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HYBRID FULL HORIZON-ASYMPTOTIC OBSERVER FOR BIOPROCESSES

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Abstract: The full horizon observer is a stochastic nonlinear observer that does not require any parameter tuning and whose optimal feature results directly from the identification cost function of the initial conditions. The efficiency of this observer is, however, strongly dependent on the model quality. On the other hand, the asymptotic observer does not require a kinetic model. However, its convergence is function of the experimental conditions. The aim of this study is to build a hybrid observer which allows to jointly estimate the state and identify on-line the confidence in the kinetic model. Simulations of fed-batch bacterial cultures show very satisfactory results.

Keywords: State observers, nonlinear systems, biotechnology, fermentation processes.

1. INTRODUCTION

Bioprocess knowledge, monitoring and control are key elements to insure optimal working and product quality. As the process becomes more complex (reactor design, biocatalysts, products...) more information over the dynamic of the main constituents are required. If sensors for some process variables are well established (dissolved oxygen, pH, temperature...) some do not exist or involve several problems (particularly for biological state variables) : they are not sterilizable, they require discrete and rare samples and provide measurements sometimes with a long time of analysis, the sensors and their maintenance are very expensive and finally they can degrade the hydrodynamics properties of complex bioreactors. These problems lead to consider the software sensors which combine available hardware sensors signals and a mathematical model in order to provide on-line measurements estimates in continuous time. The estimation algorithm that provides an on-line state estimate converging towards the true state of the process is called a state observer.

Several estimation techniques dealing with the non-linear models involved in bioprocesses have been proposed in the literature. Applying these techniques to bioprocess currently highlights the major advantages and drawbacks of these state observers. On one hand, exponential observers like extended Kalman filters or full horizon observers (Bogaerts and Hanus, 2001) are strongly dependent on the model quality. On the other hand the asymptotic observer (Bastin and Dochain, 1990) does not require any knowledge of the kinetic model which is most of time badly known. However the rate of convergence of this state observer is completely determined by the experimental conditions (namely the dilution rate). This may lead to very slow convergence in the case of low dilution rate, and the observer does not converge at all in the case of batch cultures.

Several solutions have been proposed in order to overcome these problems of convergence or dependency on model quality. In the usual trade-off solutions, either the model identification is added to the state estimation problem (Dubach and Märkl, 1992)(Ghoul *et al.*, 1991), or the known

part of the model is fixed a priori (Pelletier, 1995). Another trade-off solution is to fix the model structure parameters and to consider the model quality by introducing a confidence parameter. This latter solutions has lead to the hybrid observers. The asymptotic-Kalman observer (Bogaerts, 1999) and the hybrid observer proposed by (Lemesle and Gouzé, 2001) evolves between two limit cases, the extended Kalman filter, respectively the high gain observer, and the asymptotic observer of Bastin and Dochain according to this confidence parameter (evaluated on-line in the first hybrid observer and *a priori* fixed in the second one). In this paper a hybrid full horizon-asymptotic which follows the same concept of the asymptotic-Kalman observer is proposed. The continuous variation of the confidence parameters results in a continuous variation of the hybrid observer structure, the two limit cases being (rigorously) the full horizon (100% confidence) and asymptotic (0% confidence) observers.
This paper is organized as follows. The second section recalls the framework of macroscopic reaction schemes and their associated mass balances used for bioprocess modelling. Based on this framework section 3 describes the full horizon observer and section 4 the asymptotic observer. Section 5 is devoted to the hybrid full horizon asymptotic observer. The performance of this observer is illustrated on a simulation example in section 6. Finally, section 7 draws some conclusions.

