real world. The nominal plant is usually a lower order system than the real plant, because highly complicated components are rather than modeled.

One widespread approach of describing uncertainties is the unstructured formulation. Even if the precise uncertainty dynamics is unknown, usually an upper bound could be defined in frequency domain in order to characterize the mismatch. Complex uncertainties, neglected dynamics, respectively their (frequency depending) bounds could be classified into several groups. Two major types (not counting the more complicated structures) of complex uncertainty could be distinguished; the additive and the multiplicative blocks (at the plant output or input for MIMO systems). The choice of the unmodeled dynamics is predestined by the engineer and by the application, since it hangs on the modelling aspects. Nevertheless, the choice is always to involve a certain amount of a priori information.

In our case, the input multiplicative uncertainty is preferred, because it specifies the digression, the frequency depending difference (in percentage) between the nominal and the actual plant. The formal definition of the multiplicative uncertainty is given by:

$$M(G_n, W_m) := \left\{ G : \left| \frac{G(i\omega) - G_n(i\omega)}{G_n(i\omega)} \right| \leq \left| W_m r(i\omega) \right| \right\} \qquad (4)$$

At each frequency, $|W_m(i\omega)|$ represents the percentage of the difference between all of the plants represented by $M(G_n, W_m)$ and the nominal plant model G_n. In that sense, $M(G_n, W_m)$ represents a set of possible plants, centered at G_n. On a Nyquist plot, at a given frequency ωs it can be thought as a disk of radius $|W_m(i\omega_s)G_n(i\omega_s)|$, centered at $G_n(i\omega_s)$. On the other hand, the complex-valued (sometimes vector) Δ_m is assumed to be stable and unknown with a H_∞ norm lower or equal to 1.

The linearized model in question said to be good fidelity up to 0.71 − 1 rad/min, but it degrades rapidly at higher frequency than 1 rad/min due to neglected nonlinear dynamics, cross channel coupling errors, actuator modeling error etc. These types of uncertainties will be modeled by complex valued, unstructured and input multiplicative representation. The multiplicative form is chosen for convenience because it permits the intuitive interpretation of the magnitudes of uncertainty in terms of relative error percentage.

The weighting function W_e chosen for tracking errors can be thought as penalty function. W_e should be large in frequency range where small errors are desired and small where larger errors can be tolerated. Advisedly, the choice of the weights can be performed. To achieve perfect tracking (i.e. integral action) W_e weights should be large at very low frequency to imitate integrator. At the same time, good tracking property and nominal model validity can be treated as a trade-off. Uncertain model can not be forced to assure nominal performance requirements.

T_{id} is the model matching function which generally is an ideal transfer function of the plant. It has been selected on the fact to react quickly on glucose disturbance. The control input is limited and can be (norm) saturated using performance criteria W_u. Using this weight the designer can penalize larger deflections and thereby minimize control activity. The simplest weight on insulin inlet is a constant term across the frequency and with a magnitude equal to the inverse of the maximal quantity.

Weighted sensor noises W_n and external disturbances W_d are input weights. Therefore, their selection is slightly different from the definition of output scales.

The role of weights for these signals is basically the opposite of the role of weights for output weights discussed so far. Inputs to the weights are signals whose frequency responses are flat and unit size. The weights themselves contain scale factors and frequency shaping that match the size, units and frequency content of the true inputs. Input weights can be either frequency dependent or constant.

Necessary and sufficient conditions for robust stability and robust performance can be formulated in terms of the structured singular value denoted as μ, 0. Now, the design setup in Figure 1 should be formalized as a standard design problem as illustrated in Figure 2. The augmented P-K structure can be created by applying the weighting functions given above and the inputs can be written as:

$$\tilde{w} = \begin{bmatrix} r & n & h \end{bmatrix}^T, \tilde{z} = \begin{bmatrix} z_e & z_u \end{bmatrix}^T \tag{5}$$

By introducing the lower LFT of the (P,K) pair, i.e. $M = F_l(P,K)$, one gets back the $\Delta - M$ structure (Figure 2). The robustness and performance analysis of the augmented plant can be fulfilled by the partition blocks of the M:

$$\begin{bmatrix} e \\ \tilde{z} \end{bmatrix} = \begin{bmatrix} M_{11} & M_{12} \\ M_{21} & M_{22} \end{bmatrix} \begin{bmatrix} d \\ \tilde{w} \end{bmatrix} \tag{6}$$

Assume that Δ_m is a member of the bounded subset:

$$\mathbf{B\Delta} = \left\{ \Delta_m \in \Delta \;\middle|\; \overline{\sigma}\{\Delta\}_m < 1 \right\} \tag{7}$$

where Δ is defined by:

$$\Delta = \left\{ diag\left(\delta_1^c I_{r_1}, \ldots, \delta_{m_c}^c I_{r_{m_c}}, \Delta_1, \ldots, \Delta_n\right), \delta_i^c \in C, \Delta_j \in C^{m_j \times m_j} \right\} \tag{8}$$

where the ith repeated complex scalar block is r_i x r_i and the jth full block is m_j x m_j.

