Second-order sliding mode observer for multiple kinetic rates estimation in bioprocesses

Sebastián Nuñez [a,b,*], Hernán De Battista [a,b], Fabricio Garelli [a,b], Alejandro Vignoni [c], Jesús Picó [c]

[a] CONICET, Argentina
[b] LEICI, Facultad de Ingeniería, Universidad Nacional de La Plata (UNLP), Calle 48 esq. 116s/n, La Plata, Argentina
[c] Institut d'Automàtica i Informàtica Industrial, Universitat Politècnica de València, Camí de Vera s/n, Valencia, Spain

ABSTRACT

Specific kinetic rates are key variables regarding metabolic activity in bioprocesses. They are non-linear functions of concentrations and operating conditions and therefore of difficult access for process control. In this paper, a multiple kinetic rates observer based on second-order sliding mode ideas is proposed. The main difference with other proposals is that smooth estimates are achieved in finite-time without adding additional dynamics. The resulting estimator is robust against uncertainty in the model of the estimated variables. Experimental results from continuous fermentation of *S. cerevisiae* are presented, where microbial specific growth rate and net ethanol production rate are estimated.

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1. Introduction

Nowadays, biotechnological processes are applied in a wide range of industries for the production of enzymes, recombinant proteins, and high-value metabolic products. An important control problem of these processes is to achieve a desired metabolic condition (Jobé et al., 2003). The specific reaction rates contain information that is closely related to microbial activity. The knowledge of these signals have at least two relevant applications. First, reaction rates can be used in closed-loop control for improving process productivity. For instance, certain industrial problems have been related to the problem of regulating the specific growth rate (μ) of microorganism (Ren & Yuan, 2005; Soons, Voogt, van Straten, & van Boxtel, 2006). Second, the on-line availability of such information during the cultivation stage enhances bioprocess monitoring, which is essential for quality control, process reproducibility and early problem detection (Vojinovi, Cabral, & Fonseca, 2006).

Regretfully, specific reaction rates are in general not accessible since they are unmeasurable and uncertain non-linear functions of states (concentrations) and operating conditions (temperature, pH, pressure, etc). In this context, the use of observers (*software sensors*) to obtain an on-line estimation of specific rates avoids the problem of model identification while adds information for closed-loop control schemes and culture studies (Farza, Busawon, & Hammouri, 1998).

A survey of relevant methods applied to state estimation in bioprocesses can be found in Venkateswarlu (2004). Particularly, several model-based observers have been proposed for the reaction rate estimation problem. They include adaptive estimator for microbial growth rate in Bastin and Dochain (1986), extended Kalman filter in Shimizu, Takamatsu, Shioya, and Suga (1989), asymptotic observers for parameter estimation in Bastin and Dochain (1990), high gain observers of specific rates in Farza et al. (1998), Gauthier, Hammouri, and Othman (1992), and Martinez-Guerra, Garrido, and Osorio-Miron (2001), and sliding mode based observers in Picó, De Battista, and Garelli (2009), Rahman, Spurgeon, and Yan (2010), and De Battista, Picó, Garelli, and Vignoni (2011). Other approach, which does not rely on process model but requires training data sets, is based on artificial neural networks (Karakuzu, Türker, & Öztürk, 2006).

In the sliding mode observers (SMO), the idea is to enforce a sliding regime on the subspace for which the state estimation error is zero by means of a discontinuous action. Then, the observer output copies the measured state despite disturbances and allows the reconstruction of the signal of interest (De Battista, Picó, Garelli, & Navarro, 2012; Edwards & Spurgeon, 1998). In the problem of kinetic rates estimation, the unknown signals appear

* Corresponding author at: LEICI, C.C. 91 (1900), La Plata, Argentina. Tel./fax: +54 221 425 9306.
E-mail addresses: sebastian.nuniez@ing.unlp.edu.ar (S. Nuñez), deba@ing.unlp.edu.ar (H. De Battista), fabricio@ing.unlp.edu.ar (F. Garelli), alvig2@upv.es (A. Vignoni), jpico@ai2.upv.es (J. Picó).

