Parametric Sensitivity Analysis of a Multiple Model Adaptive Predictive Control for Regulation of Mean Arterial Blood Pressure

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Abstract: Postsurgical complication of hypertension may occur in cardiac patients. To decrease the chances of complication it is necessary to lower high blood pressure as soon as possible. Continuous infusion of vasodilator drugs, such as sodium nitroprusside (Nipride), would quickly lower the blood pressure in most patients. However, each patient has a different sensitivity to infusion of Nipride. The parameters and the time delays of the blood pressure control system are initially unknown. Moreover, the parameters of the transfer function associated with a particular patient change over time. The objective of the study is to develop a procedure for blood pressure control in the presence of uncertainty of parameters and considerable time delays. In this paper, a sensitivity analysis was performed, changing the parameter that controls the convergence rate of weight factors (V). The simulation results showed significant changes in settling time (T_s), stressing the importance of this parameter on the control model definition. Considering a $V = 0.05$ was obtained $T_s = 195$s and, for same patient, $T_s = 510$s by increasing the value to $V = 0.4$, with the Root Mean Square Error (RMSE) varying but always lower than 1%.

1 INTRODUCTION

Arterial hypertension is an important risk factor responsible to cause cardiovascular diseases, being responsible for 54% of the deaths caused by stroke. Twenty-nine percent (29%) of the world's population has arterial hypertension with Brazil contributing to 22% to 44%, depending on the region (Mion et al., 2016). These numbers become very important as high blood pressure is directly associated to cerebrovascular events, coronary arterial disease and mortality (Kochar and Woods, 1990).

In order to reduce the risk of postoperative complications, the blood pressure needs to be controlled in a quick and effective way. One way to achieve this is to apply the infusion of vasodilators drugs such as Sodium NitroPrusside (SNP). However, each patient has, usually, a different sensibility to the drug and this, in general, varies with time and an overdose of the drug can cause serious and undesirable side effects.

Drug Delivery Systems are the devices that are used to infuse the drug into the human body at a particular rate for a given time period. These systems are widely used in cardiovascular surgical treatments and Intensive Care Units (ICU). The drugs that are used during treatments are mainly used to control the blood pressure. Control of such drugs during surgeries and in ICU are very tedious since manual control are done by anaesthetists which is not accurate and takes time (Sowparnika et al., 2017).

Blood pressure control of a patient under the influence of SNP, that is a vasodilator, is modelled through an uncertain model (Slate, 1980; Maitelli and Yoneyama, 1997). A multi-model approach is used in order to control the blood pressure under the influence of this drug. Multi-model approaches are commonly applied to control non-linear systems that operates in long ranges (Cavalcanti et al., 2007; Cavalcanti et al., 2009; Silva et al., 2010; Silva, 2010; Silva et al., 2015).

The basic idea of Multiple Model Adaptive Control (MMAC) procedure is based upon the assumption that the plant (model which indicates the relation between mean arterial pressure (MAP) of a patient under the influence of SNP) can be represented by a finite number of models and, for

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each model a controller can be priori designed (Silva et al., 2015).

The objective of this paper is to develop an adaptive method control for a blood pressure management for any patient without changing the controller. In this work, a multi-model adaptive control (MMAC) is used to control the MAP. Thus, a set of models is chosen and a Smith Predictor based Generalized Predictive Control (SPGPC) is designed for each chosen model. A validity function is defined in order to calculate the weight of each controller. The weight factor selected considers the residual error between the output of a given model and the plant (patient) output. Moreover, an analysis of the influence of the parameter controlling the convergence rate of the weight factors was carried out.

2 PROBLEM FORMULATION

An automated drug SNP infusion system for blood pressure control should produce good response characteristics, such as pressure undershoot (i.e., maximum excursion below commanded level) less than 10 *mmHg*, 20 percent settling time of 300-600 *seconds*, steady-state error within *+5 mmHg* (Silva, 2015).

A mathematical model of the mean arterial pressure (MAP) of a patient under the influence of SNP that was developed by (Slate, 1980) is given by:

$$MAP(t) = P_0 - \Delta P(t) + v(t) \tag{1}$$

where MAP is the mean arterial pressure, P_o is the initial blood pressure, $\Delta P(t)$ the change in pressure caused by the SNP infusion, and $v(t)$ is a stochastic background noise. A continuous-time deterministic model describing the relationship between the change in the blood pressure and drug infusion rate (Slate, 1980) is as follows:

$$\Delta P(s) = \frac{Ke^{-T_i s}(1+\alpha e^{-T_c s})}{1+\tau s} I(s) \tag{2}$$

where $\Delta P(s)$ is the arterial blood pressure variation, $I(s)$ is the infusion rate, K is drug sensitivity, α is the recirculation constant, T_i is the inertial transport delay, T_c is the recirculation time delay, and τ is a time constant.

