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Robust estimation for hybrid models of genetic networks

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Abstract— **In this paper we consider state estimation problems with Boolean measurements for a classical negative loop genetic network governed by a piecewise affine (PWA) model. In the first part, an observer is proposed for the case where full state Boolean measurements are available. In particular sliding modes may occur and this leads to finite time convergence for the observer. In the second part we discuss state estimation with partial state Boolean measurements. A naive approach based on algebraic computation is proposed to solve the initial condition inverse problem. In the third part the observer is used to identify some unknown but fixed parameters of the model. We also investigate the robustness of the observer for a parametric uncertain model, and show that the error bound is proportional to the magnitude of the uncertainty.**

I. INTRODUCTION

This work deals with the observation aspect of a class of hybrid systems with discrete measurements. More precisely, we consider in this paper a class of piecewise affine (PWA) systems which is used to model simplified genetic regulatory networks. This approach is useful to the qualitative understanding of biological networks.

The PWA system framework was first introduced by Glass in the early 70's (see for instance [8]) and has been studied for decades. In particular, we will focus on the analysis of a basic motif, the negative feedback loop, which describes the interactions among n genes: gene x_2 inhibits gene x_1, gene x_{i+1} activates gene x_i ($i = 2 \dots, n-1$) and gene x_1 activates gene x_n. For example, it is shown in [13] that under some assumption on the parameters, a 2-dimensional negative loop system behaves as a damped oscillator. For higher-dimensional case, it is proved that the system converges to a limit cycle.

From a mathematical biology point of view, oscillations play an important role since rhythmic phenomena are quite common in living organisms. For this purpose, control problems for PWA systems are considered in [4] to generate and destroy oscillatory behavior for the PWA model of 2-node negative loop genetic network by PWA controls.

We are interested here in state estimation problems with Boolean measurements, that is to say, the only available knowledge (complete or partial) is whether the protein concentrations are above or below some threshold values. This kind of problem is interesting because due to the experimental techniques used (such as microarray technique), very often the measurements of genes expression are only qualitative, e.g., the gene is strongly or weakly expressed (cf. [9] and [7]). In some sense this kind of 'fuzzy-like' output represents also the robustness in the measurements.

For PWA systems, the observability problem is considered in [1]. Sliding mode observers can also be used (e.g. see [15]) with the measurement taken as a part of the state vector. These methods cannot be applied directly in our case because we only have qualitative measurements. Systems with quantized output observations are also widely studied. In the case where the measurements are only the sign-observations of the state without precise value, [10] investigate the observability problem of linear systems without switches. In [2], a quantized state feedback control strategy is proposed to stabilize linear systems. The quantizer considered is a set of right-continuous step functions. This method cannot be applied here because our model is a discontinuous system. In [6] the authors analyze the global convergence for a class of neural networks where the neuron activations are modeled by discontinuous functions, but the observability problem is not considered.

In our paper [11] we proposed a simple observer for a 2-dimensional negative loop system with full state Boolean measurements. The observer converges with at least the same rate as the nominal system. Moreover, thanks to the sliding motion, one can obtain *finite time* convergence after two switches (in the best case where one takes the 'optimal' initial condition for the observer). This property is interesting because for example, for a damped oscillator which converges in finite time, it is important to estimate the state variables before they converge to the stable focus. Here we extend the observer to the n-dimensional loop.

We next consider the state estimation problem with partial Boolean measurements, for $n = 2$. Unfortunately one cannot apply the same type of observer as in the full measurements case. Indeed the system is observable if and only if the state variables are located in two different half-planes. Instead, it is possible to solve the initial condition inverse problem by an algebraic approach.

Finally we check the robustness of our observer for parametric perturbed systems. Two types of perturbations are considered: 1) unknown variation on the synthesis coefficients, and 2) uncertainty on the threshold values. For the first point we propose an adaptive dichotomy algorithm to identify the unknown parameter. For the second one, we will show that the observer is robust in the practical sense.

This paper is organized as follows. We introduce the n-dimensional PWA system in Section 2. An exponentially convergent observer with complete Boolean measurements is given in Section 3, together with the sliding mode existence

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condition and some convergence time estimation. In Section 4 an approach is proposed to determine the initial condition in the partial Boolean measurement case. In Section 5 we investigate the robustness of the observer for some parametric perturbed and uncertain models.

