Robust H_∞ Blood – Glucose Control with *Mathematica*

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Abstract: A robust control design on frequency domain using Mathematica is presented for regularization of glucose level in Type I diabetes persons under intensive care. The method originally proposed under Mathematica by Helton and Merino, [1] – now with an improved disturbance rejection constraint inequality – is employed, using the three-state minimal patient model of [2]. The robustness of the resulted high-order linear controller is demonstrated by nonlinear closed loop state-space simulation, in case of standard meal disturbances and compared with H∞ design implemented with the mu-toolbox of Matlab. The controller designed with model parameters representing the most favorable plant dynamics from the point of view of control purposes, can operate properly even in case of parameter values of the worst-case scenario.

Keywords: glucose-insulin control, disturbance rejection, robust control, Mathematica

1 Introduction

Blood-glucose control is one of the most difficult control problems to be solved in biomedical engineering. The main reason is that patients are extremely diverse in their dynamics and in addition their characteristics are time-varying. The investigations of [3] discourage the use of a low complexity control such as PID, if high level of performance is desired. To design an optimal, high quality control, one needs a relevant model of the process as well as a proper control technique. There are several studies in both areas. For example, [4] analyzed the different models of glucose-insulin interactions in human body, while [5], [6], [7] studied the applications of traditional and modern control techniques for blood-glucose regulation.

However, probably the best way to approach the problem is to consider the system model and the applied control technique together, [8] or [9]. Models for diabetic systems are imprecise by nature, therefore some research works are concentrated on adaptive control techniques using on-line parameter estimation, [10], others suggest robust control design as [11].

In this study, the authors present a robust control design on frequency domain using *Mathematica* for regularization of glucose level in Type I diabetes persons under intensive care. The corresponding *Mathematica* program package, OPTDesign, was originally developed by [1].

Here we have slightly improved this technique by suggesting an effective disturbance rejection constraint inequality for the disturbance transfer function. Our study is based on the minimal patient model of [2]. In order to check the quality, especially the robustness of our control, the controller is designed with the most favorable model parameter values, but tested with the values representing the worst-case scenario in terms of difficulty of the system dynamics for control purposes.

The technique of the computations and closed loop simulations, employing the *Mathematica* Application, Control System Professional Suite, (CSPS) together with OPTDesign, have been already demonstrated by [12] for a simple water-level control problem.

2 Model Equations

Several different models of diabetic systems exist in the literature including, for example, the very detailed 21st-order metabolic model of Sorensen, [13]. 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 the three-state minimal patient model of Bergman, [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 [14]: $p_1 = 0.028$, $p_2 = 0.025$, $p_3 = 0.00013$, $p_4 = 5/54$, $G_B = 110$, $Y_B = 1.5$, $V_L = 120$.

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:

$$i_0 = p_4 Y_B V_L = 16.667 \tag{2}$$

Loading CSPS of *Mathematica* the linearized system around the vicinity of the steady-state can be calculated as well as our interested transfer function from the glucose concentration $G(s)$ to the input vector $\{h(s)\ i(s)\}$:

$$\begin{aligned} H_{G\to i}(s) &= \frac{1.19\cdot 10^{-4}}{s^3 + 0.1456s^2 + 0.0056s + 6.48\cdot 10^{-5}} \\ H_{G\to h}(s) &= \frac{s + 0.025}{s^2 + 0.53s + 0.0007} \end{aligned} \tag{3}$$

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

3 Concept of the Robust Control Design

3.1 Performance Requirements

Considering the complementary sensitivity function of a general closed loop system, [15]:

$$T(s) = \frac{P(s)C(s)}{1 + P(s)C(s)} \tag{4}$$

where $P(s)$ represents the transfer function of the considered plant, and $C(s)$ the transfer function of the controller, the robust control method on frequency domain implemented in OPTDesign briefly can be summarized by satisfying the following conditions, [1]:

T must satisfy disk inequality:

$$\left|K(i\omega) - T(i\omega)\right| \le R(i\omega) \qquad \text{for } \omega_a \le \omega \le \omega_b \tag{5}$$

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;

Defining the gain-phase margin as $m = \inf|1 + PC|$, the constraint should be:

$$|T(i\omega) - 1| \leq \frac{1}{m} \qquad \text{for all } \omega \tag{6}$$

The bandwidth of the complementary sensitivity function ($T(i\omega)$) should be below than $1/\sqrt{2}$ or in other words below -3 dB, [15].