2. MACROSCOPIC REACTION SCHEMES AND MASS BALANCES FOR BIOPROCESS MODELLING

A bioprocess can be described by a reaction scheme defined by a set of M reactions (Bastin and Dochain, 1990). Such a reaction scheme can be expressed by:

$$\sum_{i \in R_k} (-\nu_{i,k})\xi_i \overset{\varphi_k}{\to} \sum_{j \in P_k} \nu_{j,k}\xi_j \qquad k \in [1, M] \qquad (1)$$

where
- $\nu_{i,k}$ and $\nu_{j,k}$ are the pseudo-stoichiometric coefficients or yield coefficients;
- φ_k is the reaction rate;
- ξ_i is the i^{th} component;
- $R_k(P_k)$ is the set of ξ_i which are reactants (products) in the reaction k;
- M is the number of reactions.

Assuming that the bioprocess takes place in a perfectly stirred bioreactor, the system dynamics can be described by a model resulting from mass balances for the macroscopic species involved in the reaction scheme:

$$\frac{d\xi(t)}{dt} = K\varphi(\xi, t) - D(t)\xi(t) + F(t) - Q(t) \quad (2)$$

where
- $\xi \in \Re^N$ is the vector of concentrations;
- $K \in \Re^{N \times M}$ is the pseudo-stoichiometric coefficients matrix ($M \leq N$);
- $\varphi \in \Re^M$ is the vector of reaction rates;
- $D \in \Re$ is the dilution rate;
- $F \in \Re^N$ is the vector of external feed rates;
- $Q \in \Re^N$ is the vector of gaseous outflow rates.

In the sequel, the external feed rates and gaseous outflow rates are put together in a vector

$$u(t) = F(t) - Q(t) \quad (3)$$

Let:

$$\xi^T = [\xi_1^T \quad \xi_2^T] \quad (4)$$

where $\xi_1 \in \Re^L (L \leqslant N)$ contains the elements of ξ which are measured :

$$\xi_1 = C\xi = [I_L \quad O_{L,N-L}]\xi \quad (5)$$

These measurements are provided by discrete samples $y(t_k)$:

$$y(t_k) = C\xi(t_k) + \epsilon(t_k) \quad (6)$$

ϵ being a white noise sequence normally distributed with $E[\epsilon(t_k)] = 0$ and $E[\epsilon(t_k)\epsilon^T(t_k)] = \delta_{k,l}Q(t_k)$.

The other elements $\xi_2 \in \Re^{(N-L)}$ of ξ are the variables which are not measured.

3. THE FULL HORIZON OBSERVER

The full horizon observer (FHO) is a stochastic observer that consists in integrating the simulation model between two measurements (prediction) starting with the most likely initial conditions identified on the base of all the available measurements (correction). This nonlinear observer does not require any parameter tuning and its optimal feature results directly from the identification cost function of the initial conditions (Bogaerts and Hanus, 2000),(Bogaerts and Hanus, 2001). The efficiency of this observer is, however, strongly dependent on the model quality and particularly, in the case of a bioprocess, on the quality of the kinetic model.

The prediction equation of the full horizon observer is defined as

$$\begin{cases} \dfrac{d\hat{\xi}(t)}{dt} &= K\varphi(\hat{\xi}, t) - D(t)\hat{\xi}(t) + u(t) \\ \hat{\xi}(t) &= g(t, u(t), \hat{\xi}_{0/k}) \qquad \forall t \in [t_k, t_{k+1}] \end{cases} \quad (7)$$

where $g(t, u(t), \hat{\xi}_{0/k})$ is the prediction of $\xi(t)$ on the time interval $[t_k, t_{k+1}]$ deduced from the integration of equ. (2) from the most likely initial conditions $\hat{\xi}_{0/k}$. These latter are identified by solving a nonlinear optimization problem on the basis of all the measurements $y(t_j), j \in [1,k]$ available up to time k :

$$\begin{aligned}\hat{\xi}_{0/k} &= \underset{\xi_0}{Argmin} J_k(\xi_0) \\ &= \frac{1}{2}\underset{\xi_0}{Argmin}\sum_{j=1}^{k}\epsilon^T(t_j)Q^{-1}\epsilon(t_j)\end{aligned} \quad (8)$$

Where $\epsilon(t_j) = y(t_j) - Cg(t_j, u(t), \xi_0)$

Note that a necessary condition of existence of the solution (8) is that the number of available measurements is greater or equal to the number of initial states to identify (Bogaerts and Hanus, 2000).

