

## OPTIMAL STATE ESTIMATION AND ON-LINE OPTIMISATION OF A BIOCHEMICAL REACTOR

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An on-line optimising control strategy involving a two level extended Kalman filter (EKF) for dynamic model identification and a functional conjugate gradient method for determining optimal operating condition is proposed and applied to a biochemical reactor. The optimiser incorporates the identified model and determines the optimal operating condition while maximising the process performance. This strategy is computationally advantageous as it involves separate estimation of states and process parameters in reduced dimensions. In addition to assisting on-line dynamic optimisation, the estimated time varying uncertain process parameter information can also be useful for continuous monitoring of the process. This strategy ensures that the biochemical reactor is operated at the optimal operation while taking care of the disturbances that are encountered during operation. The simulation results demonstrate the usefulness of the two level EKF assisted dynamic optimizer for on-line optimising control of uncertain nonlinear biochemical systems.

**Keywords:** bioprocess monitoring, dynamic simulation, model identification, optimisation; control

### 1. INTRODUCTION

Bioprocess technology is currently employed for the production of various commodity and fine chemicals. Optimal operation of bioreactors can be achieved by means of the operational strategies derived based on the optimisation approaches known as dynamic optimisation and on-line optimisation. The determination of the open-loop time varying control policies that maximises or minimises a given performance index is referred to as optimal control/dynamic optimisation. The optimal control policies that ensure the satisfaction of the product property requirements and the operational constraints can be calculated off-line, which are then implemented on-line so that the system is operated in accordance with these control policies. Optimal control is a widely used approach and various techniques have been reported for chemical processes including bioreactors (Bryson and Ho, 1975; Catalina and Gabriela, 2007; Jimmy et al., 2010; Jin et al., 2011; Peroni et al., 2005; Thomas and Kiparissides, 1984; Xie et al., 2001). However, on-line optimising control is a promising approach to fulfill the requirement of monitoring and control of bioreactors. Optimising control deals with the problem of changing the operating conditions of a dynamic process on-line to achieve economic optimum. In recent years, various optimising control techniques have been reported for different applications including bioreactors (Beluham et al., 1995; Chen et al., 1998; Kim et al., 1991; Noda et al., 2000; Zhou et al., 1999). In bioprocesses, several factors such as complex nature of microorganism growth, disturbance dynamics, parameter uncertainties and noisy process variables severely affect the operating

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performance. The on-line optimising control scheme has to take into account such changes and continuously reevaluate the process to maximise its economic production. Since bioprocess conditions are ever changing, the optimisation algorithm should incorporate a model whose parameters need to be continuously identified on-line. Thus, the selection of a model structure plays an important role in on-line optimisation. It is usual to view nonlinear systems as linear systems and compensate for nonlinearities through adaptation of linear model parameters. On-line optimisation involving adaptive process models has been widely employed to biochemical processes (Jang et al., 1987; Hamer and Richenberg, 1988; Harmon et al., 1987; Rolf and Lim, 1985; Ryhiner et al., 1992). In most of those applications, a linear process model with a simple structure is employed and convergence in parameters and efficiency in operation is achieved. Those studies are based on steady state optimisation involving an identification period between optimisation steps to compute steady state gain to predict process output. When process parameters change widely, methods based on steady state/linear models fail to achieve convergence. Process models based on fundamental physical and chemical laws are preferred for on-line optimisation to empirical input-output models because of their wide range of validity and physically more meaningful variables to identify. In addition, some of the bioprocess variables are not available as direct measurements and they need to be estimated on-line using known process measurements. Therefore, the state/parameter estimation scheme also becomes an integral part of on-line optimisation. On-line optimisation based on a physical process model involves the procedure of continuously revising the dynamic model, thus characterizing the process during transients and eliminating the need to wait for steady states. During steady state operation, the dynamic model acts as a steady state model to deduce the optimum. Jang et al. (1987) have presented a two-phase approach based on a physical process model in which the first phase is concerned with the on-line estimation of states and parameters of nonlinear process model and the second phase deals with the determination of optimum operating strategy. The state and parameter estimation problem is solved by using a nonlinear programming approach, which generally requires more computational effort. It has been mentioned that the estimation problem must be executed whenever a change of reasonable magnitude is anticipated in the parameters. However, since the changes in the identified parameters are reflected by measured data and if the measurements are noisy, it is difficult to observe the incipient changes in the process from the parameter estimates. Moreover, due to the use of samples in aggregate, it is not possible to extract instantaneous changes in process parameters. If such time varying process parameters are available more frequently, they can be readily incorporated in on-line optimisation scheme to characterize the real process operation.

In this work, an on-line optimising control strategy involving a computationally efficient two level extended Kalman filter (EKF) for dynamic model identification with separate estimation of states and parameters, and a functional conjugate gradient method for determining optimal operating condition is presented and applied to a biochemical reactor. The dynamic model involved in the estimation module represents the true dynamics of the system incorporating physical, chemical and biological parameters. The two level extended Kalman filter employed in the estimation module is computationally efficient as it provides separate estimation of states and uncertain process parameters. In the estimation module, measurements are filtered, measured/unmeasured states are estimated and process parameters are identified at every sampling instant and incorporated in the optimiser to compute the optimal operating condition that maximises the process performance. The performance of the on-line optimising control strategy of this work is evaluated through simulation by applying it to a biochemical reactor.

## 2. ON-LINE OPTIMISING CONTROL STRATEGY

This strategy consists of a two level extended Kalman filter (EKF) as an estimation module and a functional conjugate gradient method as an optimisation module. The estimation module provides the estimates of measured/unmeasured process states and uncertain process parameters which are then

incorporated in the optimisation module to determine the optimal operating condition. The estimation and optimisation modules are repeatedly in tandem to follow continually changing input disturbances and process parameters. A schematic of the proposed on-line optimising control strategy is shown in Fig. 1.

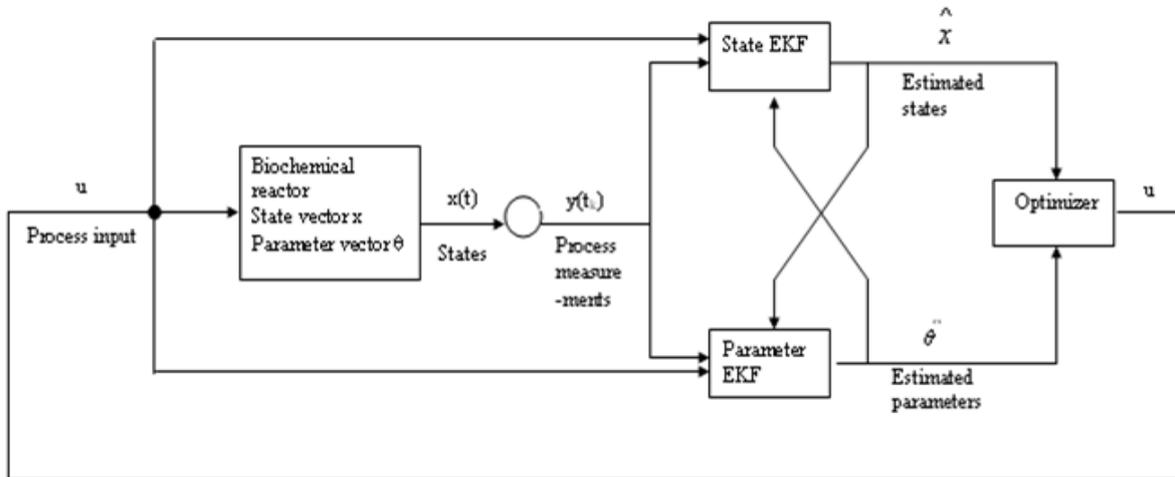


Fig. 1. Two level EKF assisted on-line optimisation control scheme

### 2.1. State and parameter estimation

Methods based on filtering and observation are more useful for state and parameter estimation in nonlinear processes. Such methods can filter out the noise in the process measurements and provide optimal estimates for states and parameters. The extended kalman filter (EKF) is a widely used method of filtering and observation. The EKF is a heuristic filter based on the linearised dynamics of a system, and has become the standard for state and parameter estimation of nonlinear systems. Many successful applications of EKF for state and parameter estimation have been reported (Gudi et al., 1994; Frederic et al., 2011; Venkateswarlu, 2004; Venkateswarlu and Avantika, 2001; Venkateswarlu and Gangiah, 1992). EKF provides a combined estimation of states and parameters involving full size matrix operations. If the state and parameter estimation is carried out separately, the computational effort can be reduced considerably due to the involvement of matrix calculations in reduced dimensions. Thus in this study, a method of two level extended Kalman filter is presented for separate estimation of states and parameters. The estimation scheme is similar to that employed for process fault diagnosis via state and parameter estimation (Venkateswarlu et al., 1992).

By considering time varying parameters in the process model, the expressions for states and parameters are given by:

$$\dot{x}(t) = f_x(x, \theta, t) + w_x(t), \quad x(0) = x_0 \quad (1)$$

$$\dot{\theta}(t) = p_\theta(x, \theta, t) + w_\theta(t), \quad \theta(0) = \theta_0 \quad (2)$$

where  $f_x$  and  $p_\theta$  are nonlinear functions of states  $x$ , parameters  $\theta$  and also input  $u$ . The  $w_x$  and  $w_\theta$  are process noise with covariance matrices  $Q_x$  and  $Q_\theta$ . The nonlinear observation model can be expressed as

$$y(t_k) = h_k(x, \theta, t) + v(t_k) \quad (3)$$

where  $h$  is a nonlinear function of states and parameters, and  $v$  is observation noise with zero mean. The linear measurement relation is given by

$$y(t_k) = Hx(t_k) + v(t_k) \tag{4}$$

The states,  $x(t)$  and parameters,  $\theta(t)$  of Eqs. (1) and (2) can be estimated on-line using the known measurements,  $y(t_k)$  in conjunction with the process model.

### 2.2. Two-level extended Kalman filter

By this method, states are estimated separately in the first level by a state extended Kalman filter and in the second level, uncertain process parameters are identified separately by a parameter extended Kalman filter. States and parameters are exchanged between the estimators for each new value of measurement. A schematic of the state estimator is shown in Fig. 1.

#### 2.2.1 State estimation filter

Starting with an initial estimate,  $\hat{x}_0$  and its covariance,  $P_{x0}$ , the correct estimate,  $\hat{x}(t_k/t_k)$  and its associate covariance,  $P_x(t_k/t_k)$  at time  $t_k$  are computed using the following equations:

$$\left. \begin{aligned} P_x(t_k/t_k)^{-1} &= P_x(t_k/t_{k-1})^{-1} + H_x^T(t_k)R^{-1}H_x(t_k) \\ K_x(t_k) &= P_x(t_k/t_k)H_x^T(t_k)R^{-1} \\ \hat{x}(t_k/t_k) &= \hat{x}(t_k/t_{k-1}) + K_x(t_k)\{y(t_k) - h_k[\hat{x}(t_k/t_{k-1}), \hat{\theta}(t_k/t_{k-1})]\} \end{aligned} \right\} \tag{5}$$

The propagated expressions for the estimate and its covariance from  $t_k$  to  $t_{k+1}$  are:

$$\left. \begin{aligned} \hat{x}(t/t_k) &= f_x[\hat{x}(t/t_k), \hat{\theta}(t/t_k), t] \\ P_x(t/t_k) &= F_x[\hat{x}(t/t_k)]P_x(t/t_k) + P_x(t/t_k)F_x^T[\hat{x}(t/t_k)] + Q_x \end{aligned} \right\} \tag{6}$$

where

$$F_x[\hat{x}(t/t_k)] = \left. \frac{\partial f_x}{\partial x} \right|_{\substack{x=\hat{x}(t/t_k) \\ \theta=\hat{\theta}(t/t_k)}}, \quad H_x(t_k) = \left. \frac{\partial h_k}{\partial x} \right|_{\substack{x=\hat{x}(t_k/t_{k-1}) \\ \theta=\hat{\theta}(t_k/t_{k-1})}}$$

The propagated expressions at time  $t_{k+1}$ ,  $\hat{x}(t_{k+1}/t_k)$  and  $P_x(t_{k+1}/t_k)$  form the recursive initial conditions for correction.

#### 2.2.2 Parameter identification filter

Starting with the parameter estimate,  $\hat{\theta}_0$  and its covariance,  $P_{\theta 0}$ , the correct estimate  $\hat{\theta}(t_k/t_k)$  and its covariance  $P_\theta(t_k/t_k)$ , at time  $t_k$  are computed using the following equations:

$$\left. \begin{aligned} P_\theta(t_k/t_k)^{-1} &= P_\theta(t_k/t_{k-1})^{-1} + H_\theta^T(t_k)R^{-1}H_\theta(t_k) \\ K_\theta(t_k) &= P_\theta(t_k/t_k)H_\theta^T(t_k)R^{-1} \\ \hat{\theta}(t_k/t_k) &= \hat{\theta}(t_k/t_{k-1}) + K_\theta(t_k)\{y(t_k) - h_k[\hat{x}(t_k/t_{k-1}), \hat{\theta}(t_k/t_{k-1})]\} \end{aligned} \right\} \tag{7}$$

The propagating expressions for the estimate and its covariance from  $t_k$  to  $t_{k+1}$  are:

$$\left. \begin{aligned} \hat{\theta}(t/t_k) &= p_\theta[\hat{x}(t/t_k), \hat{\theta}(t/t_k), t] \\ P_\theta(t/t_k) &= G_\theta[\hat{\theta}(t/t_k)]P_\theta(t/t_k) + P_\theta(t/t_k)G_\theta^T[\hat{\theta}(t/t_k)] + Q_\theta \end{aligned} \right\} \tag{8}$$

where

$$G_{\theta}[\theta(t/t_k)] = \frac{\partial p_{\theta}}{\partial \theta} \Big|_{\theta=\hat{\theta}(t/t_k)}^{x=\hat{x}(x(t/t_k))}, \quad H_{\theta}(t_k) = \frac{dh_k}{d\theta} \Big|_{\theta=\hat{\theta}(t_k/t_{k-1})} = \frac{\partial h_k}{\partial \theta} + \frac{\partial h_k}{\partial \hat{x}(t_k/t_{k-1})} \cdot \frac{d\hat{x}(t_k/t_{k-1})}{d\theta} \Big|_{\theta=\hat{\theta}(t_k/t_{k-1})}$$

The propagated expressions at time  $t_{k+1}$ ,  $\hat{\theta}(t_{k+1}/t_k)$  and  $P_{\theta}(t_{k+1}/t_k)$  form the recursive initial conditions for correction. The initial covariance matrices  $P_{x0}$  and  $P_{\theta 0}$  are used to reflect errors in the initial states and parameters. The process and observation noise covariance matrices  $Q_x$ ,  $Q_{\theta}$  and  $R$  are used to reflect uncertainty in the process model and measurements. The matrices  $P_{x0}$ ,  $P_{\theta 0}$ ,  $Q_x$ ,  $Q_{\theta}$  and  $R$  are generally selected as design parameters. The performance index  $J$  of the two level extended Kalman filter is expressed by:

$$J = \sum_{k=1}^N \left\{ (x(0) - \hat{x}(0))^T P_{x0}^{-1} (x(0) - \hat{x}(0)) + (\theta(0) - \hat{\theta}(0))^T P_{\theta 0}^{-1} (\theta(0) - \hat{\theta}(0)) \right\} + \left\{ (y(t_k) - h_k(\hat{x}(t_k), \hat{\theta}(t_k)))^T R^{-1} (y(t_k) - h_k(\hat{x}(t_k), \hat{\theta}(t_k))) \right\} + \left\{ (x(t_k) - \hat{x}(t_k))^T Q_x^{-1} (x(t_k) - \hat{x}(t_k)) + (\theta(t_k) - \hat{\theta}(t_k))^T Q_{\theta}^{-1} (\theta(t_k) - \hat{\theta}(t_k)) \right\} \quad (9)$$

### 2.3. On-line optimisation

The on-line optimising control problem can be stated in an abstract form as follows: Given an operating point with measurements,  $y$  and a set of manipulated inputs,  $u$ , determine the values of  $u$  as a function of time that maximize the measure of profitability of the plant while meeting the operating constraints of the process. For the optimisation problem, the nonlinear plant and the measurement model expressions can be rewritten as

$$\dot{x} = f(x, u, \theta, t) \quad (10)$$

$$y = g(x, u, \theta, t) \quad (11)$$

The operating constraints are expressed as

$$e(x, u, \theta, t) \leq 0 \quad (12)$$

In these equations,  $x$  represents state variables,  $u$  is manipulated input and  $\theta$  denotes unknown parameters and unmeasured disturbances. This type of physical process model has a wide range of applicability for identifying more meaningful variables. However, if a more detailed model is used, computational complexity increases. So a compromise has to be made between the level of detail used and the number of parameters estimated on-line. Since the optimiser incorporates the states and parameters identified through separate estimation with less computational requirement, physical process models of higher dimensions can be employed with this strategy.

The optimisation problem determines the optimal operating condition,  $u(t)$  by maximising the objective functional or performance index

$$I = \int \phi(x, u, \theta, t) dt \quad (13)$$

subject to the model equations and constraints, Eqs. (10)-(12).

#### 2.3.1. Functional conjugate gradient method

The conjugate gradient method generates a set of mutually conjugate direction vectors using the gradient vector as the basis. The conjugate gradient method when applied to functional optimisation is called functional conjugate gradient method. This method involves successive approximation in the

control domain, utilising the gradient to compute a new control function in each iteration. The implementation of the method involves the following procedure (Fletcher and Reeves, 1964).

The objective function in Eq. (13) is in the form

$$I = \int f_0(x, u, \theta, t) dt \quad (14)$$

The Hamiltonian is formulated as

$$H = f_0 + \lambda^T f \quad (15)$$

where  $\lambda$  represents a set of adjoint variables, the relation of which is given by

$$-\dot{\lambda}_i = \frac{\partial H}{\partial x_i} \quad (16)$$

The gradient,  $g$  and the direction,  $\xi$  are calculated as

$$g^i(t) = \frac{\partial H}{\partial u}(t) \quad (17)$$

and

$$\xi^{i+1}(t) = -g^{i+1}(t) + \beta^i \xi^i(t), \quad 0 \leq t \leq \tau \quad (18)$$

where  $\beta^i = \frac{\int_0^\tau (g^{i+1})^2 dt}{\int_0^\tau (g^i)^2 dt}$ .

The initial conditions are taken to be

$$g^0(t) = g(u^0) \quad \text{and} \quad \xi^0(t) = -g(u^0), \quad 0 \leq t \leq \tau \quad (19)$$

The performance of the above on-line optimising control strategy is evaluated by applying to the following biochemical system.

#### 2.4. Application system

A dynamic model of the chemostat is described by the following differential equations (Harmon et al., 1987):

$$\begin{aligned} \frac{dc}{dt} &= \frac{\mu_m w c}{k_s + w} - Dc \\ \frac{ds}{dt} &= -\frac{1}{Y} \frac{\mu_m s c}{k_s + s} + D(s_f - s) \\ \frac{dw}{dt} &= a(s - w) \end{aligned} \quad (20)$$

where  $c$  is the biomass concentration,  $s$  the substrate concentration,  $w$  is the weighted average of previous substrate concentrations,  $s_f$  is the substrate feed concentration,  $D$  is the dilution rate,  $\mu_m$  is the maximum specific growth rate,  $k_s$  is the monod constant and  $Y$  is the yield. The parameter  $a$  is the delay term which is a measure of the organisms' ability to adjust their growth rate when a change in the condition of the chemostat occurs. For a constant volume fermentation, the product  $Dc$  is clearly a productivity measure, where  $D$  is the dilution rate and  $c$  is the biomass concentration. The on-line

optimising control strategy determines the optimal dilution rate that maximises the productivity,  $Dc$ . The parameters  $s_f$  and  $\mu_m$  are estimated at each sample time at the identification phase and incorporated in the optimizer. The nominal process parameter values used in this simulation are:  $\mu_m=0.7 \text{ h}^{-1}$ ,  $k_s=22 \text{ g l}^{-1}$ ,  $Y=0.5$ ,  $a=3 \text{ h}^{-1}$ ,  $s_f=30 \text{ g l}^{-1}$ ,  $c(0)=14.153 \text{ g l}^{-1}$ ,  $s(0) = w(0) = 1.6923 \text{ g l}^{-1}$ .

### 3. RESULTS AND DISCUSSION

In a biochemical reactor, the objective is to maximise the productivity measure,  $Dc$  through optimisation of the manipulated input,  $D$  while taking care of the uncertainties in feed concentration,  $s_f$  and the specific growth rate,  $\mu_m$ . Since, the disturbances affect the process over time, it is necessary to continuously revise the process model using the most recent measurements. The measurements available from the process are concentrations of  $c$  and  $s$ . The state  $w$  is not measured on-line and has to be estimated along with the parameters  $s_f$  and  $\mu_m$ .

The mathematical model of the process is integrated numerically using a step size of 0.1 h. The simulated process measurements of every 0.1 h are used for optimal state estimation and on-line optimisation. In order to reflect the real situation, the measurements are corrupted with a zero mean random Gaussian noise of about 1% of their actual values. The filter design parameters such as the initial state and parameter noise covariance matrices ( $P_{x0}, P_{\theta 0}$ ), the process noise covariance matrices ( $Q_x, Q_\theta$ ) and the observation noise covariance matrix ( $R$ ) are initially selected using process variable and noise information and further tuned so as to obtain better estimator performance. These filter design parameters are given in Table 1. The two level EKF is thus designed and applied to estimate  $s_f$ ,  $\mu_m$  and  $w$  using the known measurements  $c$  and  $s$ . The identified model is incorporated in the optimiser to determine dilution rate,  $D$ .

Table 1. Filter design parameters

$P_{x0}$	$P_{\theta 0}$	$Q_1$	$Q_2$	$R$
$\begin{bmatrix} 0.0005 & 0 \\ 0 & 0.0005 \end{bmatrix}$	$\begin{bmatrix} 0.0005 & 0.0 \\ 0.0 & 0.0005 \end{bmatrix}$	$\begin{bmatrix} 0.2 & 0.0 \\ 0.0 & 0.2 \end{bmatrix}$	$\begin{bmatrix} 0.2 & 0.0 \\ 0.0 & 0.2 \end{bmatrix}$	$\begin{bmatrix} 1.0 & 0.0 \\ 0.0 & 1.0 \end{bmatrix}$

The sensitivity of the estimator in conjunction with the optimiser is investigated for normal process operation by studying the effect of filter design parameters as well as measurement noise. Table 2 shows the quantitative performance of the estimator evaluated for an operating period of 60 hrs for normal process operation. The ISE values shown in Table 2 are the summated squared differences between the actual states of  $x$ ,  $s$  and  $w$  obtained through numerical simulation and those corresponding to estimated states. The results shown in Table 2 are obtained by changing each of the filter design parameter while keeping the remaining parameters unchanged. This ISE measure reflects the performance measure of Eq. (9) in simplest form. From these results it can be observed that there is no significant change in estimator performance for 10 times increase or decrease of filter design parameters from their initially set values. Decreasing the measurement noise has shown a moderate influence on the estimator performance, while increasing it to a higher level has shown considerable influence on the estimator performance. The results thus indicate the stability of the estimator towards the effect of filter design parameters.

The estimated state responses using normal process measurements with zero mean random Gaussian noise of about 1% to their actual values are shown in Fig. 2. The true values shown in Fig. 2 represent the numerical values obtained from the solution of model equations. The estimated profiles in Fig. 2 correspond to the biomass and substrate concentrations beginning from their initial values of 14.153

g/L and 1.6923 g/L, respectively. These results indicate a close correspondence between the estimated and true states. Fig. 3 shows the results of the estimated process parameters, the optimal dilution rate and the process performance measure based on measurements corresponding to normal process parameters. Fig. 4 shows the results of the estimated process parameters, the optimal dilution rate and the process performance measure involving normal noisy measurements corresponding to change in  $s_f$  from 30 to 25 /l at 30 hrs and change in  $u_m$  from 0.7 to 0.85 h<sup>-1</sup> at 40 hrs during the operation. The identified process parameters in Figs. 3 and 4 show that they are in close agreement with their corresponding true values. The optimal dilution rate and the process performance measure in Fig. 4 exhibit the fast tracking ability of the optimiser to adapt the process disturbances.

Table 2. Estimator performance for different levels of filter design parameters and noise

Filter design Parameter/noise	Level	ISE
Initial state Covariance matrix	$P_{x0}/10$	3.2539
	$P_{x0}$	3.2463
	$10P_{x0}$	3.1763
	$P_{\theta}/10$	3.2473
	$P_{\theta}$	3.2463
	$10P_{\theta}$	3.2362
Process noise Covariance matrix	$Q_x/10$	3.3738
	$Q_x$	3.2463
	$10Q_x$	3.366
	$Q_{\theta}/10$	3.2463
	$Q_{\theta}$	3.2463
	$10Q_{\theta}$	3.2463
Observation noise covariance matrix	$R/10$	3.0188
	$R$	3.2463
	$10R$	3.3828
Observation noise	$v/10$	2.7995
	$v$	3.2463
	$10v$	12.2576

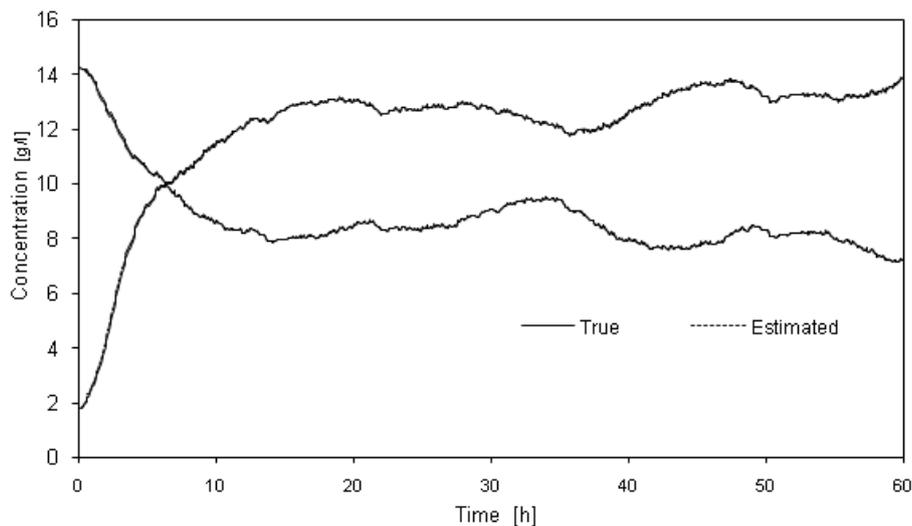


Fig. 2. State estimation results of two level EKF assisted on-line optimiser with no parameter uncertainties

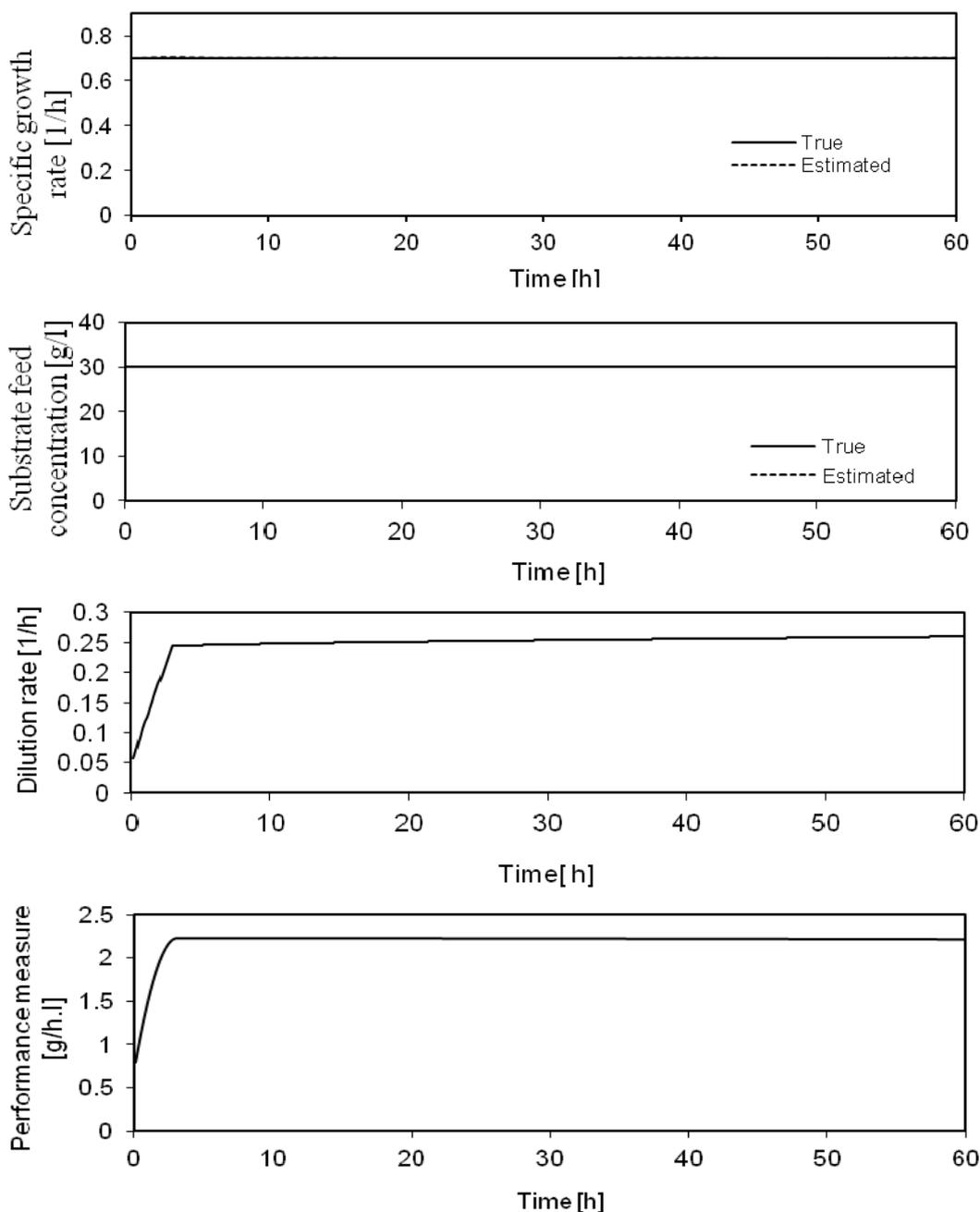


Fig. 3. Results of two level EKF assisted on-line optimiser with no parameter uncertainties

The performance of the estimator is also studied for changes in both  $s_f$  and  $u_m$ . Fig. 5 shows the results of the estimated process parameters, the optimal dilution rate and the process performance measure for change in  $s_f$  from 30 to 25 g/l at 30 hrs and change in  $u_m$  from 0.7 to 0.85 h<sup>-1</sup> at 40 hrs during operation when the measurements with zero mean random Gaussian noise of 5 times higher than the normal noise are employed. The results in Fig. 5 indicate how the optimal dilution rate influences the process performance for changes in  $s_f$  and  $u_m$  in the presence of more noise in the measurements. Because of the presence of more noise in the measurements, the specific growth rate initially deviates from the true value and after some time it reaches and tracks the true value quite well. These results show the noise filtering ability of the estimator and the performance of the optimiser in establishing the optimal operating conditions in the presence of uncertain parameters. The proposed strategy is also evaluated by considering measurements available at wider sampling instants. The discrete updating step of the two-level EKF has the flexibility to incorporate the measurements available at wider sampling instants while iterating the continuous prediction step with lower integration time. Fig. 6 shows the results of

the strategy with parameter uncertainties when measurements of 0.5 hr. sampling instant with zero mean random Gaussian noise of 5 times higher than the initially considered noise are employed. These results show that the on-line optimising control strategy of this study can be employed with the noisy measurements sampled at wider discrete time instants. The results demonstrate a better performance of the two-level EKF supported dynamic optimiser for optimal control of biochemical reactor in the presence of sudden and gradual process parameter uncertainties as well as noise in the measurements.

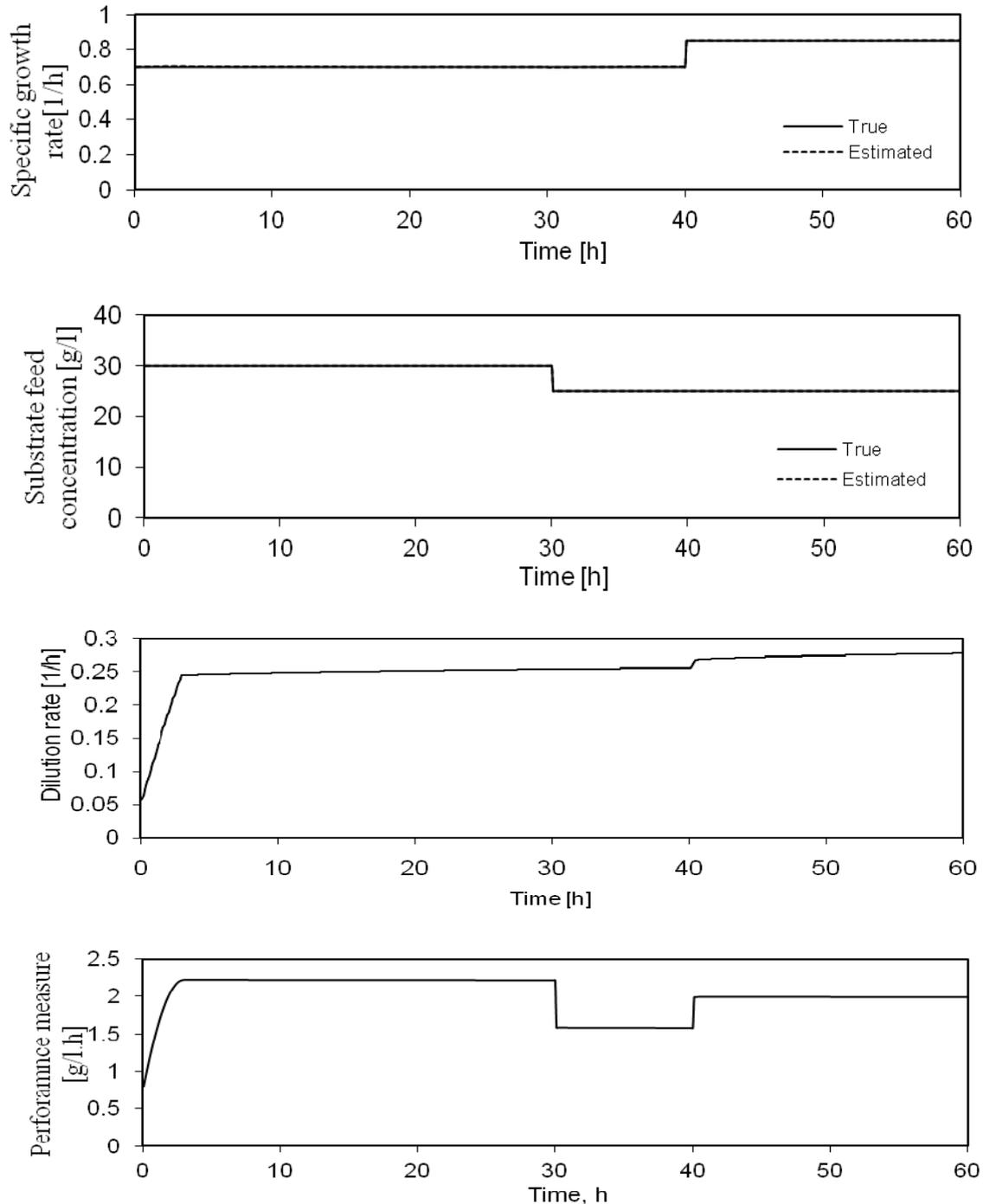


Fig. 4. Results of two level EKF assisted on-line optimiser in the presence of parameter uncertainties

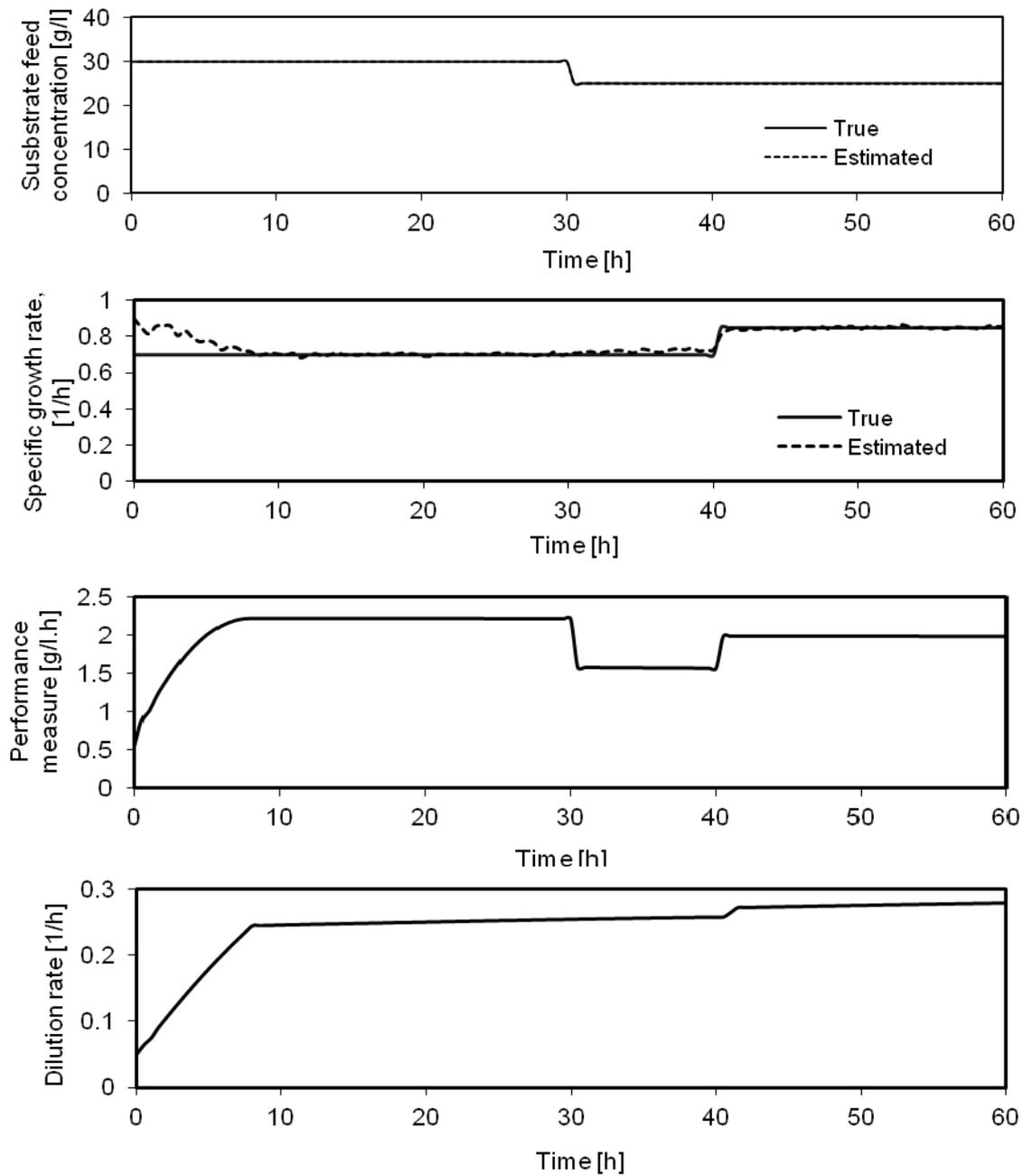


Fig. 5. Results of two-level EKF assisted online optimiser in the presence of parameter uncertainties

