ROBUST CONTROL ALGORITHMS FOR BLOOD GLUCOSE CONTROL USING MATHEMATICA

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ABSTRACT

Application of modern robust control methods using Mathematica are presented in this case-study for blood glucose control of Type I diabetic patients under intensive care. The methods are applied on the minimal model of Bergman [1], using computer algebra. Two modern robust control methods are exemplified: the disturbance rejection LQ control or minimax control (as an extension of the classical LQ control) and the robust H_∞ control. It is shown the minimax control has limitations in practice, but employing reduced Gröbner basis on rational field, it is possible to approximate the theoretical solution and so getting a better solution than LQ does. In case of H_∞ control, the graphical method in frequency domain – implemented under Mathematica by [2] – is extended with a disturbance rejection constraint and the robustness of the resulted high-order linear controller is demonstrated by nonlinear closed loop simulation in state-space, in case of standard meal disturbances. The symbolic and numeric computations were carried out with Mathematica 5.2 and with its CSPS Application, as well as with MATLAB 6.5.

Keywords: *Glucose control, minimax control, H_∞ control, reduced Gröbner basis, Mathematica*

1. INTRODUCTION

In many biomedical systems, external controller provides the necessary input, because the human body could not ensure it. The outer control might be partially or fully automated. The self-regulation has several strict requirements, but once it has been designed it permits not only to facilitate the patient's life suffering from the disease, but also to optimize (if necessary) the amount of the used dosage.

Due to the extremely diverse dynamics of the patients, the blood-glucose control is one of the most difficult control problems to be solved in biomedical engineering.

It was several times formulated [3], [4], [5] that closed-loop glucose regulation requires three steps: a glucose sensor, an insulin pump, and a control algorithm able to determine (based on the glucose measurements) the necessary insulin dosage.

Regarding the control strategies applied, the palette is very wide [6], starting from classical control strategies like PID control [7], optimal control [8], to the modern control techniques like adaptive control [9], neuro-fuzzy algorithms [10], model predictive control [3], [11], [12], but also post-modern control strategies, like H_∞ control [4], [5], H_2/H_∞ control [13], μ-synthesis [14], Linear Parameter Varying (LPV) technique [15].

To design an optimal, high quality control, one needs a relevant model of the process as well as a proper control technique. Classical control is not a benefic solution, if high level of performance is desired [3].

The article presents modern robust control methods of the Bergman minimal model [1] of Type I diabetic patients under intensive care using computer algebra under *Mathematica*: the disturbance rejection LQ control or minimax control (as extension of the classical LQ control) and the robust H_∞ control.

First the minimax control is presented and it is shown that it has limitations in practice. However, employing reduced Gröbner basis on rational field, it is possible to approximate the obtained theoretical solution and so getting a better solution than LQ does.

In case of H_∞ control, for the graphical method in frequency domain implemented under *Mathematica* by [2] an extension, a disturbance rejection constraint is proposed for the requirement envelope. The robustness of the resulted high-order linear controller is demonstrated by nonlinear closed loop simulation in state-space, in case of standard meal disturbances.

The symbolic and numerical computations were carried out with *Mathematica* 5.2, with its Control System Professional Suite Application (CSPS), as well as with MATLAB 6.5.

2. MATERIALS AND METHODS

2.1. Model equations

Several different models of diabetic systems exist in the literature including, for example, the very detailed 21th-order metabolic model of Sorensen [16]. However, to have a system that on one hand, can be readily handled from the point of view of control design, but on the other hand represents the biological process properly, the authors considered Bergman's three-state minimal patient model [2]:

$$\begin{aligned}\dot{G}(t) &= -p_1 G(t) - (G(t)+G_B)X(t) + h(t)\\ \dot{X}(t) &= -p_2 X(t) + p_3 Y(t)\\ \dot{Y}(t) &= -p_4 (Y(t)+Y_B) + i(t)/V_L\end{aligned} \tag{1}$$

where the three state variables (as well as outputs) are the plasma glucose deviation $G(t)$ (mg/dL), remote compartment insulin utilization $X(t)$ (1/min), and plasma insulin deviation $Y(t)$ (mU/dL). The control variable is the exogenous insulin infusion rate, $i(t)$ (mU/min), whereas the exogenous glucose infusion rate $h(t)$ (mg/dL min) represents the disturbance.

Other variables represent parameters of system (1). The physiological parameters are G_B the basal glucose level (mg/dL), Y_B basal insulin level (mU/dL), V_L the insulin distribution volume (dL) and p_1, p_2, p_3, p_4 represent the model parameters.