The corresponding discrete-time deterministic model for this process can be given as follows:

$$\Delta P(t) = \frac{q^{-d}(b_o + b_m q^{-m})}{1 - a_1 q^{-1}} I(t); b_o > 0 \tag{3}$$

where q^{-1} denotes a unit delay operator. The parameters b_o, b_m, a_1, d, and m are obtained from the sampled version of the continuous-time model given in (2).

A range of typical values for the parameters of the model (2) for different patients is given by (Slate, 1980). Using these values and the sampling time T_s equal to 15 s, a range of values for the parameters in model (3) can be computed. It is given in Table 1.

Table 1: Range of values for parameters of the discrete-time deterministic plant model for sampling time of 15 s.

Parameter	Minimum	Maximum	Nominal
b_o	0.053	3.546	0.187
b_m	0	1.418	0.075
a_1	0.606	0.779	0.741
d	2	5	3
m	2	5	3

3 MULTIPLE MODEL ADAPTIVE CONTROL METHOD

The Multiple Model Adaptive Control (MMAC) procedure, is based upon the assumption that the plant can be represented by a finite number of models and, for each model a controller can be priori designed.

An adaptive mechanism is then need to decide which controller should be dominant for a given plant. One procedure for solving this problem is to consider a weighted sum of all the controller outputs, where the weighting factors are determined by the relative residuals between the plant response and the model responses (Silva et al., 2015). Figure 1 depicts the block diagram of the MMAC scheme using the SPGPC in controller bank. The equations that describe the model is presented on Table 2, and are explained in more detail in the following subsections.

3.1 Model Bank Design

The model bank consists of a number of models with constant parameters that characterize the individual plant subspace (He et al., 1986).

These models should have the same structure as the plant, and is described by Equation (4). Where the output pressure from model j is calculated by (5).

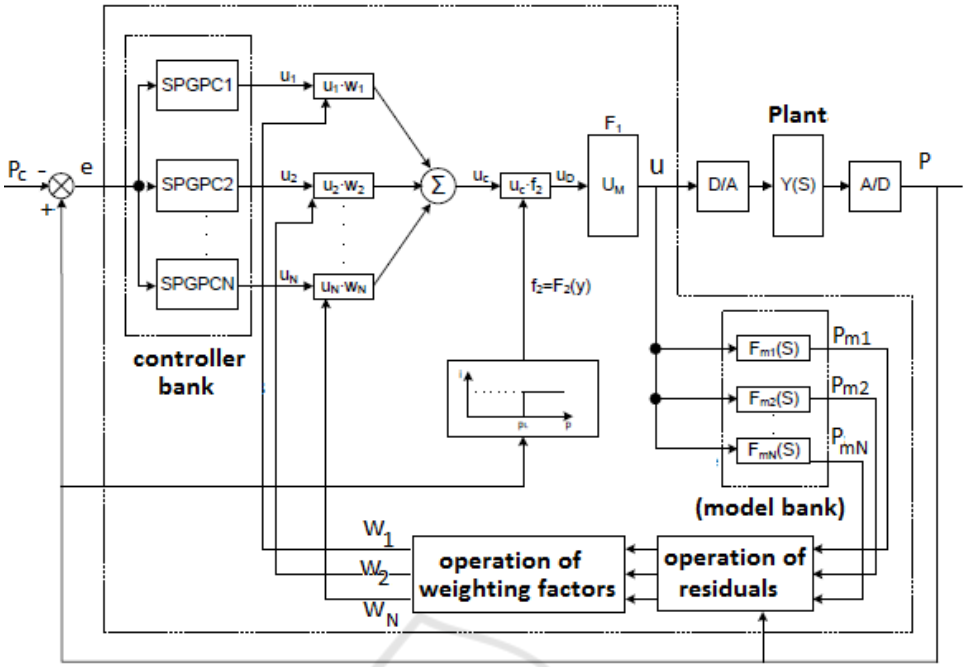

Figure 1: MMAC schema (Silva, 2015).