As pointed out by Bogaerts and Hanus (2000, 2001) this method provides a continuous-time estimation based on rare and asynchronous measurement samples, consists of a stochastic approach, is a true nonlinear approach (no approximation such as linearization), does not require any tuning, may be theoretically analysed (e.g., state estimation correction) and provides confidence intervals for the state estimates. However, it requires the full knowledge of the model structure (2).

4. THE ASYMPTOTIC OBSERVER

The establishment of the asymptotic observer (Bastin and Dochain, 1990) is based on the following conditions : $\varphi(\xi, t)$ is unknown, K is known, $L = dim(\xi_1) \geqslant p = rank(K)$;

Hence, there always exists a partition

$$\xi^T = [\xi_a^T \; \xi_b^T] \quad (9)$$

so that the corresponding partition

$$K^T = [K_a^T \; K_b^T] \quad (10)$$

involves a matrix $K_a \in \Re^{p\times M}$ of full row rank. Given such a partition of K, the following matrix equation

$$A_0 K_a + K_b = 0_{N-p,M} \quad (11)$$

has always a unique solution $A_0 \in \Re^{(N-p)\times M}$. We can therefore define an auxiliary vector $Z \in \Re^{(N-p)}$:

$$Z(t) = A_0\xi_a(t) + \xi_b(t) \quad (12)$$

whose dynamics is independent of the kinetics $\varphi(\xi, t)$:

$$\frac{dZ(t)}{dt} = -D(t)Z(t) + A_0 u_a(t) + u_b(t) \quad (13)$$

where $u^T = [u_a^T u_b^T]$ is the partition of u corresponding to the partition of ξ. It is possible to write the vector Z as a linear combination of the vectors ξ_1 and ξ_2 of measured and non measured states :

$$Z = A_1\xi_1 + A_2\xi_2 \quad (14)$$

where $A_1 \in \Re^{(N-p)\times L}$ and $A_2 \in \Re^{(N-p)\times(N-L)}$. The asymptotic observer is finally defined by :

$$\begin{cases}\dfrac{d\hat{Z}(t)}{dt} = -D(t)\hat{Z}(t) + A_0U_1(t) + U_2(t) \\ \hat{\xi}_2(t) = A_2^+(\hat{Z}(t) - A_1\xi_1(t))\end{cases} \quad (15)$$

where $A_2^+ \in \Re^{(N-L)\times(N-p)}$ is a left pseudo-inverse of A_2.

In the sequel, for the sake of simplicity, the partition $\xi^T = [\xi_1^T\xi_2^T]$ will be chosen so that $\xi^T = [\xi_a^T\xi_b^T]$. In this particular case, the asymptotic observer (15) can be replaced by

$$\begin{cases}\dfrac{d\hat{Z}(t)}{dt} = -D\hat{Z}(t) + A_0U_1(t) + U_2(t) \\ \hat{\xi}_2(t) = \hat{Z}(t) - A_0\xi_1(t)\end{cases} \quad (16)$$

with

$$A_0K_1 + K_2 = 0_{N-p,M} \quad (17)$$

and $K^T = [K_1^T K_2^T]$ and $u^T = [u_1^T u_2^T]$ the partition of K and u corresponding to the state partition of $\xi^T = [\xi_1^T\xi_2^T]$.

If the asymptotic observer presents the major advantage to be independent of the reaction rate function $\varphi(\xi, t)$ in (2) it has also some drawbacks:

- its convergence is function of the experimental conditions (namely the dilution rate). This observer may therefore not converge (batch process) or converge very slowly (low dilution rate);
- the approach is completely deterministic and therefore does not take into account the measurement noises;
- if only descrete measurement are available, it becomes necessary to extrapolate the samples in continuous time.

