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Design of a switched robust control scheme for drug delivery in blood pressure regulation ⋆

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Abstract: A control algorithm based on switching robust controllers is presented for a Linear Parameter Varying (LPV) time-delay system modeling automatic infusion of vasodilator drug to regulate postsurgical hypertension. The system is scheduled along a measurable signal trajectory. The prospective controllers are robustly designed at various operating points forming a finite set of robust controllers and then a hysteresis switching is performed between neighboring robust controllers for a larger operating range of the LPV system. The stability of the switching LPV system for the entire operating range is ensured by providing a sufficient condition in terms of bound on the scheduling signal variation using the concept of dwell time. Simulation results are provided to verify the performance of the designed control scheme.

Keywords: Time-delay system, LPV system, Uncertain system, Robust control, Hysteresis switching, Biomedical control system, Life sciences

1. INTRODUCTION

The regulation of postoperative hypertension is essential during general clinical and operative scenarios to decrease bleeding. It becomes particularly vital for postoperative cardiac patients suffering from Myocardinal Revascularization for a quick recovery because they do not possess an autonomic capability of regulating their increased blood pressure and an external infusion of a vasodilator drug (a drug facilitating blood flow due to decrease in vascular resistance) is needed to reduce their high blood pressure, see Mitchell (1982) and Koch-Weser (1974) for more details.

A formal research for the development of automatic control schemes for regulation of postoperative hypertension dates back to the late 1970's when Slate et al. (1979) presented an experimentally validated mathematical model relating the patient's blood pressure response to the injection of Sodium Nitroprusside (SNP) drug. The blood pressure response of the model was in agreement with the response observed in actual postsurgical patients. From 1970's through 1980's, many contributions were made towards fixed gain Proportional-Integral-Derivative (PID) controllers for postoperative hypertension regulation as in Sheppard et al. (1979), Smolen et al. (1979), De Asla et al. (1985) and Pardini et al. (1988). From late 1980's, there has been a remarkable shift in trend towards the use of adaptive controllers for blood pressure regulation. The adaptive controllers found in literature for blood pressure regulation can be classified as: Self Tuning Regulators (STR), Model Reference Adaptive Controllers (MRAC) and Multiple Model Adaptive Controllers (MMAC). See Isaka and Sebald (1993) for a complete summary of these adaptive controllers and their application for the regulation of blood pressure.

Recently, Luspay and Grigoriadis (2015) introduced the concept of LPV control for regulation of postsurgical hypertension. They used a Multiple Model Extended Kalman Filter (MMEKF) algorithm for online estimation of blood pressure response model parameters and a LPV control algorithm for the regulation of blood pressure. Ahmed and Özbay (2015) proposed switching PI Smith-predictor based robust controllers for a LPV time-delay system modeling automatic administration of SNP drug in postsurgical scenario. This paper is an extension of our previous work. In this work, we provide a finite dimensional approximation of the original LPV time-delay model representing the blood pressure response to drug infusion. We also provide a sufficient condition for stability of the switching LPV finite-dimensional approximated system based on the idea of Yan and Özbay (2007).

The rest of the paper is organized as follows. In Section 2, mathematical description of the process, design constraints and formulation of the LPV framework are presented. In Section 3, the switching robust control scheme is given for the LPV system under consideration. Section 4 discusses the stability of the switching LPV system. Finally, Section 5 presents simulation results to verify the performance of our proposed control algorithm.

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2. PROBLEM DEFINITION

2.1 Model description

The model relating patient's blood pressure response to the infusion of a vasodilator drug is given by the continuous-time, third order, stable, time-delayed transfer function $\Sigma(s)$ as

$$\Sigma(s) := \frac{\Delta P_d(s)}{I(s)} = \frac{K(\tau_3 s+1)e^{-Ts}}{(\tau_1 s+1)[(\tau_2 s+1)(\tau_3 s+1)-\alpha]} \quad (1)$$

where $I(s)$ is the Laplace transform of the drug delivery rate in $\frac{ml}{h}$ and $\Delta P_d(s)$ is the Laplace transform of the change in blood pressure in $mmHg$. In (1), K is the patient's sensitivity to the drug in $mmHg\left(m\ h^{-1}\right)^{-1}$, T is the initial injection delay in seconds, α is the drug fraction recirculating and, finally τ_1, τ_2 and τ_3 are the time constants in seconds for vasodilator drug action, flow through pulmonary circulation and flow through systemic circulation, respectively. The Mean Arterial Pressure (MAP) is given as

$$MAP(t) = \Delta P_d(t) + P_0 \quad (2)$$

where $P_0 = 150\ mmHg$ is the initial blood pressure, which is known and fixed.

