ADAPTIVE SWITCHING CONTROL OF QUADRATICALLY STABILIZABLE UNCERTAIN SYSTEMS WITH AN ANESTHESIA APPLICATION

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Abstract: The problem of controlling nonlinear noisy systems affected by large possibly non-parametric uncertainties is approached via the introduction of a supervisor which, whenever needed, switches on, in feedback to the plant, a controller selected from a finite set of predesigned controllers. An application to automatic drug delivery for anesthesia is presented to illustrate the method.

Keywords: Supervisory control, Lyapunov methods, Robust stability, Adaptive Control

1. INTRODUCTION

Control of time-varying plants in the presence of large uncertainties typically requires the introduction of adaptation in the feedback loop. However, conventional continuous adaptation is not always capable of performing satisfactorily mainly because of its inherent difficulty in taking advantage of prior knowledge of potential plant changes and/or of suitable candidate controllers.

In recent years, adaptive *switching supervisory control* (SSC) has emerged as an alternative approach for tackling the problem (Hespanha and Liberzon, 2001; Hespanha and Morse, 1999; Hilhorst *et al.*, 1994; Zhivoglyadov *et al.*, 2001) with its appealing inherent feature of resembling an adaptive version of classic gain-scheduling control which has been successful in so many applications. As a matter of fact, SSC aims at extending gain-scheduling control to cases where the supervisor has no full information on the current dynamical behaviour of the plant to be controlled. A typical situation is the one where only records of past plant I/O data are available in order to let the supervisor decide whether the current controller is adequate, and, in the negative, select another candidate controller.

Switching mechanisms are usually based on a supervisory logic whereby a controller is falsified whenever the inferred behaviour of another controller turns out to be better than the one actually achieved by the currently operating controller. Whenever this happens, the candidate controller with the best inferred behaviour is switched on in feedback to the plant, replacing the currently operating controller. The main contribution of this paper is to present falsification and inference criteria integrated in a new supervisory switching logic, whereby no prior information on disturbance bounds is required, nor specific knowledge of plant models, not even in the form of an uncertain parametric system of equations. In particular, the method may apply to situations in which the plant model (possibly nonlinear) is very poorly known (non-parametric uncertainties) provided that the state of the system be accessible for measurement.

2. PROBLEM FORMULATION

Consider a discrete time nonlinear system of the following form:

$$x_{t+1} = \tilde{f}(x_t, u_t, d_t) \qquad (1)$$
$$\tilde{f}(x, u, d) \doteq f(x, d) + g(x, u)$$

with states $x \in \mathbb{R}^n$, control inputs $u \in \mathcal{U} \subset \mathbb{R}^p$, and exogenous bounded disturbances $d_t \in \mathcal{D} \subset \mathbb{R}^q$. The aim is to design a supervisory control strategy, capable of orchestrate, based on I/O data, the switching among a finite family of candidate controllers in such a way that the resulting closed-loop system be stable. Moreover, we would like to allow the largest possible amount of a priori uncertainty on the plant (1). In particular, nothing is assumed on the function f which can be completely unknown. Knowledge of the function $g(x, u)$ is needed in the preliminary prototype version of the algorithm that we are going to develop; however, as shown in a subsequent section, it can in principle be neglected at the expense of some performance degradation. The control law is selected among a finite family of N state-feedbacks:

$$u_t = k_i(x_t) \qquad i = 1 \dots N. \qquad (2)$$

Notice that, thanks to the special decoupled form of (1) it is possible, based on the knowledge of the current and past states and inputs, to compute the one-step ahead state prediction based on the i-th feedback

$$x(t|i) := \tilde{f}(x_{t-1}, k_i(x_{t-1}), d_{t-1})$$
$$= x_t + g(x_{t-1}, k_i(x_{t-1})) - g(x_{t-1}, u_{t-1})$$

viz. the value of the state at t if the i-th controller would have been used in the loop at $t - 1$. The switching algorithm we propose improves on the one in (Angeli and Mosca, 2004) as no a priori knowledge of a Lyapunov function cover is assumed to be known.

