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Nonlinear regulation for a continuous bioreactor via a numerical uncertainty observer

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Abstract

A robust adaptive control strategy for a class of continuous-flow bioreactor process where the intrinsic reaction rates are poorly know is provided. A numerical observer is used to obtain on-line discrete estimates of the main uncertainties (kinetics term, yield production, and biomass concentration) of a continuous bioreactor. With this estimate, a linearizing feedback control law is obtained which provides robust regulation against uncertainties, disturbances and additive noise on the substrate concentration measurements. The performance of the closed-loop system is illustrated via numerical simulations.

Keywords: Nonlinear regulation; Continuous bioreactor; Biomass; Kinetics

1. Introduction

Optimization of continuous-flow bioreactors can be generally achieved by maintaining the process outputs close to their desired values over a time interval of interest. In particular, during the course of the process the cell and substrate concentrations are to be close to prespecified steady-states, and the latter are choosing to optimize certain performance criteria. Their corresponding control problem commonly consists of two stages. In the first stage, the process that starts from some initial state is to be brought close to the desired steady-state, while in the second stage, the objective is to maintain the process outputs close to their desired values over large time intervals. Such a problem is rendered complex due to the highly nonlinear nature of the process, and since the control objective is to be achieved in the presence of parameter time variations and substantial unmodeled dynamics. The later effects generally tend to deteriorate the performance of the process in a direction of a lower productivity.

A major difficulty in the monitoring and control of bioprocesses is the lack of reliable and simple sensors for following the evolution of the main state variables and parameters such as biomass, product and growth rate. This absence of direct on-line measurements devices has lead to the development of elemental balancing techniques, to provide on-line estimates of state variables. Excellent reviews of these estimation techniques are provided in Ref. [1].

The first attempts to estimate unknown variables related to the continuous bioreactor involved macroscopic component balances. While this may be accurate for a steady-state estimation, this is not the case of the yield coefficient, which varies during transient growth period [2].

In order to extend this approach for the transient period, an instantaneous discrete algorithm has been proposed [3]. This technique is based on a mass balance to estimate the uncertainty terms supposing that the substrate concentration is available for discrete measurement. Aguilar et al. [3] provided a stability proof of the closed-loop system. However, the approach mentioned above becomes unstable when measurements are noisy.

In this work, we follow the basic ideas presented in a previous work to design controller with uncertainty compensation. To reduce adverse effects caused by noisy measurements, we propose an on-line estimation strategy for the unknown kinetic terms through a relatively new class of observers which are based on the solution of a set of algebraic equations that represents the mismatch between the output dynamics and a reference dynamical system. With this estimate and the methodology proposed by Isidori [4], a linearizing feedback control law was designed that is robust in

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the presence of uncertainties and disturbances in the process model and noisy measurements. As in the control design proposed in Ref. [3], our method is restricted to a particular class of model structures in which uncertainty appears as an additive uncertainty.

2. Process model

An important goal of controlling continuous bioreactors is to achieve and maintain a desired steady-state operating point. The characteristics of the steady-state and the dynamic behavior of the given process are important considerations when designing a control scheme to effectively regulate a system. The analysis of the process begins with the development of a mathematical model approximating the behavior of the process. The bioreactors are generally modeled as continuous stirred tank reactors (CSTR). The dynamic behavior of these processes is highly nonlinear and can originate multiplicity of steady-states or self-sustained oscillations [5–7].

It is common with bioreactors to develop models using a set of ordinary differential equations. For a constant-volume vessel with a pure culture feed with a sterile flow, mass balances for biomass (cell) and limiting substrate concentrations lead to the following equations.

$$\dot{X} = -DX + \mu(S)X \quad (1)$$

$$\dot{S} = D(S_f - S) - (1/Y_d)\mu(S)X \quad (2)$$

where D is the dilution rate, Y_d is the yield coefficient and $\mu(S)$ is the specific grow rate.

Despite some objections to the Monod equation, this one and variations thereon are probably the most widely used models of microbial growth, primarily because they are simple and mathematically tractable. Through steady-state analysis, several researches conclude that nontrivial multiplicity and oscillatory phenomena were not possible for a constant yield.

