A Soft Sensor for Biomass in a Batch Process with Delayed Measurements

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Abstract: This paper presents a soft sensor to estimate the biomass concentration in a batch bioprocess used in production of δ-endotoxins of *Bacillus thuringiensis*, subject to delayed measurements. The soft sensor proposed is based on a cascade observer-predictor algorithm. The observer stage is based on a class of second order sliding mode algorithms, allowing a fixed-time estimation of the biomass. Additionally, the prediction stage offsets the effect of the delay in measurements. Simulations show the feasibility of the proposed observer.

Keywords: cascade observer-predictor, delayed measurements, δ-endotoxins production of *Bacillus thuringiensis*, fixed-time observer, Smith predictor.

1. INTRODUCTION

Measuring variables in industrial processes, such as bioprocess, is necessary to carry out tasks of control, diagnosis and fault detection, identification and monitoring (Walcott et al., 1987; Dochain, 2003). For some variables, the work of measurement is hard, costly and difficult to perform due to the unavailability of reliable devices, time delays, errors in the measurement system, high costs of devices and hostile environments for primary measuring devices (Bequette, 2002). Therefore, in order to make estimates by measurements of other variables related directly or indirectly to the variable difficult to measure has been used the state estimators. This dynamic systems are applied to a specific process, with a combination of software and hardware, and they are commonly named as virtual sensors or soft sensors.

However, the soft sensors technology transfer to industrial bioprocesses require to solve some problems such as observer schemes that allowing the use of delayed measurements. To overcome such problem, some authors have developed different methods to incorporate nonuniform and delayed information in state estimation techniques. In (Gopalakrishnan et al., 2011; Guo and Huang, 2015; Guo et al., 2014) have incorporated asynchronous and delayed information to stochastic estimation techniques (Kalman filter and its modifications) but these only apply to discrete systems. Other authors present deterministic estimation techniques with asynchronous and delayed measurement for hybrid systems, with a continuous model for the process and a discrete model for the effects of sensor and sampling. These observers are grouped into three types: Piecewise (Wang et al., 2015), Cascade (Khosravian et al., 2015b,a) and distributed (Zeng and Liu, 2015). This deterministic techniques can to solve the problems of estimating independently or in stages. This feature allows adaptation and extension to solving future problems in state estimation. For example, a mathematical application of a high gain observer in cascade with a predictor was proposed in (Khosravian et al., 2015a). However, a few papers show applications in state estimation in bioprocess with delayed measurements (Zhao et al., 2015).

Therefore, in this paper a cascade observer-predictor for the process of δ-endotoxins production process of *Bt* with fixed time convergence and delayed measurements is considered. The cascade observer-predictor structure is based on the observer presented in (Khosravian et al., 2015b,a) and the Sliding Mode Observer (SMO) proposed in (Sánchez et al., 2015). The proposed observer allows the exact and fixed-time reconstruction of the biomass (vegetative cells and sporulated cells) in the reactor when measurements are delayed.

In the following, the Section 2 presents the mathematical model δ-endotoxins production process of *Bt* with Delayed Measurement. The cascade observer-predictor is presented in Section 3 and presents some mathematical preliminaries in order to introduce the basics of fixed time stability and predictor stability. The Section 4 presents simulation results of the cascade observer-predictor for the δ-endotoxins production process of *Bt*. Finally, the conclusions of this paper are exposed in the Section 5.

2. BATCH PROCESS MODEL WITH DELAYED MEASUREMENT

The model of the δ-endotoxins production of *Bt* proposed on (Amicarelli et al., 2010; Rómoli et al., 2016) is used. In this paper the block-wise form of the equations is modified to allow a straightforward design of a second order sliding mode observer. The model equations are

$$\begin{aligned}
\dot{s}_p &= -\left(\frac{\mu(s_p,o_d)}{y_{x/s}} + m_s\right) x_v \\
\dot{o}_d &= K_3 Q_A\left(o_d^* - o_d\right) - K_1\left(\mu(s_p,o_d) - k_e(t)\right)x_v \\
&\quad - K_2\left(x_v + x_s\right) \\
\dot{x}_v &= \left(\mu - k_s(s_p) - k_e(t)\right)x_v \\
\dot{x}_s &= k_s x_v
\end{aligned} \tag{1}$$