Table 2: Equations used in the MMAC schema.

Equation	
$\Delta P_{mj}(k) = \frac{q^{-d}(b_{oj} + b_m q^{-m})}{1 - a_1 q^{-1}} u(k); b_{0j} > 0 \ \ (j = 1, \dots, N)$ where $\Delta P_{mj}(k)$ is the change in the jth model output, u(k)is the model input, P_0 is the initial value	(4)
$P_{mj}(k) = \Delta P_{mj}(k) + P_0 \ \ (j = 1, \dots, N)$	(5)
$R_j^2(k) = \{[P_{mj}(k) - P(k)] / (P_0 - P_c)\}^2$	(6)
$u_c(k) = \sum_{j=1}^{N} W_i(k) u_j(k)$ where *N* is the number of models, $u_c(k)$ is the control variable, $u_j(k)$ are the individual controller outputs and $W_j(k)$ are the weighting factors.	(7)
$W_j^{'}(k) = \frac{\exp[-R_j^2 / 2V^2] W_j(k-1)}{\sum_{i=1}^{N} \exp[-R_i^2 / 2V^2] W_i(k-1)}$	(8)
$W_j \ (k) = \begin{cases} W_j^{'}(k) & W_j^{'}(k) > \delta \\ \delta & W_j^{'}(k) \le \delta \end{cases}$	(9)
$W_j \ (k) = \frac{[W_j \ (k)]^2}{\sum_{i=1}^{N} [W_i(k)]^2}$	(10)
$W_j(0) = W_j'(0) = \frac{1}{N} \quad (j = 1, \dots, N)$ where *N* is the number of models	(11)
$e(k) = p(k) - p_c$	(12)

Table 2: Equations used in the MMAC schema (cont.).

$u = F_1(u_D) = 0$, *if* $u_D < 0$; $= F_1(u_D) = u_D$, *if* $u_D \leq U_M$; $= F_1(u_D) = U_M$, *if* $u_D > U_M$.	(13)
$F_2(p(k)) = 1$, *for* $p(k) \geq p_L$; *or* $F_2(p(k)) = 0$, *for* $p(k) < p_L$. *Where* p_L *is defined as* $p_L = p_c - 20$ *and* p_c *is the commanded pressure setpoint*	(14)

The relative residual $R_j^2(k)$ will be defined as the normalized squared error between plant and model (6). At each sample time *k*, the model that has the smallest residual is defined as the matching model, which will be used to represent the plant characteristics.

3.2 Control Algorithm

To reach desirable system performance and to guarantee patient safety, the control algorithm should converge quickly to the optimal values and should react to time varying plant characteristics, as well as ensure a reasonable rate of blood pressure change. Table 2 shows the main equations used inr the MMAC control algorithm that will be explained following. Thus, the control was computed as a weighted sum of controller bank signals, and represented by the equation (7).

The weights were selected in 3 steps:

1. Recursive update calculated by (8);
2. Bounding away from zero by (9)
3. Normalization by (10)

where $R_j(k)$ are the residuals and defined in (6), *V* is a parameter controlling the convergence rate of *W'j(k)* with $R_j(k)$ and δ is a threshold to limit the importance of past information.

Equations (7) and (8) express the basic relationship between the control, the weighting factors, and the relative residuals. Equation (9) is used to delimit the importance of past information enabling the adaptive mechanism quickly react to the new information about the plant characteristics. Equation (10) is used to normalize the weighting factors so that their square sum is equal to unity.

The parameter *V* in (8) plays an important role in controlling the convergence rate of $W_j(k)$. To see this, let $R_m(k)$ and $W_m(k)$ represent the residual and the weighting factor corresponding to the matching model, then:

$$R_m(k) < Rj(k) \quad (for\ j \neq m) \tag{15}$$

From (8) and (10) it can be seen that:

$$\frac{W_j(k)}{W_m(k)} = \left\{exp\left[-\frac{1}{V^2}\left(R_j^2 - R_m^2\right)\right]\right\}\frac{W_j(k-1)}{W_m(k-1)} \tag{16}$$

Thus, for rapid convergence of $W_j(k)$, a smaller value of *V* is desired; however, an excessive reduction in *V* could cause a computer overflow. In the algorithm, the initial weighting factors $W_j(0)$ and the threshold δ must be determined a priori. Since the plant gain may be located in any position in the plant parameter space, the values for $W_j(0)$ were assumed to be uniform and calculated by (11).
From (8), it is observed that a large value of δ will improve the sensitivity of the algorithm to the new plant information.
In Fig. 1, since the plant gain is negative, the system error is expressed as (12). Where K is the sampling time and p_c, is the commanded or set-point pressure level.