Using an experimental continuous bioreactor, Dibiaso et al. [6] verify the existence of multiple steady-states. Using proportional feedback control, an unstable steady-state was maintained by manipulating the dilution rate. After reaching the steady-state, the control loop was opened and the system settled to a new steady-state, demonstrating the multiplicity.

Suppose that the specific growth rate is given by Monod's model, and the yield coefficient varies according to Crooke et al. [5]:

$$Y_d = 0.01 + 0.03S \quad (3)$$

$$\mu(S) = \frac{0.3S}{1.75 + S} \quad (4)$$

for $D = 0.14\ h^{-1}$ and $S_f = 35.0\ g\ l^{-1}$, Tsao and Wu [8] reported that the open-loop reactor presents two steady-states and a limit cycle which is present at the nonwash-out steady-state of the reactor ($X = 1.872$, $S = 1.531$).

3. Numerical uncertainty observer algorithm

When it is desired to design a feedback linearizing control law for a nonlinear system, it is well known that model uncertainties produce a closed-loop behavior which has a poor performance or even instability [9]. In order to use this approach, it is necessary to get an estimate of the uncertainties. The closer this estimate is to the real value, the better is the performance of the resulting controller.

Let $\psi(S,t) = \mu(S)X(t)/Y_d$ represents the uncertainty associated with the substrate dynamics. Then Eq. (2) can be rewritten as:

$$\dot{S} = D(S_f - S) - \psi(S,t) \quad (5)$$

In general, $\psi(S,t)$ has the following properties:
(a) $\psi(S,t)$ is continuous and differentiable over the whole range of interest.
(b) $\psi(S,t) \in [\psi_{min}, \psi_{max}]$ for all positive S, t.

Let us construct the following auxiliary dynamical system

$$\dot{\hat{S}} = D(S_f - \hat{S}) - \hat{\psi} \quad (6)$$

When the solutions of the systems (5) and (6) are the same for all time after some time $t^* > 0$ (i.e., $\hat{S}(t) \to S(t)$ as $t \to t^* > 0$), then $\hat{\psi}$ is an estimate of ψ. In order to estimate uncertainties, it is not necessary that $\hat{S}(0) = S(0)$. However, since substrate concentration is assumed to be measured, the initial condition $\hat{S}(0) = S(0)$ is a reasonable assumption. If $y \equiv S - \hat{S}$ represents the mismatch between systems (5) and (6), then the dynamics associated with y is governed by:

$$\dot{y} = f(y, \hat{\psi}, t) = \psi - \hat{\psi} \quad (7)$$

The aim of the observation algorithm is to design a methodology such that $\hat{\psi}$ can drive the system (7) to a desired target value $y_d = 0$. The structure of the observer is based on the methodology proposed by Ostojic [10]. If the tracking error is defined as $e = y_d - y$, we consider the problem of finding a relationship for $\hat{\psi}$ which will bring the tracking error to zero. Moreover, it is desired a relationship that force the error to exhibit an asymptotically stable linear dynamics

$$\dot{e} + ce = 0 \quad (8)$$

where $c > 0$ is a design parameter. Let us define the following manifold

$$\sigma = \dot{e} + ce \quad (9)$$

which can be rewritten as

$$\sigma = \dot{y}_d - f(y, \hat{\psi}, t) + ce \quad (10)$$

Eq. (10) shows that σ depends on $\hat{\psi}$ explicitly and then indicates that one can find a relationship that leads to the desired behavior (Eq. (9)), simply by solving $\sigma = 0$ for $\hat{\psi}$. Then, the solution to the uncertainty estimation problem can be reduced to finding a solution $\hat{\psi}(t)$ of the nonstationary equation

$$\sigma(\hat{\psi}(t), t) = 0 \quad (11)$$

There are two ways to find a solution of Eq. (11). The first one is an analytical methodology. This approach starts from the assumption of a whole knowledge of the relationship given by Eq. (7). As this equation contains the uncertain term ψ, this approach can not be used. The alternative approach is to implement a numerical solution of Eq. (11) through standard nonlinear finding roots methodologies. This work is employed with this approach, using a *Successive Substitutions Algorithm*, whose structure is similar to a discrete finite-difference observer [3]. Considering the properties of $\psi(S,t)$ mentioned above, one can use the results on convergence for fixed point iterative methodologies, and this gives the way for solving Eq. (11).

