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An observer for a piecewise affine genetic network model with Boolean observations

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***Abstract*— In this paper we consider the state reconstruction problem with Boolean measurements for a genetic network governed by a piecewise affine (PWA) model. A Luenberger-like observer is proposed and we undertake an investigation of its convergence rate. The approach of Filippov is used to define the solution on the surface of discontinuity. In particular sliding modes may occur in some cases and this leads to *finite-time* convergence for the observer. A transition graph is given for the coupled observer-nominal system in general case. To minimize the convergence time, different convergence scenarios are discussed for optimizing the choice of initial condition of the observer.**

I. Introduction

A large number of biological networks consist of many individual components interacting through complex positive and negative feedback loops and it is difficult to understand, by an intuitive approach, the resulting behaviors and their relation with the actual functioning of the systems. So, a piecewise affine (PWA) framework allows a rigorous mathematical modeling and analysis approach, which is useful to the qualitative understanding of biological networks. Our analysis focuses on PWA systems with discrete measurements and our results are related to the topics of hybrid systems, quantized control and synchronization.

In this paper we consider a classical genetic regulatory network with negative feedback loop, which is composed of two genes A and B who interact with each other, more precisely, A activates B and B inhibits A (see [19]).

Under the assumptions of quasi-steady state of mRNAs and simplification of the synthetic rates in the activation and inhibition by step functions (instead of Hill functions, for details of different frameworks comparison according to various assumptions, see for instance [16]), the qualitative model can be described by a 2-dimensional PWA time-invariant system. The piecewise linear model was first introduced by [10] and has been well studied for decades (see e.g. [6], [15] and [18]).

This model has a simple structure of biological interest. It is shown in [18] that, under some assumption on the parameters, the solution behaves like a damped oscillator, which tends to a stable focus. In mathematical biology, oscillations play an important role since rhythmic phenomena are quite common in living organisms, such as circadian oscillations, oscillations in blood production or neural activity (e.g. Parkinson's disease). Analysis and manipulation of periodic behaviors of biological systems has become more and more important at both theoretical and experimental levels. For example, some PWA controls are proposed in [5] to generate and destroy oscillatory behavior in the above 2-dimensional PWA activation-inhibition network model. Qualitative control problems (in which only three positive values were allowed according to the synthesis levels) have been considered in [4] for the bistable switch model (where two genes inhibit each other mutually) with single bounded input.

We are interested here in state reconstruction problems with Boolean measurements, that is to say, we only know (partially) whether the protein concentrations are above or below some threshold values. This kind of state reconstruction problems is interesting because very often the measurements of genes expression are only qualitative due to the experimental techniques used, e.g., the gene is strongly or weakly expressed (cf. [12] and [9]).

From a mathematical point of view, this problem has two distinct aspects when compared to classical observation problems: firstly, the model is a switching dynamical system (PWA), and secondly we have only Boolean measurements (step functions). In this paper we propose to estimate the protein concentrations through an auxiliary system, that is, an observer, by using their locations w.r.t. the threshold values. Moreover, the convergence rate can be accelerated by setting the gain value and by choosing the initial condition. In some special cases with the sliding motions one has convergence in *finite time* for the observer. The convergence time in general cases is also investigated. We believe that such state reconstruction problems with Boolean measurements have not yet been addressed in the literature.

For PWA systems, the authors of [2] have considered the observability problem. In [11], both deterministic and particle filtering approaches are considered for a class of discrete time PWA systems. Specially for the first approach, a Luenberger observer is proposed such that the error system is also a switching system. The correction term contains only the output vector and its estimate. Sliding mode observers can also be used (e.g. see [20] and [1]) by taking additionally the sign of the mismatch between output and its estimate. For both cases, all the observer designs within the literature (as far as we know) are dealt with the measurement taken as a part of the state vector, that is, one needs (partially) the continuous values (with errors possibly) of these state variables. 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

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only the sign-observations of the state without precise value, [13] investigates on the observability problem of continuous-/discrete-time linear systems (without switches). In [3], a quantized state feedback control strategy is proposed to stabilize linear systems in both continuous-/discrete-time cases. 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 [8] the authors analyze the global convergence for a class of neural networks where the neuron activations are modeled by discontinuous functions, but observability problem is not considered.

This paper is organized as follows. We introduce the PWA model and the observation problem in Section II. An exponentially convergent observer is proposed in Section III, and an alternative approach is discussed. In Section IV we analyze the sliding mode solutions and finite-time convergence of the observer. The convergence time in general case is investigated in Section V. Some possible generalisations are mentioned in Section VI.

II. PWA systems with Boolean measurements

The piecewise affine model is described by the system (Σ) as follows:

$$\begin{cases} \dot{x}_1 = k_1 s^-(x_2,\theta_2) - d_1 x_1, \\ \dot{x}_2 = k_2 s^+(x_1,\theta_1) - d_2 x_2 \end{cases} \tag{II.1}$$

with the step functions defined by

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

and

$$s^-(x_i,\theta_i) = 1 - s^+(x_i,\theta_i).$$

The state variables $x_i \in \mathbb{R}_{\geq 0}$, $i = 1,2$, denote the protein concentrations of genes, 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.