II. PWA MODEL AND PROBLEM STATEMENT

Consider an n-node genetic network

$$\begin{array}{ccccc} x_2 & \dashv & x_1 & \rightarrow & x_n \\ \uparrow & & & & \downarrow \\ x_3 & \leftarrow & \cdots & \leftarrow & x_{n-1} \end{array}$$

which represents a negative feedback loop in a complex regulatory network. The symbols $\vdash$ and $\rightarrow$ denote respectively gene inhibition and activation (see for instance [14] for an example in biology).

The classical PWA model of the above network, presented in [14] is described by population balance equations as follows:

$$\begin{array}{rcl} \dot{x}_1 & = & k_1(1 - s^+(x_2, \theta_2)) - d_1 x_1, \\ & \vdots & \\ \dot{x}_i & = & k_i s^+(x_{i+1}, \theta_{i+1}) - d_i x_i, \qquad 2 \le i \le n-1 \\ & \vdots & \\ \dot{x}_n & = & k_n s^+(x_1, \theta_1) - d_n x_n \end{array}$$

with the step function defined by

$$s^+(x_i, \theta_i) = \begin{cases} 1, & \text{if } x_i > \theta_i, \\ 0, & \text{if } x_i < \theta_i. \end{cases} \qquad (1)$$

The state variables $x \in \mathbb{R}^n_{\ge 0}$, denote the protein concentrations, and the positive constant parameters k_i, d_i and θ_i, $i = 1, 2$, denote, respectively, the translation (production) rates, the degradation rates, and the threshold concentrations.

More generally, we rewrite the hybrid system (with possible inputs) into matrix form:

$$\dot{x} = Ka + KS(x, \theta) - \Gamma x + U(t) \qquad (2)$$

with $a = [1\ 0\ \ldots\ 0]'$, $S(x, \theta) = \text{vect}(s^+(x_i, \theta_i))$ and

$$\Gamma = \text{diag}(d_i), \quad K = \begin{pmatrix} 0 & -k_1 & 0 & \cdots & 0 \\ 0 & 0 & k_2 & \ddots & \vdots \\ \vdots & \ddots & \ddots & \ddots & 0 \\ 0 & \cdots & 0 & \ddots & k_{n-1} \\ k_n & 0 & \cdots & \cdots & 0 \end{pmatrix},$$

vector $U(t) \in \mathbb{R}^n_{\ge 0}$ denotes the inputs of external stimulation.

It is well known that under the assumption on the parameters

$$\frac{k_i}{d_i} > \theta_i, \quad i = 1, \ldots, n, \qquad (3)$$

the system without inputs ($U = 0$) is a damped oscillator when $n = 2$ and it converges to a limit cycle when $n \ge 3$ (see [13]). Using the notation in [13], the oscillatory trajectory of (2) can be represented by a state transition graph of a Boolean mapping of $S(x, \theta)$ (for the elements of the set $E = \{x \in \mathbb{R}^n_{\ge 0}, x_i \ne \theta_i\}$), which is a $2n$-cyclic attractor as follows:

$$\begin{array}{ccccccccc} 100\ldots00 & \rightarrow & 100\ldots01 & \rightarrow & \cdots & \rightarrow & 101\ldots11 & \rightarrow & 111\ldots11 \\ \uparrow & & & & & & & & \downarrow \\ 000\ldots00 & \leftarrow & 010\ldots00 & \leftarrow & \cdots & \leftarrow & 011\ldots10 & \leftarrow & 011\ldots11 \end{array}$$

in which the i-th component equals to $s^+(x_i, \theta_i)$. For the sake of simplicity, denote the regular domains (orthants) of $\mathbb{R}^n_{\ge 0}$ by

$$\begin{array}{rcl} D_1^- & = & \{x \in E\,,\ S(x, \theta) = [000\ldots00]\} \\ D_2^- & = & \{x \in E\,,\ S(x, \theta) = [010\ldots00]\} \\ & \vdots & \\ D_n^- & = & \{x \in E\,,\ S(x, \theta) = [011\ldots11]\} \\ D_1^+ & = & \{x \in E\,,\ S(x, \theta) = [111\ldots11]\} \\ D_2^+ & = & \{x \in E\,,\ S(x, \theta) = [101\ldots11]\} \\ & \vdots & \\ D_n^+ & = & \{x \in E\,,\ S(x, \theta) = [100\ldots00]\} \end{array} \qquad (4)$$

according to the above transition graph against the direction of the arrows.