This model, adopted from Martin et al. (1987), is a variant of empirically validated model of Slate et al. (1979). The model consists of three first-order sections depicting drug action, systemic circulation and pulmonary circulation as shown in Fig. 1. Later, this model was also adopted by Malagutti et al. (2013) and Malagutti (2014) for their research work.

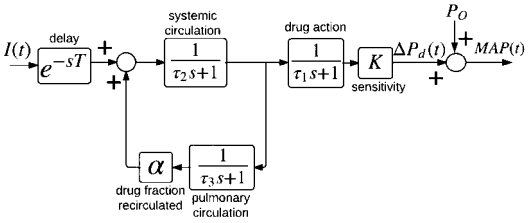

Fig. 1. Compartmental model proposed by Martin et al. (1987)

It has been shown by Wood et al. (1987) that the patient's sensitivity to the drug varies not only from patient to patient but also within the individual patient. Therefore, treating the variability in intra-patient response to the drug infusion, we consider the patient's sensitivity to the drug as a time-varying measurable signal, $K(t) \in [-9.5, -0.25]\ mmHg\left(m\ h^{-1}\right)^{-1}$. A MMEKF algorithm can be employed for an online estimate of $K(t)$ as shown in Luspay and Grigoriadis (2014). Treating the variability in inter-patient response to the drug injection, drug fraction recirculating $\alpha \in [0.25, 0.65]$ and initial injection delay $T \in [20, 60]$ sec are considered to be uncertainties of considerably large and known ranges. The ranges of these uncertainties are also in accordance with the clinical validated data, Meijers et al. (1997). The nominal values of α and T are taken to be $\alpha_0 = 0.5$ and $T_0 = 50$ sec, respectively, see Slate et al. (1979) and Malagutti et al. (2013) for more discussion. We assume the time constants $\tau_1 = 50$ sec, $\tau_2 = 30$ sec and $\tau_3 = 10$ sec to be known and fixed, Martin et al. (1987).

2.2 Design Constraints and Performance Specifications

Our main aim is to reduce the blood pressure from an initial value of 150 $mmHg$ to a final value of 100 $mmHg$ and maintain this level within ± 5 $mmHg$ of final value considering uncertainties in T and α, and time-variation in measurable scheduling signal $K(t)$. Based on our earlier work Ahmed and Özbay (2015) and Malagutti (2014), the design constraints and performance specifications for postsurgical hypertension regulation problem are listed below:

- The maximum settling time should preferably be ≤ 10 min but it must not exceed 15 min,
- MAP should be within $[70, 120]$ $(mmHg)$ once it settles to this interval in order to be in agreement with the normal physiological blood pressure limits,
- MAP should be within ± 5 $mmHg$ of 100 $mmHg$ during steady state,
- MAP should not drop below the danger threshold of 70 $mmHg$,
- The acceptable range of vasodilator SNP drug injection is $0 \leq I(t) \leq 180\ ml\ h^{-1}$ due to toxic side effects of SNP,
- The response of system must not be oscillatory or unstable at anytime.

2.3 Formulation of the LPV framework

Considering the range of uncertainties in model parameters and to fulfill the performance specifications, we have chosen a third-order Padé approximation (3) to insert the time delay into the model dynamics.

$$e^{-sT} \approx P_{T,3}(s) = \frac{1 - Ts/2 + (Ts)^2/10 - (Ts)^3/120}{1 + Ts/2 + (Ts)^2/10 + (Ts)^3/120} \quad (3)$$

Therefore, a finite-dimensional approximation of (1) can be modeled as

$$\Sigma_a(s) := \frac{K(\tau_3 s+1)P_{T,3}(s)}{(\tau_1 s+1)[(\tau_2 s+1)(\tau_3 s+1)-\alpha]} \quad (4)$$

Considering $K(t)$ to be a measurable scheduling signal, and defining input variable as $u(t) = I(t)$ and output variable as $y(t) = \Delta P_d(t)$, we can formulate a LPV framework for the model given in (4) as

$$\begin{aligned} \dot{\mathbf{x}}(t) &= \mathbf{A}\ \mathbf{x}(t) + \mathbf{B}(K(t))\ u(t) \\ y(t) &= \mathbf{C}\ \mathbf{x}(t) \end{aligned} \quad (5)$$

where $\mathbf{x}(t)$ is the state vector defined as

$$\mathbf{x}(t) = [x_1(t)\ x_2(t)\ x_3(t)\ x_4(t)\ x_5(t)\ x_6(t)]^T.$$

The system matrix $\mathbf{A}$ is given by