3. THE IDEAL SUPERVISORY ALGORITHM

We first describe a prototype version of the algorithm, which already exhibits the main features of the approach, although its applicability is restricted in practice by the need of considering a growing number of past I/O data. The switching logic operates by comparing a set of performance signals Δ_t^i generated as follows

$$\Delta_t^i := \min D_i$$

$$\text{subject to } D_i \in \mathbb{R}, P_i = P_i' \in \mathbb{R}^{n \times n}$$

$$x(k|i)' P_i x(k|i) - \lambda x_{k-1}' P_i x_{k-1} \leq D_i \qquad (3)$$
$$\text{for all } k \in [1, t]$$

$$D_i \geq 0 \qquad \mathrm{I} \leq P_i \; (\leq MI)$$

where the constants $M > 1$ and $0 < \lambda < 1$ are parameter knobs of the supervisor.

Remark 3.1. It is useful to provide hints on the meaning of M. This is clearly an upper-bound on the condition number of P and hence an a priori bound on the eccentricity of the ellipsoidal level sets of the Lyapunov function the algorithm is seeking. Knowledge of this upperbound allows to limit the search of a decreasing quadratic function within a compact space and, through some analysis techniques that we discuss in the subsequent Section, will provide us with an estimate of the needed past data window. □

The following lemma is an easy consequence of (3).

Lemma 3.2. Let the system (1) be **quadratically stabilizable** with contraction rate λ for some controller $k_i(x)$, (and P_i condition number less than M) , viz. there exists $P_i : \; I \leq P_i(\leq MI)$ so that for all x, d

$$\tilde{f}(x, k_i(x), d)' P_i \tilde{f}(x, k_i(x), d) - \lambda x' P_i x \leq \gamma_i(|d|) \qquad (4)$$

for some $\mathcal{K}_\infty$ function γ_i. Then, there exists an index $i \in \{1 \dots N\}$ such that for all $t \in \mathbb{Z}_+$

$$\Delta_t^i \leq \max_{\tau \in [1, t-1]} \gamma_i(|d_\tau|) \qquad (5)$$

□

Let $i_t^\star$ denote the controller in the loop at time t with $i_0^\star$ arbitrarily initialized. We adopt a switching logic with hysteresis defined as follows:

$$i_t^\star := \arg\min_i \{\Delta_t^i - \varepsilon \delta_{i i_{t-1}^\star}\} \qquad (6)$$

where $\varepsilon > 0$ plays the role of an additive hysteresis constant, and δ_{ij} is the Kroneker's δ. The following holds:

Lemma 3.3. Assume that system (1) is fed at time $t \in \mathbb{Z}_+$ by the control $u_t = k_{i_t^\star}(x_t)$ where $i_t^\star$ is selected according to (6). Then, the number of controller switchings up to time t, that we denote by η_t, can be upperbounded as follows:

$$\eta_t \leq (N+1) \cdot \left\lceil \frac{\min_i \Delta_t^i}{\varepsilon} \right\rceil \qquad (7)$$

where $\lceil y \rceil$ denotes the smallest integer greater than or equal to y. □

For the proof of the previous lemma, see (Angeli and Mosca, 2004) (Lemma 3.3).

Practical Input-to-State Stability (ISS) for the overall scheme can now be proved.

Theorem 1. Let the plant be quadratically stabilizable with the P condition number upperbounded by M as in (4) for some controller $k_i(x)$. Then, system (1) controlled by the supervised state-feedback:

$$u_t = k_{i_t^\star}(x_t)$$

where $i_t^\star$ is selected according to the supervisory logic in (3) and (6), is practically Input to State Stable. □