Notice that the step function (1) is not defined on the threshold θ_i. Thus, whenever $x_i = \theta_i$ for some i, (2) should be defined as a differential inclusion and the solution should be interpreted in the sense of Filippov (cf. [5]).

As mentioned in the introduction, we are interested in state reconstruction problem with Boolean measurements. The only available outputs are the positions of the state variables x_i w.r.t. the thresholds θ_i. (cf. Fig. 1)

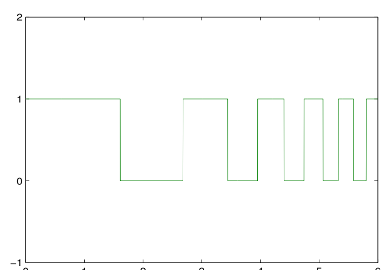

Fig. 1. Boolean output $y_i(t) = s^+(x_i, \theta_i)(t)$ available for the state estimation problem.

We define the following problems:

(P1) *estimate the protein concentrations x, under the complete Boolean observations on regional location of x_i w.r.t. θ_i (i.e., the values of $s^+(x_i, \theta_i)$ or $s^-(x_i, \theta_i)$, i=1, …, n). Furthermore, the convergence rate of the observer should be faster than the intrinsic convergence rate of the dynamical system to its stable state.*

(P2) *the same objective as in (P1) under some partial Boolean observation, i.e., only some of $s^+(x_i, \theta_i)$, ($i = 1, \ldots, n$) is known.*

III. Observer under full Boolean measurements

A. Observer design

Given a dynamical system, an observer is an auxiliary system that produces an estimation of the current state by using available registered observations.

For the problem (*P1*) with complete Boolean state measurements

$$y = S(x, \theta), \tag{5}$$

we extend our 2-D piecewise Luenberger-like observer in [11], as follows :

$$\dot{\hat{x}} = Ka + KS(\hat{x}, \theta) - \Gamma\hat{x} + U(t) + G \cdot (y - S(\hat{x}, \theta)) \tag{6}$$

with $G = K + \text{diag}(\beta_i)$, β_i some positive constants.

Let $\varepsilon = x - \hat{x}$. We obtain the error system

$$\dot{\varepsilon} = -\Gamma\varepsilon - \text{diag}(\beta_i) \cdot [S(x, \theta) - S(\hat{x}, \theta)]. \tag{7}$$

It is clear that if one takes $\beta_i = 0$ then (7) becomes $\dot{\varepsilon} = -\text{diag}(d_i) \cdot \varepsilon$, and the convergence rate of the observer is $d = \min\{d_i\}$. But this is just a detector, and we are interested in accelerating the convergence rate of the error, that is, find some $l > d$ such that $\dot{\varepsilon} < -l\varepsilon$.

Theorem 1: The observer (6) is exponentially convergent. Moreover its convergence rate can be accelerated by setting the gain value.

Proof: By taking $V(\varepsilon) = \varepsilon^T\varepsilon/2$ as candidate Lyapunov function, we have

$$\frac{dV}{dt} \leq \sum_{i=1}^{n}\{-\min(\beta_i)\varepsilon_i[s^+(x_i, \theta_i) - s^+(\hat{x}_i, \theta_i)] - d_i\varepsilon_i^2\}. \tag{8}$$

Define $\Delta(x_i, \hat{x}_i) = (x_i - \hat{x}_i)[s^+(x_i, \theta_i) - s^+(\hat{x}_i, \theta_i)]$. Notice that $\Delta(x_i, \hat{x}_i) \geq 0$. Indeed, we have

$$\Delta(x_i, \hat{x}_i)\begin{cases} = |x_i - \hat{x}_i|, & \text{if } (x_i - \theta_i)(\hat{x}_i - \theta_i) < 0, \\ = 0, & \text{if } (x_i - \theta_i)(\hat{x}_i - \theta_i) > 0 \\ & \text{or } x_i = \hat{x}_i = \theta_i, \\ \in [0, |x_i - \hat{x}_i|], & \text{if } x_i \neq \theta_i, \hat{x}_i = \theta_i \\ & \text{or } x_i = \theta_i, \hat{x}_i \neq \theta_i. \end{cases}$$

Hence the derivative of V is negative definite, moreover V is radially unbounded, thus the error system is GAS.