Theorem 1 [10]. Let $\hat{\psi}(t)=F(\hat{\psi},t)$ be a real nonstationary equation with an exact solution $\psi^*(t)$. Let $\psi(t_{k+1})=F(\psi(t_k),t_k)$, with $\psi(t_0)$ known, be the resulting recursive formula to compute estimates of $\psi^*(t)$ at instants $t_k=t_0+hk$, where h is a constant and $k=1, 2, \ldots, k_\infty$. Then, in order the estimation error $\varepsilon(t_k)=\psi(t_k)-\psi^*(t_k)$ be bounded for all k, it is sufficient that

1. Both $F(\psi,t)$ and $\psi^*(t)$ are continuously differentiable, and
2. There exists a constant M such that the condition

$$\left|\frac{\partial F(\psi,t)}{\partial \psi}\right| \le M<1$$

holds in a region containing $\psi(t_0)$, $\psi(t_1)$ and $\psi^*(t)$ for all $t\in[t_0, t_0+hk_\infty]$. The estimation error is bounded by:

$$|\varepsilon(t_k)| \le M^k|\varepsilon(t_0)| + hN\frac{1-M^k}{1-M}, \text{ where } k=1, 2, \ldots, k_\infty$$

$$N=\sup\left|\frac{\partial F(\psi,t)}{\partial t}+\psi^*(t)\frac{\partial F(\psi,t)}{\partial \psi}\right|, t\in[t_0, t_0+hk_\infty].$$

The proof of the above theorem can be found in Ref. [10]. To use the result of Theorem 1, one can rewrite $\sigma(\hat{\psi}(t),t)=0$ into an equivalent form:

$$\hat{\psi}(t)=F(\hat{\psi},t) \tag{12}$$

Then $\hat{\psi}(t_{k+1})=F(\hat{\psi}(t_k),t_k)$, $\hat{\psi}(t_{k+1})\in[\psi_{\min}, \psi_{\max}]$ defines the recursive estimation law for Eq. (7).

The transformation of Eq. (11) to Eq. (12) is not unique. In this work, the successive substitution method is used, where $F(\hat{\psi},t)=\hat{\psi}+\lambda\sigma(\hat{\psi},t)$ and λ is a (*relaxation*) fixed parameter. With these definitions, the recursive estimation law for Eq. (7) can be rewritten as

$$\hat{\psi}(t_{k+1})=\hat{\psi}(t_k)+\lambda\sigma(\hat{\psi}(t_k),t_k) \tag{13}$$

In applications, $\sigma(\hat{\psi}(t_k),t_k)$ is calculated using Eq. (9) rather than Eq. (10). Thus, the estimator (Eq. (13)) does not require explicit knowledge of plant parameters. The structure of the system (9) is needed only to determine bounds on the parameter λ, but is not necessary to calculate the estimate $\hat{\psi}(t)$. The parameter λ is chosen in such a way that iteration (Eq. (13)) becomes convergent. From Theorem 1, it is easy to verify that the condition for $\hat{\psi}(t)$ to be an asymptotic observer of $\psi(t)$ is

$$0<\lambda\frac{\partial f(y,\hat{\psi},t)}{\partial \psi}<2.$$

From Eq. (7), we obtain:

$$-2<\lambda<0 \tag{14}$$

It is important to point out that in order to satisfy the conditions for Theorem 1, if the resulting uncertainty estimate obtained from Eq. (14) is lower than $\psi_{\min}$, then $\hat{\psi}(t_k)$ is taken as $\psi_{\min}$. In the opposite case, if the resulting uncertainty estimate obtained from Eq. (14) is larger than $\psi_{\max}$, then $\hat{\psi}(t_k)$ is taken as $\psi_{\max}$. As in the strategy proposed by Khalil [9], the bounds $\psi_{\min}$, $\psi_{\max}$ in $\hat{\psi}(t_k)$ reduces the adverse effects introduced by the nonlinear peaking phenomenon [11].

4. The nonideal control strategy

The objective of this work is to design a control law for D in such a way that the dynamics of S can be driven to a desired trajectory given by $S^{\text{ref}}(t)$. If $S^{\text{ref}}(t)$ has a constant value, the control problem becomes a regulation problem.

