2013 European Control Conference (ECC)
July 17-19, 2013, Zürich, Switzerland.

Guaranteed Robust Optimal Experiment Design for Nonlinear Dynamic Systems

Dries Telen, Boris Houska, Filip Logist, Moritz Diehl, and Jan Van Impe

Abstract— **This paper is about optimal experiment design for uncertain nonlinear dynamic processes. We are interested in designing experiments which allow to identify the unknown states and parameters of a differential equation from noisy measurements. Here, unpredictable process noise or structural model-plant mismatches can be an additional complication. In this case, robustness aspects have to be taken into account as the experiment has to be planned under incomplete information. The paper discusses problem formulations and numerical solution approaches for this type of robust optimal experiment design problems under bounded uncertainties. The corresponding techniques are illustrated in the design of experiments for a fedbatch bioreactor.**

I. INTRODUCTION

In the last decades, optimal experiment design (OED) techniques have gained increasing attention. This is due to the fact that it is often difficult to identify parameters in nonlinear dynamic systems. Especially, for cost intensive applications, it can be beneficial to design a control input in such a way that the experiment yields as much information as possible, see [3] for an overview.

An important challenge in OED is that the experiment has to be planned under incomplete information due to the presence of unknown parameters. This problem becomes even more challenging if unpredictable process disturbances occur during the experiment. In [9] it is suggested to take robustness aspects into account by analyzing the influence of the unknowns on the Fisher information matrix in a linear approximation, other approaches have been suggested in [14], [13] and the references therein. However, robust experiment design appears to be an open reseach field [4].

In this paper, we compute the variance-covariance by using a Riccati differential equation [15] which can also take time varying uncertainties into account. We also propose a novel approach for robust optimal experiment design. Here, our aim is to provide guarantees on the information content of an experiment using techniques from the field of ellipsoidal calculus [5], [10] and guaranteed state estimation [1]. By applying this ellipsoidal set propagation, we obtain a rigorously robust optimal experiment design. We show that the proposed technique is conservative and accounts for all nonlinearities. In addition it only requires first order sensitivities whereas existing methods [9] require second order sensitivities in the problem formulation.

We start in Section II with an introduction to different formulations of OED problems for nonlinear dynamic systems. In Section III we extend this formulation for guaranteed bounds on the uncertainty for the case of affine uncertainty systems. We discuss how robustness aspects in OED can be taken into account in Section IV. The corresponding techniques are illustrated in Section V where we analyze robust experiment designs for a fed-batch bioreactor. The paper concludes in Section VI.

II. EXISTING OED ALGORITHMS

In this section we introduce first the classic formulation of optimal experiment design. In the second part, we show how to compute an approximation of the variance-covariance matrix by using Riccati differential equations.
Let us consider the following uncertain dynamic system:

$$\forall t \in [0,T] : \dot{y}(t) \quad = \quad g(y(t),p,u(t),w(t)), \tag{1}$$

with $y(0) = y_0$. Here, $y(t) \in \mathbb{R}^{n_y}$ denotes the state, $p \in \mathbb{R}^{n_p}$ an unknown but time-invariant parameter, $u(t) \in \mathbb{R}^{n_u}$ a control input which we want to optimize, and $w(t) \in \mathbb{R}^{n_w}$ an unknown and time-varying input. Note that for the theoretical considerations in this paper, we will use an alternative notation which stacks the parameters to the states. More precisely, we define an augmented state $x(t) := (y(t)^\top, p^\top)^\top$ such that:

$$\dot{x}(t) = f(x(t),u(t),w(t)) := (g(y(t),p,u(t),w(t))^\top, 0^\top)^\top, \tag{2}$$

with $x(0) = (y_0^\top, p^\top)^\top$. Most of the traditional formulations of optimal experiment design analyze how accurately the unknown parameter p can be measured with the experiment at hand. However, we suggest in the current paper a more general framework which allows optionally to analyze the joint information about the parameter p and the state $y(t)$. This motivates us to collect these variables in one vector $x(t)$ aiming at a more compact notation. Thus, the unknowns which we want to estimate are now part of the initial value $x(0)$ and the time varying input w. Finally, we plan to take measurements of the form $\eta(t) := z(t) + v(t) \in \mathbb{R}^{n_z}$, where the output relation $z(t) = H(x(t))$ may in general be nonlinear, too. Here, $v(t)$ denotes the measurement error.

Dries Telen, Filip Logist, and Jan Van Impe are with the Department of Chemical Engineering, KU Leuven, Willem de Croylaan 46, B-3001 Leuven-Heverlee, Belgium.

Boris Houska is with the Centre for Process Systems Engineering & Department of Chemical Engineering, Imperial College London Roderic Hill Building - Room C509, South Kensington Campus, London, SW7 2AZ

Moritz Diehl is with the Department of Electrical Engineering, KU Leuven, Kasteelpark Arenberg 10, B-3001 Leuven-Heverlee, Belgium.

Contact: `jan.vanimpe@cit.kuleuven.be`

A. Classic OED problem formulation

In the following, we are interested in the case that the uncertainty functions w and v are stochastic white noise for which positive semi-definite matrices $V(t)$ and $W(t)$ are given by:

$$\begin{array}{ll} \mathbb{E}\{w(t)\} = 0, & \mathbb{E}\{w(t)w(t')\} = W(t)\delta(t-t') , \\ \mathbb{E}\{v(t)\} = 0, & \mathbb{E}\{v(t)v(t')\} = V(t)\delta(t-t') \end{array} \tag{3}$$

for all $t, t' \in \mathbb{R}$. The initial value $x(0) \in \mathscr{N}(\eta_0, P_0)$ is assumed to be a random variable with Gaussian distribution with given variance-covariance matrix $P_0 \in \mathbb{R}^{n_x \times n_x}$ and given expectation $\eta_0 \in \mathbb{R}^{n_x}$.