Moreover, although $\dot{V} = -\text{diag}(d_i)\varepsilon^T\varepsilon$ when $(x_i - \theta_i)(\hat{x}_i - \theta_i) > 0$, $\forall i = 1, 2$, the situation will change when x or $\hat{x}$ passes from one orthant to another. Suppose that x hits the threshold θ_j before $\hat{x}$ does. Notice that for the negative loop systems under the assumption (3), each threshold is a transparent wall (cf. [12]), then x will leave θ_j and this leads to $(x_j - \theta_j)(\hat{x}_j - \theta_j) < 0$. Hence we have

$$\frac{dV}{dt} \leq -\beta_j|\varepsilon_j| - \sum_{i=1}^{n} d_i\varepsilon_i^2.$$

In other words, the convergence rate can be accelerated by setting the values of β_i. For the case when $\hat{x}$ hits the threshold θ_j before x does, with some β_j large enough, there exists sliding mode along θ_j, i.e., $\hat{x}_j = \theta_j$ until x hits θ_j (see Proposition 2 below). The j-coordinate of x and $\hat{x}$ will be synchronized in finite time. ∎

For the sake of simplicity, we discuss the problem in the 2-D case (for the idea of proof, see [11]). We can obtain an estimation of 'practical' convergence time for the observer, that means convergence is acceptable if the error enters a small neighborhood of zero after a finite time:

Proposition 1: In the general case, the error enters a small neighborhood of zero after at most

$$T_{max} = \sum_{i=1}^{2}\max\Big\{\frac{1}{d_i}\ln\Big(\frac{k_i}{d_i\theta_i}\Big), \frac{1}{d_i}\ln\Big(\frac{k_i}{k_i - d_i\theta_i}\Big)\Big\} + \frac{2}{d}\ln\Big(\frac{\beta + \max(k_1, k_2)}{\beta + \min\limits_{i=1,2}(d_i\theta_i, k_i - d_i\theta_i)}\Big).$$

Remark 1: Proposition 1 means that in general one has only 'almost-synchronization' on i-coordinates. This can be improved by using a simple *linear tracking technique* if we know furthermore the delay δt between system switch time t_1 and observer switch time $\hat{t}_1$ on the same half-threshold (the values of t_1 and $\hat{t}_1$ are not necessary). For an arbitrary given $\tau > \delta t$, in order to get exact synchronization, it suffices to accelerate the observer dynamics by switching the observer (2) to a new system

$$\dot{\hat{x}}_i = -d'_i\hat{x}_i - k'_i s^\sigma(\hat{x}_j, \theta_j), \qquad i \neq j \tag{9}$$

with

$$\frac{d'_i}{d_i} = \frac{k'_i}{k_i} = \frac{\tau}{\tau - \delta t} \tag{10}$$

during the period τ, with the switch function

$$\Xi(t) = |s^+(x_i, \theta_i)(t) - s^+(\hat{x}_i, \theta_i)(t)|.$$

At the end of τ, we have exactly $\hat{x}_i = x_i$ and we switch the system (9) back to the observer (2).

B. Sliding motion and initial condition choice

An important property of hybrid systems is that sliding motion may exist on the switching domains [15]. We give here a sliding mode existence condition which depends on the gain value β.

Proposition 2: If $\hat{x}$ is in a neighborhood of the hyperplane θ_i, $i = 1, \ldots, n$, then a sliding mode may occur on θ_i if $x \in D_i^\sigma$, $\sigma \in \{+, -\}$ and $\beta > \max\limits_i\{d_i\theta_i, k_i - d_i\theta_i\}$.

The proof is omitted here due to space constraints, the idea can be found in [11]. Thanks to this property, we can set a practical optimal initial condition for the observer to guarantee a sliding mode at both of the thresholds, in order to obtain exact convergence in finite time. It can be also seen as the synchronization on each coordinate (cf. Fig. 2).

Corollary 1: Let the initial condition of the observer be $\hat{x}_i(0) = \theta_i$, $i = 1, \ldots, n$. Then the convergence time is optimal in the sense that it will not exceed the observation time

$$T_{obs} = \sum_{i=1}^{n}\max\Big\{\frac{1}{d_i}\ln\Big(\frac{k_i}{d_i\theta_i}\Big), \frac{1}{d_i}\ln\Big(\frac{k_i}{k_i - d_i\theta_i}\Big)\Big\} \tag{11}$$

whatever the initial condition of the nominal system is.