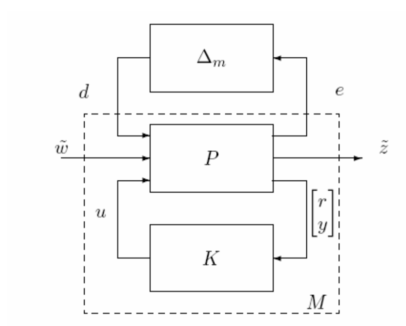

Figure 2
Generalized Δ – P - K structure

Robust stability is equivalent to:

$$\left\| M_{11} \right\|_{\infty} < 1 \tag{9}$$

The authors restrict the set of perturbation to $\Delta \in \mathbf{B\Delta}$ and therefore condition (9) might be conservative. A less conservative solution of the problem is to structure uncertainties. This is the structured singular value μ. The structured singular value can be defined as:

$$\mu_{\Delta}(M) = \frac{1}{min_{\Delta}(\overline{\sigma}\{\Delta\} : \Delta \in \Delta, det(I + \Delta M) = 0)} \tag{10}$$

unless no $\Delta \in \mathbf{\Delta}$ makes $I\text{-}M\Delta$ singular, in which case $\mu_{\Delta}(M)=0$. Thus $1/\mu_{\Delta}(M)$ is the "size" of the smallest perturbation Δ, measured by its maximum singular value, which makes $det(I\text{-}M\Delta) = 0$.

From definition of μ, the robust stability can be reformulated as:

$$\sup_{\omega} \mu(M_{11}) < 1 \Leftrightarrow \left\| \mu(M_{11}) \right\|_{\infty} < 1 \tag{11}$$

The main goal of our synthesis is to guarantee robust performance (RP). The closed-loop system achieves robust performance if the performance objective is met:

$$\sup_{\omega} \mu(M) < 1 \Leftrightarrow \left\| \mu(M) \right\|_{\infty} < 1 \tag{12}$$

The aim of the μ synthesis is to minimize the peak value of $\mu_{\Delta}(.)$ of the closed-loop M for all stabilizing controllers K, [23].

4 Example

In this section the robust servo glucose-insulin controller is designed and applied through the model-based diabetic patient system.

First, the weighting functions are defined and then a two degree of freedom μ synthesis demonstrates the necessity of structuring uncertainties. Unlike the control synthesis, the closed loop simulation was experimented on nonlinear plant given by (1).

The first step (the control synthesis) is the choice of the input multiplicative weight W_m, comprehending the neglected actuator dynamics. At low frequency, where the linear model is supposed to be satisfactory, the relative mismatch was adjusted to 10%. Moreover, above 1 rad/min it starts to grow up (the cross over frequency is about 30 rad/min) and at higher frequency shape the linear model is fully uncertain, the weight is over 100%.

The ideal tracking model T_{id} from the reference to the insulin measured output is a first order lag with $T = 120$ min time constant (due to Oral Glucose Tolerance Test measurements) and unity steady-state gain.

To assure good tracking performance W_e was increased at lower frequency up to 100. Therefore, based on the small gain theorem [24], the permitted tracking error in this range is over 0.01 μU/ml. More the weight is decreased in frequency, more the tracking slip is larger.

Uncertain system can not be forced to properly follow the reference signal. A slightly damped dynamic input weight is applied to filter the disturbance input, the glucose inlet. The cut off frequency of the W_d is around 20 rad/min.

Usually, measurement noise corrupts the outputs. The general percentage of the incorporating noise, by channel, might not be over 2 − 5%. During the design process the W_n anticipates 5% measurement noise. The synthesis is high sensitive even for a moderated change in the error term of insulin noise.

The control input, i.e. the insulin inlet was maximized, because one can not use as many control energy as desired. The input inverse scale W_u permits to use a maximal, normalized and constant control input 38.525 μU/ml, [18].