Let us assume for a moment that we have already taken measurements $\eta(t)$ for $t \in [0,T]$ using a given control input u. In this situation, we are interested in solving a nonlinear parameter estimation problem in order to compute the maximum likelihood estimate of the state. As we consider nonlinear dynamic systems, we do not have an explicit expression for this maximum likelihood estimate. Consequently, we have to compute the state estimate by solving a nonlinear optimal control problem of the form:

$$\begin{array}{rl} (x^*, w^*) := & \underset{x(\cdot),w(\cdot)}{\operatorname{argmin}} J[x(\cdot), w(\cdot)] \\ \text{s.t.} & \dot{x}(t) \ = \ f(x(t), u(t), w(t)) \end{array}$$

with $t \in [0,T]$. Here, the objective J is a least-squares term:

$$\begin{array}{l} J[x(\cdot), w(\cdot)] \ := \ \|x(0) - \eta_0\|^2_{P_0^{-1}} + \int_0^T \|w(t)\|^2_{W(t)^{-1}} \, \mathrm{d}t \\ + \int_0^T \|H(x(t)) - \eta(t)\|^2_{V(t)^{-1}} \, \mathrm{d}t , \end{array}$$

while (x^*, w^*) denotes the maximum likehood estimate for the state and noise, respectively. In this context and also in the following sections we use the notation $\|x\|^2_Y := x^\top Y x$ in order to denote weighted Euclidean norms for positive definite weighting matrices Y. In the field of optimal experiment design we are interested in computing and optimizing the variance-covariance matrix of the maximum likelihood estimate $x^*(T)$ for the final state without knowing the measurements η yet.

One of the most broadly used formulations of optimal experiment design for parameter estimation [3] is based on the Fisher information matrix:

$$F[t,u] := P_0^{-1} + \int_0^t \frac{\partial H(x(\tau))}{\partial x_0}^\top V(\tau)^{-1} \frac{\partial H(x(\tau))}{\partial x_0} \, \mathrm{d}\tau. \tag{4}$$

Note that $F[t,u]$ is a symmetric and positive semi-definite matrix but with different dimensions, i.e., $n_x \times n_x$, as $x_0 \in \mathbb{R}^{n_x}$ collects all unknown initial values which we want to estimate. In the following, we introduce the short hands:

$$C(\tau) := \frac{\partial H(x(\tau))}{\partial x} \quad \text{and} \quad S(\tau) := \frac{\partial x(\tau)}{\partial x_0} ,$$

where $S(t)$ can also be computed from a variational differential equation of the form:

$$\dot{S}(\tau) = A(\tau)S(\tau) \quad \text{with} \quad S(0) = I$$

$$A(\tau) := \frac{\partial f(x(\tau), u(\tau), 0)}{\partial x} , \ B(\tau) := \frac{\partial f(x(\tau), u(\tau), 0)}{\partial w} .$$

Now, the Fisher information matrix can also be written as:

$$F[t,u] = P_0^{-1} + \int_0^t S(\tau)^\top C(\tau)^\top V(\tau)^{-1} C(\tau) S(\tau) \, \mathrm{d}\tau .$$

Under the assumption of unbiased and uncorrelated Gaussian noise, the (approximate) Fisher information matrix (FIM) has an interesting property: its inverse $F[t,u]^{-1}$ approximates the parameter estimation variance-covariance matrix [11].

B. Riccati-OED formulation

For the special case that we are looking for a maximum likelihood estimate of the states $\xi(t) \in \mathbb{R}^{n_x}$, it is well-known [8] that the optimal solution can be computed by using an affine observer equation of the form:

$$\begin{array}{rcl} \dot{\xi}(t) & = & A(t)\xi(t) + d(u(t)) + L(t)\left[\eta(t) - C(t)\xi(t)\right] , \\ \xi(0) & = & \xi_0 , \end{array}$$

where $L(t) \in \mathbb{R}^{n_x \times n_y}$ is the Kalman gain. The corresponding variance-covariance matrix $P(t)$ of this estimate can be obtained by a forward simulation of the Ricatti equation, which can be written as:

$$\begin{array}{rcl} \dot{P}[t,u] & = & A_\mathrm{e}(t)P(t) + P(t)A_\mathrm{e}(t)^\top + Q_\mathrm{e}(t) \\ P[0,u] & = & P_0 . \end{array} \tag{5}$$

Here, we use the short hands:

$$\begin{array}{rcl} A_\mathrm{e}(t) & := & A(t) - L(t)C(t) , \\ Q_\mathrm{e}(t) & := & B(t)W(t)B(t)^\top + L(t)V(t)L(t)^\top . \end{array}$$

In [15], we show that this variance-covariance matrix is related to the Fisher information matrix as defined in the previous section. Also note that the above Riccati formulation to obtain the variance-covariance matrix is exact for the uncertainty affine case. In the nonlinear case this variance-covariance matrix is a first order approximation. The main point is now that the matrix functions $A_\mathrm{e}(t)$ and $Q_\mathrm{e}(t)$, and consequently also the function P, can be influenced by the control input u. Thus, u can be regarded as a variable which can be used to optimize some optimal experiment design objective, e.g., the A-criterium $\Phi(P(T)) = \mathrm{Tr}(P(T))$ at a given time $T > 0$.