in the time-derivative of the states. First-order sliding mode observers were developed in Picó et al. (2009) to deal with specific growth rate and substrate estimation from on-line biomass measurement. Although the exact estimation of μ was a high-frequency discontinuous signal, it was useful for constructing the substrate observer. The resulting estimates were robust under typical model uncertainties while exhibiting first order dynamics. In Rahman et al. (2010), substrate measurements were used to estimate the substrate consumption rate. The observer error dynamics is exponentially stable whereas model uncertainties and disturbances are rejected. Thereafter, in De Battista et al. (2011) a second-order sliding mode observer of μ was presented. More precisely, the proposal is a modified version of the "super twisting" algorithm, a high-order sliding mode algorithm presented in Levant (1998). In this case, the observer provides smooth estimation that exhibits finite-time convergence and is robust to typical process model uncertainties.

This work is intended to generalise preliminary results in De Battista et al. (2011). The multiple rates estimation problem requires to deal with an additional time-varying function. Therefore, further modifications are required in both the observer's structure as in the proposition of stability conditions. From bioprocess control viewpoint, the goal is to add information about the microorganism activity so as to increase on-line signals for closed-loop control and bioprocess monitoring. Therefore, the observer proposed here is applied to estimate p specific kinetic rates of production or consumption based on p related on-line measurements of process variables. The main difference with other continuous time proposals is that the estimates are achieved in finite-time and from then on, no additional dynamics is added. Besides, differing from first-order SM proposals the resulting estimations are smooth. Consequently, no additional smoothing elements would be required in closed-loop configurations. Further, robustness is expected since no model of each kinetic rate is assumed.

The rest of the paper is organised as follows. In Section 2 the problem to be solved and a typical state-space model for a bioprocess in a stirred-tank are presented. Then, in Section 3, the proposed observer is formulated. Section 4 presents results in which microbial specific growth rate and net ethanol production rate in continuous fermentation of *Saccharomyces cerevisiae* are estimated from experimental data. Finally, in Section 5, concluding remarks are given.

2. Bioprocess model and problem statement

A biotechnological process taking place in a stirred tank can be described by the following state-space model (Bastin & Dochain, 1990):

$$\frac{d\boldsymbol{\xi}}{dt} = \boldsymbol{K}\boldsymbol{r}(\boldsymbol{\xi}, t) - D(t)\boldsymbol{\xi}(t) + \boldsymbol{F}(t) - \boldsymbol{Q}(\boldsymbol{\xi}), \tag{1}$$

where $\boldsymbol{\xi}(t) \in \mathbb{R}_+^n$ is the state vector, $\boldsymbol{K}$ an $(n \times m)$ pseudo-stoichiometric coefficients matrix, $\boldsymbol{r}(\cdot) \in \mathbb{R}^m$ the reaction rates vector, $D(t) \in \mathbb{R}_+$ the dilution rate, $\boldsymbol{F}(t) \in \mathbb{R}_+^n$ the input flow rate vector and $\boldsymbol{Q}(\boldsymbol{\xi}) \in \mathbb{R}_+^n$ the gaseous outflow rate vector.

Eq. (1) describes the dynamics of the (bio)chemical species in the culture, which evolves according to m reaction rates $\boldsymbol{r}(\boldsymbol{\xi}, t)$. Since the reactions can take place only in the presence of certain necessary reactants, $r_i(\cdot)$ is zero whenever the concentration of one of the required reactants is zero. Then, the reactions can be factorised as $r_i(\boldsymbol{\xi}, t) = \alpha_i(\boldsymbol{\xi}, t) \prod_{j \in \mathcal{J}_i} \xi_j$ where $\alpha_i(\cdot)$ is generally a non-linear function and $\mathcal{J}_i$ denotes the set of required reactants (Bastin

& Dochain, 1990). In matrix form, this results in

$$\boldsymbol{r}(\boldsymbol{\xi}, t) = \boldsymbol{G}(\boldsymbol{\xi}, t)\boldsymbol{\alpha}(\boldsymbol{\xi}, t), \tag{2}$$

where $\boldsymbol{G}(\boldsymbol{\xi}, t)$ is an $(m \times m)$ state-dependent diagonal matrix.