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 $C(i\omega) \leq \frac{\alpha_r}{|\omega|^n}$ inequality is held, then for large ω frequencies it is true that $T(i\omega) \leq |P(i\omega)C(i\omega)|$, or by other words:

$$|T(i\omega)| \leq \alpha_r \frac{|P(i\omega)|}{|\omega|^n} \qquad \text{for } |\omega| > \omega_r \tag{7}$$

In addition we introduced a new condition for disturbance rejection requirement, considering $P_d(s)$ the transfer function of the disturbance and having the sensitivity transfer function ($1-T(s)$), the inequality should be:

$$|1 - T(i\omega)| \leq \frac{c}{|P_d(i\omega)|} \tag{8}$$

where c is a constant less than 1.

These requirements all together can be summarized in the requirement envelope presented in Figure 1.

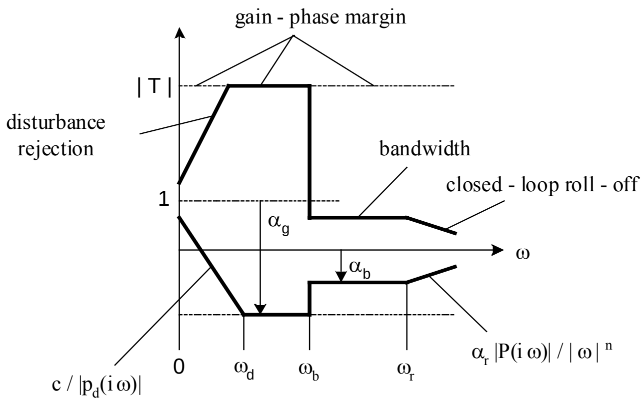

Figure 1

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: $c = 0.95$; $\alpha_r = 8.7641*10^{-7}$; $n = 2$; $\omega_d = 2.65$; $\omega_b = 4$; $\omega_r = 6.5$; $\alpha_g = 2.5$; $\alpha_b = 0.9$. Results are shown in Figure 2.

3.2 Optimizing Performance Function

Assuming that *T(s)* has no right-half plane (RHP) poles (is internally stable), the designing problem can be formulated as it follows:

Given a plant *P(s)*, a set of performance requirements **P** and a set $I = \left\{ T(s) \in RH^{\infty} \right\}$ of rational internally stable transfer functions the task is to determine optimal $T \in I$ which satisfies **P**.

Starting from (5) the performance requirements can be expressed in form of disk inequalities, which can be written in the following way:

$$\frac{1}{R(i\omega)^2}(|K(i\omega) - T(i\omega)|)^2 \le 1 \qquad \text{for } \forall\omega \tag{9}$$

Now, for a given *T* it can be calculated the largest value of the left-hand side:

$$\gamma(T) = \sup_{\omega}\left(\frac{1}{R(i\omega)^2}(|K(i\omega) - T(i\omega)|)^2\right) \tag{10}$$

If *T* is optimal (T^*), it means that $\gamma(T^*) \le \gamma(T)$ for all $T \in I$ and satisfying **P**. By other words this means:

$$\gamma^* = \inf_{T} \sup_{\omega}\left(\frac{1}{R(i\omega)^2}(|K(i\omega) - T(i\omega)|)^2\right) \tag{11}$$

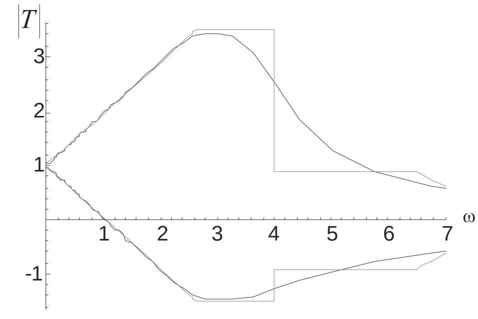

Figure 2

The actual original and smoothed requirements envelopes

This γ^* value is basically the solution of the H_∞ suboptimal problem, [15]. This value should be in the [0,1] interval to guarantee robust performance.

Running OPTDesign for the requirement envelope shown in Figure 2, the obtained result for γ^* was 0.3679. This value was also checked with the mu-toolbox of Matlab and a very similar result was obtained. The numerical values of the optimal T^* inside the considered constraining envelope is presented in Figure 3. With γ^* calculated, we have checked the performance requirements similarly as in [12].

The numerical values of these optimal T^* will be approximated with a proper rational function, in our with a 20th order one. The local error of this approximation can be seen in Figure 4.

Then, applying (3) and (4) we can express the transfer function of the control part, *C(s)*. In order to simulate the non-linear closed-loop in time domain we should convert *C(s)* in state-space form.