It is well known that under the following assumption on the parameters:

$$\phi_i = \frac{k_i}{d_i} > \theta_i, \quad i = 1,2. \tag{II.2}$$

the system tends to a stable focus (θ_1,θ_2) as a damped oscillator (see [18]).

Notice that the step functions are not defined on the thresholds. Since on a threshold each differential equation in (II.1) has discontinuous righthand side, it should be defined as an differential inclusion and the solution should be interpreted in the sense of Filippov [7], that is, an absolutely continuous vector-valued function $x(t)$ defined on an interval I which satisfies the differential inclusion almost everywhere on I.

As mentioned in the introduction, we are interested in state reconstruction problem with Boolean measurements, i.e., we only know the positions of the state variables x_i w.r.t. the thresholds θ_i. We define the following problem

***(P)**: design an observer for (II.1) to estimate the protein concentrations x_i, $i = 1,2$, with 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=1,2). Furthermore, the convergence rate of the observer should be faster than the intrinsic convergence rate of the dynamical system to its stable state.*

III. Observer with complete Boolean observations

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 (P) with complete Boolean measurements

$$y_1 = s^+(x_1,\theta_1), \qquad y_2 = s^+(x_2,\theta_2), \tag{III.1}$$

we propose a simple piecewise Luenberger-like observer $(\hat{\Sigma})$:

$$\begin{pmatrix} \dot{\hat{x}}_1 \\ \dot{\hat{x}}_2 \end{pmatrix} = \begin{pmatrix} -d_1\hat{x}_1 - k_1 s^-(\hat{x}_2,\theta_2) \\ -d_2\hat{x}_2 + k_2 s^+(\hat{x}_1,\theta_1) \end{pmatrix} + \begin{pmatrix} \beta_1 & -k_1 \\ k_2 & \beta_2 \end{pmatrix} \begin{pmatrix} y_1 - s^+(\hat{x}_1,\theta_1) \\ y_2 - s^+(\hat{x}_2,\theta_2) \end{pmatrix} \tag{III.2}$$

with β_i, $i = 1,2$ some positive constants.

Theorem 3.1: The observer (III.2) is exponentially convergent. Moreover its convergence rate can be accelerated by setting the gain value.

Proof : By taking $\varepsilon = x - \hat{x}$ we have the error equation

$$\begin{pmatrix} \dot{\varepsilon}_1 \\ \dot{\varepsilon}_2 \end{pmatrix} = \begin{pmatrix} -d_1\varepsilon_1 \\ -d_2\varepsilon_2 \end{pmatrix} - \begin{pmatrix} \beta_1[s^+(x_1,\theta_1) - s^+(\hat{x}_1,\theta_1)] \\ \beta_2[s^+(x_2,\theta_2) - s^+(\hat{x}_2,\theta_2)] \end{pmatrix} . \tag{III.3}$$

Taking $V(\varepsilon) = \varepsilon^T\varepsilon/2$ as Lyapunov candidate function with $\varepsilon = (\varepsilon_1\ \varepsilon_2)^T$, we have

$$\frac{dV}{dt} \leq -\min(\beta_1,\beta_2)\sum_{i=1}^{2}\{\varepsilon_i[s^+(x_i,\theta_i) - s^+(\hat{x}_i,\theta_i)] - d_i\varepsilon_i^2\}. \tag{III.4}$$

Define $\Delta(x_i,\hat{x}_i) = (x_i - \hat{x}_i)[s^+(x_i,\theta_i) - s^+(\hat{x}_i,\theta_i)]$, $i = 1,2$. Notice that $\Delta(x_i,\hat{x}_i) \geq 0$. Indeed, we have

$$\Delta(x_i,\hat{x}_i) \begin{cases} = |x_i - \hat{x}_i|, & \text{if } (x_i-\theta_i)(\hat{x}_i-\theta_i) < 0, \\ = 0, & \text{if } (x_i-\theta_i)(\hat{x}_i-\theta_i) > 0 \\ & \text{or } x_i = \hat{x}_i = \theta_i, \\ \in [0, |x_i - \hat{x}_i|], & \text{if } x_i \neq \theta_i, \hat{x}_i = \theta_i \\ & \text{or } x_i = \theta_i, \hat{x}_i \neq \theta_i. \end{cases} \tag{III.5}$$

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

It is clear that if one takes $\beta = 0$ then the error equation becomes $\dot{\varepsilon} = -\mathrm{diag}(d_1,d_2)\cdot\varepsilon$, and the convergence rate of the observer is $d = \min\{d_1,d_2\}$. But this is just a detector, we are interested in accelerating the convergence rate of the error, that is, find some $l > d$ such that $\dot{\varepsilon} < -l\varepsilon$.