where s_p is the substrate concentration, o_d is the dissolved oxygen concentration, x_v is the vegetative cells concentration, x_s is the sporulated cells concentration, μ is the specific growth rate, $y_{x/s}$ is the growth yield, m_s is the maintenance constant, Q_A is the airflow that enters the bio-reactor, o_d^* is the oxygen saturation concentration, K_1 is the oxygen consumption dimensionless constant by growth, K_2 is the oxygen consumption constant for maintenance, K_3 is the ventilation constant, k_s is the spore formation kinetics and $k_e(t)$ is the specific cell death rate. Furthermore, the constitutive equations for $\mu(s_p, o_d)$ (Monod-based), $k_s(s_p)$ and $k_e(t)$ are given by:

$$\begin{aligned}
\mu(s_p,o_d) &= \mu_{\max}\frac{s_p}{K_s + s_p}\frac{o_d}{K_o + o_d} \\
k_s(s_p) &= k_{s,\max}\left(\frac{1}{1+e^{G_s(s_p - P_s)}} - \frac{1}{1+e^{G_s(s_{p,\mathrm{ini}} - P_s)}}\right) \\
k_e(t) &= k_{e,\max}\left(\frac{1}{1+e^{-G_e(t - P_e)}} - \frac{1}{1+e^{-G_e(t_{\mathrm{ini}} - P_e)}}\right)
\end{aligned} \tag{2}$$

where $\mu_{\max}$ is the maximum specific growth rate, K_s is the substrate saturation constant, K_o is the oxygen saturation constant,$k_{s,\max}$ is the maximum spore formation, $k_{e,\max}$ is the maximum specific cell death rate, G_s is the gain constant of the sigmoid equation for spore formation rate, G_e is the gain constant of the sigmoid equation for specific cell death rate, P_s is the position constant of the sigmoid equation for spore formation rate, P_e is the position constant of the sigmoid equation for specific cell death rate, $s_{p,\mathrm{ini}}$ is the initial glucose concentration and t_{ini} is the initial fermentation time.

Assumption 2.1. It is assumed that the measurements of the outputs s_p and o_d are continuously measured with a delay time $\tau > 0$. The delay τ is considered to be known and constant.

Defining $x_1 = s_p$, $x_2 = o_d$, $x_3 = x_v$, $x_4 = x_s$ and considering the Assumption 2.1, the model (1) can be written as:

$$\begin{aligned}
\dot{x}_1(t) &= b_1(x_1(t), x_2(t))x_3(t) \\
\dot{x}_2(t) &= b_{21}(x_1(t), x_2(t))x_3(t) \\
&\quad + f_2(x_2(t)) + b_{22}x_4(t) \\
\dot{x}_3(t) &= b_3(x_1(t), x_2(t))x_3(t) \\
\dot{x}_4(t) &= b_4(x_1(t))x_3(t)
\end{aligned} \tag{3}$$

where

$$\begin{aligned}
b_1(x_1(t),x_2(t)) &= -\left(\frac{\mu(x_1(t),x_2(t))}{y_{x/s}} + m_s\right) \\
f_2(x_2(t)) &= K_3 Q_A\left(o_d^* - x_2(t)\right) \\
b_{21}(x_1(t),x_2(t)) &= -K_1(\mu(x_1(t),x_2(t)) - k_e(t)) - K_2 \\
b_{22} &= -K_2 \\
b_3(x_1(t),x_2(t)) &= \mu(x_1(t),x_2(t)) - k_s(x_1(t)) - k_e(t) \\
b_4(x_1(t)) &= k_s(x_1(t))
\end{aligned} \tag{4}$$

and with the measurements

$$y\left(t\right) = \left[x_1\left(t-\tau\right)\ x_2\left(t-\tau\right)\right]^T \tag{5}$$

The block-wise form (3)-(5) allows a straightforward design of a second order sliding mode observer. The nominal parameters for the system (3) are given in Table 1.

Table 1. Nominal Parameters of the BT model.