To reduce the size of the state-space form we use the *MinimalRealization* technique built in CSPS. As a result we have obtained a sixth order LTI model (matrix *D* is zero):

$$A=\begin{pmatrix} -5.488 & 0.189 & 0.0042 & -0.002 & -7.34\cdot 10^{-6} & -1.27\cdot 10^{-6} \\ -39.61 & -5.99 & -0.1335 & 0.066 & 2.29\cdot 10^{-4} & 3.96\cdot 10^{-5} \\ 81.03 & 12.05 & -1.754 & 0.876 & 0.003 & 5.23\cdot 10^{-4} \\ 3823.16 & 568.03 & -83.024 & -5.837 & -0.02 & -0.003 \\ 50135.2 & 7448.91 & -1088.6 & -76.22 & -13.21 & -2.31 \\ -205374 & -30513.7 & 4459.35 & 312.25 & 54.54 & 5.26 \end{pmatrix}$$

$$B=\begin{pmatrix} -2.52\cdot 10^{-5} & 1.87\cdot 10^{-4} & 0.00038 & 0.018 & 0.237 & -0.97 \end{pmatrix}^T \tag{12}$$

$$C=\begin{pmatrix} -4.597\cdot 10^{10} & 1.94\cdot 10^{9} & 1.123\cdot 10^{8} & -1.064\cdot 10^{8} & 170668 & -33566 \end{pmatrix}$$

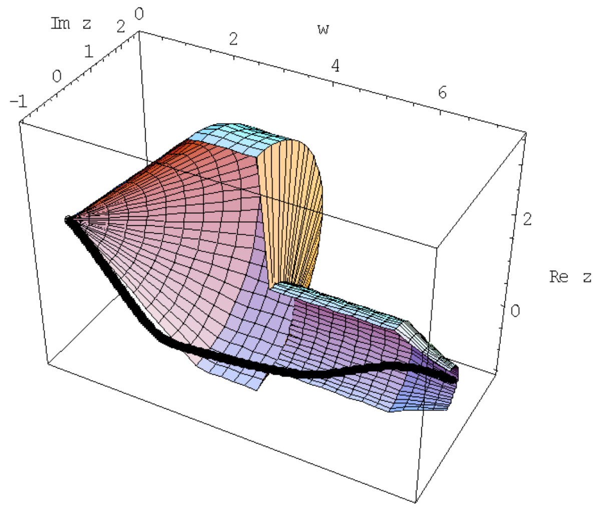

Figure 3

The numerical values of the optimal T^* inside the considered constraining envelope

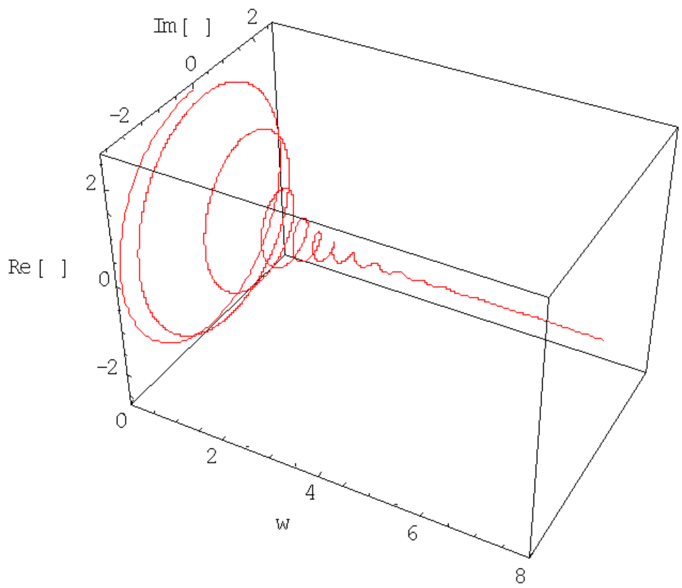

Figure 4

The local error of the rational function approximation of the optimal 20^{th} order T (in 10^{-4})

4 Simulating the Nonlinear Closed-Loop Dynamics for Blood-Glucose System

4.1 Non-linear Closed Loop Model Simulation

Using the parameters given at the beginning of this paper, (2), the performance of the control was tested by using a standard meal disturbance with about six hour duration, modeled by [16] and given in Figure 5.

Using the designed controller, the controlled dynamics of the blood glucose and insulin infusion are presented in Figure 6 and Figure 7.