The precise study of convergence rate will be discussed in Section IV.

B. Some remarks

It is well known that in some sense the state reconstruction problem is equivalent to the initial condition inverse problem. In our particular case where the system is piecewise affine, the explicit solution of linear equations in each regular domain (orthant) can be easily computed, which depends on its initial condition in the domain:

$$x_i(t) = (x_{i0} - \Phi_i)e^{-d_i t} + \Phi_i, \quad i = 1,2$$

with the *focal points* depending on the initial condition

$$\Phi_1 = \phi_1 s^-(x_{20}, \theta_2), \qquad \Phi_2 = \phi_2 s^+(x_{10}, \theta_1).$$

In addition, in the above negative feedback loop system all the switching domains are transparent walls (see [15]).

Notice that the measurements $s^+(x_i, \theta_i)$ are time-varying functions, so we know the instant t_n when each switch $x_i(t_n) = \theta_i$ occurs and the interval of time in which the trajectory stays in each regular domain. The history of the measurements allows us to determine the initial condition back in time, which is unknown *a priori* in the observation problem. Indeed, in each regular domain the two equations are decoupled and the rates d_i are known together with the switch time, then the starting point and ending point of the trajectory in each domain can be determined uniquely.

To apply this method we need a minimum observation time T since the system should hit two switching domains. To see this, denote by t_1, t_2 respectively the time for the system to hit the first two switching domains. Without loss of generality, suppose that after t_1 the trajectory hits first the vertical threshold θ_1 at some point $P_1 = (\theta_1, \tilde{x}_{20})$, and t_2 later it hits the horizontal threshold θ_2 at $P_2 = (\tilde{x}_{10}, \theta_2)$. On the other hand, the time needed for the system to get to P_2 from P_1 is

$$t_{P_1 \to P_2} = \frac{1}{d_1}\ln\left(\frac{\theta_1 - \phi_1}{\tilde{x}_{10} - \phi_1}\right) = \frac{1}{d_2}\ln\left(\frac{\tilde{x}_{20} - \phi_2}{\theta_2 - \phi_2}\right)$$

with ϕ_i defined in (II.2). By setting $t_2 = t_{P_1 \to P_2}$ we can compute explicitly $\tilde{x}_{10}$ and $\tilde{x}_{20}$. Thus the exact initial condition can be determined with the value of $\tilde{x}_{20}$ and the measured time t_1. We can obtain the upper bound of $T_{\max}$:

$$T_{\max} = \sum_{i=1}^{2} \max\left\{\frac{1}{d_i}\ln\left(\frac{\phi_i}{\theta_i}\right), \frac{1}{d_i}\ln\left(\frac{\phi_i}{\phi_i - \theta_i}\right)\right\}. \qquad \text{(III.6)}$$

Though this alternative approach does work for our simple example, the observer design is still important because:

1) the inverse approach needs precise time measurement to guarantee the precision of the initial condition reconstruction;

2) we are also interested in the *online* estimation of the state variables before the necessary time to determine the exact initial condition. The advantage of the dynamical observer (in contrast to an algebraic computation) is to have an adaptive estimation which is robust to small perturbation in the parameters.

IV. Sliding mode solution and finite time convergence for the observer

Denote by D_i^σ, $i \in \{1,2\}$, $\sigma \in \{+,-\}$, the four *regular domains*:

$$\begin{aligned}
D_1^- &= \{x \in \mathbb{R}^2_{\geq 0}, 0 < x_1 < \theta_1, 0 < x_2 < \theta_2\},\\
D_2^- &= \{x \in \mathbb{R}^2_{\geq 0}, 0 < x_1 < \theta_1, x_2 > \theta_2\},\\
D_1^+ &= \{x \in \mathbb{R}^2_{\geq 0}, x_1 > \theta_1, x_2 > \theta_2\},\\
D_2^+ &= \{x \in \mathbb{R}^2_{\geq 0}, x_1 > \theta_1, 0 < x_2 < \theta_2\}.
\end{aligned}$$

and S_i^σ, $i \in \{1,2\}$, $\sigma \in \{+,-\}$ the four *switching domains*:

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

Denote by Γ (resp. $\hat{\Gamma}$) the trajectory of (Σ) (resp. $(\hat{\Sigma})$) and we use the index 0 to denote their initial locations. We also use the notations $\phi_i = k_i/d_i$, $i = 1,2$.

A. Existence of sliding mode

Notice that the error system is a switching system, so a sliding mode may occur. In this case, one of the state variables remains constant while the other evolves towards a point determined by the signs of the vector fields. Geometrically, the trajectory of the solution will evolve on a switching domain (sliding surface), see Fig. 1.