Parameter	Values	Unit
$\mu_{\max}$	0.65	h^{-1}
$y_{x/s}$	0.37	$g \cdot g^{-1}$
K_s	3	$g \cdot L^{-1}$
K_o	1×10^{-4}	$g \cdot L^{-1}$
m_s	5×10^{-3}	$g \cdot g^{-1} \cdot h^{-1}$
$k_{s,\max}$	0.5	h^{-1}
G_s	1	$g \cdot L^{-1}$
P_s	1	$g \cdot L^{-1}$
$k_{e,\max}$	0.1	h^{-1}
G_e	5	h
P_e	4.9	h
K_1	3.795×10^{-3}	dimensionless
K_2	0.729×10^{-3}	h^{-1}
K_3	2.114×10^{-3}	L^{-1}
Q_A	1320	$L \cdot h^{-1}$
o_d^*	0.00759	$g \cdot L^{-1}$
t_{ini}	0	h
$s_{p,\mathrm{ini}}$	32	$g \cdot L^{-1}$

3. PROPOSED SOFT SENSOR SCHEME

3.1 Observability Analysis

Let the vector $\mathcal{H}$ which contains the measured outputs of the system (3), $x_1(t-\tau)$, $x_2(t-\tau)$ and their derivatives be defined as

$$\mathcal{H} = \left[\, x_1(t-\tau)\ x_2(t-\tau)\ \dot{x}_1(t-\tau)\ \dot{x}_2(t-\tau)\,\right]^T \tag{6}$$

Similarly to the analysis presented in Sánchez et al. (2015), the observability analysis for the system (3) determines the existence of a diffeomorphism between the vector $\mathcal{H}$ and the delayed state vector $x = \left[\, x_1(t-\tau)\ x_2(t-\tau)\ x_3(t-\tau)\ x_4(t-\tau)\,\right]^T$.

The existence of this diffeomorphism can be evaluated, at least locally, by checking if the observability matrix defined as $\mathcal{O} = \frac{\partial \mathcal{H}}{\partial x(t-\tau)}$ is invertible. For the system (3), the observability matrix is calculated from (6) and is given by

$$\mathcal{O} = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ * & * & b_1(x_1(t-\tau), x_2(t-\tau)) & 0 \\ * & * & b_{21}(x_1(t-\tau), x_2(t-\tau)) & b_{22} \end{bmatrix} \quad (7)$$

where it follows that the determinant of (7) is $\det(\mathcal{O}) = b_{22}b_1(x_1(t-\tau), x_2(t-\tau))$. Therefore, this system is observable for $t \geq \tau$. However, it can be shown that $|\det(\mathcal{O})|$ achieves a very small value (about 1×10^{-9}), which compromises the numerical invertibility of the observability matrix $\mathcal{O}$ (Sánchez et al., 2015).

To overcome this numerical drawback, the following scaling transformation of the state is proposed:

$$\begin{aligned} x_{1s}(t-\tau) &= \beta_1 x_1(t-\tau) \\ x_{2s}(t-\tau) &= \beta_2 x_2(t-\tau) \end{aligned} \quad (8)$$

with β_1 and β_2 real positive constants to be defined thereafter.

Thus, using the notation $x_i^\tau = x_i(t-\tau)$ for $i = 1, \ldots, 4$, the system (3) under the scaling (8) becomes:

$$\begin{aligned} \dot{x}_{1s}^\tau &= b_1^s(x_1^\tau, x_2^\tau)x_3^\tau \\ \dot{x}_{2s}^\tau &= f_2^s(x_2^\tau) + b_{21}^s(x_1^\tau, x_2^\tau)x_3 + b_{22}^s x_4^\tau \\ \dot{x}_3^\tau &= b_3(x_1^\tau, x_2^\tau)x_3^\tau \\ \dot{x}_4^\tau &= b_4(x_1^\tau)x_3^\tau \end{aligned} \quad (9)$$

where $b_1^s(x_1^\tau, x_2^\tau) = \beta_1 b_1(x_1^\tau, x_2^\tau)$, $f_2^s(x_2^\tau) = \beta_2 f_2(x_2^\tau)$, $b_{21}^s(x_1^\tau, x_2^\tau) = \beta_2 b_{21}(x_1^\tau, x_2^\tau)$ and $b_{22}^s = \beta_2 b_{22}$.

3.2 Observer-Predictor Scheme

In this section a cascade observer-predictor scheme is represented. Based in the structure presented in Khosravian et al. (2015b), the proposed scheme is composed for a SMO and Smith predictor. A block diagram of this proposal is shown in Figure 1. In this figure the sensor block separately block process is proposed to clarify, in this paper, the problem of delay occurs in the dynamics of the sensor.