Proof 3.4. Let $\|d\|_\infty$ be bounded (if d is unbounded nothing is left to prove as the ISS claim is void). By virtue of Lemma 3.2, $\min_i \Delta_t^i \leq \gamma(\|d\|_\infty)$. Therefore, exploiting (7) the switching stops in finite time. From that time on, call it t_0, $i_t^\star \equiv i^\star$, and a sequence of matrices P_t exists, $I \leq P_t \leq MI$, so that for the closed-loop trajectory corresponding to the $i^\star$ controller:

$$x_k' P_t x_k - \lambda x_{k-1}' P_t x_{k-1} \leq \min_i \Delta_t^i + \varepsilon$$

for all $k \in [t_0+1, t]$. Since by Lemma 1, $\min\{D_t^i\} \leq \gamma(\|d\|_\infty)$ we can conclude that:

$$x_k' P_t x_k - \lambda x_{k-1}' P_t x_{k-1} \leq \gamma(\|d\|_\infty) + \varepsilon$$

for all $k \in [t_0+1, t]$. Assume without loss of generality $P_t \to \bar{P}$ as $t \to +\infty$. Fix an arbitrary finite $k > t_0$ we have:

$$x_k' P_t x_k - \lambda x_{k-1}' P_t x_{k-1} \leq \gamma(\|d\|_\infty) + \varepsilon$$

for all $t \geq k$. Hence, going to the limit as $t \to +\infty$ yields:

$$x_k' \bar{P} x_k - \lambda x_{k-1}' \bar{P} x_(k-1) \leq \gamma(\|d\|_\infty) + \varepsilon.$$

Since k is arbitrary we may conclude for $V(x_t) := x_t' \bar{P} x_t$.

$$V(x_t) \leq V(x_{t_0}) \lambda^{(t-t_0)} + \frac{\gamma(\|d\|_\infty) + \varepsilon}{1-\lambda}.$$

This concludes the proof of Practical Input-to-State Stability.

4. FINITE WINDOW LENGTH

The algorithm in the previous Section entails, at each time step, the solution of an LMI of linearly growing dimension. This is a serious drawback of the algorithm which keeps its validity only as a conceptual scheme. Hereafter we discuss the possibility of limiting the amount of past data to a finite window length without affecting in a significant manner the stability features of the prototype algorithm. To this end we consider the following modified performance criteria:

$$\begin{gathered} \Delta_t^i := \min D_i \\ \text{subject to } D_i \in \mathbb{R}, P_i = P_i' \in \mathbb{R}^{n \times n} \\ x(j|i)' P_i x(j|i) - \lambda x_{j-1}' P_i x_{j-1} \leq D_i \\ \text{for all } \ j \in [t-L, t] \\ D_i \geq \Delta_{t-1}^i \qquad \mathrm{I} \leq P_i \leq MI. \end{gathered} \qquad (8)$$

There are two fundamental differences with respect to (3). First of all, only a finite window length of $L+1$ past samples for the state are considered. As a consequence, monotonicity of the signals Δ_t^i could, in principle, be lost; this is why the monotonicity property is enforced by letting $D_i \geq \Delta_t^i$ in the optimization (8). It is clear that Lemma 3.2 holds even in this new set-up. We are now ready to prove the Main Result of the paper.

Theorem 2. Let the plant be quadratically stabilizable with condition number upperbounded by M for some controller $k_i(x)$. Then, system (1) controlled by the supervised state-feedback:

$$u_t = k_{i_t^\star}(x_t)$$

where $i_t^\star$ is selected according to the supervisory logic in (8) and (6), is practically Input to State Stable provided that

$$L \geq M \frac{\lambda}{1-\lambda}. \qquad (9)$$

□

Proof 4.1. Let $\|d\|_\infty$ be bounded (if d is unbounded nothing is left to prove as the ISS property trivially holds). By virtue of Lemma 3.2, $\min_i \Delta_t^i \leq \gamma(\|d\|_\infty)$. Therefore, exploiting (7) the switching stops in finite time. From that time on (let us relabel this as t_0 and assume without loss of generality $t_0 > L$), $i_t^\star \equiv i^\star$, and a sequence of matrices P_t exists, $I \leq P_t \leq MI$, so that for the closed-loop trajectory corresponding to the $i^\star$ controller:

$$x_k' P_t x_k - \lambda x_{k-1}' P_t x_{k-1} \leq \min_i \Delta_t^i + \varepsilon \qquad (10)$$