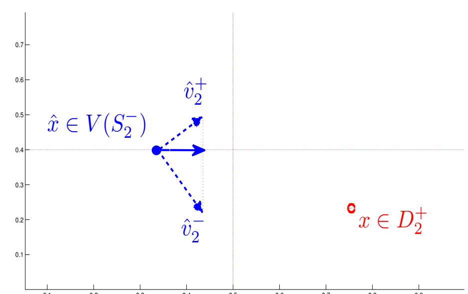

Fig. 1. The sliding mode in a neighborhood of the switching domain S_2^- for the observer.

Recall the assumption on the parameters (II.2), hence there exists some small η such that $k_i/d_i \geq \theta_i + \eta$. It is well known that a sufficient condition for sliding mode to exist on some hyperplane $s = 0$ is

$$\lim_{s \to 0^-} \dot{s} \cdot \lim_{s \to 0^+} \dot{s} < 0. \qquad \text{(IV.1)}$$

Clearly there exists no sliding mode for the nominal system. For example, to check the nonexistence of sliding mode on $x_2 = \theta_2$, we take the righthand side of the second equation in (II.1): $k_2 s^+(x_1, \theta_1) - d_1 x_2$ with $x_2 \in [\theta_2 - \delta, \theta_2 + \delta]$, $0 < \delta < \eta$. If x belongs to the left half-plane, one has $s^+(x_1, \theta_1) = 0$. Hence $-d_1(\theta_2 - \delta)$ and $-d_1(\theta_2 + \delta)$ are both negative. If x belongs to the right half-plane, then $s^+(x_1, \theta_1) = 1$, we have both $k_2 - d_1(\theta_2 - \delta)$ and $k_2 - d_1(\theta_2 + \delta)$ positive. For the same reason, there is no sliding mode for a detector.

TABLE I

THE VALUES OF (ψ_1,ψ_2) IN (IV.2), ACCORDING TO x AND $\hat{x}$ LOCATIONS.

$\hat{x}\in$ \ $x\in$	D_1^-	D_2^-	D_1^+	D_2^+
D_1^-	$(k_1,0)$	$(0,\beta)$	$(\beta,\beta+k_2)$	$(\beta+k_1,k_2)$
D_2^-	$(k_1,-\beta)$	$(0,0)$	(β,k_2)	$(\beta+k_1,-\beta+k_2)$
D_1^+	$(-\beta+k_1,0)$	$(-\beta,\beta)$	$(0,k_2)$	$(k_1,-\beta+k_2)$
D_2^+	$(-\beta+k_1,-\beta)$	$(-\beta,0)$	$(0,\beta+k_2)$	(k_1,k_2)

This is not the case for the observer with a sufficient large gain value. In fact, we can give a sufficient condition for the existence of a sliding mode.

Proposition 4.1: If $\hat{x}$ is in a neighborhood of θ_i, $i=1,2$, then a sliding mode may occur on θ_i if $x\in D_i^\sigma$, $\sigma\in\{+,-\}$ and $\beta>\max\{d_i\theta_i,k_i-d_i\theta_i\}$.

Proof: Take the righthand side of the first equation in (III.2):

$$\hat{v}_1=k_1s^-(x_2,\theta_2)+\beta s^+(x_1,\theta_1)-\beta s^+(\hat{x}_1,\theta_1)-d_1\hat{x}_1$$

with $\hat{x}_1\in[\theta_1-\delta,\theta_1+\delta]$, $0<\delta<\eta$. If $x\in D_1^-$, i.e., $s^+(x_1,\theta_1)=1$ and $s^-(x_2,\theta_2)=1$, then we have

$$\begin{cases}\hat{v}_1^-=k_1-d_1(\theta_1-\delta)>0,\\ \hat{v}_1^+=k_1-\beta-d_1(\theta_1+\delta)<0,\ \text{with}\ \beta_1>k_1-d_1\theta_1.\end{cases}$$

Hence we have a sliding mode on θ_1. A similar reasoning leads to the existence of sliding mode on θ_1 when $x\in D_1^+$ and $\beta>d_1\theta_1$. When $x\in D_2^+$ (resp. $x\in D_2^-$), it is easy to see that both v_1^+ and v_1^- are positive (resp. negative), hence there is no sliding mode in these cases. One can check the existence of sliding mode on θ_2 in the same way by taking the righthand side of the second equation in $(\hat{\Sigma})$. ∎

So the existence of sliding mode depends not only on the location of x w.r.t. a threshold, but also the direction of the oscillation. In our case where the oscillation is anti-clockwise, the sliding mode may occur on a threshold where $\hat{x}$ is nearby only when x is behind the threshold.

B. Some properties of sliding mode solutions

In fact, the observer can be written as

$$\begin{cases}\dot{\hat{x}}_1=-d_1\hat{x}_1+\psi_1,\\ \dot{\hat{x}}_2=-d_2\hat{x}_2+\psi_2,\end{cases}\tag{IV.2}$$

where the values of (ψ_1,ψ_2) are given by Table I. Thus the observer has $(\Psi_1,\Psi_2)=(\psi_1/d_1,\psi_2/d_2)$ as its focal point according to different locations of x and $\hat{x}$.