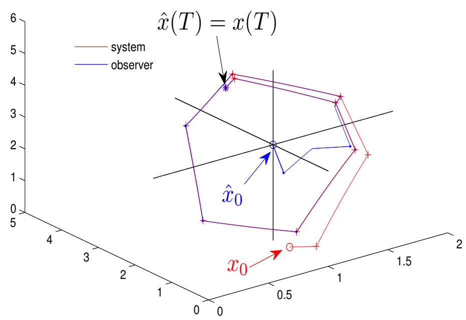

Fig. 2. A 3-D example for the convergence with sliding modes: the observer starting from $(\theta_1, \theta_2, \theta_3)$ converges to the nominal system in finite time.

IV. Estimation under partial Boolean measurements

In this section we investigate the state estimation problem ($P2$) in the 2-D case. Without loss of generality, suppose that we have only $y = s^+(x_1, \theta_1)$ as output. Clearly, the system is not observable in each orthant since the step function s^+ is not injective for any $x_1' \neq x_1$ such that $(x_1' - \theta_1)(x_1 - \theta_1) > 0$. In addition, we have no information about vector field $\dot{x}_2$. Hence, we cannot apply the same observer design as in Section 3 because the nominal system switches at the threshold θ_2.

For the complete Boolean measurements case, we have mentioned in [11] that there is a naive approach based on the algebraic computation to solve the initial condition inverse problem. This *back-in-time* approach can also be applied for the partial Boolean measurement case. More precisely, by taking into account the explicit form of the solution, one can use the history of the partial observation to determine the initial condition of the nominal system.

Indeed, notice that the time needed for the system to travel through each half-plane is an increasing function w.r.t. $|x_i - \theta_i|$. To explain the method, consider an example. Suppose that the initial condition $(x_1^{(0)}, x_2^{(0)}) \in (0, \theta_1) \times (0, \theta_2)$. The trajectory hits successively at $(\theta_1, x_2^{(1)})$, $(x_1^{(2)}, \theta_2)$ and $(\theta_1, x_2^{(3)})$ after T, $T + \Delta T'$ and $T + \Delta T$ respectively, with $\Delta T'$ unknown and

$$\Delta T = \frac{1}{d_1}\left\{ \ln\left(\frac{\theta_1 - \frac{k_1}{d_1}s^-(x_2^{(1)}, \theta_2)}{x_1^{(2)} - \frac{k_1}{d_1}s^-(x_2^{(1)}, \theta_2)}\right) + \ln\left(\frac{x_1^{(2)} - \frac{k_1}{d_1}s^-(x_2^{(3)}, \theta_2)}{\theta_1 - \frac{k_1}{d_1}s^-(x_2^{(3)}, \theta_2)}\right)\right\},$$

in which $s^-(x_2^{(1)}, \theta_2)$ and $s^-(x_2^{(3)}, \theta_2)$ are known. Hence one can determine the value of $x_1^{(2)}$ if the duration ΔT is known. Notice that the time partition of the trajectory in each orthant can be determined by using the explicit form of the solution. This allows us to compute the value of $x_2^{(1)}$. Using this method once again, one can determine the initial condition $x_2^{(0)}$ if T is measured. The x_1-coordinate of the initial condition can be obtained in similar way.

In summary, we do not need to know the value of $\Delta T'$, only the values of switching time on θ_1 are necessary to solve the initial problem. With this approach, we can determine the initial condition after a full turn, which corresponds to two successive switches on the threshold θ_1.

The drawbacks of this approach are:
1) precise time measurement is needed to guarantee the precision of the initial condition reconstruction;
2) it does not offer a real time state estimation before the necessary time to determine the initial condition.

V. Robustness analysis of observer for model with parametric perturbations

Now we consider some parametric perturbed systems and will check the robustness of our observer. We focus on two types of perturbations: 1) unknown variation on the synthesis coefficients k_i, and 2) uncertainty on the threshold values θ_i.

A. Parametric identification

Consider the 2-D model with complete Boolean state measurements. Suppose that there exist some unknown (but fixed and bounded) variations of the parameters k_i, $i = 1, 2$, say $\tilde{k}_i = k_i + \Delta k_i$ with $k_i^- \leq \Delta k_i \leq k_i^+$. The objective is to identify the values of Δk_i.