5. THE HYBRID FULL HORIZON-ASYMPTOTIC OBSERVER

The general idea of the full horizon-asymptotic observer is to use the advantages of the FHO when the model is of good quality and to evolve towards the asymptotic observer when the confidence in the kinetic model becomes very low.

In order to take count of this confidence in the kinetic model and to allow the evolution of this observer towards the asymptotic one according to this degree of confidence the following modifications of the full horizon observer are proposed:

- the state transformation proposed by Bogaerts (Bogaerts, 1999) :

$$Z_1 = \xi_1 \quad (18)$$

$$Z_2 = \xi_2 + (1-\delta)A_0\xi_1 \quad (19)$$

where A_0 is the solution of (17) and δ is supposed to belong to the interval [0,1];

- a weighted output injection in the estimate $\hat{\xi}_1$

$$\hat{\xi}_1 = \delta \hat{Z}_1 + (1-\delta) y \qquad (20)$$

- the extension of the state estimate $\hat{Z}$ to :

$$\hat{Z}^T = [\hat{Z}_1^T \hat{Z}_2^T \delta] \qquad (21)$$

- the addition of a recall term towards the FHO in the correction equation. Without this term a solution of the optimization problem would be $\delta = 0$, leading directly the observer to an asymptotic one.

$$\frac{(1-\hat{\delta})}{\sigma_\delta^2} \qquad (22)$$

where σ_δ^2 is the degree of confidence in the kinetic model;

- the addition of a recall term towards the initial conditions $\hat{Z}_0^2$ of the asymptotic observer :

$$(1-\hat{\delta})([\hat{\xi}_2^0(Z_0) - \xi_2^{0^*}]^T Q_{\xi_2^{0^*}}^{-1} [\hat{\xi}_2^0(Z_0) - \xi_2^{0^*}]) \qquad (23)$$

where

. $\hat{\xi}_2^0$ is the estimate of the initial conditions of the non measured elements of ξ deduced from the estimation of $\hat{Z}_0$ and equation (19);
. $\xi_2^{0^*}$ is an initial guess on $\hat{\xi}_2^0$;
. $Q_{\xi_2^{0^*}}$ is the covariance matrix of $\xi_2^{0^*} - \xi_2^0$.

In order to build a continuous measurement $y(t)$ on the basis of the discrete samples $y(t_k)$, a linear extrapolation is used :

$$y(t) = \begin{cases} y(t_k) + (t - t_k) * \dfrac{y(t_k) - y(t_{k-1})}{t_k - t_{k-1}} \\ \qquad\qquad t_1 \leqslant t_k \leqslant t \leqslant t_{k+1} \\ y(0) \qquad\qquad 0 \leqslant t \leqslant t_1 \end{cases} \qquad (24)$$

From these modifications, it is possible to derive the hybrid full horizon-asymptotic observer :

$$\begin{cases} \dfrac{d\hat{Z}_1}{dt} = K_1 \varphi(\hat{Z}_1, \hat{\xi}_2) - D\hat{Z}_1 + u_1 \\ \dfrac{d\hat{Z}_2}{dt} = \delta K_2 \varphi(\hat{Z}_1, \hat{\xi}_2) - D\hat{Z}_2 + u_2 + (1-\delta) A_0 u_1 \\ \dfrac{d\delta}{dt} = 0 \\ \hat{\xi}_1 = \delta \hat{Z}_1 + (1-\delta) y \\ \hat{\xi}_2 = \hat{Z}_2 - (1-\delta) A_0 \hat{\xi}_1 \qquad \forall t \in [t_k, t_{k+1}] \end{cases} \qquad (25)$$

$$\hat{Z}_{0/k} = \frac{1}{2} \underset{Z_0}{Argmin} \sum_{j=1}^{k} \epsilon^T(t_j) Q^{-1} \epsilon(t_j) + \frac{1-\hat{\delta}}{\sigma_\delta^2} + (1-\hat{\delta})(\epsilon^{0T} Q_{\xi_2^{0^*}}^{-1} \epsilon^0) \qquad (26)$$

where
- $\epsilon(t_j) = y(t_j) - \hat{\xi}_1(t_j, u(t), Z_0)$
- $\epsilon^0 = \hat{\xi}_2^0(Z_0) - \xi_2^{0^*}$