Suppose the dynamical behavior of S is given by Eq. (5), then the linearizing control law that imposes a first-order behavior to S is the following equation:

$$D=\frac{1}{S_f-S}(\psi+k(S-S^{\text{ref}})) \tag{15}$$

If k is chosen such that $k<0$, then Eq. (15) drives S asymptotically to S^{ref}. However, as ψ is unknown, then D given by Eq. (15) is also unknown. Instead of using ψ to evaluate Eq. (15), in this work it is proposed to use the estimate $\hat{\psi}(t)$ given by Eq. (13), such that Eq. (15) can be expressed as:

$$D(t_k)=\frac{1}{S_f-S(t_k)}(\hat{\psi}(t_k)+k(S(t_k)-S^{\text{ref}})) \tag{16}$$

Consider the particular case where the parameters λ and c are chosen as -1 and 0, respectively. Then, using the definition for y ($y\equiv S-\hat{S}$) and recalling that $y_d=\dot{y}_d=0$, the observer (13) can be written as:

$$\hat{\psi}(t_{k+1})=\hat{\psi}(t_k)+\dot{S}(t_k)-\dot{\hat{S}}(t_k)=\dot{S}(t_k)-D(S_f-S(t_k)) \tag{17}$$

If discrete-time measurements of S are available for time intervals τ, the time derivative of S can be approximated by backwards finite differences, and Eq. (15) takes the following form:

$$\hat{\psi}(t_{k+1})=\frac{S(t_k)-S(t_{k-1})}{\tau}-D(S_f-S(t_k)) \tag{18}$$

which is equal to the discrete-time estimator reported in Ref. [3].

Aguilar et al. [3] proved that the closed-loop behavior of the systems (1)–(2) with the uncertainty estimator given by Eq. (18), is asymptotically stable as $\tau \to 0$. Considering a sufficiently small control parameter τ/k, the closed-loop trajectories can be driven to an arbitrary small neighborhood from the reference value S^{ref}.

5. Effect of the noise on the measurements

The performance of the closed-loop system with a control law given by Eq. (16) and the uncertainty term estimated by Eq. (18) is satisfactory when the measurements are noise free. However, when the measurements are noisy, the uncertainty estimate $\hat{\psi}(t)$ is affected by a term which becomes unbounded as $\tau \to 0$.

Let $\delta(t_k)$ be an additive noise with zero mean value and uniform distribution, which is associated with the substrate measurements at the time t_k. Then, the measured substrate concentration at the time t_k is given in the following form:

$$S^m(t_k) = S(t_k) + \delta(t_k) \tag{19}$$

where $S^m(t_k)$ is the measured substrate concentration value used in the evaluation of the controllers (13) and (16). Eqs. (18) and (19) yield

$$\hat{\psi}(t_{k+1}) = \frac{S(t_k) - S(t_{k-1})}{\tau} - D(S_f - S(t_k)) + \frac{\Delta\delta(t_k)}{\tau} \tag{20}$$

where $\Delta\delta(t_k) = \delta(t_k) - \delta(t_{k-1})$. From the discussion on Section 5, the uncertainty estimate becomes closer to the real one when sampling interval becomes smaller, however, this implies that the last term in Eq. (20) becomes unbounded despite the value of $\Delta\delta(t_k)$. That is, $(\Delta\delta(t_k)/\tau) \to \infty$ as $\tau \to 0$.

Considering the noise measurement effect on the uncertainty estimator given by Eq. (13), the following expression is obtained:

$$\hat{\psi}(t_{k+1}) = \hat{\psi}(t_k) + \lambda\sigma(\hat{\psi}(t_k), t_k) - \lambda\left(\frac{\Delta\delta(t_k)}{\tau} + c\delta(t_k)\right) \tag{21}$$

Notice that the uncertainty estimate contains an additional term which involves the noise measurements effect, however, its effect can be reduced by taking the value of λ sufficiently small. In this way, the estimate given by Eq. (21) resembles the structure showed in Eq. (13), with analogous convergence properties.

6. Numerical results

In order to illustrate the dynamic behavior of the close-loop system, numerical simulations of a continuous bioreactor were implemented according to the model described in Section 2. The parameter values for the controllers (13) and (18) were chosen as: $k = 1.0\ h^{-1}$, $\lambda = -0.1, -0.05, 0.001$; $c = 0.5\ h^{-1}$. Initial conditions for the controller were chosen as $\hat{S}(t_0) = S(0)$, $\hat{\psi}(t_0) = 2.3\ g\ l^{-1}\ h^{-1}$. From open loop simulations, it was found that the lower and upper bounds on $\hat{\psi}(t_k)$ are: $\psi_{min} = 0\ g\ l^{-1}\ h^{-1}$, $\psi_{max} = 10.0\ g\ l^{-1}\ h^{-1}$.

The prescribed setpoint is $S^{ref}(t) = 1.538\ g\ l^{-1}$, which corresponds to an unstable open-loop equilibrium point. The initial conditions for the system are: $S(0) = 10.0\ g\ l^{-1}$, $X(0) = 2.0\ g\ l^{-1}$. A sustained perturbation on the concentration of substrate feed flow was taken according to the following expression

$$S_f = S_f^0 + A\sin(\omega t) \tag{22}$$

where $S_f^0 = 35.0\ g\ l^{-1}$, $A = 5.0\ g\ l^{-1}$, and $\omega = 0.2\ h^{-1}$.

In order to evaluate the influence of noisy measurements on the controller performance and the reduction of its effects through the observer parameter λ, numerical simulation with the conditions described above was implemented for different values of λ. The noise in the substrate concentration measurement $\delta(t_k)$ was taken as a random number in $[-0.1, 0.1]$ (about 10% measurement error).

Fig. 1 presents the transient behavior of $S(t)$. Observe that $S(t)$ is maintained around the setpoint despite perturbations, uncertainties and noisy measurements; that is, the controllers (13) and (18) provide practical regulation. According to the results in Section 5, the peaking phenomena on the substrate concentration become less severe as the parameter λ becomes smaller. It is interesting to note that despite the parameter λ acts like a low-pass (noise) filter, the dynamical response of the substrate concentration remains almost the same, even λ was reduced one order in magnitude.

Fig. 2 shows the transient behavior of the real and the estimated uncertainties. It can be observed that the estimate of the uncertain term is maintained around the real value. The

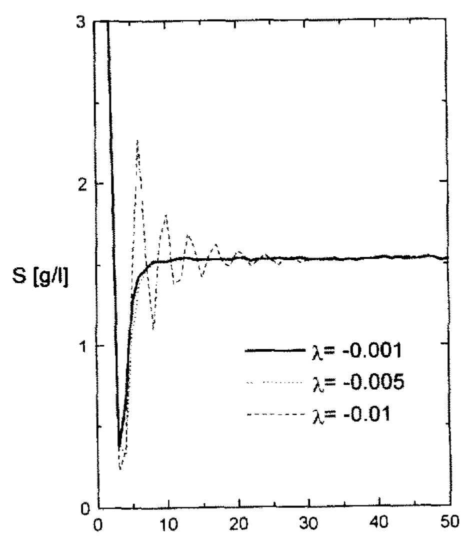

Fig. 1. Closed-loop behavior of the substrate concentration for different values of the observer parameter λ.

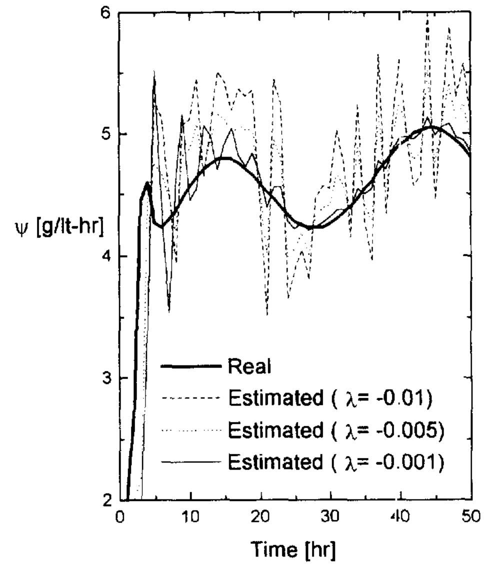

Fig. 2. Comparison of the dynamical behavior of the real and estimate uncertainties for different values of the observer parameter λ.