When we aim at designing an experiment in order to estimate the uncertain parameters, we will only take a subset of the matrix P into account by introducing the following positive semi-definite scaling matrix:

$$\Sigma \ = \ \begin{pmatrix} 0 & I \end{pmatrix}, \tag{6}$$

with $I \in \mathbb{R}^{n_p \times n_p}$. In other words, we are interested in a nonlinear optimal control problem of the form:

$$\begin{array}{ll} \inf\limits_{P(\cdot),u(\cdot),L(\cdot)} & \Phi\left(\Sigma P(T) \Sigma^\top\right) \\ \text{s.t.} & \left\{ \begin{array}{rcl} \dot{P}(t) & = & A_\mathrm{e}(t)P(t) + P(t)A_\mathrm{e}(t)^\top + Q_\mathrm{e}(t) \\ P(0) & = & P_0 \\ u(t) & \in & \mathbb{U}(t) \quad \text{for all } t \in [0,T] . \end{array} \right. \end{array} \tag{7}$$

In this context, the set $\mathbb{U}(t) \subseteq \mathbb{R}^{n_u}$ can be used to represent control constraints. Note that the optimal control problem (7) can also be considered in combination with other choices of the quality measure Φ such as D-criterion ($\det(\Sigma P \Sigma^\top)$) and E-criterion ($\lambda_{\max}(\Sigma P \Sigma^\top)$).

For a more elaborate discussion on OED-criteria, we refer to [3]. Remark that these criteria can be formulated either for the variance-covariance matrix or the Fisher information matrix. Note that if $V(t)$ is invertible, the minimization over the function L can explicitly be eliminated, as we can use Kalman's relation $L(t) = P(t)C(t)^T V(t)^{-1}$. However, it should be kept in mind that the resulting formulation is in general still a non-convex optimal control problem in u, i.e., the elimination of L does only help in the sense that we have less optimization variables left. For the case when we have affine state constraints, we refer to [12].

III. OED BASED ON GUARANTEED STATE ESTIMATION

In this section, we first introduce the notions of guaranteed state estimation for uncertainty affine dynamic systems by employing ellipsoidal calculus. In the second part we illustrate how we can employ this formulation for optimal experiment design.

Let us first consider an uncertainty affine dynamic system of the form:

$$\begin{aligned} \dot{x}(t) &= A(u(t))x(t) + B(u(t))w(t) + d(u(t)) \\ x(0) &= x_0 \, . \end{aligned} \tag{8}$$

Here, the system coefficients A, B and d may depend nonlinearly on the control input $u(t)$. In the previous section, we assumed the uncertainties v, w, and x_0 to be random variables. When we have the following given uncertainty sets $\mathbb{V}(t) \subseteq \mathbb{R}^{n_y}$, $\mathbb{W}(t) \subseteq \mathbb{R}^{n_w}$, and $\mathbb{X}_0 \subseteq \mathbb{R}^{n_y}$, i.e., our information is of the form $v(t) \in \mathbb{V}(t)$, $w(t) \in \mathbb{W}(t)$, and $x_0 \in \mathbb{X}_0$, we can construct a compact set that includes with guarantee the states (and thus the parameters) of the system which are consistent with the measurements and the bounded noise which is the field of "Guaranteed State Estimation".

Assuming for a moment that we have taken measurements $\eta(t)$ of the output $y(t)$ for all $t \in [0,T]$ and for a given u, the aim is thus to find the smallest set $X(T) \subseteq \mathbb{R}^{n_x}$ for which we can guarantee that it contains the state $x(T)$ at time T using all the information that we have.

A possible method to compute this compact set is the ellipsoidal bounding of the states [1] or use zonotope and interval arithmetic to obtain the compact set [2].

A. Ellipsoidal Approach for Guaranteed State Estimation

Note that if the sets $\mathbb{V}(t), \mathbb{W}(t)$, and $\mathbb{X}_0$ are convex while the dynamic system is uncertainty affine, then the set $X(T)$ is convex, as an intersection of convex sets is convex.

Unfortunately, it is in general very expensive to compute the set $X(T)$. Thus, we directly concentrate on outer approximations of $X(T)$. This can for example be done by using ellipsoids. Here, we assume that the sets $\mathbb{V}(t)$ are ellipsoids of the form:

$$\mathbb{V}(t) \;=\; \mathscr{E}(V(t)) \;:=\; \left\{ \, V(t)^{\frac{1}{2}} v \, \middle| \, \exists v \in \mathbb{R}^{n_y} : \; v^T v \;\leq\; 1 \right\} ,$$

where $V(t) \in \mathbb{S}_+^{n_y \times n_y}$ is given. The sets $\mathbb{W}(t) = \mathscr{E}(W(t))$ and $\mathbb{X}_0 = \mathscr{E}(P_0)$ with $W(t) \in \mathbb{S}_+^{n_w \times n_w}$ and $P_0 \in \mathbb{S}_+^{n_x \times n_x}$ are assumed to be ellipsoidal, too. Now, we plan to employ the following technical result, which has originally been proposed by [10]:

Lemma 1: Let $L : [0,T] \to \mathbb{R}^{n_x \times n_y}$ and $\kappa : [0,T] \to \mathbb{R}^2_{++}$ be any given functions. If there exist functions $\xi : [0,T] \to \mathbb{R}^{n_x}$ and $P : [0,T] \to \mathbb{R}^{n_x \times n_x}$ which satisfy on the interval $[0,T]$ the differential equations:

$$\begin{aligned} \dot{\xi}(t) &= A_{\mathrm{e}}(t)\xi(t) + d(u(t)) + L(t)\eta(t) \, , \; \xi(0) = \xi_0 \, , \\ \dot{P}(t) &= A_{\mathrm{e}}(t)P(t) + P(t)A_{\mathrm{e}}(t)^\top + (\kappa_1(t) + \kappa_2(t))P(t) \\ & \quad \tfrac{1}{\kappa_1(t)}B(t)W(t)B(t)^\top + \tfrac{1}{\kappa_2(t)}L(t)V(t)L(t)^\top \, , \\ P(0) &= P_0 \, , \end{aligned}$$

then we can guarantee that we have:

$$x(t) \in \mathscr{E}(\xi(t), P(t)) \;:=\; \left\{ \, \xi(t) + P(t)^{\frac{1}{2}} v \, \middle| \, \exists v : \; v^T v \;\leq\; 1 \right\}$$

for all $t \in [0,T]$, i.e., $\xi(t)$ can be regarded as a state estimate whose error is bounded by the ellipsoid $\mathscr{E}(P(t))$. Here,

$$A_{\mathrm{e}}(t) \;:=\; A(u(t)) - L(t)C(t)$$

is defined as in the previous section.

Remarkably, it can even be shown that we have:

$$\bigcap_{L(\cdot), \kappa(\cdot) > 0} \mathscr{E}(\xi(T), P(T)) \;=\; X(T) \, , \tag{9}$$

i.e., the intersection of all outer approximations which can be generated with Lemma 1 is coinciding with the exact set valued solution of the guaranteed state estimation problem. The proof of this statement and the above Lemma can both be found in [10].

B. OED formulation based on Guaranteed Estimation

In this paper, we employ the achievements in ellipsoidal calculus of the previous section and transfer them to the context of optimal experiment design. Here, we are interested in optimal control problems of the form:

$$\begin{aligned} & \inf_{P(\cdot), u(\cdot), \kappa(\cdot) > 0, L(\cdot)} \quad \Phi\left(\Sigma P(T) \Sigma^\top\right) \qquad \text{s.t.} \\ & \dot{P}(t) = A_{\mathrm{e}}(t)P(t) + P(t)A_{\mathrm{e}}(t)^\top + (\kappa_1(t) + \kappa_2(t))P(t) + \\ & \qquad \tfrac{1}{\kappa_1(t)}B(t)W(t)B(t)^\top + \tfrac{1}{\kappa_2(t)}L(t)V(t)L(t)^\top \\ & P(0) = P_0 \\ & u(t) \in \mathbb{U}(t) \quad \text{for all } t \in [0,T] \, . \end{aligned} \tag{10}$$

Formulation (10) allows us to design an experiment for which we can guarantee that the difference between the real state $x^*(T)$ (and thus also the real parameter value) at time T and the corresponding identification result $\hat{x}(T)$ (and thus the estimated parameter value) satisfies $\hat{x}(T) - x^*(T) \in \mathscr{E}(P(T))$.

Let us assume for a moment that we can compute the corresponding set $X(T)$, then we would like to optimize a generalized design criterion $\widetilde{\Phi}(X(T))$ which depends on the set $X(T)$. Here, we assume that the function $\widetilde{\Phi}$ satisfies the following fundamental properties:

1) The function $\widetilde{\Phi}$ is translationally invariant, i.e., we have
$$\widetilde{\Phi}(\{a\} \oplus X(T)) \; = \; \widetilde{\Phi}(X(T))$$
for all vectors $a \in \mathbb{R}^{n_x}$. Here, $\oplus$ denotes the Minkowski sum of two sets.
2) The function $\widetilde{\Phi}$ is monotonically increasing, i.e., we have for all sets $X, Y \subseteq \mathbb{R}^{n_x}$ with $X \subseteq Y$ a relation of the form $\widetilde{\Phi}(X) \; \leq \; \widetilde{\Phi}(Y)$.

Here, we could for example regard choices of the form:

$$\begin{aligned}
\widetilde{\Phi}_{\mathrm{A}}(X(T)) \quad &:= \quad (n_x+2)\int_{X(T)} \left\| x - \int_{X(T)} \xi \, \mathrm{d}\xi \right\|_2^2 \mathrm{d}x \, , \\
\widetilde{\Phi}_{\mathrm{D}}(X(T)) \quad &:= \quad \frac{\Gamma\left(\frac{n_x}{2}+1\right)}{\pi^{\frac{n_x}{2}}} \int_{X(T)} 1 \, \mathrm{d}x \, , \\
\widetilde{\Phi}_{\mathrm{E}}(X(T)) \quad &:= \quad \max_{a,b \in X(T)} \frac{1}{2} \|a-b\|_2 \, ,
\end{aligned}$$

which we propose to call the generalized *A*-, *D*-, and *E*-criterion, respectively. As any feasible solution P of the problem (10) satisfies by construction $X(T) \subseteq \mathscr{E}(P(T))$, we know that we have:

$$\widetilde{\Phi}_{\mathrm{E}}(X(T)) \; \leq \; \widetilde{\Phi}_{\mathrm{E}}(\mathscr{E}(P(T))) \; = \; \lambda_{\max}(P(T)) \; = \; \Phi_{\mathrm{E}}(P(T)) \, .$$

In other words, if we optimize the E-criterion using formulation (10), the objective value will be an upper bound on the generalized E-criterion. Similar statements hold for the generalized A- or D-criterion, as we have relations of the form $\widetilde{\Phi}_{\mathrm{A}}(X(T)) \leq \Phi_{\mathrm{A}}(P(T))$ and $\widetilde{\Phi}_{\mathrm{D}}(X(T)) \leq \Phi_{\mathrm{D}}(P(T))$.