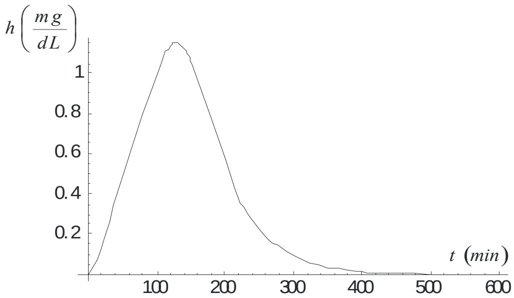

Figure 5

Considered exogenous glucose infusion (meal disturbance), by [16]

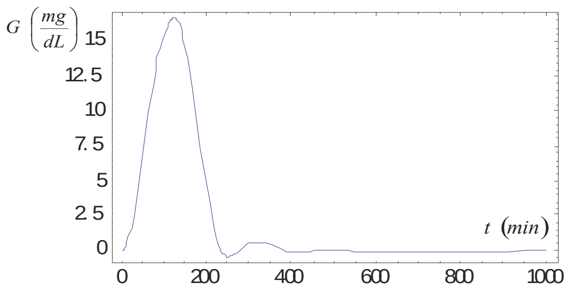

Figure 6

Controlled dynamics of blood glucose concentration, *G(t)*

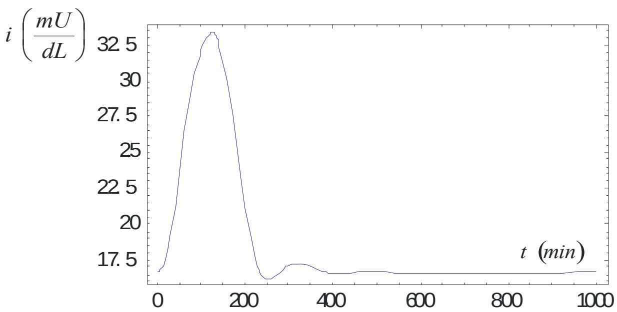

Figure 7
The corresponding insulin infusion rate, *i(t)*

4.2 Testing Robustness of the Controller

The investigations of [3] showed that for limiting case of model parameter $p_1 = 0$, the system is unable to regulate the glucose level on its own. Indeed, the eigenvalues of the linearized model in case $p_1 = 0$ are {- 0.0925926, - 0.025, 0}, so the open loop system is unstable, but controllable. The result of the simulation carried out with the same controller, but with nonlinear plant model having the value of $p_1 = 0$, shows that the compensator is able to control the system even in this case, although the quality of the control is not so good, than it was in case $p_1 = 0.028$ (Figure 8, Figure 9).

These results are very similar to those obtained in [3] (in case of the NMPC control method, where the best result were obtained, and where the controller was originally designed for instable situation, $p_1 = 0$).

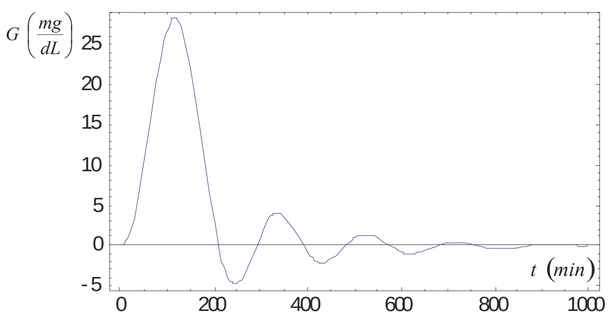

Figure 8
The controlled dynamics of blood glucose, *G(t)* in case of unstable plant, $p_1 = 0$

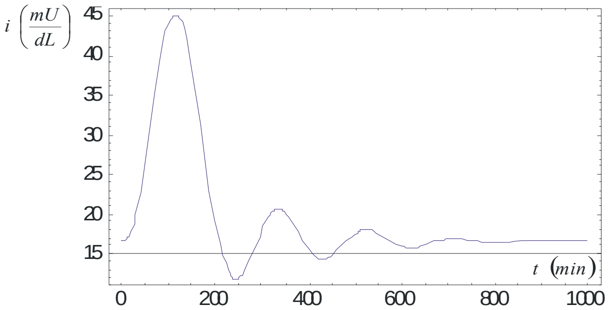

Figure 9

The corresponding insulin infusion rate, *i(t)* in case of $p_1 = 0$

Conclusions

A practical method has been presented for designing a robust controller to regulate glucose-insulin system for Type I diabetic patients under intensive care. Employing *Mathematica* CSPS Application together with the OPTDesign package developed by [1], 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, even in case when the model parameters have changed and the system became unstable.

The proposed design procedure can be easily adapted to other problems, where uncertainty plays an important role and robustness of the control is undispensable.

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