For patient safety, two nonlinear units are built into the system. The nonlinear unit limiting infusion rate is given by (13). Where U_M is the allowed maximum infusion rate. The other nonlinear unit is used to turn off the infusion if and when hypotension occurs (Slate, 1980). Its expression is given by (14).

4 SIMULATION RESULTS AND SENSITIVY ANALYSIS

Computer simulations were used to evaluate the response of the system design (Section 4) over a representative plant parameter envelope. It were studied the response to step command in the presence of plant background noise, the adaptation of the algorithm to time-varying plant parameter. Tables 3 and 4, show, the parameters of models bank and patients tested, respectively.

Figure 2 shows a 3D chart, where it is possible to visualize the parameters b_0, b_m and a_1 of the models present in Tables 3 and 4.

The regime blood pressure considered was *150 mmHg* and the multi-model controller deviation reference of *-50 mmHg*. The plant background noise *v(t)* was simulated as a white Gaussian noise sequence with standard deviation of *2 mmHg*.

Table 3: Parameters of the models bank.

Model	Parameters				
	b_0	b_m	a_1	d	m
M1	0,053	0	0,606	3	3
M2	0,053	0	0,779	3	3
M3	0,053	1,418	0,606	3	3
M4	0,053	1,418	0,779	3	3
M5	3,546	0	0,606	3	3
M6	3,546	0	0,779	3	3
M7	3,546	1,418	0,606	3	3
M8	3,546	1,418	0,779	3	3
M9	0,187	0,075	0,741	3	3

Table 4: parameters of the patients tested.

Patient	Parameters				
	b_0	b_m	a_1	d	m
1	1,799	0,709	0,690	3	3
2	2,672	1,063	0,735	3	3
3	0,103	0,100	0,779	3	3
4	0,318	0,076	0,697	3	3
5	2,820	1,360	0,719	3	3
6	2,155	0,372	0,719	3	3
7	1,025	0,775	0,771	3	3

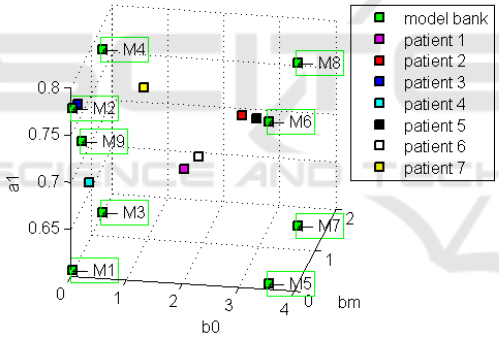

Figure 2: Parameters of the models bank and patients tested.

A sensitivity analysis was performed, changing the parameter that control the convergence rate of weight factors (V in Equation (8)) and computing the performance indexes as follows:

1) **T_s** – Settling Time = the time required for the response curve to reach and stay within a range of 5% of the set point value;

2) Root Mean Square Erro (RMSE)

$$\textbf{RMSE} = \sqrt{\frac{\sum_{i=1}^{N}(e_i)^2}{N}}; \quad (17)$$

3) Root Mean Square Control Effort (RMSU)

$$\textbf{RMSU} = \sqrt{\frac{\sum_{i=1}^{N}(u_i - u_{i-1})^2}{N}}. \quad (18)$$

Table 5 shows the relationship between parameter V and values obtained for T_s, RMSE and RMSU for each simulated patient, presented in table 4.

The maximum, minimum and mean values of T_s, RMSE and RMSU of Table 5 were represented in the figures 3, 4, 5, respectively.

Figures 6, 7 and 8 show blood pressure, infusion rate and weight factors for patient 1, using V = 0.05, respectively.

The simulations results presented in Figure 8 shown the convergence process of the weighting factors $W_j(k)$, with the global control effort to be calculated relatively to the closest model (less residual error).

Figure 6 shows that the schema leads the blood pressure of the chosen patient to the set reference. These results also show that the MMSPGPC algorithm is robust even in the presence of the plant background noise.

Table 5: Relationship between parameter V and values obtained for T_s, RMSE and RMSU for each simulated patient.