Note that the problem formulation (10) finds in general only upper bounds on the above generalized design criteria.

IV. A NOVEL ROBUST OED ALGORITHM

In this section we extend the guaranteed state estimation idea for nonlinear dynamic system. This formulation will connect with the OED formulations based on Riccati differential equations from Section II-B. In the second part of this section, we introduce a conservative estimation of the nonlinearities which will yield the guaranteed robust OED formulation.

A. Linear Approximation Techniques

In general models in (bio)chemical engineering tend to be nonlinear, so we have to extend the approach outlined in the previous section. A possible practical solution to this problem is to analyze the influence of the uncertain inputs v, w, and x_0 on the estimate $x^*(T)$ in a linear approximation. The corresponding technique leads to a reasonably tractable approximate optimal experiment design formulation. If we transfer this idea to our notation, the linear approximation approach leads to an optimal control problem of the form:

$$\begin{array}{cl}
\inf\limits_{\xi(\cdot),P(\cdot),\kappa(\cdot)>0,u(\cdot),L(\cdot)} & \Phi\left(\Sigma P(T) \Sigma^\top\right) \\
\text{s.t.} & \left\{ \begin{array}{rcl}
\dot{P}(t) & = & A_{\mathrm{e}}(t)P(t) + P(t)A_{\mathrm{e}}(t)^\top + Q_{\mathrm{e}}(t) \\
P(0) & = & P_0 \\
\dot{\xi}(t) & = & f(\xi(t),u(t),0) \\
\xi(0) & = & \xi_0 \\
u(t) & \in & \mathbb{U}(t) \quad \text{for all } t \in [0,T] \, .
\end{array} \right.
\end{array} \qquad (11)$$

Here, the functions:

$$\begin{aligned}
& A_{\mathrm{e}}(t) := \tfrac{\partial f(\xi(t),u(t),0)}{\partial x} - L(t)\tfrac{\partial H(\xi(t))}{\partial x} \quad \text{and} \\
& Q_{\mathrm{e}}(t) := \tfrac{1}{\kappa_1(t)} \tfrac{\partial f(\xi(t),u(t),0)}{\partial w} W(t) \left(\tfrac{\partial f(\xi(t),u(t),0)}{\partial w}\right)^\top \\
& \quad +(\kappa_1(t)+\kappa_2(t))P(t) + \tfrac{1}{\kappa_2(t)} L(t)V(t)L(t)^\top
\end{aligned}$$

require the computation of derivatives of f and H with respect to x and w. The only difference is that the matrix functions A, B, C are replaced with the corresponding derivatives of the functions f and H as we do in the Riccati OED formulation of Section II-B.

B. Robust Approximation Techniques

We are interested in solving generalized optimal experiment design problems which may formally be written as:

$$\min_{u(\cdot)} \; \widetilde{\Phi}(X(T)) \quad \text{s.t.:} \quad \forall t \in [0,T]: \; u(t) \in \mathbb{U}(t) \, ,$$

where $X(T)$ is the smallest set in which the state $x(T)$ can be guaranteed to be by using all available information. We are interested in computing conservative outer approximations of the set $X(T)$.

Let us regard the following nonlinear filter equation with linear learning gain:

$$\begin{aligned}
\dot{\xi}(t) \quad &= \quad f(\xi(t),u(t),0) + L(t)\left[\eta(t) - H(\xi(t))\right] \, , \\
\xi(0) \quad &= \quad \xi_0 \, .
\end{aligned}$$

As the unknown real state satisfies the differential equation $\dot{x}(t) \; = \; f(x(t),u(t),w(t))$, we may write the dynamic equation for the measurement error $e := x - \xi$ in the form:

$$\begin{aligned}
\dot{e}(t) \quad = \quad & [A(t) - L(t)C(t)]\, e(t) + B(t)w(t) + L(t)v(t) \\
& + f_{\mathrm{N}}(x(t),\xi(t),w(t)) \, ,
\end{aligned}$$

where we use the short hands:

$$\begin{aligned}
& A(t) := \tfrac{\partial f(\xi(t),u(t),0)}{\partial x} \quad B(t) := \tfrac{\partial f(\xi(t),u(t),0)}{\partial w} \quad C(t) := \tfrac{\partial H(\xi(t))}{\partial x} \\
& f_{\mathrm{N}}(x(t),\xi(t),w(t)) \; := \; f(x(t),u(t),w(t)) - f(\xi(t),u(t),0) \\
& \qquad\qquad -A(t)[x(t)-\xi(t)] - B(t)w(t) \\
& \qquad\qquad +L(t)\left[H(\xi(t)) - C(t)[x(t)-\xi(t)]\right] \, .
\end{aligned}$$