The $\alpha_i(\cdot)$ defined in (2) are called the *specific* reaction rates per unit of *each* reactant (other definitions such as per unit of biomass are usually used, see Perrier, Feyo de Azevedo, Ferreira, & Dochain, 2000). These non-linear time-varying functions provide important knowledge about the bioprocess (e.g. microbial specific growth rate, oxygen specific uptake rate, specific production rate of metabolites) but its modelling and parameter identification can be extremely difficult. In order to add information about the process (possibly for on-line process control), a software sensor of specific reaction rates will be developed.

Particularly, the goal is to derive a robust observer of a subset of p specific reaction rates, namely $\boldsymbol{\alpha}_p(t) = [\alpha_1(t), ..., \alpha_p(t)]^T$. To this end, let us consider that p available measurements of $\boldsymbol{\xi}(t)$ are rearranged in a vector $\boldsymbol{z}$, i.e. $\boldsymbol{z}(t) = [\xi_1(t), ..., \xi_p(t)]^T$. Let $\boldsymbol{K}_p$ and $\boldsymbol{G}_p(\cdot)$ be the corresponding $(p \times p)$ submatrices of $\boldsymbol{K}$ and $\boldsymbol{G}(\cdot)$, respectively whereas $\boldsymbol{F}_p$ and $\boldsymbol{Q}_p$ are the corresponding $(p \times 1)$ vectors arranged from $\boldsymbol{F}$ and $\boldsymbol{Q}$. Assume the following:

Assumption 1. The state variables are positive and bounded.

Assumption 2. $\boldsymbol{G}_p$, $\boldsymbol{F}_p$ and $\boldsymbol{Q}_p$ are available.

Assumption 3. A bound for each α_i time derivative $\overline{\rho}_i > 0$ is known.

Assumption 4. The matrix $\boldsymbol{K}_p$ is invertible.

Assumption 5. Diagonal matrices $\boldsymbol{G}_1$, $\boldsymbol{G}_2$ such that $\boldsymbol{0} < \boldsymbol{G}_1 \leq \boldsymbol{G}_p(\cdot) \leq \boldsymbol{G}_2$ holds are known.

Note that Assumption 1 holds for the bioprocess variables (e.g. component concentrations and volume). Assumption 2 is a common assumption in the literature regarding the availability of certain on-line measurements (e.g Perrier et al., 2000). Assumption 3 states that a bound of each kinetic dynamics is available, which can be determined from practice knowledge of the bioprocess. Assumption 4 ensures that p reaction rates can be estimated from the p measured variables. Otherwise, the measured vector would not provide enough information about the reactions. From the discussion of Eq. (2), the elements of $\boldsymbol{G}_p$ are products of state variables which all remain positive and bounded. In the event that one required reactant vanishes, then at least one reaction no longer takes place. In that case, the estimation of the reaction rate has no sense and consequently the estimation problem should be reconsidered. The diagonal elements of $\boldsymbol{G}_1$ and $\boldsymbol{G}_2$ in Assumption 5 should be selected by the user based on his own knowledge about the particular process being monitored.

Now, from the model (1) and the previous discussion, the following system is considered

$$\frac{d\boldsymbol{z}}{dt} = \boldsymbol{K}_p \boldsymbol{G}_p(\cdot)\boldsymbol{\alpha}_p(\boldsymbol{\xi}, t) - D\boldsymbol{z} + \boldsymbol{F}_p - \boldsymbol{Q}_p, \tag{3}$$

$$\frac{d\boldsymbol{\alpha}_p}{dt} = \boldsymbol{R}\boldsymbol{\rho}(t), \tag{4}$$

in which $\boldsymbol{\alpha}_p(t)$ is the vector of specific kinetic rates to be estimated and $\boldsymbol{R} = diag\{\overline{\rho}_i\}$ arranges the bounds of the time derivatives. Note that $\boldsymbol{\rho}(t)$ is a vector of p unknown continuous functions where $\|\boldsymbol{\rho}(t)\|_\infty \leq 1$ holds.