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LQG/LTR CONTROLLER DESIGN FOR AN ANAESTHESIA INFUSION SYSTEM

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ABSTRACT

By the possibility of anaesthesia control systems development, this paper aims to show an robust control application of the Linear Quadratic Gaussian with loop transfer recovery (LQG/LTR) design methodology on the frequency domain after an introduction of LQR (linear quadratic regulator), to an anaesthesia infusion multivariable system representing a patient under a infusion of an anaesthetic and a muscle relaxant, with the medium arterial pressure and Paralysis being monitored.

1. INTRODUCTION

At the medical science, anesthetists diary face themselves a series of hemodynamic and respiratory variables that need to be monitored and kept in well defined ranges, to maintain optimal conditions to surgery practices. For example, at nervous system, thoracic and abdominal systems it is necessary a neuromuscular blocking to its realization with safeness (Simanski 2009).

Clinical anesthetists have as mainly tasks (Linkens 1992):

- The maintenance of an unconsciousness state induced by medicaments
- Induction of muscular blocking
- Analgesia (process of pain release)

The international association to the study of pain (IASP) defines pain as the uncomfortable sensation and emotional experience, associated to tissue lesion or potential, or described in terms related to the specific lesion.

The maintenance of unconsciousness and muscular blocking are applied at surgery environments, and analgesia has a relation to post-operatory situations. The primary question to these three principal tasks of clinical anesthetist is the measurement and determination of the pain quantity (Linkens 1992). This occurs because pain has subjective magnitude, and the acceptable limits vary from person to person, depending on the anxiety of the patient and on the moment of its quantification as the culture of the patient, and in some cases during the process of pain measurement the patient

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needs to be awake and cooperating, what not always is possible (Slullitel 1998).

By this scenario and the development of quick response medicaments, as *Mivacurium Propofol* and *Remifetanil* (they proportionate measurement of its effects), it makes possible the automatic control approach to automatic infusion systems (Simanski 2009).

2. MONITORING OF THE ANESTHESIA PROCESS

Despite it is not possible to make a direct measurement of analgesia and unconsciousness yet, some physiological signals can be effectively related to them. By (Simanski 2009), the unconsciousness level can be related to cortical activity, and (Linkens 1992) affirms that it can be monitored by medium arterial pressure and medium systolic pressure, too. Analgesia can be determined by EEG (Electroencephalogram).

The use of EEG to monitor analgesia is known since 1940, when it was discovered that patients under it effects presented lower frequency brain waves, with a bigger amplitude if compared to an EEG signal of a person without that did not receive a dose. Today, by the advent of digital signal processing, Fourier analysis is applied to electroencephalogram signals to obtain its frequency distribution, and some frequencies are related to a situation where analgesia is applied (Simanski 2009).

Another modern approach to monitor analgesia consists in HRV technique (Heart rate variability). The applicability of it consists in the fact that under painful stimulus, fluctuations on the respiratory pattern occur on a patient, what can be related to cardiac frequency. The measurement is made by the comparison of wave forms at an ECG dispositive (electrocardiogram) (Simanski 2009). The level of unconsciousness can be monitored through physiological signals simultaneously, as cardiac frequency, sweating, medium arterial pressure and lacrimation (Linkens 1992). Between the topics in respect to anesthesia practice, the one that can be easily measured is the muscular relaxing; By (Linkens 1992), a common approach is the observation of electromyography (accompaniment of electric signals generated by excitable membranes).

3. MODEL DESCRIPTION

The model analyzed in this document is a 2 input 2 output system representing an infusion pump system. By definition, an infusion pump is a medical device that is used to deliver fluids into a patient's body in a controlled manner, and may deliver nutrients or medications (Medical 2010). The system is delivering doses of *atracurium* and *isoflurane* in vapor form (inputs) and is measuring the medium arterial pressure and induced unconsciousness (Paralysis, as outputs). Fig. 1 shows a kind of infusion pump.

The *atracurium* is a muscular relaxant of intermediary duration and intravenous injection, recommended for surgery applications. More details about this medicament can be found at (Dailymed 2012), and *isoflurane* is an anesthetic used in general anesthesia (Isoflurane 2012). The model matches a signal of MAP (medium arterial pressure) as an indicator of anesthesia level and EMG (electromyography) signal as

indicator of muscular relaxing.