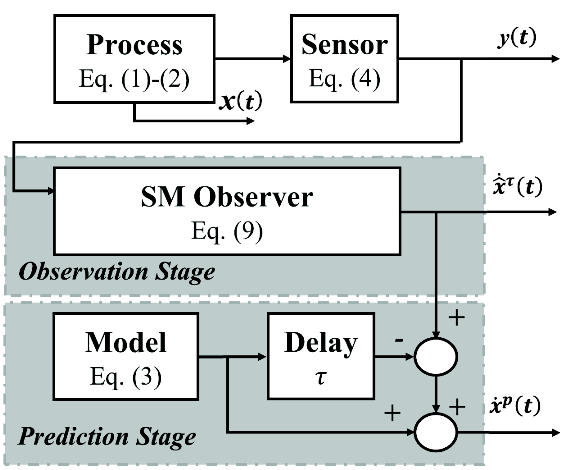

Figure 1. Observer-Predictor scheme

An explanation of the scheme of Figure 1 is as follows.

Observation Stage (SM Observer): First, from (8)-(9) the following Sliding Mode Observer is proposed in order to provide an estimation of the delayed state variables:

$$\begin{aligned} \hat{x}_1^\tau &= \beta_1^{-1}\hat{x}_{1s}^\tau \\ \hat{x}_2^\tau &= \beta_2^{-1}\hat{x}_{2s}^\tau \\ \dot{\hat{x}}_{1s}^\tau &= b_1^s(\hat{x}_1^\tau, \hat{x}_2^\tau)\hat{x}_3^\tau + k_{11}\phi_1(\tilde{x}_{1s}^\tau) \\ \dot{\hat{x}}_{2s}^\tau &= f_2^s(\hat{x}_2^\tau) + b_{21}^s(\hat{x}_1^\tau, \hat{x}_2^\tau)\hat{x}_3^\tau + b_{22}^s\hat{x}_4^\tau + k_{21}\phi_1(\tilde{x}_{2s}^\tau) \\ \dot{\hat{x}}_3^\tau &= b_3(\hat{x}_1^\tau, \hat{x}_2^\tau)\hat{x}_3^\tau + k_{12}\left[b_1^s(\hat{x}_1^\tau, \hat{x}_2^\tau)\right]^{-1}\phi_2(\tilde{x}_{1s}^\tau) \\ \dot{\hat{x}}_4^\tau &= b_4(\hat{x}_1^\tau)\hat{x}_3^\tau + k_{22}\left[b_{22}^s\right]^{-1}\phi_2(\tilde{x}_{2s}^\tau) \end{aligned} \quad (10)$$

where $\hat{x}_1^\tau$, $\hat{x}_2^\tau$, $\hat{x}_{1s}^\tau$, $\hat{x}_{2s}^\tau$, $\hat{x}_3^\tau$ and $\hat{x}_4^\tau$ are the estimates of x_1^τ, x_2^τ, x_{1s}^τ, x_{2s}^τ, x_3^τ and x_4^τ, respectively; $\tilde{x}_{1s}^\tau = x_{1s}^\tau - \hat{x}_{1s}^\tau$ and $\tilde{x}_{2s}^\tau = x_{2s}^\tau - \hat{x}_{2s}^\tau$ are the error variables; the observer input injections $\phi_1(\cdot)$ and $\phi_2(\cdot)$ are of the form $\phi_1(\cdot) = \lfloor\cdot\rceil^{\frac{1}{2}} + \theta\lfloor\cdot\rceil^{\frac{3}{2}}$ and $\phi_2(\cdot) = \frac{1}{2}\lfloor\cdot\rceil^0 + 2\theta\cdot + \frac{3}{2}\theta^2\lfloor\cdot\rceil^2$, with the parameter $\theta \geq 0$, the function $\lfloor\cdot\rceil^\alpha = |\cdot|^\alpha \mathrm{sign}(\cdot)$ is defined for $\alpha \geq 0$, where $\mathrm{sign}(x) = 1$ for $x > 0$, $\mathrm{sign}(x) = -1$ for $x < 0$ and $\mathrm{sign}(0) \in \{-1, 1\}$; and λ_1, $\lambda_2 > 0$, and k_{11}, k_{12}, k_{21}, k_{22} are the observer positive gains.

The SMO (10) was proposed in a previous paper (Sánchez et al., 2015). This observer is fixed-time convergent and also has time-invariance property, according to the definition of Khosravian et al. (2015a). A detailed stability test of observer (10) without delay in measurements has been previously published (Sánchez et al., 2015). However, the problem considered in this paper is to estimate the current state $x(t)$ when the measurements of the output are delayed such that the output measurement at time t is $y(t) = h(x(t-\tau))$ for some know constant delay $\tau \geq 0$. In this sense a prediction stage it is proposed to offset the effect of the delay in the measurement.