The next results show that sliding mode solutions guarantee the synchronization of one of the coordinates of the observer and the system, i.e., $x_i(T)=\hat{x}_i(T)$ for some i at the end of a sliding mode.

Lemma 4.2: Let $T(x_0)$ (resp. $\hat{T}(x_0)$) be the time for a trajectory Γ starting from x_0 (resp. $\hat{x}_0$) to hit the first switching domain S_i^σ. Then T (resp. $\hat{T}$) is an increasing function w.r.t. $|x_{i0}-\theta_i|$ (resp. $|x_{i0}-\theta_i|$).

Proof: It is easy to compute

$$T(x_0)=\frac{1}{d_i}\ln\Big(\frac{x_{i0}-\Phi_i}{\theta_i-\Phi_i}\Big)=\frac{1}{d_i}\ln\Big(1+\frac{x_{i0}-\theta_i}{\theta_i-\Phi_i}\Big)\tag{IV.3}$$

with $(x_{i0}-\theta_i)(\theta_i-\Phi_i)>0$ by the assumption (II.2). The result follows. By similar reasoning with

$$\hat{T}(x_0)=\frac{1}{d_i}\ln\Big(\frac{\hat{x}_{i0}-\Psi_i}{\theta_i-\Psi_i}\Big)=\frac{1}{d_i}\ln\Big(1+\frac{\hat{x}_{i0}-\theta_i}{\theta_i-\Psi_i}\Big),\tag{IV.4}$$

one can obtain the analogous result for $\hat{T}$. ∎

Notice that $T(x_0)$ cannot be computed directly because the value of x_{20} is unknown *a priori*. Even though the exact value of $T(x_0)$ is not available, one can use its upper bound to estimate the upper bound of the total convergence time.

Proposition 4.3: Let T (resp. $\hat{T}$) be the time for a trajectory Γ (resp. $\hat{\Gamma}$) to hit its first switching domain. Then there is a sliding mode only if $T>\hat{T}$, with the sliding time $T_{SM}=T-\hat{T}$. Given initial conditions x_0 of the observation system and $\hat{x}_0$ of the observer, both belong to a same regular domain, the ending point of the sliding mode on S_1^σ (resp. S_2^σ) can be determined by an auxiliary trajectory $\tilde{\Gamma}$ of (Σ) starting from the point $(\hat{x}_{10},x_{20})$ (resp. $(x_{10},\hat{x}_{20})$).

As shown in the diagram Fig. 4 , the only possible step after sliding mode is the case where x and $\hat{x}$ enter into a same regular domain with at least one of the coordinates synchronized.

C. Convergence of the observer in finite time

Since an observer is a software sensor for the model, we can set its initial condition $\hat{x}_0$ in order to guarantee an optimal convergence time, wherever the initial condition x_0 of the model is located. In our case the best choice for $\hat{x}_0$ is the intersection point (θ_1,θ_2). In fact, in this case the state variables $\hat{x}$ of the observer evolve either on a switching domain as sliding mode, or together with x on a same regular domain (see Fig. 2, in contrast with Fig. 3 representing the convergence without sliding mode).

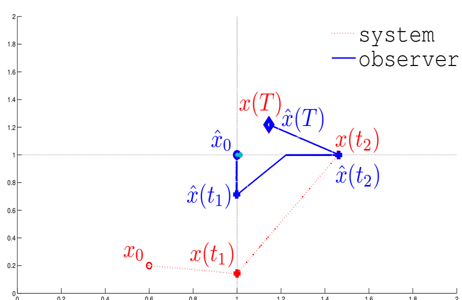

Fig. 2. Convergence with sliding modes: the observer starting from (θ_1,θ_2) converges to the nominal system in finite time.

Proposition 4.4: For $\hat{\Gamma}$ starting from (θ_1,θ_2), there is a sliding mode on the switching domain which Γ will hit first.

Proof: At the point (θ_1,θ_2), the solution of the observer should be interpreted in sense of Filippov, as the solution of the differential inclusion

$$(\dot{\hat{x}}_1\ \dot{\hat{x}}_2)^T\in H(\theta_1,\theta_2),$$

where $H(\theta_1,\theta_2)$ is the convex hull of the vector fields in the regular domains $D\in\{D_i^\sigma,i=1,2,\sigma\in\{+,-\}\}$, whose boundary ∂D contain (θ_1,θ_2)

$$H(\theta_1,\theta_2)=\overline{co}\{(\hat{v}_1^D(\theta_1,\theta_2)\ \hat{v}_2^D(\theta_1,\theta_2))^T,\ (\theta_1,\theta_2)\in\partial D\}$$

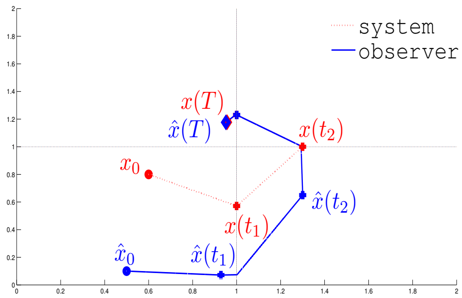

Fig. 3. Convergence without sliding mode: the error converges into a small neighborhood of zero in finite time. This case will be studied in Section V.