The unities of the variables for the model are as follows: MAP is measured in mmHg, the paralysis rate is unitary as the infusion rate of *atracurium*, the *isoflurane* rate is percentual and time is measured in minutes.

Fig. 1 Model of an infusion pump (Diytrade® 2010)

As in (Linkens 1992), the transfer matrix that represents the model is given by

$$\begin{bmatrix} Paralysis \\ \Delta MAP \end{bmatrix} = \begin{bmatrix} G_{11}(s) & G_{12}(s) \\ 0 & G_{22}(s) \end{bmatrix} \begin{bmatrix} U_1(s) \\ U_2(s) \end{bmatrix} \quad (1)$$

where

$$G_{11}(s) = \frac{e^{-s}(1 + 10{,}64s)}{(1 + 3{,}08s)(1 + 4{,}81s)(1 + 34{,}36s)} \quad (2)$$

$$G_{12}(s) = \frac{0{,}27e^{-s}}{(1 + 2{,}83s)(1 + 1{,}25s)} \quad (3)$$

$$G_{22}(s) = \frac{-15e^{-42s}}{(1 + 2s)} \quad (4)$$

$$U_1(s) = Atracurium\ Infusion\ Rate$$
$$U_2(s) = Percentual\ of\ Isoflurane\ Vapor$$

To the development of LQG/LTR controller, first the Gilbert transform was applied at the transfer matrix (Kaylath 1980). The Gilbert transform proportionate the acquisition of a minimal order (and as consequence, controllability and observability guaranteed)

state space representation, besides diagonal. The dead-time of the transfer functions that are present in Eqs. (2)-(4) were modeled with Pade first order approximation (Aguirre 2007), as in Eqs. (5) and (6).

$$e^{-\tau_d} = \frac{Q_n(-\tau_d s)}{Q_n(\tau_d s)} \tag{5}$$

$$Q_n(s) = \sum_{j=0}^{n} \frac{(n+j)!}{j(n-j)!} (\tau_d s)^{n-j} \tag{6}$$

The system in (1) after the application of Gilbert's transform is showed bellow:

$$\begin{cases} \dot{x} = Ax + Bu \\ y = Cx + Du \end{cases} \tag{7}$$

$$\dot{x} = \begin{bmatrix} -0{,}3247 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & -0{,}2079 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & -0{,}0291 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -2 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & -0{,}8 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & -0{,}3534 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -0{,}5 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & -4{,}762 \end{bmatrix} \boldsymbol{x} + \begin{bmatrix} 250{,}8 & 0 \\ -158{,}5 & 0 \\ -25{,}76 & 0 \\ 0 & -2{,}024 \\ -65{,}6 & 5{,}225 \\ 0 & -3{,}2 \\ 0 & -1{,}235 \\ 0 & 2{,}235 \end{bmatrix} \mathbf{u} \tag{8}$$

By the values of principal diagonal, it can be observed that the system is stable. A simulation of the step response on each input individually was done in Matlab® to verify the reference following performance of the system, and it did not present a satisfactory behavior, it can be seen in Fig. 2. For biomedical system, robustness is a fundamental pre requisite to the project of control system, because the lack of disturbance rejection and incorrect filtering could result on undesirable situations for patients (as in medicament infusion system), and even cause death. This makes robustness necessary in this kind of application.

When the unitary step was applied at first input, the system stabilized around the value of -1000 (Paralysis normalized as unitary, first output), and the second output did not show visible variation. When the step was applied to the second input, MAP varied from 0 to -2 mmHg. The system without controller demonstrates a contrary effect of the step application, by the presence of positive zeros of transmission, so a controller must be design to the correct reference tracking. The design of the LQG/LTR controller is presented in the following section.