This Algorithm allows the observer to evolve between the FHO and the asymptotic one according to the value of $\hat{\delta}$ that depends itself on the quality of the kinetic model. Indeed, δ being one of the optimization parameters, if the model is of good quality a $\hat{\delta}$ tending towards 1 will contribute to a low cost function value. On the other hand, if the model is of bad quality, a $\hat{\delta}$ tending towards 0 will contribute to a low cost function value. It is easy to show that the two extreme cases are δ fixed to 1 (corresponding rigorously to the FHO) and δ fixed to 0 (corresponding rigorously to the asymptotic observer). Indeed, for δ fixed to 1, the last two terms of (26) vanish and (25) and (26) become equivalent to (7) and (8). In the case of δ fixed to 0, the first term of (26) vanishes, the second one becomes constant and the last one is minimized for $\hat{\xi}_2^0(Z0) = \xi_2^{0^*}$. Hence the minimization of (26) always leads to the latter condition, which means that there is no more correction in the procedure. Finally, (25), with δ fixed to 0 and $\hat{\xi}_2^0(Z0) = \xi_2^{0^*}$ is equivalent to (16). Note that this theory can be extended to the general case where the partition $\xi^T = [\xi_a^T \xi_b^T]$ does not correspond to the partition $[\xi_1^T \xi_2^T]$. The following section illustrates the performance of this hybrid observer on a simulation example.

6. EXAMPLE ON A SIMULATED FED-BATCH BACTERIAL CULTURE

Consider a fed-batch bacterial fermentation supposed to take place in a perfectly stirred bioreactor. Consider the following reaction scheme :

$$\nu_S S \xrightarrow{\varphi} \overset{\frown}{X} \qquad (27)$$

where S denotes the substrate, X the biomass, and ν_S the yield coefficient. $\overset{\frown}{X}$ denotes an autocatalytic reaction. The mass balance corresponding to this reaction scheme is :

$$\frac{dC_S(t)}{dt} = \nu_S \varphi(C_S(t), X(t)) - D(t) C_S(t) + D(t) C_S^{in} \qquad (28)$$

$$\frac{dC_X(t)}{dt} = \varphi(C_S(t), X(t)) - D(t) C_X(t) \qquad (29)$$

where $C_S(t)$ and $C_X(t)$ are the substrate and biomass concentrations, $D(t)$ is the dilution rate, φ is the reaction rate and C_S^{in} is the substrate concentration in the feeding medium. The reaction rate φ will be described by using the Monod law:

$$\varphi = C_X \frac{\mu_{max} S}{K_m + S} \qquad (30)$$

The numerical values used for the simulation are derived from (Holmberg, 1983) where this model has been identified for a batch culture of B. thuringiensis : $\nu_S = 0.5g(10^{11}cell)^{-1}$; $K_m = 12gl^{-1}$; $\mu_{max} = 1.4h^{-1}$; $C_S(0) = 12gl^{-1}$; $C_X(0) = 1.410^{11}cell\ l^{-1}$; $S^{in} = 20gl^{-1}$; $D(t) = 0.01t[h^{-1}]$.

The simulation of this process is presented in figure 1. In the sequel, this simulation will be considered as the real process from which discrete samples of the substrate are supposed to be measured with a sampling time of $1h$. A white measurement noise of zero mean and $0.5gl^{-1}$standard deviation has been added to these measurements.

In order to illustrate the performance of the full horizon-asymptotic observer the biomass concentration will be estimated thanks to the algorithm proposed in section 5, with $A_0 = \frac{1}{\nu_S}$, $\varphi = C_X \frac{\mu_{max}\hat{Z}_1}{K_m+\hat{Z}_1}$, $\sigma_\delta^2 = 0.01$, $C_X^{0^*} = 1$, $Q_{C_X^{0^*}} = 0.01$.

