Robust Blood-Glucose Control of Type I Diabetes Patients Under Intensive Care Using Mathematica

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INTRODUCTION

This article presents a robust control design method on frequency domain using *Mathematica* for regularization of glucose level in Type I diabetes persons under intensive care. The method originally proposed under *Mathematica* by Helton and Merino (1998) is now improved with a disturbance rejection constraint inequality, and is tested on the three-state minimal model. Nonlinear closed loop simulation in state-space, in case of standard meal disturbances, demonstrates the robustness of the resulted high-order linear controller. The obtained results are compared with H_∞ design implemented with Matlab, proving that the controller (for the considered model parameters) can operate properly, even in case of parameter values of the worst-case scenario.

The 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 Hernjak and Doyle (2005) 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 (Parker, Doyle, & Peppas, 2001).

The mostly used model, and also the simplest one, proved to be the minimal model of Bergman, Philips, and Cobelli (1981), but its shortcoming is its big sensitivity 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 (e.g., de Gaetano and Arino (2000) analyzed the different models of glucose-insulin interactions in human body). Also, more general models have been used in the literature, like the model developed by Hovorka, Shojaee-Moradie, Carroll, Chassin, Gowrie, Jackson, Tudor, Umpleby, and Jones (2002), or the 21^{st} order nonlinear model of Sorensen (1985).

However, probably the best way to approach the problem of blood-glucose control is to consider the system model and the applied control technique together (Makroglou, Li, & Kuang, 2006; Parker et al., 2001). As models of diabetic systems are imprecise by nature, some research works are concentrated on adaptive control techniques using online parameter estimation (e.g., Lin, Chase, Shaw, Doran, Hann, Robertson, Browne, Lotz, Wake, & Broughton, 2004), others like Ruiz-Velazquez, Femat, and Campos-Delgado (2004) or Parker, Doyle, Ward, and Peppas (2000) suggest robust control design.

This study focuses on robust control design, for regulating glucose level in Type I diabetes patients under intensive care. The investigations were done using the minimal patient model of Bergman et al. (1981). The method applied using *Mathematica* lays on a different approach by that under Matlab. The corresponding *Mathematica* program package OPTDesign was originally developed by Helton and Merino (1998). The technique of the computations and closed loop simulations, employing the *Mathematica* Application, Control System Professional Suite (CSPS), together with OPTDesign, has been already demonstrated by Palancz (2006).

Mathematica is a mathematical program capable to work step by step, like a mathematical reasoning machine. In this way, it offers a more didactic approach as Matlab, which is focused on solving the problems in a more technical way (Palancz, Benyo, & Kovacs, 2005).

Here the authors have slightly improved this technique by suggesting an effective disturbance rejection constraint inequality for the disturbance transfer function. In order to check the quality, especially the robustness, 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. Results are compared with those obtained by Hernjak and Doyle (2005).

MODEL EQUATIONS

The three-state minimal patient model of Bergman et al. (1981) consists of the following equations:

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

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 given by Equation 1. The physiological parameters are G_B (mg/dL) the basal glucose level, Y_B (mU/dL) basal insulin level, V_L (dL) the insulin distribution volume and p_1, p_2, p_3, p_4 as the model parameters. As numerical values, the authors worked with the numerical values determined by Furler, Kraegen, Smallwood, and Chisolm (1985): p_1 = 0.028 (1/min), p_2 = 0.025 (1/min), p_3 = 0.00013 (dL/(min^2 mU)), p_4 = 5/54 (1/min), G_B = 110 (mg/dL), Y_B = 1.5 (mU/dL), V_L = 120 (dL).

The steady-state values used for linearizing the system are: G0 = X0 = Y0 = 0, h0 = 0, and for i0:

$$i_0 = p_4 Y_B V_L = 16.667 \text{ (mU/min)} \tag{2}$$

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.

CONCEPT OF THE ROBUST CONTROL DESIGN

Performance Requirements

Considering the complementary sensitivity function of a general closed loop system (Zhou, 1996):

$$T(s) = \frac{P(s)C(s)}{1+P(s)C(s)} \tag{3}$$

where P(s) represents the transfer function of the considered plant, and C(s) the transfer function of the controller. As a result, the robust control method on frequency domain implemented by OPTDesign briefly can be summarized, satisfying the following conditions (Helton & Merino, 1998):

1. T must satisfy disk inequality:

   $$|K(i\omega) - T(i\omega)| \le R(i\omega), \text{ for } \omega_a \le \omega \le \omega_b \tag{4}$$

   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 $m = \inf |1+PC|$, the constraint should be:

   $$|T(i\omega) - 1| \le \frac{1}{m}, \text{ for all } \omega \tag{5}$$

3. The bandwidth of the complementary sensitivity function (T(iω)) should be below than 1/√2 or in other words below -3 dB (Zhou, 1996).
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 $T(i\omega) \le |P(i\omega)C(i\omega)|$, or by other words: