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A study on the convergence of observer-based kinetics estimators in stirred tank bioreactors

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This paper is devoted to the tuning problem of an observer-based algorithm for the on-line estimation of reaction rates in stirred tank bioreactors. The relation between the dynamics of convergence and the tuning procedure is explored. The method proposed imposes a variable second-order dynamics on the convergence of the estimator. This approach is shown to compare favourably with a pole placement based technique, in an application to a baker's yeast fed-batch fermentation. Copyright ©1996 Published by Elsevier Science Ltd

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Two of the major problems limiting the use of modern control techniques in bioprocess operation are the difficulty of modelling the growth kinetics of micro-organisms and the lack of cheap and reliable sensors of biological variables. Extended Kalman filters represent a possible solution for state and parameter estimation. However, it is known that this methodology is often difficult to apply to problems involving non-linear systems with time varying parameters, particularly when in the presence of noisy measurements[1]. Model-based state observers and observer-based parameter estimators represent recent developments which may overcome these difficulties of lack of information and/or appropriate sensor technology. Bastin and Dochain[2] proposed a methodology for state and parameter estimation based upon the concepts of a 'general dynamical model for bioreactors' and of 'minimal kinetic modelling'. The system is represented by:

$$\frac{d\xi}{dt} = KH(\xi)\rho(\xi) - D\xi + F - Q(\xi) \tag{1}$$

where ξ is the state vector (the set of n component concentrations), K is an $(n \times m)$ yield coefficients matrix, D the dilution rate, F the feed rate vector with $\dim(F) = n$ and Q the gaseous outflow rate vector with $\dim(Q) = n$. The reaction rates are defined as $\varphi(\xi) = H(\xi)\rho(\xi)$ to take advantage of any possible knowledge of the kinetic model, $H(\xi)$ being a $(m \times r)$ matrix of known functions of the state and $\rho(\xi)$ a vector of r unknown functions of the state.

For the on-line estimation of reaction rates, when the yield coefficients are known and constant, the proposed observer-based estimator[2] is expressed by:

$$\frac{d\hat{\xi}}{dt} = KH(\xi)\hat{\rho} - D\xi + F - Q - \Omega(\xi - \hat{\xi}) \tag{2a}$$

$$\frac{d\hat{\rho}}{dt} = [KH(\xi)]^{T}\Gamma(\xi - \hat{\xi}) \tag{2c}$$

The structure for the regression Equation (2b) obeys stability requirements for the related linear time varying (LTV) perturbed system.

A difficulty in the application of this methodology is in the tuning of the gain matrices Ω and Γ, which are design parameters at the disposal of the user for the control of the stability and tracking properties of the algorithm. This problem is discussed by Pomerleau and Perrier[3] who proposed a pole placement based tuning for the estimation of the three specific growth rates involved in a baker's yeast fed-batch fermentation.

This paper is devoted to the tuning problem of this estimator. An alternative approach is presented which is based on the concept of assuming that the estimated kinetics follow a second-order dynamic response to the true reaction kinetics changes. It will be shown that, under mild restrictions, the method proposed imposes a piecewise second-order dynamics to the convergence of the estimator (i.e. with natural period of oscillation and damping coefficients which change in each sampling interval).

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Second-order dynamics based tuning

The kinetics estimator can be based on a subset of r equations of the full state space model, provided that they involve all the r parameters that need to be estimated[3,4]:

(i) Denoting by subscript s the redimensioned vectors and matrices related to such sub-space, a reformulated dynamical model is conveniently adopted by considering the transformation $\Phi = K_s^{-1}\xi_s$, where K_s is the relevant yield coefficients matrix of dimension $r \times m$.
This leads to:

$$\frac{d\psi}{dt} = H(\xi)\rho - D\psi + K_s^{-1}(F_s - Q_s(\xi)) \tag{3}$$

(ii) The kinetics estimator can then be re-written as:

$$\frac{d\hat{\psi}}{dt} = H\hat{\rho} - D\psi + K_s^{-1}(F_s - Q_s - \Omega_s(\psi - \hat{\psi}) \tag{4a}$$

$$\frac{d\hat{\rho}}{dt} = H^T\Gamma_s(\psi - \hat{\psi}) \tag{4b}$$

Equation (4a) is obtained by direct transformation of Equation (2a), whereas Equation (4b) is the result of the same type of stability considerations which led to Equation (2b).

The dynamics of the observation error is obtained by subtracting Equation (4a) from Equation (3):

$$\frac{d(\psi - \hat{\psi})}{dt} = H(\rho - \hat{\rho}) + \Omega_s(\psi - \hat{\psi}) \tag{5}$$

Assuming that matrix Γ_s is such that $[H(\xi)]^T\Gamma_s$ is a constant matrix, then differentiating Equation (4b) gives:

$$\frac{d^2\hat{\rho}}{dt^2} = H^T\Gamma_s\frac{d(\psi - \hat{\psi})}{dt} \tag{6}$$

Moreover, if $H(\xi)$ is a diagonal matrix, then combining Equations (4b), (5), and (6) and setting:

$$\Omega_s = \text{diag}\{-\omega_i\} \text{ and } \Gamma_s = H(\xi)^{-1}\text{diag}\{\gamma_i\} \tag{7a,b}$$

with ω_i, $\gamma_i \in \mathbb{R}^+$, the following result is obtained:

$$\tau_i^2\frac{d^2\hat{\rho}_i}{dt^2} + 2\zeta_i\tau_i\frac{d\hat{\rho}_i}{dt} + \hat{\rho}_i = \rho_i \qquad i = 1,\ldots,r \tag{8a}$$

with

$$\tau_i = (\gamma_i h_i)^{-0.5} \text{ and } \zeta_i = 0.5\omega_i(\gamma_i h_i)^{-0.5} \tag{8b,c}$$

where h_i refers to the diagonal elements of matrix $H(\xi)$.

Remark 1

Equations (8b) and (8c) show that each parameter follows a second-order dynamic response to the true parameter changes with a natural period of oscillation τ_i and a damping coefficient ζ_i. Nevertheless they are functions of the system state, and hence are time variant.

Remark 2

In the general case of H being a varying state dependent matrix, the algorithm is restricted to the condition $m = r$. The other restriction to be obeyed is that H is diagonal. Both conditions, however, are observed in a large and significant number of bioprocess reactions.

Remark 3

In the restricted number of cases where the matrix product K_sH (with dimensions $r \times r$) is time independent, the transformation to be performed should be $\psi = [K_sH]^{-1}\zeta_s$. For such cases it can be immediately concluded that both $m > r$ and $m < r$ can be accommodated.

The application of this methodology to the estimation problems of completely unknown and of partially known reaction rates is summarized in *Table 1*.

Case study – Baker's yeast fed-batch fermentation

The process model

Yeast growth may be characterized by three metabolic pathways:

$$S + O \xrightarrow{\mu_S^o} X + C \tag{9a}$$

$$S \xrightarrow{\mu_S^r} X + C + E \tag{9b}$$

$$E + O \xrightarrow{\mu_O^e} X + C \tag{9c}$$

where S: glucose; C: oxygen; X: biomass; E: ethanol; G: carbon dioxide and μ_S^o, μ_S^r, μ_E^e: specific growth rates for the three pathways. Pathways (9a) (9b) and (9c) refer respectively to the respiratory growth on glucose (oxidative pathway), fermentative growth on glucose (reductive pathway) and the respiratory growth on ethanol (oxidative pathway).

Table 1 Second-order dynamics based tuning for estimation of reaction kinetics

	Fully unknown	Partially unknown rates	
	reaction rates	Specific growth rates	Kinetic term[a]
$\rho(\xi)$ =	$\varphi(\xi)$	$\mu(\xi)$	$\alpha(\xi)$
$H(\xi)$ =	I_r	diag(X)	diag(g_i)
τ_i =	$\gamma_i^{-0.5}$	$(\gamma_i X)^{-0.5}$	$(\gamma g_i)^{-0.5}$
ζ_i =	$^1/_2\omega_i\gamma_i^{-0.5}$	$^1/_2\omega_i(\gamma_i X)^{-0.5}$	$^1/_2\omega_i(\gamma_i g_i)^{-0.5}$

[a] g_i, product of reactants concentration in reaction i

The dynamic model for the fed-batch fermentor is obtained from a mass balance on the components, considering that the reactor is well mixed, the yield coefficients are constant and the dynamics of the gas phase can be neglected. The mass balances, in terms of concentration, take the matrix form of the general dynamic model (Equation 1):

$$\frac{d}{dt}\begin{bmatrix} X \\ S \\ E \\ C \\ G \end{bmatrix} = \begin{bmatrix} 1 & 1 & 1 \\ -k_1 & -k_2 & 0 \\ 0 & k_3 & -k_4 \\ -k_5 & 0 & -k_6 \\ k_7 & k_8 & k_9 \end{bmatrix} \begin{bmatrix} \mu_s^o \\ \mu_s^r \\ \mu_e^o \end{bmatrix} X - D \begin{bmatrix} X \\ S \\ E \\ C \\ G \end{bmatrix} + \begin{bmatrix} 0 \\ DS_{in} \\ 0 \\ OTR \\ 0 \end{bmatrix} - \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \\ CTR \end{bmatrix} \tag{10}$$

where S_{in} is the substrate concentration in the feed, OTR is the oxygen transfer rate and CTR is the carbon dioxide transfer rate.

The kinetic model proposed by Sonnleitner and Käppeli[5] was used for simulation purposes. It is assumed that the baker's yeast fed-batch process can only be either in an ethanol production state or in an ethanol consumption state, this meaning that the yeast can only grow by two pathways simultaneously: pathways (9a) and (9b) corresponding to ethanol production, and pathways (9a) and (9c) corresponding to ethanol consumption.

The kinetics estimator

The 'observer-based kinetics estimator' (Equations (4)) is applied to the two partial models reflecting the two process states mentioned above, taking the form:

$$\frac{d\hat{\psi}}{dt} = H\hat{\mu} - D\psi + K_s^{-1}(F_s - Q_s) - \Omega_s(\psi - \hat{\psi}) \tag{11a}$$

$$\frac{d\hat{\mu}}{dt} = X\Gamma_s(\psi - \hat{\psi}) \tag{11b}$$

where $\psi = K_s^{-1}\xi_s$, $\xi_s = [C\ G]^T$, $(F_s - Q_s) = [OTR - CTR]^T$, and with the estimated specific growth rates vector $\hat{\mu}$ switching between $[\mu_s^o, \mu_s^r]$ and $[\mu_s^o, \mu_e^o]$.

The use of Equations (11) requires the on-line knowledge of biomass concentration. This is achieved by means of a 'Luenberger-type asymptotic observer'[6] which enables the on-line estimation of X, S and E from measurement of C and G:

$$\frac{d\hat{Z}}{dt} = -D\hat{Z} + (F_2 - Q_2) - K_2K_1^{-1}(F_1 - Q_1) \tag{12a}$$

$$\hat{\xi}_2 = \hat{Z} + K_2K_1^{-1}\xi_1 \tag{12b}$$

with

$$\xi_1 = [C\ \ G]^T,\ \hat{\xi}_2 = [\hat{X}\ \ \hat{S}\ \ \hat{E}]^T$$
$$(F_1 - Q_1) = [OTR - CTR]^T$$
$$\text{and } (F_2 - Q_2) = [0\ \ DS_{in}\ \ 0]^T$$

As such, the estimation procedure consists of two steps, viz: (i) state estimation from available process measurements and (ii) specific growth rate estimation.

The process model and the kinetic model adopted were implemented in a process simulator[7,8] which supplied this two-step estimation algorithm with the simulated measured variables C, G, CTR, OTR, S_{in} and F at sampling times of 6 min.

Second-order dynamics based tuning

For this case of specific growth rate estimation, and as discussed above (*Table 1*, $h_i = X$; remark 1), the gain matrix elements γ_i cannot be made strictly constant. A suitable approximation consists of employing the gain matrices given by:

$$\gamma_i = \frac{1}{\tau_i^2 X_m} \text{ and } \omega_i = \frac{2\zeta_i}{\tau_i} \tag{13a,b}$$

where τ_i and ζ_i are the desired natural period of oscillation and damping coefficient, and X_m is a mean value of biomass estimates over each time interval. The γ_i parameters are thus taken as piecewise functions of the biomass, i.e., γ_i remains constant between measurements, being adjusted at each sampling period.

Both the state observer (Equations (12)) and the kinetics estimator (Equations (11)) were integrated with a robust variable-step numerical integration algorithm (4th/5th order Runge–Kutta type embedded scheme due to Butcher), employing along the integration linear estimates of the relevant sampled variables.