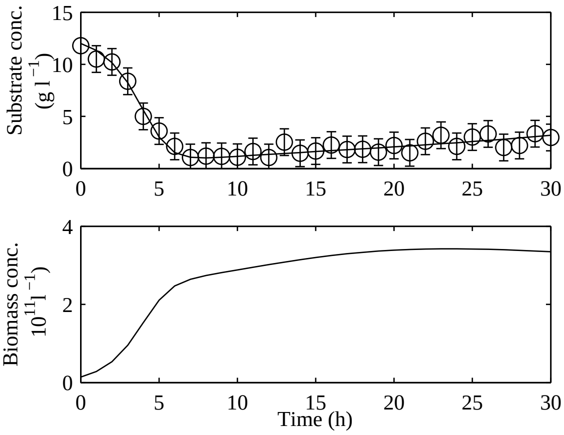

Fig. 1. Simulation of a fed-batch bacterial culture o :discrete noisy samples (with the 99 % confidence intervals),−continuous non measured signal.

This observer is used in order to estimate the biomass (X) which is not measured. Two cases are presented. First the use of the exact model (figure 2), secondly, the use of a very bad model (figure 3).

In the first situation (2), the hybrid and the FHO observers behave in a very similar way and converge rapidly to the true state. The asymptotic observer also converges but more slowly because of the low dilution rate (especially at the beginning of the experiment). The hybrid observer takes count of the model quality since $\hat{\delta}$ remains near 1. In the second case (3), at the beginning of the experiment, the hybrid observer behaves as the FHO, however, it rapidly detects the bad quality of the model and $\hat{\delta}$ evolves to 0. The hybrid observer tends therefore to the asymptotic observer and converges with it to the true state whereas the FHO diverges from the true state. Note that the parameter σ_δ appears as a tuning parameter of the hybrid observer reflecting the sensitivity of the observer to the model quality.

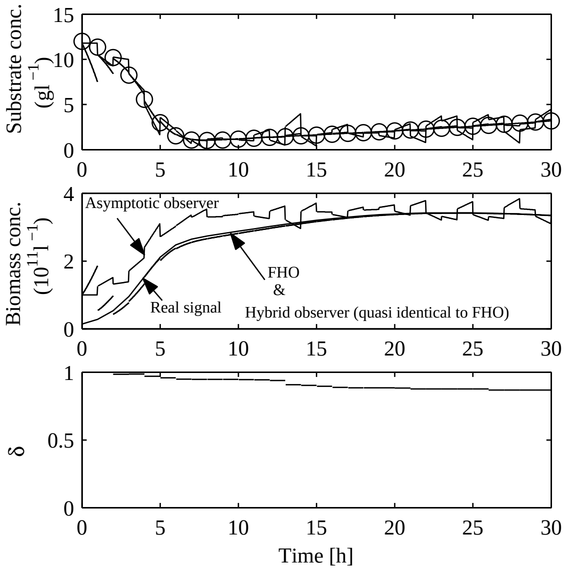

Fig. 2. Estimation of the substrate and the biomass concentrations (exact model).

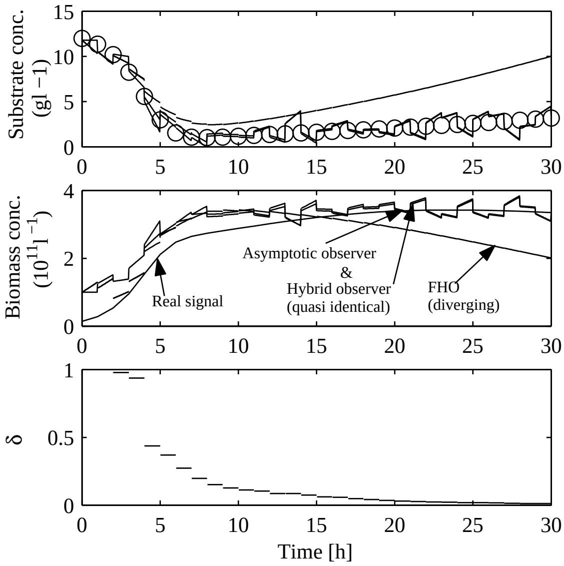

Fig. 3. Estimation of the substrate and biomass concentrations (modelling error : $\mu_{max} = 0.7h^{-1}$ and $K_m = 18gl^{-1}$ in place of $\mu_{max} = 1.4h^{-1}$ and $K_m = 12gl^{-1}$).