with $\hat{v}_i^D = \psi_i^D - d_i\theta_i$. By checking Table I, it is easy to see that for every fixed $x \in D$, ψ_i, $i \in \{1,2\}$ have only 2 possible values, denoted by ψ_i^σ, $\sigma \in \{+,-\}$. In general, we have

$$\prod_{\substack{i \in \{1,2\} \\ \sigma \in \{+,-\}}} (\psi_i^\sigma - d_i\theta_i) < 0.$$

Hence either $\hat{v}_1^+\hat{v}_2^-$ or $\hat{v}_2^+\hat{v}_2^-$ is negative. So $\hat{v}_i^+\hat{v}_i^- < 0$ implies a sliding mode on the switching domain S_i^σ with σ depending on the sign of $\hat{v}_j^+$, $j \neq i$. Moreover, the first switching domain $S_{i'}^{\sigma'}$ that Γ will hit depends on the sign of $v_{j'}$, $j' \neq i'$. Notice that $\hat{v}_j^+ v_j > 0$, so the sliding mode will exactly occur on the first switching domain that Γ will hit. ■

Theorem 4.5: For $\hat{\Gamma}$ starting from (θ_1, θ_2), the observer converges in finite time with $T_{\max}$ given by $(III.6)$ as an upper bound of the convergence time.

Proof: Suppose that $x_0 \in D_i^\sigma$, $i \in \{1,2\}$, $\sigma \in \{+,-\}$, then Γ will hit first the switching domain S_i^σ. According to Proposition 4.4, for $\hat{\Gamma}$ starting from (θ_1, θ_2) there is a sliding mode on S_i^σ. This leads to $s^+(x_j, \theta_j) = s^+(\hat{x}_j, \theta_j)$ with $j \neq i$. Moreover, we have $v_i = \hat{v}_i$. Denote by T_1 the time needed for Γ to reach S_i^σ, then at T_1 we have synchronization of the x_i-coordinate i.e., $|\varepsilon_i(T_1)| = 0$ and $|\varepsilon_j(T_1)| = |\varepsilon_j(0)|$ with $j \neq i$. Notice that $|\hat{x}_i(T_1) - \theta_i| = 0 \leq |x_i(T_1) - \theta_i|$, and by Lemma 4.2 the time T is an increasing function on $|x_i - \theta_i|$, we can conclude that $\hat{\Gamma}$ will hit the next threshold θ_j before Γ does. This leads again to a sliding mode for the observer at the next S_j^σ. With a similar reasoning as above, we have synchronization of the x_j-coordinate after a time T_2, and $|\varepsilon_j(T_1 + T_2)| = 0$. It is easy to check that the upper bound of $T_1 + T_2$ is the same to $T_{\max}$ in (III.6). ■

V. General case: accelerated convergence

Consider all the possible relative locations of x and $\hat{x}$:

(I) x and $\hat{x}$ are in a same regular domain;

(II) x and $\hat{x}$ are in two adjacent domains and Γ hits a switching domain before $\hat{\Gamma}$ does;

(III) x and are in two adjacent domains and $\hat{\Gamma}$ hits a switching domain before Γ does;

(IV) x and $\hat{x}$ are in two opposite domains;

(V) $\hat{x}$ is on a threshold and follows a sliding mode.

All the possible transitions among these cases are illustrated in Fig. 4, Each arrow line represents a possible transition between two of the five cases. Some of them (drawn by green dash lines) can be neglected under the assumptions that x is not too close to the point (θ_1, θ_2) and β is large enough.

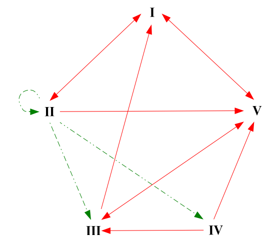

Fig. 4. Transition graph of two coupled systems (Σ) and $(\hat{\Sigma})$: all the possible state transitions according to the locations of x and $\hat{x}$. When the gain value β is large enough we consider only the transitions represented by red lines.

A. Convergence time estimation

Now we give some estimations of convergence time in general case.