Patient	**T_s**						**RMSE**						**RMSU**					
1	330	315	330	360	360	375	16,3	11,1	10,9	10,8	10,7	10,7	0,9	0,5	0,4	0,4	0,4	0,4
2	330	315	330	330	345	360	15,7	10,5	10,5	10,4	10,3	10,2	0,8	0,4	0,4	0,3	0,3	0,3
3	465	**195**	480	510	510	**510**	18,7	13,1	13,1	13,2	13,2	13,2	10,4	5,6	5,0	4,0	3,6	3,5
4	285	330	330	330	330	330	17,6	17,2	17,0	17,1	17,1	17,1	3,9	1,9	2,0	2,3	2,4	2,4
5	435	330	330	345	345	360	16,5	15,3	15,2	15,0	14,9	14,9	0,6	0,6	0,5	0,5	0,5	0,5
6	315	315	315	330	345	345	15,9	15,9	15,7	15,4	15,3	15,2	0,8	0,7	0,6	0,6	0,6	0,5
7	405	405	405	405	435	435	16,4	16,5	16,4	16,2	16,1	16,0	0,5	0,5	0,5	0,4	0,4	0,4
Average	366	315	360	373	381	388	16,7	14,2	14,1	14,0	13,9	13,9	2,5	1,5	1,3	1,2	1,2	1,1
Min	285	195	315	330	330	330	15,7	10,5	10,5	10,4	10,3	10,2	0,5	0,4	0,4	0,3	0,3	0,3
Max	465	405	480	510	510	510	**18,7**	17,2	17,0	17,1	17,1	17,1	**10,4**	5,6	5,0	4,0	3,6	3,5
V	**0,01**	**0,05**	**0,1**	**0,2**	**0,3**	**0,4**	**0,01**	**0,05**	**0,1**	**0,2**	**0,3**	**0,4**	**0,01**	**0,05**	**0,1**	**0,2**	**0,3**	**0,4**

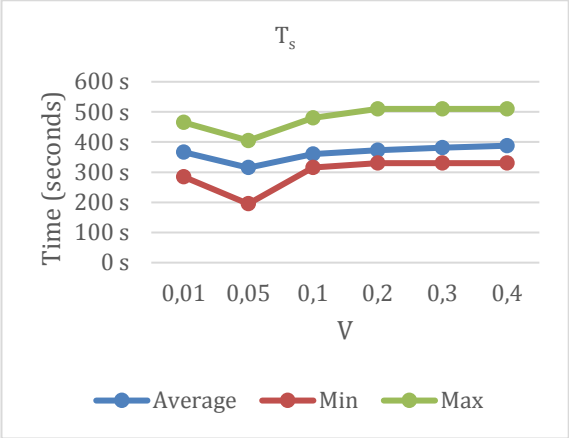

Figure 3: Average, maximum and minimum of T_s.

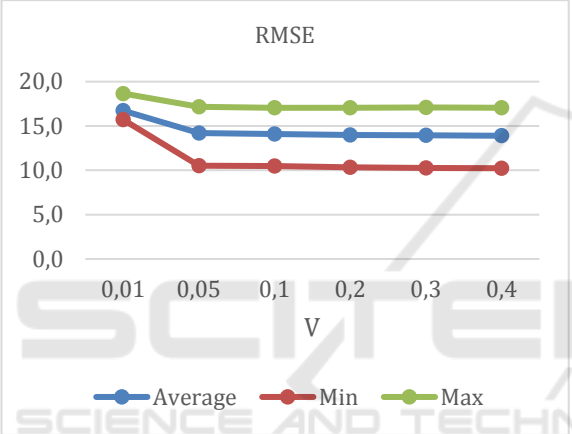

Figure 4: Average, maximum and minimum of RMSE.

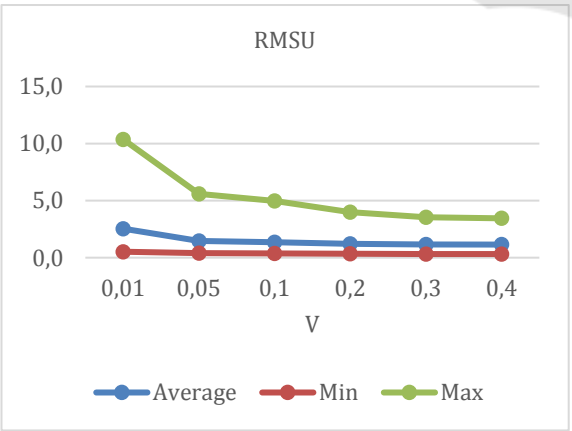

Figure 5: Average, maximum and minimum of RMSU.