Pole placement based tuning

The overall estimation procedure was also carried out, employing Euler's discretization approach and the tuning method proposed by Pomerleau and Perrier[3]. Basically, this method consists of defining time trajectories for the gain parameters in order to maintain constant the position of poles (on the discrete complex plan) of the discrete error system throughout the fermentation. The gain parameters are given by:

$$\gamma_i = \frac{(p_i - 1)^2}{\tau^2 X^2} \text{ and } \omega_i = \frac{2(p_i - 1)}{T} \tag{14a,b}$$

where p_i is the desired double pole of the error system ($0 < p_i < 1$), X is the biomass estimate and T the sampling period (and also the integration step).

Results and discussion

Figures 1, 2 and *3* illustrate the tuning procedure proposed in this work. The results in *Figure 1* are obtained

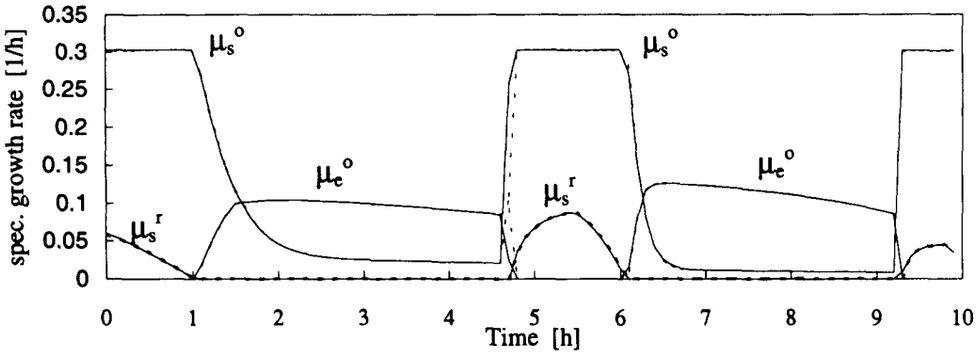

Figure 1 Specific growth rates estimation, using the second-order dynamics based tuning, with $\tau_i = 0.01$ and $\zeta_i = 0.5$. ITAE index values for estimates of μ_s^o, μ_s^r and μ_e^o, respectively = 0.10, 0.02, 0.05. (solid lines – true; dotted lines – estimates)

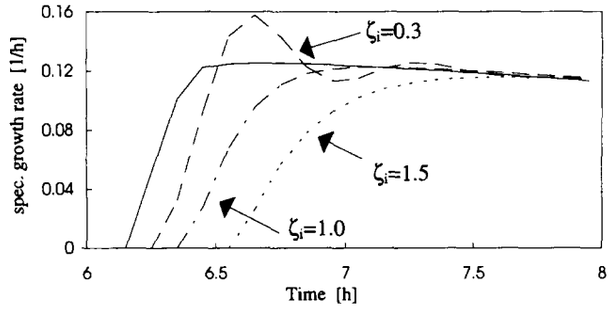

Figure 2 μ_e^o estimates for different coefficients ($\tau_i = 0.01$)

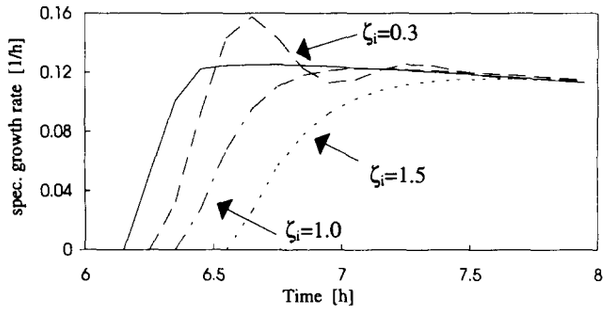

Figure 5 μ_e^o estimates for different poles

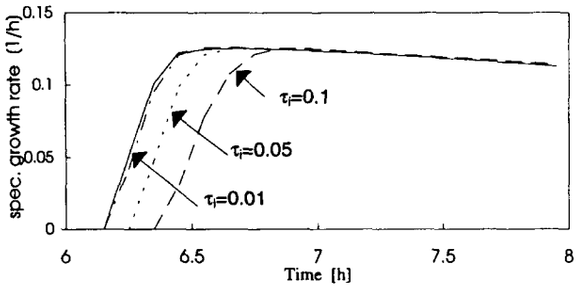

Figure 3 μ_e^o estimates for different damping coefficients' natural periods of oscillation ($\zeta_i = 0.8$)

with similar natural periods of oscillation ($\tau_i = 0.01$) and damping coefficients ($\zeta_i = 0.5$) for the three components. The influence of τ_i and ζ_i on the dynamics of convergence can be assessed from the plots in *Figures 2* and *3*. This influence is in agreement with the characteristics of a typical second-order dynamics response: for decreasing the τ_i the response becomes faster and for decreasing ζ_i the response becomes more oscillatory.