As numerical values the authors worked with the numerical values determined by [17]: p_1 = 0.028, p_2 = 0.025, p_3 = 0.00013, p_4 = 5/54, G_B = 110, Y_B = 1.5, V_L = 120.

In order to linearize the system, we need its steady-state values: $G_0 = X_0 = Y_0 = 0$, $h_0 = 0$, and for $i_0 = p_4 Y_B V_L = 16.667$.

Loading CSPS of *Mathematica* the linearized system around the vicinity of the steady-state can be calculated.

The system proved to be stable, controllable and observable, so we can move to the control algorithm.

2.2. The LQ and Minimax control methods

It is well-known [18], that the dynamics of an LTI (linear time invariant) system can be described in general form by:

$$\begin{aligned} \dot{x}(t) &= Ax(t) + Bu(t) \\ y(t) &= Cx(t) \end{aligned} \tag{2}$$

where A, B, C are constant matrices.

Using a classical LQ control, the requirement on designing is to minimize the following quadratic cost functional:

$$J(u,d) = \frac{1}{2}\int_0^\infty [\, y^T(t)Qy(t) + u^T(t)Ru(t)]dt \tag{3}$$

where Q and R are positive definite matrices. The classical LQ attempts to find an optimal control $u^*(t)$, $t \in [0,\infty]$, based on CARE (Control Algebraic Riccati Equation):

$$J(u^*) \leq J(u) \tag{4}$$

for all $u(t)$ on $t \in [0,\infty]$. So, LQ realizes an optimization in the "average" direction, [18].

For the considered glucose-insulin interaction (1), because the first component of $u(t)$ states for disturbance (representing the glucose intake in the human body which disturbs the steady-state level), it must be eliminated from LQ control.

Therefore, considering the R matrix its R_{11} component should be considerably greater than R_{22}. As a result we have chosen:

$$R = \begin{pmatrix} 1000 & 0 \\ 0 & 0.001 \end{pmatrix}, \quad Q = \begin{pmatrix} 0.001 & 0 \\ 0 & 0.001 \end{pmatrix} \tag{5}$$

As a result, the LQ gain (KLQ) can be determined by solving CARE, [19]:

$$KLQ = \begin{pmatrix} 0 & 0 \\ -0.467069 & 2.62107 \end{pmatrix} \tag{6}$$

The disturbance rejection LQ method represents a generalization of the classical LQ problem [18], and is based on the minimax criteria, where the system dynamics are generally described as before, (2).

Now the input variable $u(t)$ is separated in control input $\bar{u}(t)$ and disturbance $d(t)$, which can be considered unmeasurable:

$$\begin{aligned} \dot{x}(t) &= Ax(t) + B\bar{u}(t) + Ld(t) \\ y(t) &= Cx(t) \end{aligned} \tag{7}$$

Therefore, in this situation the quadratic cost functional will be modified with the disturbance explicitly:

$$J(\bar{u},d) = \frac{1}{2}\int_0^\infty [\, y^T(t)y(t) + \bar{u}^T(t)\bar{u}(t) - \gamma^2 d^T(t)d(t)]dt \tag{8}$$

Now, the disturbance – while it appears with negative sign – attempts to maximize the cost, while we want to find a control $\bar{u}(t)$ that minimizes the maximum cost achievable by the disturbance (by the worst case disturbance).

This is a case of the so called "worst-case" design and leads to the formulation of the following differential-game:

$$\max_{d(t)} J(\bar{u},d) \rightarrow \min_{\bar{u}(t)} J(\bar{u},d) \tag{9}$$

$\bar{u}(t)$, $d(t)$ satisfying the state equation. It was demonstrated [18] that the solution of the differential-game (9) exists, is unique and satisfies the saddle point condition:

$$J(\bar{u}^*, d) \leq J(\bar{u}, d) \leq J(\bar{u}, d^*) \tag{10}$$

where $\bar{u}^*$ is the optimal control and d^* is the worst-case disturbance.