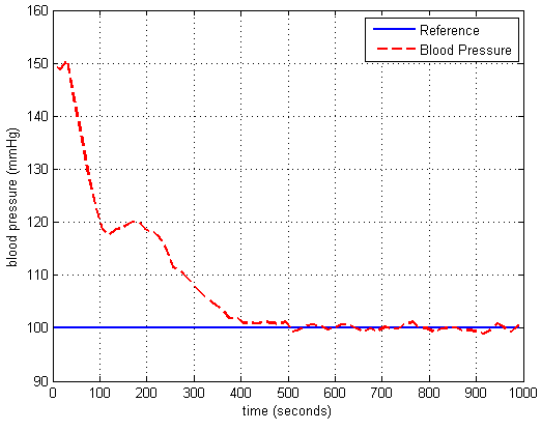

Figure 6: Blood pressure (mmHg) for the Patient 1, using *V*=0,05.

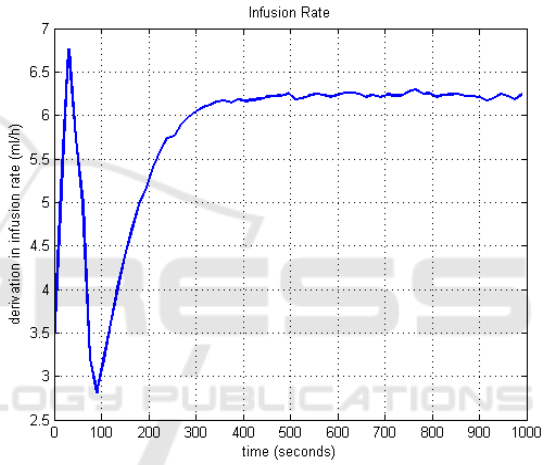

Figure 7: Infusion rate for the Patient 1, using *V*=0,05

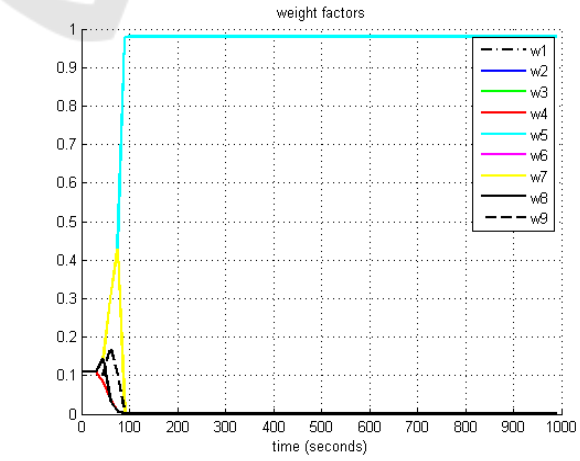

Figure 8: Weight factors for the Patient 1, using *V*=0,05.

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5 CONCLUSIONS

The results showed that the multi-model schema MMSPGPC presented has a great potential of application in uncertain systems. Even in presence of significant noise background, the presented approach has shown a reasonable result and could be applied, as first approach, in tests with animals. Others basic controllers, in order to attenuate the delay effect, may be considered.

The simulation results showed that, changes small in V can induce large changes in settling time (T_s). Where, for the patient 3, was obtained T_s = 195s using V = 0,05 and, T_s = 510s using V = 0,4, with the Root Mean Square Error (RMSE) varying less than 1% and small change in RMSU.

Moreover, the sensitivity analysis shows that for high values de V, had a slower convergence of the weight factors, thus an increase of T_s. However for low values de V, for example V = 0,05, has a faster convergence, reducing T_s, in most cases with small change in RMSU and RMSE. Although, overly faster convergence, for example $V \leq 0{,}01$, impair control, increasing the values of T_s, RMSE and RMSU.

In addition, the patient 3, which is closer to a model in models bank (see Figure 2), presented the lowest settling time (T_s = 195s) among all simulated patients (see Table 5). This suggests that, the nearness of the patient to a model in models bank, can provide a faster convergence.

In the future, robustness tests must be implemented with the submission of the system to a larger range of disturbances and parameters. Comparative studies with other control algorithms, such as robust adaptive control, they would also be important to accomplish in order to obtain the accuracy of the MMSPGPC presented

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