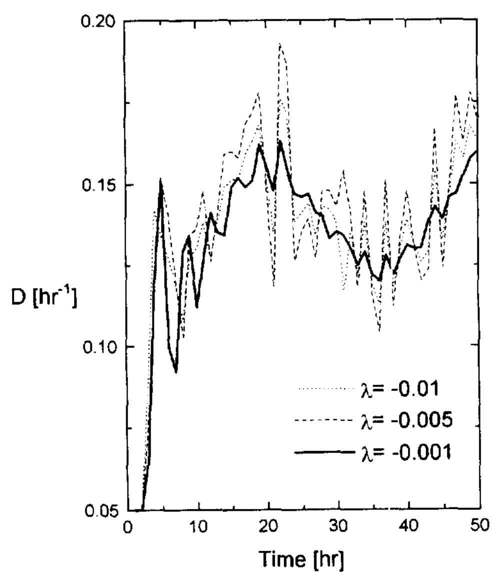

Fig. 3. Control input behavior for different values of the observer parameter λ.

size of the neighborhood was made smaller by varying the values of λ.

Fig. 3 presents the dynamical behavior of the control input D. Observe that the peaking effect induced by the noisy measurements on the control input is not too severe despite the size of the noise. Again, the peaking phenomena on the substrate concentration become less severe as the parameter λ becomes smaller.

To compare with a nonadaptive controller which does not estimate uncertainty, we have implemented a PI-controller tuned with internal model control (IMC) methodologies [12] based on a nominal linearized model. Fig. 4 presents numerical simulations with the PI-controller and the proposed controller. Although the PI-controller converges faster than the controller based on uncertainty estimation, the PI one is

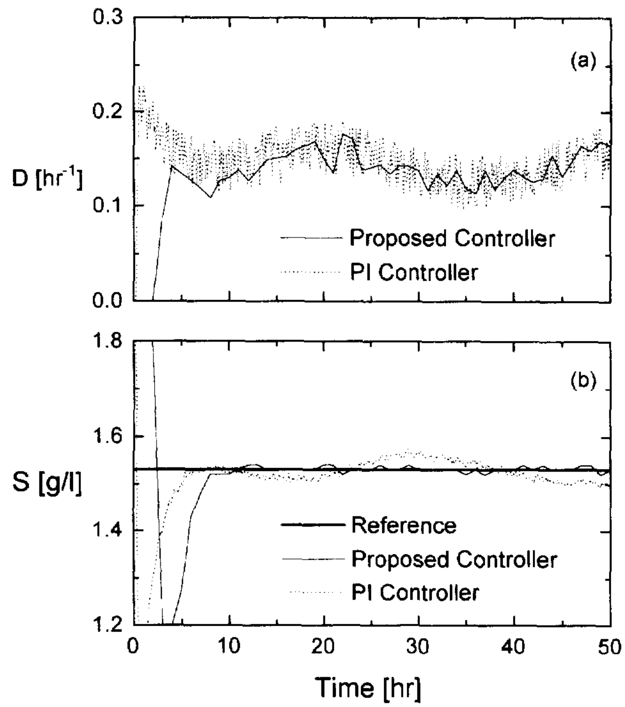

Fig. 4. Comparison of the dynamical behavior driven by a PI-controller and the proposed in this work.

more sensible to measurements noise. To reduce the adverse effects of measurements noise, an alternative is to detune the controller. However, there is no systematic procedures to detune a PI-controller in order to reduce adverse noise effects. The controller proposed in this work introduces a detuning parameter λ (relaxing parameter), for which the rule is *reduce* it up to obtain 'good' close-loop performance.

7. Concluding remarks

In this work, a control strategy for substrate concentration regulation for a continuous bioreactor in which the kinetic terms related with the specific growth rate, the yield coefficient and the biomass concentration are unknown was developed. The controller uses the on-line estimated values of kinetic terms, having practical stability even in the presence of uncertainties in the process model and additive noise on the substrate concentration measurements. Such estimates are obtained from a numerical observer. Numerical simulations of a continuous bioreactor were carried out and showed that the performance of the resulting controller is satisfactory despite uncertainties and noisy measurements.

A limitation of our method is that uncertainty estimation in closed-loop can only be realized when the uncertainty appears additively and matched (i.e., the uncertain term is in the same row of the control input). In some cases, matched uncertainty appears naturally, as in the case of bioreactors studied in this work. In other cases, such structure of uncertainty can be obtained via changes of coordinates.

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