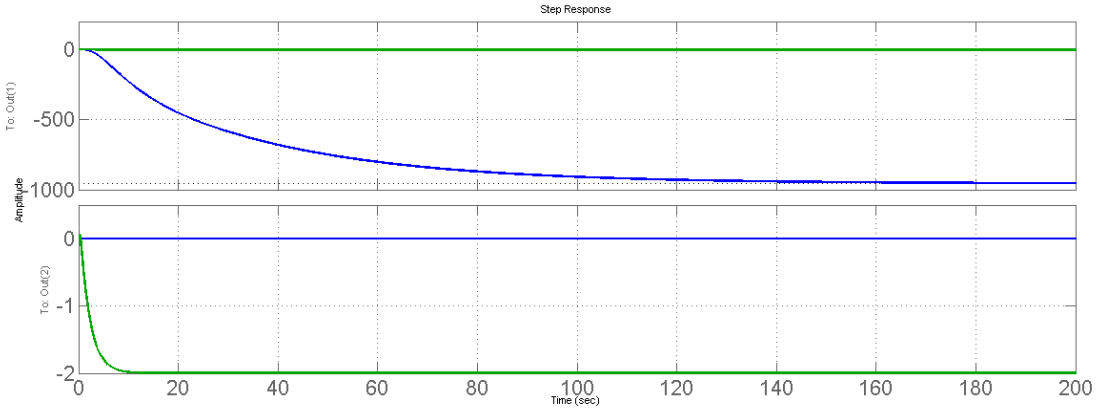

Fig. 2 Step response of the system, being applied in U_1 (upper graphic) and U_2
The blue line represents output 1 (Paralysis) and green line output 2 (MAP)

4. LQG/LTR CONTROLLER DESIGN

Before the presentation of the LQG/LTR design, first an introduction of LQR (linear quadratic regulator) (Rigely 1986, Kishor 2004) will be introduced. Consider the time invariant linear system in the state space in Eq. (10) (the temporal dependency of the variables x and u are not present for simplification for writing).

$$\begin{cases} \dot{x} = Ax + Bu \\ \quad y = Cx \end{cases} \tag{10}$$

Where A is the system's state matrix, B is control Matrix and C is output matrix, by definition. It is desired to minimize the performance index Eq. (11)

$$J = \int_0^\infty [x^T Q_c x + u^T R_c u] dt \tag{11}$$

This performance index is commonly defined as quadratic performance index, and specifies that the objective is to find a control law u(t) aiming the integral of the error that appear by the variations of state trajectories being kept low without needing a big quantity of energy. The variables Q_c and R_c are symmetric matrices chosen by the projector to determinate the relative importance of the system states and the control law. By the hypothesis of system stabilization, it can always be found a control law, as

$$u = -K_c x \tag{12}$$

That makes the closed loop system asymptotically stable resulting in a finite performance index value. K_c can be calculated through

$$K_c = R^{-1} B^T P \tag{13}$$

where *P* is the unique positive definite solution of the Riccati continuous algebraic equation

$$A^T P + AP - PBR_c{}^{-1}B^T P + Q_c = 0 \tag{14}$$

It is needed to consider if the system presents unstable trajectories that are not perceived by the performance index, the optimal control law will not change them resulting in a closed loop system unstable. If all the trajectories are demonstrated through the term $x^T Q_c x$, the stability is guaranteed and *J* will be finite. The system will be asymptotically stable if the system at Eq. (10) and the equation at Eq. (15) is detectable.

$$z = Hx \tag{15}$$

The term *H* is any matrix that $H^T H = Q_c$, with the pair [A, H] observable. As the project of the LQR has the necessity of measuring all the state variables of a determined system, it is not viable financially and in complexity (not always the state variables are known), so a Kalman filter is designed to estimate the plant states. To the LQG/LTR design, consider the system in the state space in the form:

$$\begin{cases} \dot{x} = Ax + Bu + \Gamma\xi \\ y = Cx + n \end{cases} \tag{16}$$

where ξ and n are gaussian white noises with medium value equal to zero. It is desired to minimize the performance index

$$J = E\left\{\lim_{T\to\infty}\frac{1}{T}\int_0^T [z^T z + u^T R_c u]dt\right\} \tag{17}$$

And the control law that minimizes (17) is

$$u = -K_c\hat{x} \tag{18}$$

where $\hat{x}$ is an estimation of the state x based in the measured *y*. The estimation is defined through the Kalman filter Eq. (19), with the gain matrices of the filter calculated by Eq. (20), Eqs. (21) and (22).

