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## Optimal Operation of Semi-Batch Processes with a Single Reaction

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# Optimal Operation of Semi-Batch Processes with a Single Reaction

Srinivas Palanki and Jyothy Vemuri

## Abstract

In a large number of industrial semi-batch reactor applications, a single reaction takes place in the reactor and the operational objective is to compute the optimal feed rate of reactants and the optimal batch temperature that optimizes an objective function at the end of a fixed batch time. In this work, it is shown that the optimal operating policy can be split into several time intervals. Analytical expressions for the optimal input are developed for each interval. Parametric uncertainty is handled by implementing this strategy in closed-loop. This methodology is illustrated via simulation of two semi-batch reactor applications.

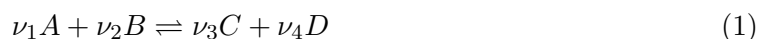
**KEYWORDS:** Dynamic Optimization, Batch Reactor Operation

## 1 INTRODUCTION AND INDUSTRIAL PRACTICE

Batch and semi-batch processes are of considerable importance to the fine chemicals and pharmaceutical industry. Since the production volumes are low, batch plants are typically *multi-product* facilities in which several different products share the same piece of equipment. With the recent trend in building small flexible plants that are close to the markets of consumption, there has been a renewed interest in batch processes (Biegler *et al.*, 1999).

A survey of industrial practice in the batch industry in the US was conducted recently (Palanki, 2002). The following characteristics were found to be common to a large number of batch industries:

- Most of the reactions are liquid phase reactions and while the final product is the result of several synthesis steps, each synthesis step is a new batch operation and typically requires different reactants and solvents and has different batch operating conditions. Some of these steps are done in the same equipment while others are done in different batch equipment.
- In each batch step, there is one chemical reaction of the type



- Most batch chemical reactors are operated at constant temperature and, if semi-batch, at constant feed rate of the reactant(s). The operating temperature and feed rate are determined *heuristically*, typically by doing a few laboratory experiments.
- A recipe, which consists of a series of time related steps, is followed in open-loop fashion at the industrial scale batch process.
- Batch-to-batch variation in product yield and quality is observed in a number of batch reactors.
- Some measurements, such as temperature, pH, viscosity and pressure are made on-line. Furthermore, periodic samples are taken for measuring concentration off-line. However, this data is typically used for determining if the batch is operating properly. This information is *not* used for making on-line adjustments to the operating strategy.

Similar characteristics of batch operation were found by surveys conducted by Hasabe and Hashimoto (1992) and Terweisch (1994). Most respondents indicated that they were interested in (i) reducing variability in product quality from batch to batch and (ii) increasing product yield in each batch. It was recognized that the open-loop strategy did not guarantee that the batch was being run optimally and could lead to substantial losses in product yield and quality over the course of several batch runs. Most respondents were interested in a methodology that would indicate what adjustments should be made on-line to achieve these objectives.

In this work, we develop a methodology for determining the optimal temperature and the optimal feeding policy for a semi-batch reactor in which a reaction of the form of eq. (1) is occurring. In section 2, the end-point optimization problem is formulated mathematically. The solution strategies available in the literature to solve this class of problems are briefly reviewed. In section 3, the solution of the end-point optimization problem is presented. It is shown that the optimal operating strategy depends on the structure of the reaction kinetics which strongly influence whether the optimal inputs should be at their constraints (upper or lower bounds) or should take a value in

the interior of their bounds. In section 4, the analytical expressions developed in section 3 are simplified for elementary irreversible and reversible reactions. In section 5, this methodology is illustrated via simulation of three semi-batch reactors. Finally, in section 6, the major conclusions of this study are summarized.

## 2 PRELIMINARIES

Batch processes are *transient* in nature; the process variables undergo significant changes during the batch cycle and there is no *steady state* (Palanki *et al.*, 1993). Unlike continuous processes, the major objective is not to keep the system at a given set-point but to follow a trajectory that results in the optimization of an objective such as yield or product quality at the *end* of the batch cycle. Such problems are called *end-point* optimization problems.