Prediction Stage (Model + Delay): Second, based on (Khosravian et al., 2015a) a Smith predictor compensating the delay may be considered as

$$\dot{x}^p(t) = \dot{\hat{x}}^\tau(t) + f(x^p(t)) - f(x^p(t-\tau)) \quad (11)$$

where the prediction of the current state is denoted by $x^p \in \mathbb{R}^n$ and $\hat{x}^\tau$ is the estimate x subject to delayed output measurements (5). Moreover, with the system model (3) and the known delay τ for output measurement (5), it is possible to know the dynamics of the predicted states without delay $f(x^p(t))$ and delayed $f(x^p(t-\tau))$.

The stability of the Observer-Predictor structure is such that the estimate state converge asymptotically/exponentially to the system trajectories (1)-(2), if the estimates provided by the Observer (SMO) converge asymptotically/exponentially to the delayed system state (Khosravian et al., 2015a). In this sense the definition of finite time convergent include asymptotically/exponentially convergent and fixed-time convergent of SMO (10) is a stronger form of finite time (Polyakov, 2012). In the next section the simulation results are presented.

4. SIMULATION RESULTS

This section presents the numerical simulation results of the proposed estimation structure. The simulations parameters were:

- Fundamental step size of $1 \times 10^{-5}[h]$. This time is small due to requirement of robust differentiation in the estimation scheme.
- Model parameters like shown on Table 1.

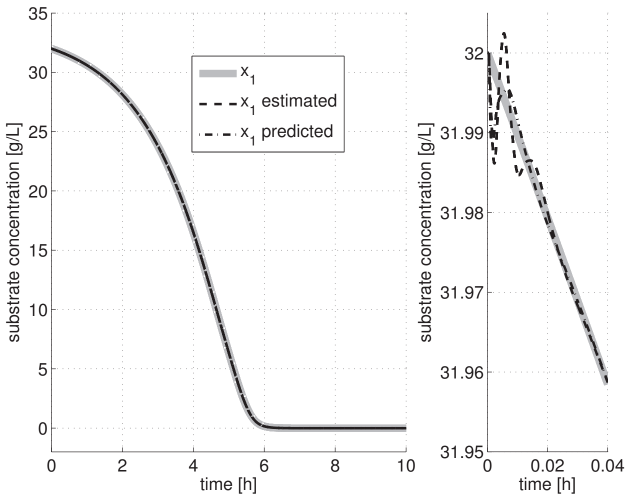

Figure 2. Substrate concentration s_p with $\tau = 5 \times 10^{-5}[h]$.

- The parameters shown in this table were taken according to the range to $20\,[\mathrm{g \cdot L^{-1}}] < s_{p,\max} < 32\,[\mathrm{g \cdot L^{-1}}]$.
- The value $s_{p,\max}$ corresponds to the initial condition of s_p since $\dot{s}_p \leq 0$.
- The substrate concentration $s_p = x_1$ and the dissolved oxygen concentration $o_d = x_2$ are assumed to be measured, noiseless and delayed, and the initial conditions $\hat{x}^{\tau}_{1s}$ and $\hat{x}^{\tau}_{2s}$ were taken as the scaled initial conditions of x_1 and x_2 respectively
- The delay is a known constant $\tau \geq 0$. However, since the vegetative cells concentration $x_v = x_3$ and the sporulated cells concentration $x_s = x_4$ aren't measured, the initial conditions $\hat{x}^{\tau}_3$ and $\hat{x}^{\tau}_4$ were taken different from x_3 and x_4, respectively.
- Another thing that should be noted is that with the selected values of β_1 and β_2, the minimum value of $|\det(\mathcal{O}_s)|$ is around 2.

Figures 2, 3, 4 and 5 show the comparison between the actual x, estimated $\hat{x}^{\tau}$ (SMO without prediction) and predicted x^p (SMO with prediction) variables corresponding to substrate concentration s_p, dissolved oxygen concentration o_d, vegetative cell concentration x_v and sporulated cells concentration x_s when the delay measurement is $\tau = 5 \times 10^{-5}[h]$. It can be noticed that, despite initial estimation error $x(0) = \left[32,\ 0.74 \times 10^{-2},\ 0.645,\ 1 \times 10{-}5\right]^T$, and $\hat{x}^{\tau}(0) = x^p(0) = \left[32,\ 0.74 \times 10^{-2},\ 6.45,\ 1\right]^T$ the fixed time convergence of the estimated variables is achieved.