for all $t \geq t_0$ and all $k \in [t-L, t]$. We define the following candidate Lyapunov function $\Pi_t := \sum_{i=0}^{L} P(t+i)$ and $V_t := x_t'\Pi_t x_t$. By Lemma 3.2 it is straightforward to verify that:

$$
\begin{aligned}
V_t &= x_t'\Pi_t x_t = \sum_{i=0}^{L} x_t' P_{t+i} x_t \\
&\leq \sum_{i=0}^{L} \lambda x_{t-1}' P_{t+i} x_{t-1} + \gamma(\|d\|_\infty) + \varepsilon \\
&= \lambda x_{t-1}'\Pi_{t-1} x_{t-1} + \gamma(\|d\|_\infty) + \varepsilon \\
&+ \lambda x_{t-1}'[P_{t+L} - P_{t-1}] x_{t-1} \\
&\leq \lambda x_{t-1}'\Pi_{t-1} x_{t-1} + \\
&+ \lambda(M-1) x_{t-1}' x_{t-1} + \gamma(\|d\|_\infty) + \varepsilon \\
&\leq \lambda(1 + (M-1)/(L+1)) x_{t-1}'\Pi_{t-1} x_{t-1} \\
&+ \gamma(\|d\|_\infty) + \varepsilon = \tilde{\lambda} V_{t-1} + \gamma(\|d\|_\infty) + \varepsilon \quad (11)
\end{aligned}
$$

where we defined $\tilde{\lambda} := \lambda(1 + (M-1)/(L+1))$. Therefore if we choose

$$L \geq M \frac{\lambda}{1-\lambda}$$

we have $\tilde{\lambda} < 1$ and this in turn implies practical ISS by virtue of (11).

5. HANDLING NON-DECOUPLED DISTURBANCES

The special form of $\tilde{f}$ allows to compute the expression of $x(t|i)$ for all $i = 1 \ldots N$; In words it allows to perform a "virtual" experiment and compute the state of the system at time t as if the $i-$th controller were in the loop at time $t-1$. This approach, which allows to evaluate the performance of controllers without actually "testing" them in feedback to the plant, has the drawback of requiring explicit knowledge of the vector function $g(x,u)$. When this is not the case, it is still possible, at the cost of performance degradation, to modify the performance signal generator according to the following set of equations:

$$
\begin{aligned}
&\delta_t^i = \min D_i \\
&\text{subject to: } D_i \in \mathbb{R}, P_i = P_i' \in \mathbb{R}^{n\times n} \\
&\quad x_k' P_i x_k - \lambda x_{k-1}' P_i x_{k-1} \leq D_i \\
&\quad \forall\, k \in [t-L, t]: \quad i_{k-1}^\star = i \\
&\quad D_i \geq \Delta_{t-1}^i \qquad \mathrm{I} \leq P_i \leq M I. \\
&\Delta_t^i = \begin{cases} \Delta_{t-1}^i & \text{if } i \neq i_{t-1}^\star \\ \delta_t^i & \text{if } i = i_{t-1}^\star \end{cases}
\end{aligned}
\tag{12}
$$

The signal generator (12) can be applied to general nonlinear systems of the form

$$x_{t+1} = \tilde{f}(x_t, u_t, d_t). \tag{13}$$

Notice that the performance signal relative to any controller, is frozen whenever the controller is not in the loop. If the controller is currently operating, the performance signal is updated and possibly increased, by imposing a quadratic dissipation inequality over the time samples, among the last $L+1$, for which a certain controller was active. By the above considerations it is clear that Lemma 3.2 still holds with the performance signals generator (12).

We are now ready to state our main result for this Section.

