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### ► To cite this version:

Olivier Sename, Corentin Briat. Discussion on: "Time-Delay Model-Based Control of the Glucose-Insulin System, by Means of a State Observer". *European Journal of Control*, 2012, 18 (6), pp.607-609. hal-00795550

**HAL Id: hal-00795550**

**<https://hal.science/hal-00795550>**

Submitted on 28 Feb 2013

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# Discussion on the article "Time-delay model-based control of the glucose-insulin system, by means of a state observer"

Olivier Sename<sup>†</sup> and Corentin Briat<sup>‡</sup>

## I. INTRODUCTION

Time-delay systems are ubiquitous in nature and engineering. Delays account for transmission, diffusion and migration phenomena as well as maturation and aging in physical, biological, ecological, epidemiological and population systems. Lotka-Volterra models describing prey-predator models or Pearl-Verhulst equations for population dynamics are instances of deterministic models aiming to describe population evolution. These models do not account for aging/maturation of the population and this is the reason why refinement of the models have been proposed [1].

Delays in epidemiological models [1] may account for incubation time, time for recovery, time for the vaccine to become active or time to be susceptible again after recovering. Models referred to as compartmental models [2], comprising SIR, SIS, SEIS models, and so on. The following simple delay-SIR model has been proposed in [3]

$$\begin{aligned}\dot{S}(t) &= -\beta S(t)I(t) \\ \dot{I}(t) &= \beta S(t)I(t) - \beta \int_h^\infty \gamma(\tau)S(t-\tau)I(t-\tau)d\tau \\ \dot{R}(t) &= \beta \int_h^\infty \gamma(\tau)S(t-\tau)I(t-\tau)d\tau\end{aligned}$$

where  $S, I$  and  $R$  represent the population of susceptible, infectious and recovered people, respectively. The delay is distributed in this model and describes the time spent being sick. The distributed delay kernel  $\gamma : [h, \infty) \rightarrow \mathbb{R}_+$  satisfies the condition  $\int_h^\infty \gamma(\tau)d\tau = 1$  and can be seen as a probability distribution. An optimal vaccination strategy has been applied on this model for controlling the disease outbreak.

Delay equations have also found applications in ecology [4], [5] where the following neutral delay model [6] for forest evolution based on Pearl-Verhulst equation has been proposed:

$$\dot{x}(t) = rx(t) \left[ 1 - \frac{x(t-\tau) + c\dot{x}(t-\tau)}{K} \right]$$

where  $x, r$  and  $K$  are the tree population, the intrinsic growth rate and the environmental carrying capacity. The additional term  $c\dot{x}(t-\tau)$  to the usual logistic equation is introduced to account for soil depletion and erosion.

The paper [7] addresses the control of the glucose-insulin system

$$\begin{aligned}\dot{G}(t) &= -K_{xgi}G(t)I(t) + \frac{T_{gh}}{V_G} \\ \dot{I}(t) &= -K_{xi}I(t) + \frac{T_i G_{max}}{V_I} f(G(t-\tau_g)) + u(t)\end{aligned}\quad (1)$$

which takes the form of a positive nonlinear system with constant discrete-delay. Above  $G$  and  $I$  denote plasma glycemia and insulinemia, respectively. The control input  $u$  is the exogenous intra-venous insulin delivery rate.

The current paper [7] addresses the design of an observer-based control law, where the controller is taken back from [8] by the same authors. The observer is designed with the assumption that only the plasma glycemia, i.e.  $G(t)$ , is measured. The observer design relies on the computation of a constant matrix  $W$ , which multiplied by the inverse of the Jacobian matrix of the observability matrix (which is nonsingular except at  $(0, 0)$ ), yields the observer-gain, see e.g. [9]. The local stability of the closed-loop system is finally proved by looking at the asymptotic stability of the origin of the linear time-varying system

$$\begin{aligned}\dot{\hat{e}}(t) &= H\hat{e}(t) + WC\xi(t) \\ \dot{\xi}(t) &= \dot{H}\xi(t) + Br_0(t)\xi(t) + r_1(t)BC\xi(t-\tau_g).\end{aligned}\quad (2)$$

A Lyapunov argument is used to infer stability of the above LTV system and the matrix gain  $W$  is designed according to some results in [10] pertaining on delay-independent robust stability of uncertain polytopic time-delay systems.

## II. TOWARDS AN LPV APPROACH FOR BIOLOGICAL SYSTEMS

### A. A first extension to LPV observers

The framework developed in the paper [7], i.e. delay and time-varying parametric uncertainties, is completely compatible with the LPV framework which assumes knowledge of the varying parameters  $r_1$  and  $r_2$ . Note that these parameters are functions of the state of the systems.

Along these lines, we can therefore imagine the following extensions:

- The observer structure may be extended to incorporate additional terms (ans gains), notably to take into account delayed information. This may lead to a more accurate estimation of the state and better convergence properties. The exact knowledge of the delay value is critical here and may be the main limitation of observer including delays. Memory-resilient observers should be a suitable solution, see e.g. [11], [12] for memory resilient controllers.

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- System (2) can be viewed as an LPV system involving two varying parameters  $r_0$  and  $r_1$ . Some of the results developed in [13], [14] may be used to design an LPV observer involving a parameter-dependent gain  $W(r_1, r_2)$  in order to improve performance of the overall observation process.

### B. Design of gain scheduled LPV controllers

The design of gain-scheduled control laws is also one of the objectives of the LPV framework. By rewriting system (1) as a quasi-LPV system of the form

$$\begin{aligned}\dot{G}(t) &= (K_{xgi}\rho(t))I(t) + \frac{T_{gh}}{V_G} \\ \dot{I}(t) &= \alpha(t)G(t - \tau_g) - K_{xi}I(t) + u(t)\end{aligned}\quad (3)$$

where  $\rho(t) = G(t)$  and

$$\alpha(t) = \frac{T_i G^{max}}{V_I} \cdot f'(\rho(t - \tau_g)). \quad (4)$$

The above system is an LPV time-delay system that has been extensively studied in [15], [16], see also references therein. Based on this formulation, gain-scheduled controllers can easily be derived.

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