$$\dot{\hat{x}} = A\hat{x} + Bu + K_f[y - C\hat{x}] \tag{19}$$

$$K_f = \Sigma C^T R_f{}^{-1} \tag{20}$$

The term Σ do not represent a mathematical operation, it is the solution of algebraic Riccati equation.

$$A\Sigma + \Sigma A^T + Q_f - \Sigma C^T R_f{}^{-1} C\Sigma \tag{21}$$

$$Q_f = \Gamma Q_0 \Gamma^T \tag{22}$$

For $Q_0 \geq 0$ and symmetric. Considering the equations from Eqs. (16)-(22), an analysis of asymptotical property of the regulator will be made. Using as control weight Eq. (23)

$$R_c = \rho N \tag{23}$$

For $\rho > 0$ and $N > 0$. Making

$$G(s) = H(sI - A)^{-1}B \tag{24}$$

With the value of $\rho \to \infty$, the optimal regulator moves possible unstable poles of the system to the left half-s plane, and not effecting stable poles. As the stability margins of the systems working with this kind of regulator are not guaranteed, the LTR (loop transfer recovery) must be designed to make the Kalman filter better, recovering feedback properties of the states guaranteeing excellent stability margins to the project. For this, the formulas of Q_f and R_f for the Kalman filter is modified as

$$Q_f = \Gamma\Gamma^T + q^2 BVB^T \tag{25}$$

$$R_f = \mu I \tag{26}$$

The term *q* is a scalar that admits a sequence of high values, and as higher its value, higher are gain and phase margins of the system. *V* is an arbitrary symmetric positive definite matrix, and μ a scalar normally defined by small numbers. For this work, the uncertainties of the model were considered at the plant inputs. A detailed description of the LQG/LTR design can be find at (Rigely 1986).000

4. SIMULATION AND RESULTS

The simulations of the project were done at the software Matlab ®. For the equalization of the gains in frequency, two integrators were added to the output of the system (to equalize high frequency gains), making it a 10th order plant. Fig. 3 shows the gains of the system with integrators.

Them, the uncertainties were added to the inputs of the plant through Eq. (27)

$$l(w) = 0.1\left(1 + j\frac{w}{5}\right) \tag{27}$$

The values of ρ and q^2 were determined as 0.01 and 10^9. Fig. 4 shows the gains of the open loop system with the addition of the controller designed.

The system with controller applied did not present a very high gain margin (the gain margin calculated for this project was equal to 3,7487 dB), and phase margin equal to 43,0146°. The values are inside the acceptable range for the system's stability, according to the equations Eqs. (28)-(31).