For the alternative pole placement procedure, the best results are obtained when the double poles are close to zero (no significant improvement is obtained when $p < 0.01$). In *Figure 4* the three specific growth rates (estimated *vs.* 'true') are represented for $p = 0.01$.

The information in *Figures 1* and *4* suggests that the 'second-order dynamics' approach produces better results than the pole placement method. This is confirmed by the error indices employed (ITAE – integral of time-weighted absolute errors) which are, for the former, an order of magnitude lower than those observed for the latter. The other possible advantage of the second-order

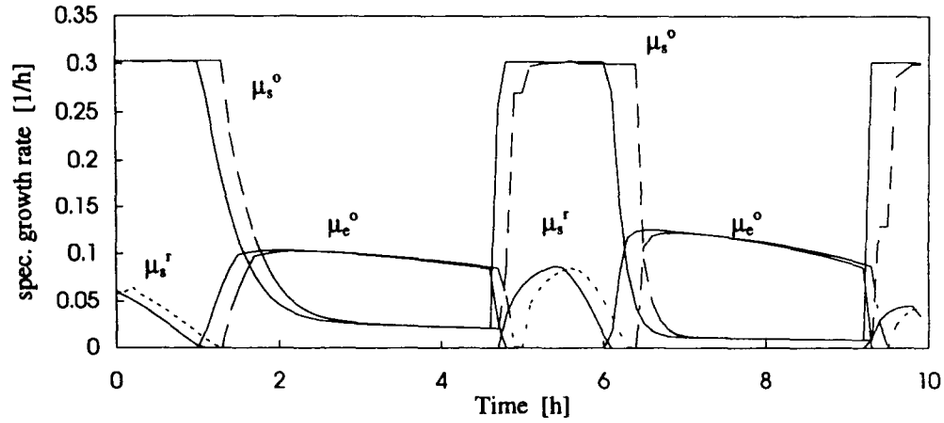

Figure 4 Specific growth rates estimation, using the second-order dynamics based tuning, with $p_i = 0.01$. ITAE index values for estimates of μ_s^o, μ_s^r and μ_e^o, respectively = 1.5, 0.34, 0.48. (solid lines – true; dotted lines – estimated)

tuning is that the choice of parameters has an intuitive basis since this type of response is widely observed in natural phenomena and its theoretical study well disseminated.

Further theoretical analysis is beyond the scope of this paper. Work is in progress which aims in particular at establishing an adaptive procedure which may lead to rigorous second-order convergence.

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Nomenclature

C	dissolved oxygen concentration
CTR	carbon dioxide transfer rate
D	dilution rate
E	dissolved ethanol concentration
F	feed rate vector
G	dissolved carbon dioxide concentration
g_i	product of reactants concentration in reaction i
$H(\xi)$	$(m \times r)$ matrix of functions of the state
k_i	yield coefficients
K	yield coefficients matrix
m	number of reaction rates
n	number of state space variables
OTR	oxygen transfer rate
p_i	double pole of the discrete error system
Q	gas removal rate vector
r	number of parameters to estimate
S	glucose concentration
S_{in}	glucose feed concentration
T	sampling period
X	biomass concentration
X_m	average value of biomass concentration over the sampling period
α	specific reaction rates vector
φ	reaction rates vector
μ	specific growth rates vector
$\hat{\mu}$	vector of estimated specific growth rates
μ_s^f	specific growth rate for the fermentative growth on glucose pathway
μ_e^o	specific growth rate for the respiratory growth on ethanol pathway
μ_s^o	specific growth rate for the respiratory growth on glucose pathway
$\rho(t)$	vector of unknown time-varying parameters
$\hat{\rho}$	vector of estimated parameters
τ_i	natural period of oscillation
ω_i, γ_i	diagonal elements of Ω and Γ
Ω, Γ	gain matrices
ξ	predicted state vector of concentrations
ξ_1	vector of measured concentrations
ξ_2	vector of non-measured concentrations
$\hat{\xi}_2$	estimated state vector of non-measured concentrations
ζ_i	damping coefficient