Proposition 5.1: If both x and $\hat{x}$ start from a regular domain, then the error enters into a small neighborhood of zero after at most $T_{\max} + 2\tilde{T}_{\max}$ with $T_{\max}$ given by (III.6) and

$$\begin{aligned} \tilde{T}_{\max}(\beta) &\leq \frac{1}{d}\ln\Big(\frac{\beta + \max(k_1,k_2)}{\beta + \min\limits_{i=1,2}(d_i\theta_i, k_i - d_i\theta_i)}\Big) \\ &\leq \frac{1}{d}\ln\Big(\frac{\beta + \max(k_1,k_2)}{\beta}\Big). \end{aligned} \quad \text{(V.1)}$$

Sketch of proof : Suppose that $\hat{\Gamma}$ hits a switching domain before Γ does, denote T_1 (resp. $\hat{T}_1(\beta)$, which depends on the gain value β) the time needed for Γ (resp. $\hat{\Gamma}$) to hit the switching domain. According to the diagram Fig. 4, there are two possibilities: either one passes from the case (I) to (V) after T_1, or from (I) to (II) after $\hat{T}_1(\beta)$. In order to study the convergence time, we use the following transition chain diagrams:

$$\begin{aligned} &I \xrightarrow{T_1} II \xrightarrow{\hat{T}_1(\beta)} I \\ &I \xrightarrow{\hat{T}_1(\beta)} V \xrightarrow{T_1 - \hat{T}_1(\beta)} I \\ &I \xrightarrow{T_1(\beta)} II \xrightarrow{\hat{T}_1(\beta)} V \xrightarrow{T_2 - \hat{T}_1(\beta)} I \end{aligned} \quad \text{(V.2)}$$

The time needed for each transition is indicated above the corresponding arrow. We return to the case (I) after at most $T^* + \tilde{T}(\beta)$ with

$$T^* = \max_{i=1,2}\Big\{\frac{1}{d_i}\ln\Big(\frac{\phi_i}{\theta_i}\Big), \frac{1}{d_i}\ln\Big(\frac{\phi_i}{\phi_i - \theta_i}\Big)\Big\}.$$

Moreover one can prove that $\tilde{T}(\beta)$ is of order $O(1/\beta)$, which means it can be sufficiently small when β is big enough.

Such a transition chain allows us to synchronize (*by sliding mode (V)*) or almost-synchronize (*by (II)*) at one of the x_i-coordinates, then the error belongs to a small ball of zero after two transition chains. We use here the notion of *(weak) practical observer* [17], that is, for any $\eta > 0$, there is an observer parametrized by a gain β such that

$$\forall(x_0, \hat{x}_0),\ \exists T > 0,\ \|\hat{x}(t) - x(t)\| \leq \eta,\ \forall t > T.$$

To see the convergence by almost-synchronization, one can take the first transition chain in (V.2) as an example. At the instant T_1 when Γ hits the switching domain, one has $x_i(T_1) =$

θ_i and we are in the case *(II)*. Suppose that the mismatch $\|\varepsilon(T_1)\|$ is not negligible. Using (IV.4), one can obtain the time for the observer to reach the threshold θ_i:

$$\hat{T}_1(\beta) = \frac{1}{d_i}\ln\Big(1+\frac{\hat{x}_i-\theta_i}{\theta_i-\beta/d_i}\Big) \approx \frac{|\varepsilon_i|}{|\beta-d_i\theta_i|}.$$

On the other hand, at $T_1+\hat{T}_1(\beta)$ one has

$$\begin{aligned} x_i(T_1+\hat{T}_1(\beta)) &= (\theta_i-\Phi_i)e^{-d_i\hat{T}_1(\beta)}+\Phi_i \\ &\approx \theta_i+d_i(\Phi_i-\theta_i)\hat{T}_1(\beta). \end{aligned}$$

So $|\varepsilon_i(T_1+\hat{T}_1(\beta))| \approx d_i(\Phi_i-\theta_i)\hat{T}_1(\beta)$ is small for β large enough, in other words, one has almost-synchronization at x_i-coordinate. More details of error estimation can be found in [14]. In particular, when two sliding modes occur successively as in Theorem 4.5, one has convergence in finite time $T_{\max}$ with zero error. ■

By similar reasoning, we obtain convergence time estimation in the other cases.

Proposition 5.2: If x and $\hat{x}$ start from two adjacent domains (resp. opposite domains), then the error enters into a small neighborhood of zero after at most $T_{\max}+3\tilde{T}_{\max}(\beta)$ (resp. $T_{\max}+2\tilde{T}_{\max}(\beta)$).

B. Practical consideration for optimal choice of initial condition for application

In this section we analyze the convergence time in the general case. The convergence rate can be accelerated by setting the gain value β, however it cannot be as fast as one likes (see Fig. 5). Indeed, the correction term is not activated when both x and $\hat{x}$ are in the same regular domain (case (I)). Comparing to the results obtained in Section IV, we see that a good choice in practice is to set the starting point of the observer at the intersection point of the thresholds. The convergence time is optimal in the sense that it will not exceed the observation time (III.6) whatever the initial condition of the nominal system is. Moreover the error reduces to zero.

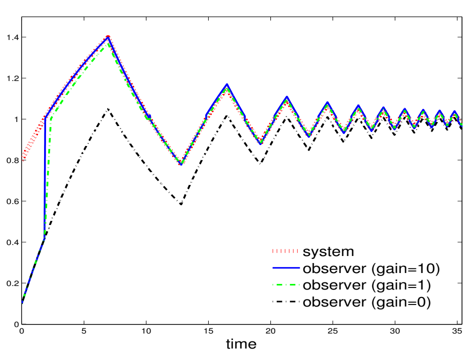

Fig. 5. The evolution of protein concentration x_1 (in red) and its estimate $\hat{x}_1$ with gain value $\beta=10$ (in blue), $\beta=1$ (in green) and without correction term (in black).