As a result, the optimal control and the worst-case disturbance are given by:

$$\bar{u}^*(t) = -B^T P x^*(t) \tag{11}$$

$$d^*(t) = \frac{1}{\gamma^2} L^T P x^*(t) \tag{12}$$

where P is the positive definite symmetric solution of the modified control algebraic Ricatti equation (MCARE):

$$PA + A^T P + C^T C - P(BB^T - \frac{1}{\gamma^2} LL^T)P = 0 \tag{13}$$

2.3. Solving the MCARE with Mathematica

Due to the fact that the not measurable $X(t)$ variable (remote compartment insulin utilization), is a slow variable [20], it can be considered zero, and so the second equation of the model (1) can be eliminated [21]. As a result the reduced linearized model becomes [22]:

$$\dot{x}(t)=\begin{pmatrix}-p_1-\frac{p_3Y_0}{p_2} & -\frac{(G_0+G_B)p_3}{p_2}\\ 0 & -p_4\end{pmatrix}x(t)+\begin{pmatrix}1 & 0\\ 0 & \frac{1}{V_L}\end{pmatrix}u(t)$$
$$y(t)=\begin{pmatrix}1 & 0\\ 0 & 1\end{pmatrix}x(t)+\begin{pmatrix}0 & 0\\ 0 & 0\end{pmatrix}u(t) \qquad (14)$$

For the solution of the MCARE equation we are looking for a symmetric solution $P=\begin{pmatrix}P_{11} & P_{12}\\ P_{21} & P_{22}\end{pmatrix}$. The complete step-by step solution under Mathematica notebook realized by the authors can be found on Wolfram Research site [19].

The critical solution of this system belongs to the critical value of the parameter γ. Crossing with γ this critical value, the solution which is real becomes imaginary and vice versa. This critical solution numerically is an ill-conditioned problem; therefore, the computation was carried out using reduced Gröbner basis on rational field, which provides solution for the unknown variables with infinite precision avoiding round-off errors. Substituting the values of the system parameters in rational form and determining the solution for the P_{11} value, the result was obtained as a fourth order monomial with γ as parameter [19], [21]. Creating a function providing the first root of this monomial, $\mathrm{Im}(P_{11}(\gamma))$, the critical value is the smallest nonzero positive root, namely [21], [22]:

$$\gamma_{crit}=\min_{\gamma>0}\left(Im\left(P_{11}(\gamma)\right)=0\right) \qquad (15)$$

Starting form a lower bound using step size Δ, the location of the critical value can be approximated with error $\varepsilon\le\Delta$. Choosing $\varepsilon = 10^{-8}$ the critical value resulted is $\gamma_{crit}=17.11742594$. Employing MATLAB v.6.5 by using the interval halving method, the same result was obtained.

However, the controller corresponding for this obtained γ_{crit} critical solution, $KLQrej=\begin{pmatrix}-0.5785 & 4.2671\\ 10.4192 & -74.5880\end{pmatrix}$ clearly shows that there is a compensation on the disturbance (glucose) part too.

This means some kind of negative injection of the glucose in the body, which is physically not possible. On the other hand, if one cancels the feedback of the disturbance and considers only the effect of the control input, no positive definite solution is obtained, and an unstable system is resulted [22]. This means that the minimax control has limitations in practice.

However, increasing the value of γ up to the value providing a positive definite solution, the question is that if in the close neighborhood of the above mentioned critical solution can we get a better result than LQ does. Investigating the above mentioned concrete situation, we have obtained a positive definite solution at $\gamma_{crit}^{*}=17.1602$ value (somewhat at 0.25 % of the γ_{crit}).

For this situation the control matrix $KLQrej=\begin{pmatrix}0 & 0\\ -59.619 & 415.648\end{pmatrix}$ provides a stable system.

2.4. H∞ control using Mathematica

The concepts of H_∞ control under *Mathematica* are presented in [2] and it represents a graphical designing procedure which differs from the literature and MATLAB approach.

The aim of the graphical method in frequency domain is to fit the complementary sensitivity function, $T(s)=\frac{P(s)C(s)}{1+P(s)C(s)}$ inside a defined requirement envelope. For this, briefly the following criteria set should be satisfied (Fig. 1):

1. T must satisfy the disk inequality:

$$\left|K(i\omega)-T(i\omega)\right|\le R(i\omega),\ \text{for } \omega_a\le\omega\le\omega_b, \qquad (16)$$

   where K and R are fixed functions that embody the desired specifications of the system. K is called the center of the disk and R is called the radius;
2. Defining the gain-phase margin as $m=inf\left|1+PC\right|$, the constraint should be:

$$\left|T(i\omega)-1\right|\le\frac{1}{m},\ \text{for all } \omega; \qquad (17)$$