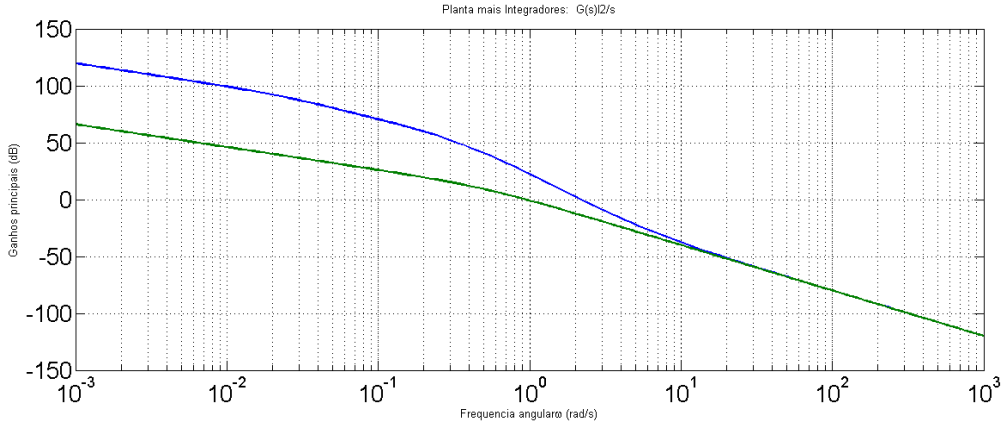

Fig. 3 Superior an Inferior gains of the plant with integrators

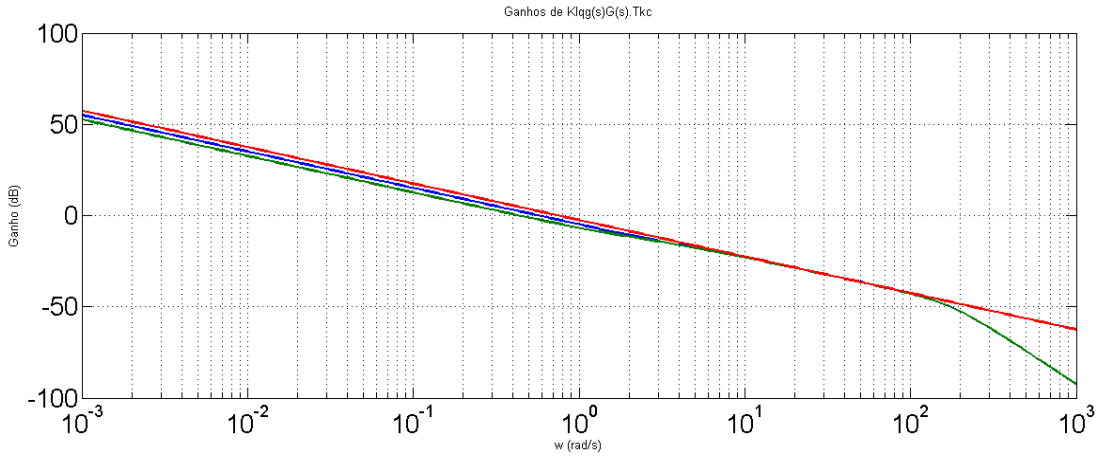

Fig. 4 Frequency gains of the open loop system with controller added

$$\frac{1}{1+\alpha_1} < MG < \frac{1}{1-\alpha_1} \tag{28}$$

or

$$\frac{1}{2} < MG < \infty \tag{29}$$

and

$$-2sen^{-1}\left({}^{\alpha_1}/_{2}\right) < MF < 2sen^{-1}\left({}^{\alpha_1}/_{2}\right) \tag{30}$$

or

$$-60° < MF < 60° \tag{31}$$

with the term α_1

$$\alpha_1 = \min_{w} \underline{\sigma}[I + G(jw)] \tag{32}$$

The frequency gains associated to the uncertainties can be seen at Fig. 5. Figs. 6 and 7 presents the outputs of the closed loop controlled system. At both inputs were applied unitary steps as performance testes of the designed system. At the Fig. 6, first was applied a step at the first input and after 30 seconds a step was applied a step at the second input, the Fig. 7 is the contrary (first step at input 2 and then another step at

input 1), with the objective to evaluate the performance of the LQG/LTR controller.