VI. CONCLUSIONS AND PERSPECTIVES

Some state reconstruction problems with Boolean measurements for a PWA model of genetic networks are addressed in this paper. An exponentially convergent observer is presented. The convergence time estimation in general case is given under different scenarios. Furthermore using sliding mode solutions in some particular cases, one obtains *finite-time* convergence for the observer. A transition graph is also given for the coupled observer-nominal system. The observer can be easily generalized for higher dimensional negative loop systems (which converge to some limit cycle, cf. [6], [18]). The proof is similar. Note that observer convergence is independent from nominal system behavior.

Future work aims to design an observer for the observation problem with partial Boolean measurements, that is, only one of $s^+(x_i,\theta_i)$, ($i=1$ or 2) is known. Another issue is the study of the robustness of the observer w.r.t. the uncertainty of the model and the parameters such as threshold values: it depends on the experimental errors, and needs further work.

REFERENCES

[1] F. Bejarano, L. Fridman and A. Poznyak. Exact state estimation for linear systems with unknown inputs based on hierarchical super-twisting algorithm. *Int. J. Robust and Nonlinear Control*, 17:1734-1753, 2007.

[2] A. Bemporad, G. Ferrari-Trecate and M. Morari. Observability and controllability of piecewise affine and hybrid systems. *IEEE Trans. Auto. Contr.*, 45(10):1864-1876, 2000.

[3] R. Brockett and D. Liberzon. Quantized feedback stabilization of linear systems. *IEEE Trans. Auto. Contr.*, 45(4):1279-1289, 2000.

[4] M. Chaves and J.-L. Gouzé. Exact control of genetic networks in qualitative framework: the bistable switch example. *Automatica*, 47: 1105-1112, 2011.

[5] R. Edwards, S. Kim and P. van den Driessche. Control design for sustained oscillation in a two-gene regulatory network. *J. Math. Biol.*, 62:453-478, 2010

[6] E. Farcot and J.-L. Gouzé. Periodic solutions of piecewise affine gene network models with non uniform decay rates: the case of a negative feedback loop. *Acta Biotheor.*, 57:429-455, 2009.

[7] A. Filippov. *Differential Equations with Discontinuous Righthand Sides*. Kluwer Academic Publishers, Dordrecht, 1988.

[8] M. Forti and P. Nistri. Global convergence of neural networks with discontinuous neuron activations. *IEEE Trans. Circuits Syst. I*, 50(11): 1421-1435, 2003.

[9] E. Gianchandani, J. Papin, N. Price, A. Joyce and B. Palsson. Matrix formalism to describe functional states of transcriptional regulatory systems. *PLoS Comput. Biol.*, 2(8):e101, 2006.

[10] L. Glass and S. Kauffman. The logical analysis of continuous, non-linear biomedical control networks. *J. Theor. Biol.*, 39:103-129, 1973.

[11] A. Juloski, W. Heemels, Y. Boers and F. Verschure. Two approaches to state estimation for a class of piecewise affine systems. *Proc. 42nd IEEE Conference on Decision and Control*, 143-148, Maui, Hawaii USA, december 2003.

[12] E. Klipp, R. Herwig, A. Kowald, C. Wierling and H. Lehrach. *Systems Biology in Practice*. Wiley-VCH, Weinheim, 2005.

[13] R. Koplon and E. Sontag. Linear systems with sign-observations. *SIAM J. Contr. Optim.*, 31(5):1245-1266, 1993.

[14] X.-D. Li, J.-L. Gouzé and M. Chaves. A Luenberger-like observer for genetic network model with Boolean observations. *manuscript*.

[15] T. Mestl, E. Plahte and S.W. Omholt. A mathematical framework for describing and analysing gene regulatory networks. *J. Theor. Biol.*, 176(2):291-300, 1995.

[16] A. Polynikis, S. Hogan and M. di Bernardo. Comparing different ODE modelling approaches for gene regulatory networks. *J. Theor. Biol.*, 261:511-530, 2009.

[17] A. Rapaport and J.-L. Gouzé. Parallelotopic and pratical observers for nonlinear uncertain systems. *Int. J. Contr.*, 76:237-251, 2003.

[18] E. Snoussi. Qualitative dynamics of piecewise-linear differential equations: a discrete mapping approach. *Dyn. Stability of Systems.*, 4: 189-207, 1989.

[19] R. Thomas and R. D'Ari. *Biological Feedback*. CRC Press Inc., Florida, 1990.

[20] V. Utkin. *Sliding Modes in Control Optimization*. Springer-Verlag, Berlin Heidelberg, 1992.