Denote by D_i^σ, $i \in \{1, 2\}$, $\sigma \in \{+, -\}$, the four *regular domains* as in (4) and S_i^σ, $i \in \{1, 2\}$, $\sigma \in \{+, -\}$ the four *switching domains*:

$$\begin{aligned} S_1^- &= \{x \in \mathbb{R}^2_{\geq 0}, x_1 = \theta_1, 0 < x_2 < \theta_2\}, \\ S_2^- &= \{x \in \mathbb{R}^2_{\geq 0}, 0 < x_1 < \theta_1, x_2 = \theta_2\}, \\ S_1^+ &= \{x \in \mathbb{R}^2_{\geq 0}, x_1 = \theta_1, x_2 > \theta_2\}, \\ S_2^+ &= \{x \in \mathbb{R}^2_{\geq 0}, x_1 > \theta_1, x_2 = \theta_2\}. \end{aligned}$$

Notice that the effect on the system of the variation Δk_i is different in each orthant according to the values of the step functions. In particular the nominal system is not affected by parametric perturbation in the orthant D_2^-. On the other hand, we need to take the perturbation into account for the remaining orthants. It is clear that different values of $\tilde{k}$ lead to different focal points for the system.

Let τ be the time for the nominal system to enter the orthant D_2^-. Launch the observer (6) at τ with the initial condition $\hat{x}(0) = (\theta_1, x(\tau))$. Since the perturbation has no effect on the system in D_2^-, one has at least almost-synchronization between the observer and the nominal system. In particular if one takes (θ_1, θ_2) as initial condition for the observer, one has a sliding mode on S_2^- and the almost-synchronization becomes to exact synchronization.

Suppose that the nominal system X and the observer $\hat{X}$ start at the same point in D_2^-. Notice that at the moment when $y_1 - S(\hat{x}_1)$ changes sign, we can determine the sign of $\tilde{k}_1 - \hat{k}_1$. This can help us to adjust the value of $\hat{k}_1$ in the next orthant.

Consider the following adaptive observer depending on each orthant:

$$\dot{\hat{x}} = \hat{K}a + \hat{K}S(\hat{x}) - \Gamma\hat{x} + U(t) + \hat{G}\cdot(y - S(\hat{x})) \quad \text{(V.1)}$$

with

$$\hat{K} = \begin{pmatrix} 0 & -k_1 - \Delta\hat{k}_1(D_j^\sigma) \\ k_2 + \Delta\hat{k}_2(D_j^\sigma) & 0 \end{pmatrix}$$

and $\hat{G} = \hat{K} + \text{diag}(\beta_i)$. Here $\Delta\hat{k}_i$ are piecewise constant functions which depend only on the values k_i^- and k_i^+.

One can take for example $\Delta\hat{k}_1(D_2^-) = (k_1^+ + k_1^-)/2$ by default. If $\hat{X}$ hits S_1^- before X does, then we deduce that $\Delta k_1 \in [k^-, \Delta\hat{k}_1(D_2^-)]$. Then we take the middle point $(k_1^+ + 3k_1^-)/4$ as a new test for $\Delta\hat{k}_1(D_2^+)$. Similarly, we take $\Delta\hat{k}_1 = (3k_1^+ + k_1^-)/4$ if X hits S_1^- before $\hat{X}$ does.

Let $k_i^{min}(D_1^-) = k_i^-$ and $k_i^{max}(D_1^-) = k_i^+$. In general, we propose a simple algorithm for the choice of $\Delta\hat{k}_i$:

$$\Delta\hat{k}_i(D_j^\sigma) = \frac{k_i^{min}(D_j^\sigma) + k_i^{max}(D_j^\sigma)}{2};$$

- $\begin{cases} k_1^{min}(D_2^+) = \Delta\hat{k}_1(D_1^-) & \text{if } y_1 - s(\hat{x}_1) > 0 \\ k_1^{max}(D_2^+) = \Delta\hat{k}_1(D_1^-) & \text{if } y_1 - s(\hat{x}_1) < 0; \end{cases}$
- $\begin{cases} k_2^{min}(D_1^+) = \Delta\hat{k}_2(D_2^+) & \text{if } y_2 - s(\hat{x}_2) > 0 \\ k_2^{max}(D_1^+) = \Delta\hat{k}_2(D_2^+) & \text{if } y_2 - s(\hat{x}_2) < 0; \end{cases}$
- $\begin{cases} k_1^{min}(D_2^-) = \Delta\hat{k}_1(D_1^+) & \text{if } y_1 - s(\hat{x}_1) < 0 \\ k_1^{max}(D_2^-) = \Delta\hat{k}_1(D_1^+) & \text{if } y_1 - s(\hat{x}_1) > 0. \end{cases}$

Repeating the procedure by refining the dichotomy, one can obtain a better estimation of Δk_i (see Fig. 3). The precision of the parametric estimation depends on the number of turns.