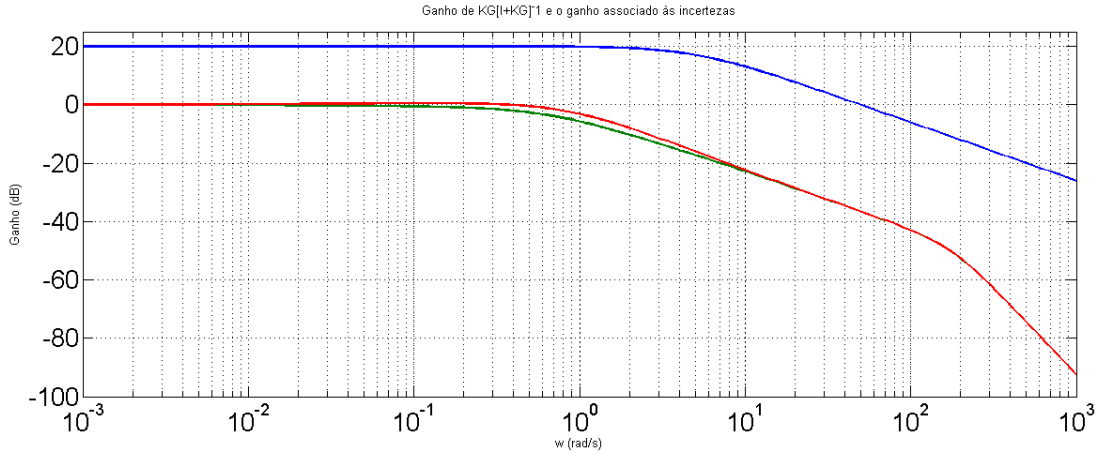

Fig. 5 Frequency gains associated to the plant uncertainties

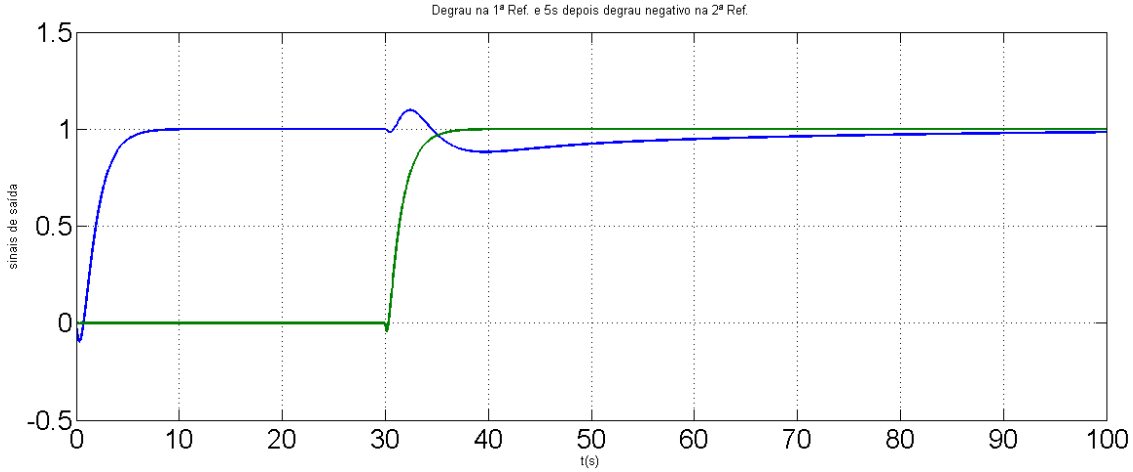

Fig. 6 Step responses of the controlled system, with the blue line representing the first input and green line the second