Theorem 3. Let the plant be quadratically stabilizable with condition number upperbounded by M for some controller $k_i(x)$. Then, system (1) controlled by the supervised state-feedback:

$$u_t = k_{i_t^\star}(x_t)$$

where $i_t^\star$ is selected according to the supervisory logic in (12) and (6), is practically Input to State Stable provided that

$$L \geq M \frac{\lambda}{1-\lambda}. \tag{14}$$

□

Proof 5.1. Let $\|d\|_\infty$ be bounded (if d is unbounded nothing is left to prove as the ISS property trivially holds). Notice that the signals Δ_t^i generated by (12) are monotone as functions of time. By virtue of Lemma 3.2, $\min_i \Delta_t^i \leq \gamma(\|d\|_\infty)$. Therefore, exploiting (7) the switching stops in finite time. Let us relabel this as $\tilde{t}_0$ and $t_0 := \tilde{t}_0 + L + 1$, so that, for all $t \geq t_0$, we are guaranteed that Δ_t^i computed according to (12) equals Δ_t^i computed according to (8). Hence, the stability proof can be carried out along the same lines as in Theorem 2.

The last piece of a priori information that needs to be removed in order to come up with a fully data-based method is the upperbound M on the condition number of the quadratic Lyapunov function P. If such an M is not known in advance we may as well adopt an algorithm in which both M and L are time-varying. We suggest the following update law:

$$M_{t+1} = \begin{cases} M_t & \text{if } i_t^\star = i_{t-1}^\star \\ 2 \cdot M_t & \text{if } i_t^\star \neq i_{t-1}^\star \end{cases}$$

An analogous update law can be used for L_t; in particular the window length will double at each switching instant. Since switching stops, M and L will become eventually constant and stability can be analyzed provided that M and L are arbitrarily initialized subject to (14).

6. APPLICATION TO NEUROMUSCULAR BLOCKADE REGULATION

The dynamic response of the neuromuscular blockade may be modelled by a cascade of a linear compartmental pharmacokinetic model (Mendonca and Lago, 1998) whose transfer function is:

$$\frac{c(s)}{u(s)} = \frac{1/\tau}{s+1/\tau}\frac{\lambda}{s+\lambda}\left(\frac{a_1}{s+\lambda_1}+\frac{a_2}{s+\lambda_2}\right) \quad (15)$$

followed by a nonlinear memoryless output function:

$$r_t = \frac{100{C_{50}}^S}{{C_{50}}^S + c_t^S} \quad (16)$$

In the former equations c_t is the effect compartment concentration, u_t is the drug infusion rate and r_t is the level of neuromuscular blockade, normalized between 0 and 100. Moreover $\vartheta \doteq [a_1\ a_2\ \lambda_1\ \lambda_2\ \lambda\ C_{50}\ S\ \tau]' \in \mathbb{R}^8$ is an uncertain parameter vector.

A general requirement in anesthesia is to ensure a suitable level of muscle relaxation in the patient. To this end, supported by clinical results, 5 robust PID controllers were designed (Manuelli and Mosca, 2003) of the following form:

$$u_t = g_c\left(1+\frac{T_s}{c_i}\frac{z}{z-1}+\frac{c_d}{T_s}\frac{z-1}{z}\right)e_t \quad (17)$$

where $e_t = ref_t - r_t$ is the difference between the desired level, set by the anaesthetist, and respectively the induced level of neuromuscular blockade. T_s is the sampling time and g_c, c_i, c_d are the controller parameters. Experimental evidence suggested that none of the previous controllers could perform satisfactorily over a broad range of patients. Therefore it seems appropriate to implement a switching supervisory algorithm which adaptively selects the controller in the loop.

It is worth noticing that, based on (2), the admissible controllers are nonlinear static state feedbacks on the contrary, the PIDs in (17) are dynamic output controllers. To cope with this discrepancy notice that:

$$A_\vartheta(d)c_t = B_\vartheta(d)u_t \quad (18)$$

or equivalently: $\Delta(d)A_\vartheta(d)c_t = B_\vartheta(d)\delta u_t$ where $\Delta(d) = 1-d$ and for the PID controllers:

$$\delta u_t = -S_i(d)e_t \quad i = 1,\ldots,5 \quad (19)$$

with

$$\begin{aligned} A_\vartheta(d) &= 1 + a_1(\vartheta)d + \ldots + a_{n_y}(\vartheta)d^{n_y} \\ B_\vartheta(d) &= b_1(\vartheta)d + \ldots + b_{n_u}(\vartheta)d^{n_u} \\ S_i(d) &= s_{i0} + s_{i1}d + \ldots + s_{in_s}d^{n_s} \end{aligned} \quad (20)$$