3. The bandwidth of the complementary sensitivity function ($T(i\omega)$) should be below than $1/\sqrt{2}$ or in other words below -3 dB [18];
4. For the closed-loop roll-off, specifying a given n and α_r as well as the roll-off frequency ω_r for which the $C(i\omega)\le\frac{\alpha_r}{|\omega|^n}$ inequality is held, then for large ω frequencies it is true that $T(i\omega)\le\left|P(i\omega)C(i\omega)\right|$, or by other words:

$$\left|T(i\omega)\right|\le\alpha_r\frac{\left|P(i\omega)\right|}{|\omega|^n},\ \text{for } |\omega|>\omega_r. \qquad (18)$$

In addition our investigations showed [21], that with an additional condition for the disturbance rejection requirement, the requirement envelope can be smoothed. Considering $P_d(s)$ the transfer function of the disturbance and having the sensitivity transfer function (1-$T(s)$), the inequality should be, [23]:

$$\left|1-T(i\omega)\right|\le\frac{c}{\left|P_d(i\omega)\right|}, \qquad (19)$$

where c is a constant less then 1.

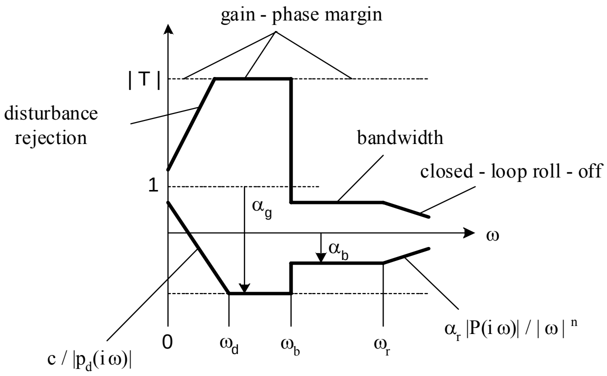

Fig. 1 Requirement envelope for robust control design in frequency domain

In order to insure the control purposes as well as the proper performance of the optimized process, the following performance requirements were chosen [23]: $c = 0.95$; $\alpha_r = 8.7641*10\text{-}7$; $n = 2$; $\omega_d = 2.65$; $\omega_b = 4$; $\omega_r = 6.5$; $\alpha_g = 2.5$; $\alpha_b = 0.9$.

As a result, we have obtained a subunitary solution of the H_∞ suboptimal problem, namely $\gamma^* = 0.3679$. This value was also checked with the mu-toolbox of Matlab and a very similar result was obtained.

With γ^* calculated, we have checked the performance requirements similarly as in [24]. The numerical values of the corresponding optimal T^* was approximated with a proper rational function, in our case a 20th order one, and having $P(s)$ known the transfer function of the control part, $C(s)$ can be determined, [23].

3. RESULTS

The performance of the control algorithms investigated above was tested for a standard meal disturbance with about six hour duration, modeled by [20] (Fig. 2).

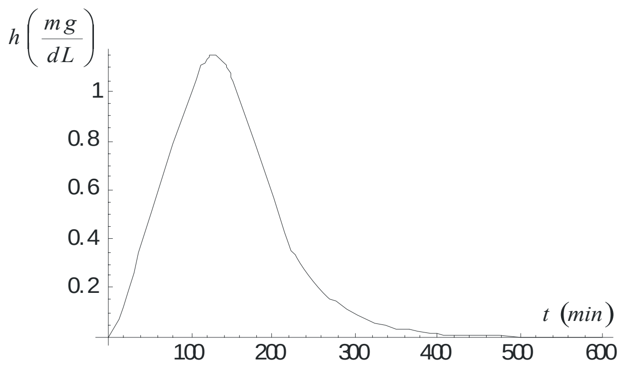

Fig. 2 Considered exogenous glucose infusion (meal disturbance), by [20]

3.1. Simulation results for the Minimax control

Although, the controller design was carried out for the reduced 2-states linear model (see section 2.3), the system is simulated for the original 3-states nonlinear model.

Comparing the results of the classical LQ control and minimax control for γ_{crit} corresponding to the physiologically interpretable case ($\gamma_{crit}^* = 17.1602$), it can be seen that even in this considered case, the disturbance rejection LQ control is more efficient than the classical LQ (Fig. 3, Fig. 4).