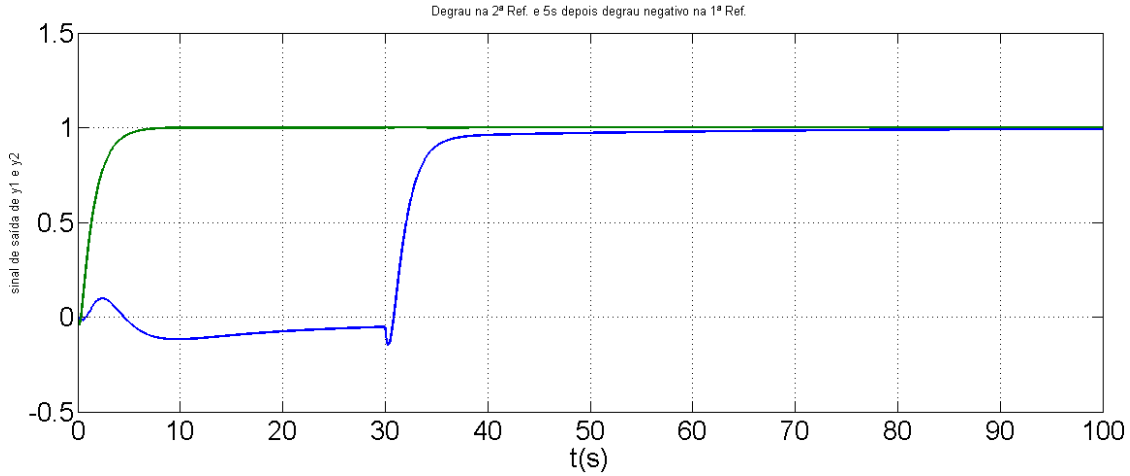

Fig. 7 Step responses for the second test

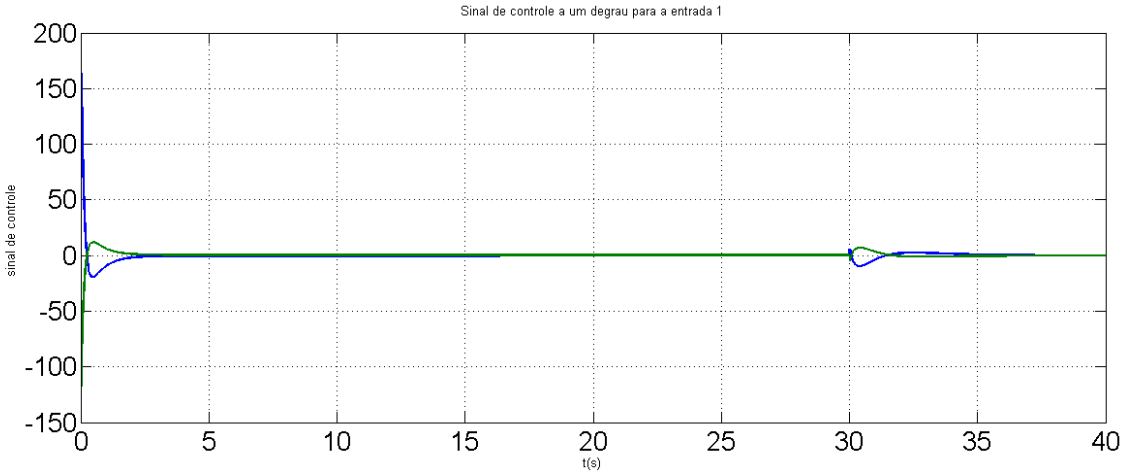

Fig. 8 Control signals of the same system at the Fig. 6

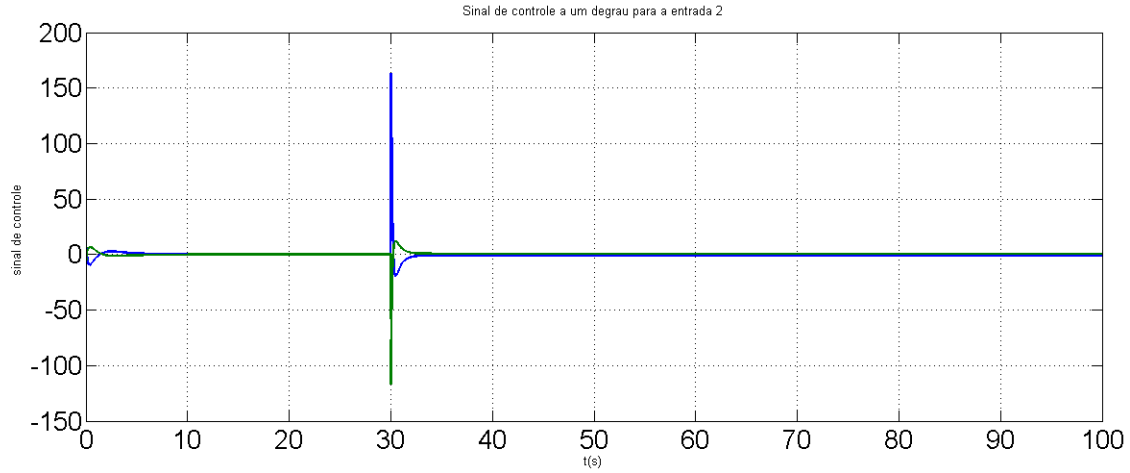

Fig. 9 Control signals of the same system at the Fig. 7

By the graphics of step responses in both situations showed at Figs. 6 and 7, it can be noted that the system was effectively decoupled, because the application of a reference at one input did not cause a big disturbance on the other, and the controlled system was capable to follow the reference without overshoot. The Figs. 8 and 9 presents the control signals of the systems (referring to Figs. 6 and 7).

The control signals are not at a high range (particularly the control signal of the Fig. 9), and this demonstrates a satisfactory performance in relation to this criteria (the controller would not spend a big quantity of energy to regulate the system). A better performance can be found by taking a better gain margin, but for other side it could elevate the control cost.

5. CONCLUSIONS

This document aimed to demonstrate a small resume of the LQR (linear quadratic

regulator) and LQG/LTR (linear quadratic Gaussian with loop transfer recovery) design procedure, with the application of this kind of controller at a multivariable system representing the infusion of two medicaments used at surgery situations, and the project demonstrated that for this model, a satisfactory behavior was determined, but as there's a big variability on the parameters of patients, for next works it is recommended the application of adaptive control, for the validation under different models.

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