where $A_\vartheta(d)$, $B_\vartheta(d)$ are the polynomials resulting from the discretization of (15) with sampling time T_s and $S_i(d)$ is a realization of the PID in (17). Since $c_t = \mathcal{NL}(\vartheta, e_t, ref_t)$, as from (16), the recursion for e_t is of the form: $\bar{A}_\vartheta(d)\mathcal{NL}(\vartheta, e_t, ref_t) = B_\vartheta(d)\delta u_t$ where $\bar{A}_\vartheta(d) = \Delta(d)A_\vartheta(d)$. Equations (15)-(17) suggest n_y=4, n_u=4 and n_s=2 as the degrees of polynomials in (20). Hence, choosing the state vector as: $\chi_t = [e_t\ e_{t-1}\ e_{t-2}\ e_{t-3}\ e_{t-4}\ \delta u_{t-1}\ \delta u_{t-2}\ \delta u_{t-3}]'$, the system evolution is described by an equation of the form: $\chi_{t+1} = f(\vartheta, \chi_t, \delta u_t, ref_t)$. Notice that this is not a minimal realization of the I/O mapping, however, in this way the supervisor can switch among static state feedback gains of the form $u_t = k_i(\chi_t)$ as specified in (2). Numerically, the local quadratic stabilizability of the plant in feedback with at least one of the controllers has been verified. Unfortunately, the high non linearity of the output function (16) does not allow to globally fulfill quadratic stability of the closed loop system. As a consequence, convergence is guaranteed only locally around the desired equilibrium. Since the neuromuscular blockade system (15)-(16) does not allow the explicit knowledge of the vector function $g(x,u)$ in (1), the approach described in Sec. 5 was applied.

In the following simulations ref_t is fixed to a constant value r_0 =10% which corresponds to a high level of neuromuscular blockade typically required in many surgical activities. The sample time is fixed to 20 sec.. During the first 10 minutes the control loop is open because the patient is assimilating the drug bolus dose injected at time t= 0 in order to induce total neuromuscular blockade in a short period of time.

The switching algorithm parameters are set to ε= 1 and λ= 0.98. The latter is chosen greater than the dominant eigenvalue of the closed loop in such a way that a desired convergence rate could be satisfied. A drawback of using a non-minimal realization is the ill-conditioning of the closed loop system matrix which imposes, in turn, a high value for the M parameter. Since, accordingly to (14), this would imply a large past data window, simulations (see figures 1, 2) were carried out ignoring the theoretical bound in (14) and L was fixed to 50 samples which appeared to be a good compromise between window length and performance of the algorithm. The same experiment was carried out with an output noise of 3% magnitude of the reference value and the algorithm (see figures 3, 4) still performs satisfactorily.

7. CONCLUSIONS

A new supervisory switching algorithm is discussed for uncertain nonlinear systems affected by

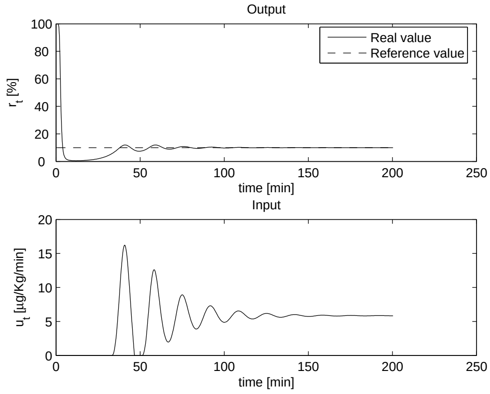

Fig. 1. Figure shows the output (top) and the input (bottom) of the plant when $\varepsilon = 1$, $\lambda = 0.98$ and $M = 10^{13}$.