Now, we assume that we manage to find an explicit nonlinearity estimate $\Omega_{\mathrm{N}}(u(t),\xi(t),P(t)) \in \mathbb{S}_+^{n_x}$ such that we have for all $w(t) \in \mathscr{E}(W(t))$ and all $e(t) \in \mathscr{E}(P(t))$ an inclusion of the form

$$f_{\mathrm{N}}(x(t),\xi(t),w(t)) \in \mathscr{E}(\Omega_{\mathrm{N}}(u(t),\xi(t),P(t))) \, .$$

If the nonlinear terms f_{N} are regarded as if they were independent uncertainties, the dynamic equation for e is uncertainty affine. Thus, we can transfer the problem formulation (10):

$$\begin{array}{cl} \inf\limits_{\xi(\cdot),P(\cdot),u(\cdot),L(\cdot),\kappa(t)} & \Phi\left(\Sigma P(T)\Sigma^{\top}\right) \\ \text{s.t.} & \left\{\begin{array}{rcl} \dot{P}(t) & = & A_{\mathrm{e}}(t)P(t)+P(t)A_{\mathrm{e}}(t)^{\top}+\Omega(P(t),\kappa(t)) \\ P(0) & = & P_0 \\ \dot{\xi}(t) & = & f(\xi(t),u(t),0) \\ \xi(0) & = & \xi_0 \\ u(t) & \in & \mathbb{U}(t) \quad \text{for all}\ t\in[0,T]\,. \end{array}\right. \end{array} \tag{12}$$

Here, $A_{\mathrm{e}}(t)$ is defined as in the previous section while $\Omega(P(t),\kappa(t))$ is defined as:

$$\begin{array}{rl} \Omega(P(t),\kappa(t)) := \sum_{i=1}^{3}\kappa_i(t)P(t) + \frac{B(u(t))W(t)B(u(t))^{\top}}{\kappa_1(t)} & \\ +\frac{L(t)V(t)L(t)^{\top}}{\kappa_2(t)} + \frac{\Omega_{\mathrm{N}}(u(t),\xi(t),P(t))}{\kappa_3(t)}\,. \end{array}$$

Now, if P is a feasible solution of the problem (12) then we must have $X(T)\subseteq\mathscr{E}(P(T))$, as the nonlinear terms have been overestimated while the assumption that the learning gain is linear introduces additional conservatism. Consequently, the formulation (12) allows us to design experiments for nonlinear dynamic systems with a-priori guarantees on the accuracy. Similar ideas for optimal control are in [7].

V. APPLICATION TO A FED-BATCH BIOREACTOR

In this section, we apply our robust optimal experiment design techniques to a fed-batch bioreactor. The described methods lead to tractable optimal control problems which are solved using the freely available ACADO-tookit [6].

A. The Fed-Batch Bioreactor Model

The dynamic model equations for our fed-batch reactor are taken from [16]:

$$\begin{array}{rcl} \frac{dC_s}{dt} & = & -\sigma C_x+\frac{u}{v}C_{s,in}-\frac{u}{v}C_s+w_0\,, \\ \frac{dC_x}{dt} & = & \mu C_x-\frac{u}{v}C_x+w_1\,, \\ \frac{dK_s}{dt} & = & 0\,, \quad \text{and} \quad \frac{dv}{dt} = u\,. \end{array} \tag{13}$$

Here, C_s is the concentration of the limiting substrate, C_x the biomass concentration, and v the bioreactor volume. Note that we control the volumetric feed rate u containing a given substrate concentration $C_{s,in}$. The specific growth rate studied in this case is the monotonic *Monod* type which is given by:

$$\mu \quad = \quad \mu_{max}\frac{C_s}{K_s+C_s}\,.$$

Finally, the substrate consumption rate is given by:

$$\sigma \quad = \quad \mu/Y_{X|S}+m\,,$$

where $Y_{X|S}$ is the yield and m the maintenance factor.

In the following we assume that the time-invariant parameter K_{s} is unknown while also the model-plant mismatch $w(t)\in\mathbb{R}^2$ is an unknown function in time. The aim is to design a measurement which is suited to identify K_s. All the remaining parameters are assumed to be given (see Table I).

TABLE I

THE KNOWN PARAMETER VALUES FOR THE FED-BATCH BIOREACTOR.

μ_{max}	$0.1\,\mathrm{h}^{-1}$	α	$1500\,\mathrm{g}$
v_{max}	$10\mathrm{L}$	β	$10.5\,\mathrm{g}$
m	0.29	$Y_{X\|S}$	0.47
$\sigma_{C_s}^2$	$10^{-2}\ \mathrm{g}^2/\mathrm{L}^2$	$\sigma_{C_x}^2$	$6.25\times10^{-4}\ \mathrm{g}^2/\mathrm{L}^2$
σ_{α}^2	$57\ \mathrm{g}^2$	σ_{β}^2	$14.3\ \mathrm{g}^2$

The initial amount of biomass available is $\beta = 10.5\,\mathrm{g}$. As the maximum volume is given by $v_{max} = 10\,\mathrm{L}$ while the total amount of limiting substrate available is denoted by α (see Table I), the initial condition for the substrate and the volume are connected via the initial value condition:

$$C_s(0)v(0)+C_{s,in}(v_{max}-v(0)) \;=\; \alpha\,, \quad C_x(0)v(0) \;=\; \beta\,.$$

Moreover, we impose the path constraints

$$0\,\tfrac{\mathrm{L}}{\mathrm{h}} \le u(t) \le 1\,\tfrac{\mathrm{L}}{\mathrm{h}} \quad \text{and} \quad 7\,\mathrm{L} \le v(t) \le 10\,\mathrm{L}\,.$$

In the following, we will always assume that the output function $z(t) = (C_{\mathrm{s}}, C_{\mathrm{x}})^T$ can be measured. The duration of the experiment to be designed is fixed to $T := 35\,\mathrm{h}$.