Using the defined weights, the nominal linear plant was augmented and the structure is shown in the Figure 1. It can easily understand, by adopting the H_∞ synthesis method (ex. γ iteration), that the robust performance prescription can not be achieved. Note, adequate H_∞ control could be found by modifying the weights. A less conservative solution might be the μ synthesis by D − K iteration for complex uncertainty, [23]. An iteration summary is shown in the Table 1. Fortunately, even the third (frequency depending) D-scales assures the robust stability, because the computed, scaled μ value is under 1.

Testing the robust servo controller, a food intake (as a disturbance) was considered. The disturbance was simulated as a sugar absorption in the body accordingly to our clinical experiments described by:

$$h(t) = 0.05 \cdot e^{-\frac{(t-10)^2}{45}} \tag{13}$$

Table 1

Differences between the H_∞ controller and μ-synthesis

Iteration	1	2	3
Controller Order	6	12	12
D-Scale Order	0	6	6
γ Achieved (H∞)	1.563	1.115	1.018
Peak value of μ	1.099	1.006	0.997

Furthermore, the time domain behavior of uncontrolled system for the above glucose intake shows that the insulin drops back to 2.2 μU/ml in 50 minutes, 0.

Figure 3 presents the applied control input (μ controller, without plant perturbation). During the different control strategies the glucose output remains the same (Figure 4).

However, in case of insulin, results are very promising (Figure 5) optimizing the necessary insulin dosage. Moreover, Figure 5 compares the μ closed-loop control under uncertainty (an input multiplicative uncertainty was used), respectively without model mismatch. The tracking performance is perturbed when the uncertainty is taken into account, since by a simple additive relation it augments the control input activity. Results have been simulated in situation without output noise, because the noise masks the variation of the insulin output presented in Figure 5.

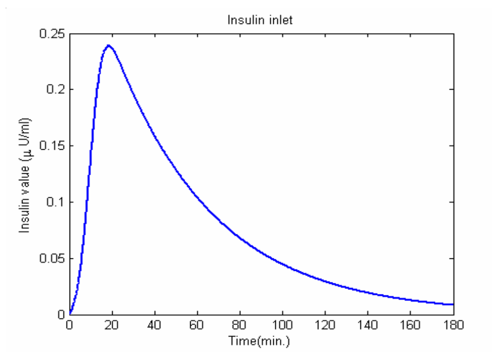

Figure 3

The necessary control input

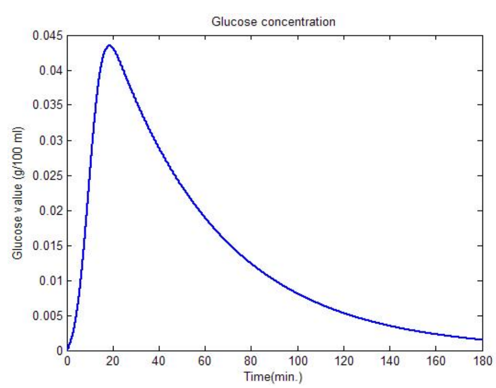

Figure 4

Glucose variation on the output

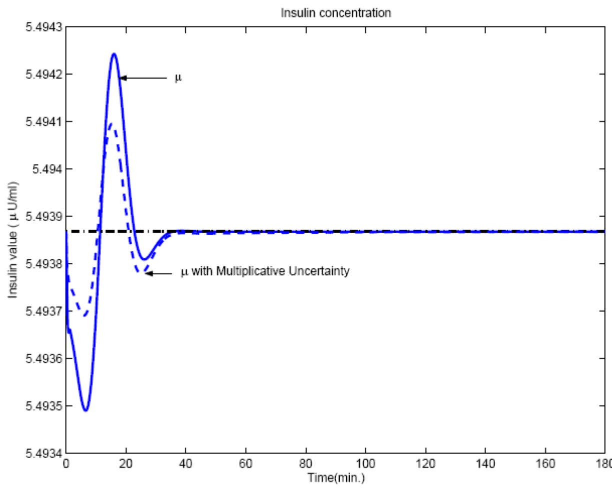

Figure 5

μ controller with and without uncertainty

Conclusions

Linear robust μ-synthesis design was applied to assure robust performance with structuring the uncertainty description of model-based glucose-insulin system. The paper exemplifies the robust control design technique for a useful biomedical application.

Diabetes mellitus is a very serious disease and its on-line control is an important research topic in nowadays. By the selected model and control algorithm, it could give advantage in practical realization. The model and the applied control strategies are not implemented yet, but after the necessary further verifications they could provide a useful help to control the blood glucose level.

Future research can be supported on mixed uncertainties. Other class of biomedical systems will be examined.

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