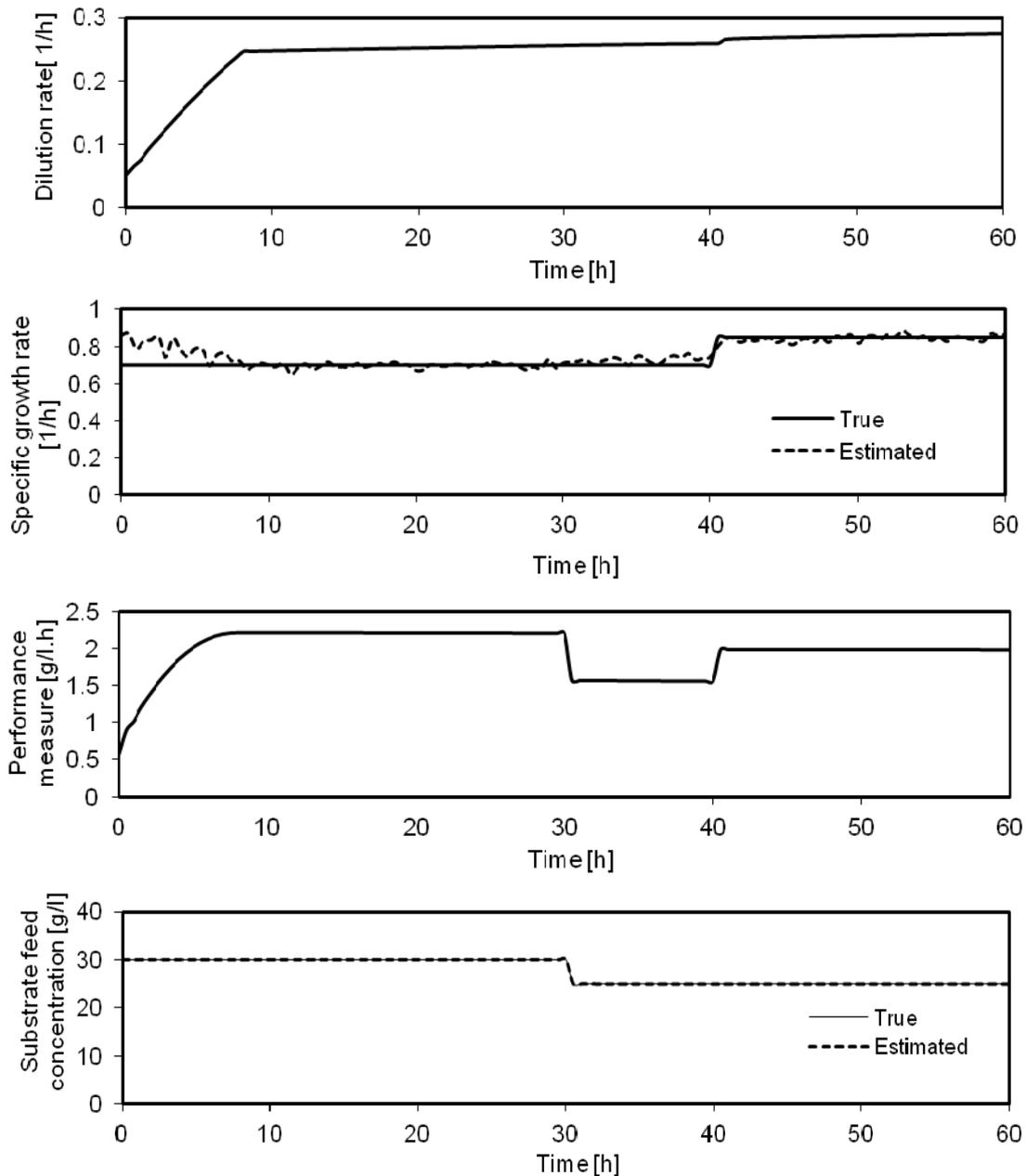


Fig. 6. Results of two-level EKF assisted on-line optimiser in the presence of parameter uncertainties

#### 4. CONCLUSIONS

Biochemical process conditions vary due to culture aging, spontaneous mutations, feed and environmental conditions. The location and amplitude of the maximum cellular productivity can change due to these conditions. In order to cope-up with the changing process conditions and disturbances, on-line identification of the dynamic process model and determination of optimal operating condition based on the identified model is necessary. The on-line optimising strategy of this study has an estimation module to provide process state and uncertain process parameter information, and an optimisation module to determine the optimal operating condition for the process. This strategy

can be conveniently implemented to physical process models of higher dimensional systems due to separate state and parameter estimation with the computations in reduced dimensions. The estimated process parameters and their variations serve to monitor the process more effectively. The results show the usefulness and reliability of the proposed approach for on-line optimisation of uncertain nonlinear dynamic systems.

## SYMBOLS

$c$	biomass concentration, g l <sup>-1</sup>
$D$	dilution rate, h <sup>-1</sup>
$Dc$	the productivity measure
$f_x$	nonlinear function of states
$f_\theta$	nonlinear function of parameters
$h$	measurement model
$k_s$	monod constant, g l <sup>-1</sup>
$P_{x0}$	initial state noise covariance matrix
$P_{\theta 0}$	initial parameter covariance matrix
$Q_x$	state model process noise covariance matrix
$Q_\theta$	parameter model process noise covariance matrix
$R$	observation noise covariance matrix
$s$	substrate concentration, g l <sup>-1</sup>
$s_f$	substrate feed concentration, g l <sup>-1</sup>
$t$	time, h
$t_k$	discrete time, h
$u$	manipulated input
$v$	observation noise
$w$	weighted average of previous substrate concentrations, g l <sup>-1</sup>
$w_x$	process noise associated with states
$w_\theta$	process noise associated with parameters
$x$	state variables
$\hat{x}$	estimated states
$y$	process measurements
$Y$	yield

### Greek symbols

$\theta$	parameters
$\hat{\theta}$	estimated parameters
$\mu$	specific growth rate h <sup>-1</sup>
$\mu_m$	maximum specific growth rate h <sup>-1</sup>

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