Figures 6 and 7 show the comparison between the actual and estimated variables corresponding to x_v and x_s when measurements of s_p and o_d are delayed with $\tau = 1 \times 10^{-1}[h]$ with SMO (SMO without prediction) and predicted x^p (SMO with prediction). Based on the presented results, it can be observed a good performance of the observer-predictor scheme proposed while the only SMO does not converge. A correct and fast estimation of x_v and x_s using the cascade observer-predictor is achieved making the proposed system suitable for observer-based control applications.

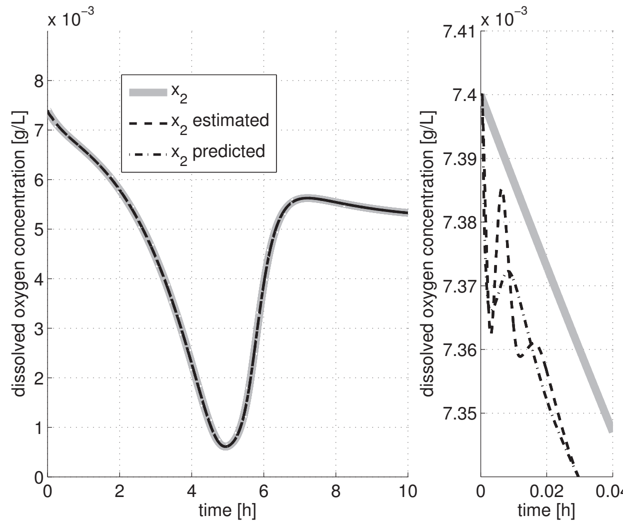

Figure 3. Dissolved oxygen concentration o_d with $\tau = 5 \times 10^{-5}[h]$.

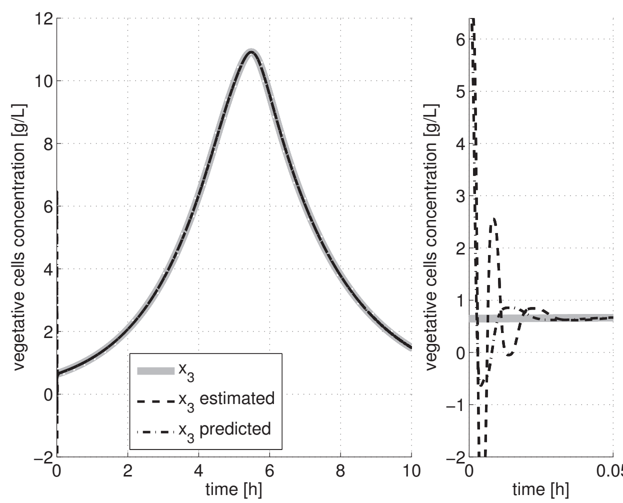

Figure 4. Vegetative cells concentration x_v with $\tau = 5 \times 10^{-5}[h]$.

Finally, Figures 8 and 9 show the effect of increased the delay measurement in s_p and o_d for estimation of x_v and x_s respectively in booth cases only SMO and SMO-predictor. The Integral Time Absolute Error (ITAE) of only SMO tends to infinity for delays in measuring higher than $\tau = 6 \times 10^{-5}[h]$, while the cascade observer-predictor scheme keep the convergence of error when the delay increase.

5. CONCLUSIONS

In this paper was presented a soft sensor to estimate the biomass in a batch bioprocess subject to delayed measurements. The soft sensor proposed is based on a cascade sliding mode observer-predictor. The observer stage is based on a class of second order sliding mode algorithms, allowing a fixed-time estimation of the biomass. The prediction stage offsets the effect of the delay in measurements. Convergence proof and numerical

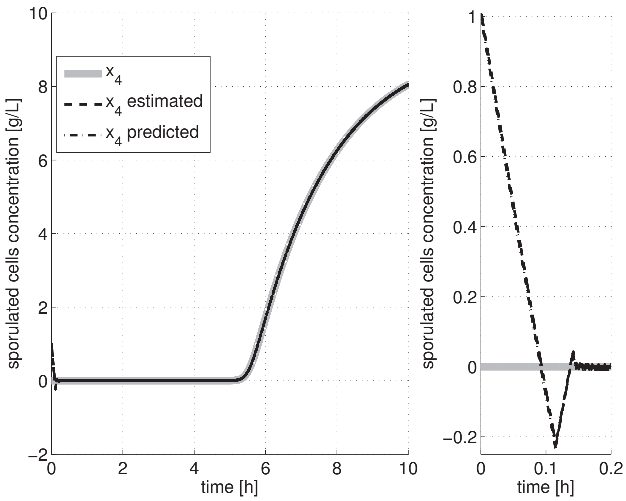

Figure 5. Sporulated cells concentration x_s with $\tau = 5 \times 10^{-5}[h]$.