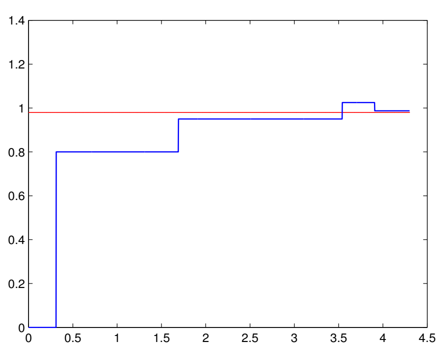

Fig. 3. The estimation of uncertain parameter variation Δk_1. The fixed variation (in red) and its estimate (in blue).

Proposition 3: After the n-th crossing of S_2^-, the bound of the relative error for the ratio $|\Delta\hat{k}_j - \Delta k_j|/|k_j^+ - k_j^-|$ between the unknown parameters and their estimates is of order $(1/4)^n \times (1/2)^n$.

Proof: By construction one can compare Δk_i with the test value $\Delta\hat{k}_i$ only when X or $\hat{X}$ hits a switching domain. Moreover each comparison reduces the relative error by $1/2$. Since each crossing contains one comparison on x_1 and two on x_2-coordinate, hence the result follows. ■

B. Uncertain measurements

Another interesting problem consists on estimating the state variables of uncertain systems when the uncertainty appears in the measurements. This is to say, the location of the concentration w.r.t. the threshold is badly measured in a small interval around the threshold. The outputs are again Boolean. In this case the information in the uncertainty interval is random and not useful. We can only use its upper and lower bounds to give an estimation.

The parametric uncertain model is described by

$$\begin{cases} \dot{x}_1 = k_1(1 - \mu^+(x_2, \theta_2; \delta_2)) - \gamma_1 x_1 \\ \dot{x}_2 = k_2\mu^+(x_1, \theta_1; \delta_1) - \gamma_2 x_2 \end{cases} \quad \text{(V.2)}$$

with μ^+ defined by

$$\mu^+(x, \theta; \delta) = \begin{cases} 0, & 0 \le x \le \theta - \delta \\ \mu_{trans}(x), & \theta - \delta \le x \le \theta + \delta \\ 1, & x \ge \theta + \delta \end{cases} \quad \text{(V.2)}$$

and $\mu_{trans} \in (0, 1)$ such that $k/\gamma > \theta \pm \delta$.

In [3], the authors have proved that the trajectories of (V.2) will finally enter the set enclosed by a limit cycle $\mathcal{C}$ (cf. the black curve in Fig. 4). The limit cycle $\mathcal{C}$ is obtained by considering the "worst case", that is, by taking $\mu^+(x_2, \theta_2) = 0, \forall x_2 > \theta_2 - \delta_2$ in the left half-plane and $\mu^+(x_2, \theta_2) = 0, \forall x_2 > \theta_2 + \delta_2$ in the right half-plane. (Similarly for $\mu^+(x_1, \theta_1)$. More details can be found in [3]).

Here we are interested in checking the robustness of the observer (6) w.r.t. the uncertainty in the measurements. The considered outputs y are of the same form as $\mu^+(x, \theta; \delta')$. For the sake of simplicity, we consider here the particular case where $\delta' = \delta$. It is worth mentioning that, even in the particular case, since μ^+ is a set-valued function, we have in general $y - \mu^+(x, \theta; \delta) \neq 0$ for $\theta - \delta \le x \le \theta + \delta$.

Construct a new observer by replacing the step function $s^+(x, \theta)$ by

$$\bar{\mu}^+(x, \theta; \delta) = \begin{cases} 0, & 0 \le x \le \theta - \delta \\ \alpha, & \theta - \delta \le x \le \theta + \delta \\ 1, & x \ge \theta + \delta \end{cases} \quad \text{(V.3)}$$

with an arbitrary $\alpha \in [0, 1]$.