B. Nominal Optimal Experiment Design

In our first case study, we assume that we have stochastic measurements of the states, where the associated variance matrix is given by $V(t) := \operatorname{diag}\left(\sigma_{C_s}^2, \sigma_{C_x}^2\right)^T$. We assume that our initial guess of K_s is of the form $\mathbb{E}\{K_s\} = 1.0\,\frac{\mathrm{g}}{\mathrm{L}}$ where the associated initial variance is

$$P_{2,2}(0) \;=\; \mathbb{E}\left\{(K_s-\mathbb{E}\{K_s\})^2\right\} \;=\; 0.5\left(\frac{\mathrm{g}}{\mathrm{L}}\right)^2\,.$$

The variances of the initial values for C_{s} and C_{x} satisfy $P_{0,0}(0)v(0)^2 = \sigma_{\alpha}^2$ and $P_{1,1}(0)v(0)^2 = \sigma_{\beta}^2$. The non-diagonal components of the matrix $P(0)$ are all 0.

For this first case study we assume $w=0$. Now, we employ the approximate optimal experiment design formulation (7) based on linearization. Here, our design objective is to minimize the predicted variance of the unknown parameter K_{s}, i.e., we define $\Phi(P) := P_{2,2}(T)$. The corresponding result is shown in Figure 1 in the form of the dotted lines. The optimized standard deviation of K_s at the end of the experiment is in a linear approximation given by

$$\sqrt{P_{2,2}(T)} \;=\; 0.15\,\frac{\mathrm{g}}{\mathrm{L}}\,.$$

This corresponds to the square-root of the objective value.

C. Robust Optimal Experiment Design

Our second case study is about robust optimal experiment design. This time we assume that we have hard bounds on the uncertainties, i.e., the measurement error satisfies $v(t)\in\mathscr{E}(V(t))$ for all $t\in[0,T]$, where $V(t)$ is given as in the previous section. Additionally, we assume that the uncertainty in the initial states and parameters satisfies the condition $x_0-\xi_0\in\mathscr{E}(P(0))$, where $P(0)$ is given as above. Finally, we regard an additional model-plant mismatch:

$$w(t)\in\mathscr{E}(W(t)) \quad \text{with} \quad W(t) \;:=\; \operatorname{diag}\left(0.1\,\frac{\mathrm{g}}{\mathrm{Ls}}, 0.1\,\frac{\mathrm{g}}{\mathrm{Ls}}\right)\,.$$

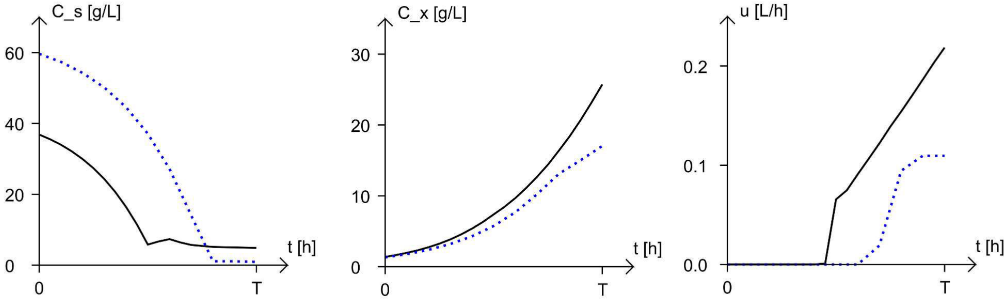

Fig. 1. The results for the expected state trajectories and the optimized control input in the case of nominal optimal experiment design (dotted lines) as well as in the case of robust optimal experiment design (solid lines).

A nonlinearity estimate for our particular right-hand side function is given by:

$$\Omega_{\mathrm{N}}(\kappa,P) \quad := \quad \mathrm{diag}\left(\frac{\mu_{\max}\upsilon}{Y_{X|S}\kappa_3}, \frac{\mu_{\max}\upsilon}{\kappa_4}, 0\right)^{\top}, \qquad (14)$$

where we use the short hands:

$$\chi \;:=\; \frac{\sqrt{P_{0,0}+2P_{0,2}+P_{2,2}}}{(K_{\mathrm{s}}+C_{\mathrm{s}})(K_{\mathrm{s}}+C_{\mathrm{s}}-\sqrt{P_{0,0}+2P_{0,2}+P_{2,2}})},$$

$$\upsilon \;=\; \chi\left[\frac{C_s C_x\sqrt{P_{0,0}+2P_{0,2}+P_{2,2}}}{K_{\mathrm{s}}+C_{\mathrm{s}}} + C_{\mathrm{s}}\sqrt{P_{1,1}} + C_{\mathrm{x}}\sqrt{P_{0,0}}\right].$$

Finally, we solve the associated robust optimal experiment design problem using formulation (12) with $\Phi(P) = P_{2,2}(T)$ as the design objective. The corresponding optimal solution is shown in Figure 1 in the form of the solid lines. The square-root of the objective value is in this case $\sqrt{P_{2,2}^{*}(T)} = 0.29\,\frac{\mathrm{g}}{\mathrm{L}}$. Thus, we know that if we perform the robustly optimized experiment we will definitely find an estimate for K_{s}^{*} which satisfies the following property. The difference $|K_{\mathrm{s}}^{*} - K_s|$ between the estimate K_{s}^{*} and the unknown real value of K_s cannot possibly be more than $0.29\,\frac{\mathrm{g}}{\mathrm{L}}$ - independent of how the uncertainty and unknowns are realized.