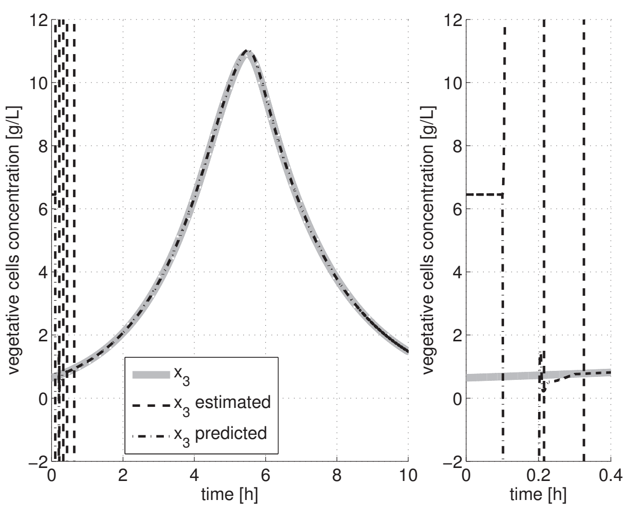

Figure 6. Vegetative cells concentration x_v with $\tau = 0.1[h]$.

simulations shown the feasibility of the cascade observer-predictor proposed.

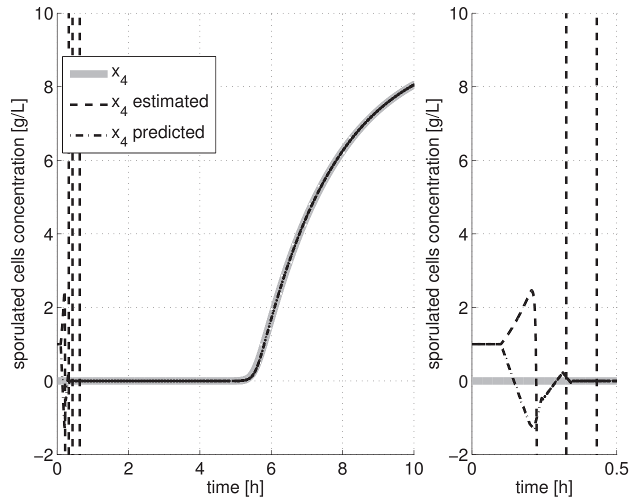

Figure 7. Sporulated cells concentration x_s with $\tau = 0.1[h]$.

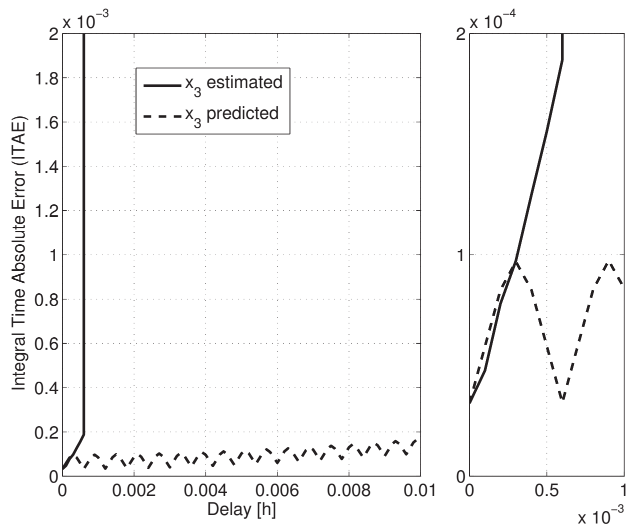

Figure 8. Delay effect to estimate x_v.

REFERENCES

Amicarelli, A., di Sciascio, F., Toibero, J.M., and Alvarez, H. (2010). Including Dissolved Oxygen Dynamics into the Bt delta-Endotoxins Production Process Model and its Application to Process Control. *Brazilian Journal of Chemical Engineering*, 27(1), 41–62.