The evolution of uncertain system and observer dynamics are illustrated in Fig. 4. The parameters α, δ_1 and δ_2 are set to be 0.5, 0.4 and 0.6 respectively. When x is not too close to the intersection of the uncertainty regions $D_\delta = [\theta_1 - \delta_1, \theta_1 + \delta_1] \times [\theta_2 - \delta_2, \theta_2 + \delta_2]$, the time that x stays in the regular domain is longer than the time it stays in the uncertainty regions. Thanks to the convergence in the regular domains, the trajectory of the observer enters the set enclosed by the limit cycle of the "worst case" and tracks quickly the nominal system. By contrast, the observer does not guarantee the convergence inside the uncertainty regions. When x is

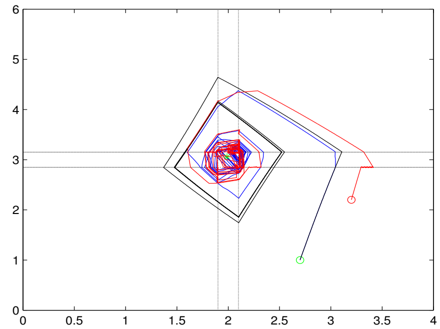

Fig. 4. The evolution of uncertain system dynamics (in blue) and its estimate with $\bar{\mu}^+$ with $\alpha = 0.5$ (in red). The black curve is the limit cycle in the worst case.

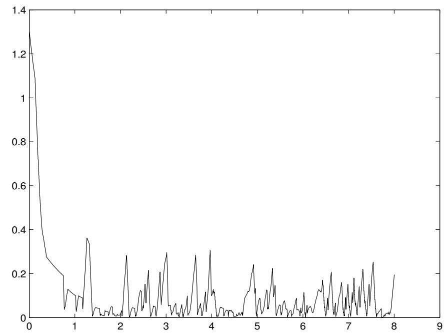

Fig. 5. The evolution of the error $\|\varepsilon\|$ between uncertain model and the observer.

too close to D_δ, one can not expect the convergence of the observer.

To check the robustness of the observer, we also compute the error estimation, which depends on the uncertainty bound size δ.

Proposition 4: Let T_1 be the time for (V.2) to travel through three regular domains. Then after T_1, with a β large enough, the error of the observer is bounded by

$$\|\varepsilon\| \leq \max\left(\frac{\delta_1}{\theta_1+\delta_1}\frac{k_2}{d_2}, \frac{\delta_1}{\frac{k_1}{d_1}-\theta_1+\delta_1}\frac{k_2}{d_2}, \frac{\delta_2}{\theta_2+\delta_2}\frac{k_1}{d_1}, \frac{\delta_2}{\frac{k_2}{d_2}-\theta_2+\delta_2}\frac{k_1}{d_1}\right).$$

Proof : With a similar reasoning as in Theorem 1, we know that $\hat{x}$ is synchronized with x after T_1. The error grows again because of the uncertainty. It is easy to check that the error growth over each uncertainty region $[\theta_i-\delta_i, \theta_i+\delta_i]$ has an upper bound equal to

$$\frac{\max(\alpha, 1-\alpha)\cdot\delta_i}{\min(\theta_i+\delta_i, \frac{k_i}{d_i}-\theta_i+\delta_i)}\cdot\frac{k_j}{d_j}, \quad i \neq j.$$

Obviously the best choice is $\alpha = 1/2$. ■

In other words, if the uncertainty bound δ in the model is relatively small w.r.t. θ_i and $k_i/d_i - \theta_i$, then the error can be considered acceptable in practical sense (see Fig. 5) because it tends to zero when $\delta \to 0$.

VI. Conclusion

Three state estimation problems with Boolean outputs for a hybrid system resulting from genetic networks are addressed in this paper. An exponentially convergent observer is presented for an n-dimensional negative loop system with full state Boolean measurements. In particular, we give a sufficient condition to guarantee existence of sliding mode. Using sliding mode solutions in this case, one obtains *finite-time* convergence for the observer. In the partial Boolean measurements case, a naive approach based on algebraic computation is proposed to solve the initial condition problem. Robustness problems are also discussed. We propose an algorithm based on dichotomy to identify the unknown parameters for parametric perturbed model and we show that our observer with complete discrete outputs is robust in the practical sense for the model with a δ uncertainty in the thresholds. The error decreases as δ decreases. Future work is focused on generalizing this robustness approach for higher dimensional systems.

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