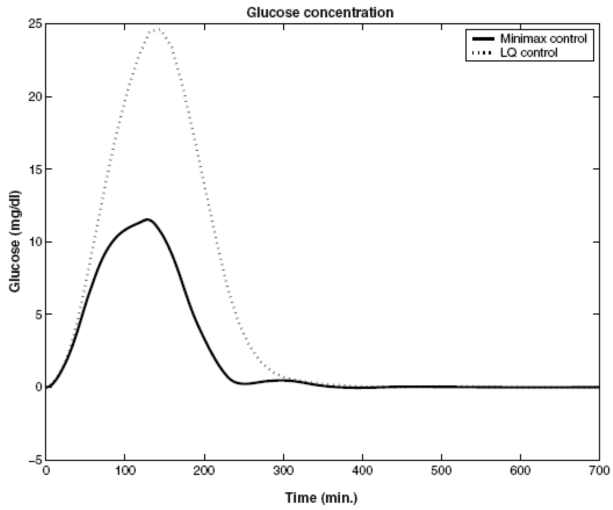

Fig. 3 Blood glucose concentration, $G(t)$ for LQ and "modified" minimax control

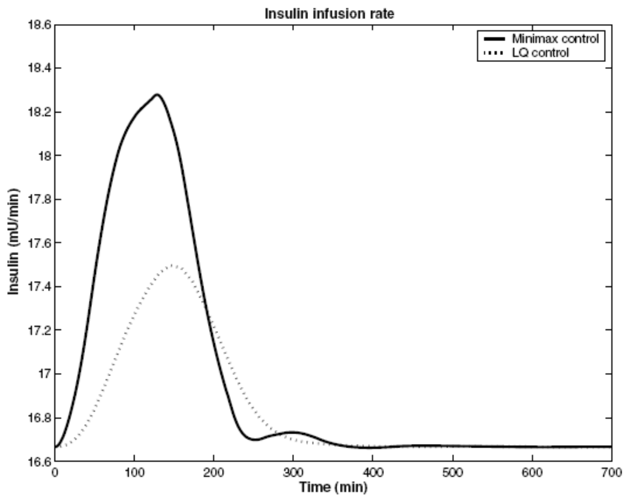

Fig. 4 Insulin infusion rate, $i(t)$ in case of LQ and "modified" minimax control

3.2. Simulation Results for the H_∞ Method

For the H_∞ method, the controlled dynamics of the blood glucose and insulin infusion are presented in Fig. 5 and Fig. 6.

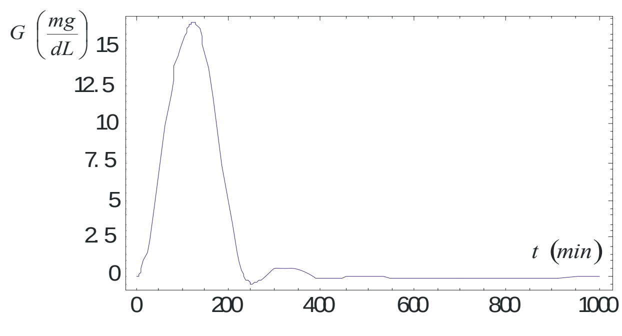

Fig. 5 Controlled dynamics of blood glucose concentration, $G(t)$

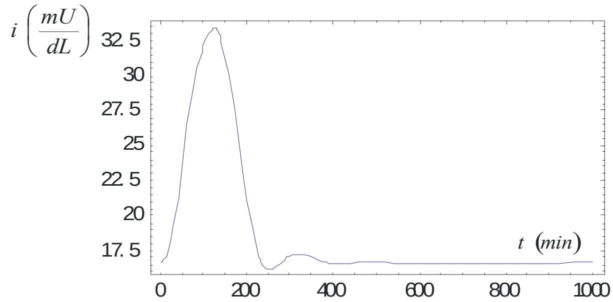

Fig. 6 The corresponding insulin infusion rate, $i(t)$

4. CONCLUSIONS

The case study presented two robust control methods using graphical interpretation and representation under *Mathematica* to regulate glucose-insulin system for Type I diabetic patients under intensive care.

For the minimax control it turned out that the critical value of γ together with the physically / physiologically realizable interpretation of a control system, will not ensure automatically a positive definite solution, if one needs a physically interpretable solution. This means that the minimax method determines the worst-case solution, but this depends on the concrete problem if it could be or could be not physically interpreted. However, even in this case it is possible to obtain a better solution than LQ does.

However, this problem can be avoided by using another numerical technique, employing the H_∞ control under *Mathematica* developed by [2]. In this case one may define a linear, high order compensator, in relatively easy way, which can be tested via nonlinear model simulation. Introducing a proper disk inequality constraint for disturbance rejection, this method is proved to be effective for providing acceptable control performance.

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