Bequette, B. (2002). Behavior of a CSTR with a recirculating jacket heat transfer system. In *Proceedings of the American Control Conference.*, volume 4, 3275 – 3280.

Dochain, D. (2003). State and parameter estimation in chemical and biochemical processes: a tutorial. *Journal of Process Control*, 13(8), 801 – 818.

Gopalakrishnan, A., Kaisare, N.S., and Narasimhan, S. (2011). Incorporating delayed and infrequent measurements in Extended Kalman Filter based nonlinear state estimation. *Journal of Process Control*, 21(1), 119–129.

Guo, Y. and Huang, B. (2015). State estimation incorporating infrequent, delayed and integral measurements. *Automatica*, 58, 32–38. doi: 10.1016/j.automatica.2015.05.001.

Guo, Y., Zhao, Y., and Huang, B. (2014). Development of soft sensor by incorporating the delayed infrequent and irregular measurements. *Journal of Process Control*, 24(11), 1733–1739.

Khosravian, A., Trumpf, J., and Mahony, R. (2015a). State Estimation for Nonlinear Systems with Delayed Output Measurements. (Cdc), 6330–6335. doi: 10.1016/j.automatica.2016.01.024.

Khosravian, A., Trumpf, J., Mahony, R., and Hamel, T. (2015b). State Estimation for Invariant Systems on Lie Groups with Delayed Output. *Automatica*, 68, 254–265.

Polyakov, A. (2012). Nonlinear feedback design for fixed-time stabilization of linear control systems. *IEEE Transactions on Automatic Control*, 57(8), 2106–2110.

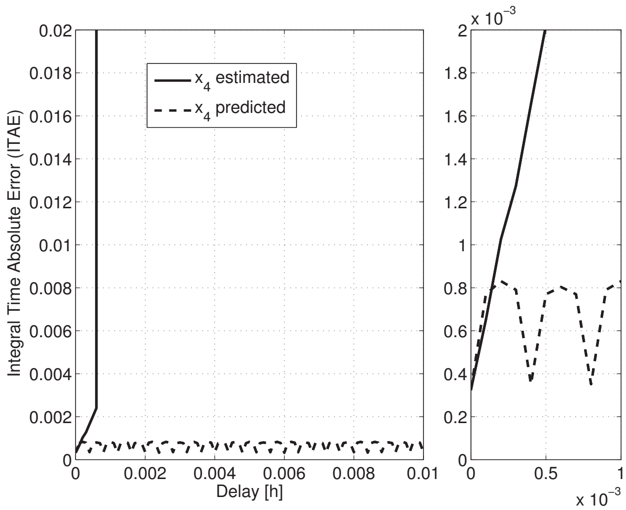

Figure 9. Delay effect to estimate x_s.

Rómoli, S., Amicarelli, A.N., Ortiz, O.A., Scaglia, G.J.E., and di Sciascio, F. (2016). Nonlinear control of the dissolved oxygen concentration integrated with a biomass estimator for production of Bacillus thuringiensis δ-endotoxins. *Computers & Chemical Engineering*, 93, 13–24. doi:10.1016/j.compchemeng.2016.05.017.

Sánchez, J.D., Isaza, J.A., Jaramillo, O., Jimenez, E., and Botero, H. (2015). A Fixed-Time Convergent Observer for Biomass in a Batch Process. In *IEEE CCAC 2015 Conference Proceedings*, volume 1, 1–4.

Walcott, B.L., Corless, M.J., and Zak, S.H. (1987). Comparative study of nonlinear state observation techniques. *Int. J. Control*, 45, 2109–2132.

Wang, H.P., Tian, Y., and Vasseur, C. (2015). Piecewise continuous hybrid systems based observer design for linear systems with variable sampling periods and delay output. *Signal Processing*, 114, 75–84. doi: 10.1016/j.sigpro.2015.01.009.

Zeng, J. and Liu, J. (2015). Distributed moving horizon state estimation: Simultaneously handling communication delays and data losses. *Systems & Control Letters*, 75, 56–68. doi:10.1016/j.sysconle.2014.11.007.

Zhao, L., Wang, J., Yu, T., Chen, K., and Liu, T. (2015). Nonlinear state estimation for fermentation process using cubature Kalman filter to incorporate delayed measurements. *Chinese Journal of Chemical Engineering*, 23(11), 1801–1810. doi:10.1016/j.cjche.2015.09.005.