VI. CONCLUSIONS AND OUTLOOK

In this paper we have proposed a technique for robust optimal experiment design. Here, we have employed a Riccati differential equation formulation that can also take time varying uncertainties into account. We have extended the ideas of guaranteed state estimation by using ellipsoidal calculus to optimal experiment design. In the proposed technique we are able to compute rigorously a robust optimal experiment design based on this ellipsoidal set propagation. The applicability of the corresponding techniques has been illustrated with a benchmark application from the field of (bio)chemical engineering.

ACKNOWLEDGMENTS

D. Telen has a Ph.D grant of the Agency for the Promotion of Innovation through Science and Technology in Flanders (IWT-Vlaanderen). J. Van Impe holds the chair Safety Engineering sponsored by the Belgian chemistry and life sciences federation essenscia. The research was supported by KUL , OT/10/035, PFV/10/002 (OPTEC), IOF-SCORES4CHEM, the Belgian Federal Science Policy Office: IAP PVII/19. This research was supported by Research Council KUL: GOA/10/09 MaNet and GOA/10/11. Flemish Government: FWO projects: 1518913N, G093013N, G.0320.08 (convex MPC), G.0377.09 (Mechatronics MPC); IWT projects: SBO LeCoPro; EU: FP7-EMBOCON (ICT-248940), FP7-SADCO (MC ITN-264735), ERC ST HIGHWIND (259 166), Eurostars SMART, ACCM.

REFERENCES

[1] I. Valyi. A.B. Kurzhanski, K. Sugimoto. Guranteed state estimation for dynamical systems: Ellipsoidal techniques. *International Journal of Adaptive Control and Signal Processing*, 8:85–101, 2006.

[2] T. Alamo, J. M. Bravo, and E. F. Camacho. Guaranteed state estimation by zonotopes. *Proceedings of the 42nd IEEE Conference on Decision and Control*, pages 5831–5836, 2005.

[3] G. Franceschini and S. Macchietto. Model-based design of experiments for parameter precision: State of the art. *Chemical Engineering Science*, 63(19):4846–4872, 2008.

[4] H. Hjalmarsson. From experiment design to closed-loop control. *Automatica*, 41:393–438, 2005.

[5] B. Houska. *Robust Optimization of Dynamic Systems*. PhD thesis, Katholieke Universiteit Leuven, 2011. (ISBN: 978-94-6018-394-2).

[6] B. Houska, H.J. Ferreau, and M. Diehl. ACADO Toolkit - an open-source framework for automatic control and dynamic optimization. *Optimal Control Applications and Methods*, 32:298–312, 2011.

[7] B. Houska, F. Logist, J. Van Impe, and M. Diehl. Robust optimization of nonlinear dynamic systems with application to a jacketed tubular reactor. *Journal of Process Control*, 22:1152–1160, 2012.

[8] R.E. Kalman. A New Approach to Linear Filtering and Prediction Problems. *Transactions of the ASME–Journal of Basic Engineering*, 82:35–45, 1960.

[9] S. Körkel, E. Kostina, H.G. Bock, and J.P. Schlöder. Numerical methods for optimal control problems in design of robust optimal experiments for nonlinear dynamic processes. *Optimization Methods and Software Journal*, 19(3-4):327–338, 2004.

[10] A.B. Kurzhanski and T.F. Fillipova. *Advances in Nonlinear Dynamics and Control. A Report from Russia.*, chapter On the Theory of Trajectory Tubes—a Mathematical Formalism for Uncertain Dynamics, Viability and Control., pages 122–188. Birkhauser, Boston, 1993.

[11] L. Ljung. *System Identification: Theory for the User*. Prentice Hall, 1999.

[12] F. Logist, B. Houska, M. Diehl, and J.F. Van Impe. Robust multi-objective optimal control of uncertain (bio)chemical processes. *Chemical Engineering Science*, 66(20):4670 – 4682, 2011.

[13] J. Martensson and H. Hjalmarsson. Robust input design using sum of squares constraints. In *14th IFAC Symposium on System Identification (SYSID06). Newcastle (Australia)*, pages 1352–1357, 2006.

[14] C.R. Rojas, J.S. Welsh, G.C. Goodwin, and A. Feuer. Robust optimal experiment design for system identification. *Automatica*, 43:993–1008, 2007.

[15] D. Telen, B. Houska, F. Logist, E. Van Derlinden, M. Diehl, and J. Van Impe. Optimal experiment design under process noise using Riccati differential equations. *Journal of Process Control*, 23:613–629, 2013.

[16] K.J. Versyck and J.F. Van Impe. Feed rate optimization for bed-batch bioreactors: from optimal process performance to optimal parameter estimation. *Chemical Engineering Communications*, 172:107–124, 1999.