These results can also be compared to the estimation of the biomass with the Kalman/asymptotic

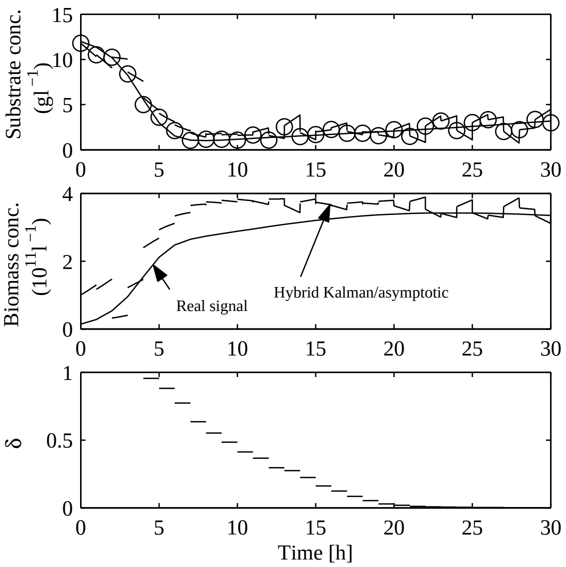

Fig. 4. Estimation of the substrate and biomass concentrations by a kalman/asymptotic observer (modelling error : $\mu_{max} = 0.7h^{-1}$ and $K_m = 18gl^{-1}$ in place of $\mu_{max} = 1.4h^{-1}$ and $K_m = 12gl^{-1}$).

hybrid observer (Bogaerts, 1999) in the case of a bad model (*cf.* figure 4). Finally, the comparaison can be made on the basis of the root of the mean square error of the biomass estimation. These values are 0.7534 $10^{11}cell\ l^{-1}$ for the full horizon observer, 0.5944 $10^{11}cell\ l^{-1}$ for the asymptotic observer, 0.4789 $10^{11}cell\ l^{-1}$ for the full horizon/asymptotic hybrid observer and 0.5561 $10^{11}cell\ l^{-1}$ for the Kalman/asymptotic hybrid observer.

7. CONCLUSION

The full horizon observer is based on the identification of the most likely initial conditions. This observer shows very interesting properties that make it particularly suitable for bioprocesses state observation. However, this observer has the major drawback to be strongly dependent on the model quality. The asymptotic observer provides an estimation of the state without any knowledge of the kinetic model. However its convergence rate is completely defined by the dilution rate.

In this paper, a new hybrid observer is proposed. The hybrid full horizon-asymptotic observer is able to evolve from the full horizon observer to the asymptotic observer according to the model quality. This evolution is driven by the ability of the observer to jointly estimate the states and to identify on-line a confidence parameter with respect to the model quality. This parameter may vary continuously from 100% to 0%. Those limits correspond rigorously to the full horizon observer (100% confidence on the kinetic model) and to the asymptotic observer (0% confidence on the kinetic model).

Simulations of fed-batch bacterial cultures show very satisfactory results. In conclusion, this contribution shows that it is possible to build a new hybrid observer evolving between the full horizon and the asymptotic observer. Note that one of the advantages of this new pair (full horizon-asymptotic observer) is the possibility to study (in future work) the mathematical properties of the state estimation error (correction, covariance) as it has been proved that these properties may be analyzed in the full horizon observer on the basis of a first order approximation (Bogaerts and Hanus, 2001).

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