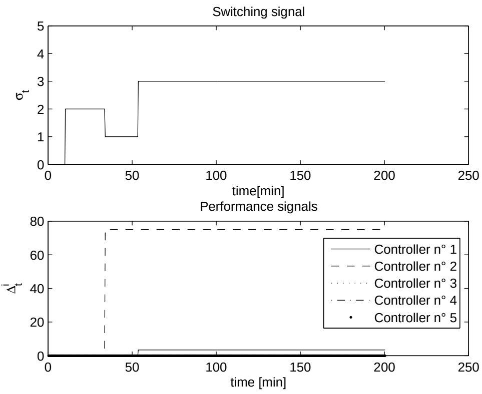

Fig. 2. Figure shows the switching signal (top) and the performance signals (bottom) relative to the 5 controllers.

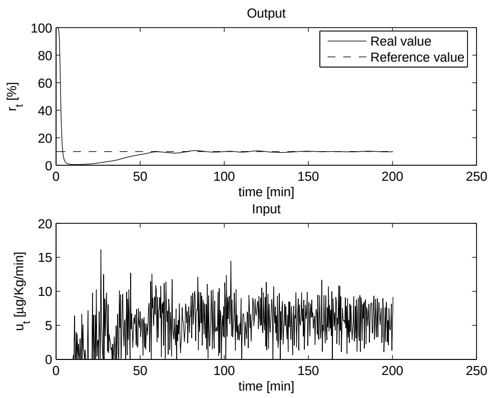

Fig. 3. Output (top) and input (bottom) are shown when a 3% amplitude noise is added on the plant output.

disturbances of unknown bounded amplitude. The method reduces to a minimum the amount of a priori information needed in order to be implemented. In particular, in its most general version can be seen as a fully data-based method. The key idea is to exploit collected data relative to each controller in order to build a quadratic Lyapunov function which is possibly decreasing along

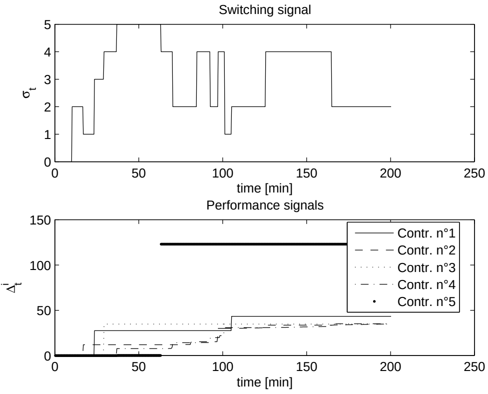

Fig. 4. Switching signal (top) and performance signals (bottom) relative to the 5 controllers are shown for the same setting as previous figure.

trajectories or at least bounded. As a by-product of the computation of the Lyapunov function, performance signals are generated which provide an estimate of the magnitude of disturbances acting on the plant. Some performance degradation is to be expected compared to similar Lyapunov-based methods which required more a priori information on the plant. Simulations for a comparisons of the two schemes are currently under investigation.

REFERENCES

Angeli, D. and E. Mosca (2004). Adaptive switching supervisory control of nonlinear systems with no prior knowledge of noise bounds. *Automatica* **40**, 449–457.

Hespanha, J. P. and A. S. Morse (1999). Stability of switched systems with average dwell-time. In: *Proc. of the 39th Conference on Dec. and Control.* Phoenix.

Hespanha, J.P. and D. Liberzon (2001). Special issue on switching and logic in adaptive control. *Int. Journal of Adaptive control and Signal processing* **15**, 211–374.

Hilhorst, R. A., J. Van Amerongen, P. Löhnbergand and H. J. A. F. Tulleken (1994). A supervisor for control of mode-switch processes. *Automatica* **30**, 1319–1331.

Manuelli, C. and E. Mosca (2003). A reduced-complexity adaptive switching supervisory control of neuromuscular blockade. In: *Proc. of the 16th Int. Conf. on Sys. Eng..* Coventry. pp. 463–466.

Mendonca, T. and P. Lago (1998). Pid control strategies for the automatic control of neuromuscular blockade. *Control Engineering Practice* **6**, 1225–1231.

Zhivoglyadov, P.V., R.H. Middleton and M. Fu (2001). Further results on localization-based switching adaptive control. *Automatica* **37**, 257–263.