### 2.1 End-Point Optimization Problem Formulation

The end-point optimization problem for a semi-batch reactor, in which a reaction of the form of eq. (1) is occurring, can be mathematically stated as follows:

Minimize the objective function

$$J = \phi(C_A(t_f), C_B(t_f), C_C(t_f), C_D(t_f), V(t_f)) \quad (2)$$

subject to

$$\begin{aligned} \frac{dC_A}{dt} &= -r_A + (C_{AF} - C_A)\frac{F}{V} \\ \frac{dC_B}{dt} &= -\frac{\nu_2}{\nu_1}r_A + (C_{BF} - C_B)\frac{F}{V} \\ \frac{dC_C}{dt} &= \frac{\nu_3}{\nu_1}r_A - C_C\frac{F}{V} \\ \frac{dC_D}{dt} &= \frac{\nu_4}{\nu_1}r_A - C_D\frac{F}{V} \\ \frac{dV}{dt} &= u \end{aligned} \quad (3)$$

Here,  $C_A$ ,  $C_B$ ,  $C_C$ , and  $C_D$  are the concentrations of species  $A$ ,  $B$ ,  $C$ , and  $D$ ,  $V$  is the reactor volume,  $r_A$  is the rate of reaction with respect to the limiting species,  $A$ , and is a function of temperature as well as concentration of the reacting species. The reaction rate  $r_A$  is a function of temperature via the reaction rate constants which are assumed to follow the Arrhenius rate law with respect to temperature (Fogler, 1999):

$$k_i = k_{i0} \exp\left(-\frac{E_i}{RT}\right) \quad (4)$$

The feed concentrations of the reactants  $A$  and  $B$  are  $C_{AF}$  and  $C_{BF}$  respectively. The manipulated inputs to the batch reactor are the volumetric feed rate of reactants,  $F$ , and the temperature,  $T$ ,

at which the batch operates. The input constraints are given by:

$$\begin{aligned} F_{min} &\leq F \leq F_{max} \\ T_{min} &\leq T \leq T_{max} \end{aligned} \quad (5)$$

The state constraints are given by:

$$\begin{aligned} C_{Amin} &\leq C_A \leq C_{Amax} \\ C_{Bmin} &\leq C_B \leq C_{Bmax} \\ C_{Cmin} &\leq C_C \leq C_{Cmax} \\ C_{Dmin} &\leq C_D \leq C_{Dmax} \\ V_{min} &\leq V \leq V_{max} \end{aligned} \quad (6)$$

The initial concentrations of species  $A$  and  $B$  are given by  $C_{A0}$  and  $C_{B0}$  respectively and it is assumed that initially there is no  $C$  or  $D$  present in the reactor. It is assumed that the reactor temperature can be changed quickly via the use of a jacket around the reactor with a heat transfer fluid. The dynamics of the jacket are assumed to be fast as compared to the reactor which is typically the case for most industrial batch reactors. The problem considered in this paper computes the desired temperature profile in the reactor. Several methods are available in the literature (e.g. Xaumier *et al.*, 2002; Soroush and Kravaris, 1993) to compute the flow rate of the heat transfer fluid in the jacket to achieve this profile.

The end-point optimization problem represented by eq. (2) and eq. (3) is of the general form: Minimize the objective function

$$J = \phi(x(t_f)) \quad (7)$$

subject to

$$\begin{aligned} \dot{x} &= f(x, u) \\ x(0) &= x_0 \\ Pu - b &\leq 0 && (\text{input constraints}) \\ Qx - c &\leq 0 && (\text{state constraints}) \end{aligned} \quad (8)$$

where  $x$  is the state vector of dimension  $n$ ,  $u$  is the input vector of dimension  $m$ ,  $f$  is a smooth vector function of dimension  $n$ ,  $Pu - b \leq 0$  represent  $p$  input constraints and  $Qx - c \leq 0$  represent  $q$  state constraints.

## 2.2 Solution Strategies

General methods for solving optimization problems of the form of eq. (7) and eq. (8) were first developed for aerospace applications in the 1950s and 1960s (Bryson and Ho, 1975). Since then, there have been a plethora of papers in the application of these methods to specific case studies of end-point optimization problems in batch processes. Two different approaches have generally been used:

1. Direct Optimization Methods
2. Indirect Optimization Methods

These methods are briefly described below:

### 2.3 Direct Optimization Methods

In this class of methods, the inputs are parameterized by a finite set of parameters. The resulting system is then coupled with an optimization algorithm to find the optimal inputs. Depending on whether the dynamic equations (8) are integrated explicitly or implicitly, two different approaches have been reported in the literature, *i.e.* the *sequential* approach and the *simultaneous* approach respectively.

In the sequential approach, the optimization is carried out in the space of the input variables only. The differential equations (8) are integrated using standard integration algorithms to evaluate the objective function (7). This corresponds to a “feasible path” approach since the differential equations are satisfied at each step of the optimization algorithm. Typically, a piecewise constant approximation over equally spaced time intervals is made for the inputs and the method is referred to as Control Vector Parameterization (CVP) in the literature (Edgar and Himmelblau, 1988). This approach has been used in a variety of batch process applications (Vassiliadis *et al.*, 1994; Sorensen *et al.*, 1996; Mujtaba and Macchietto, 1997). While the sequential approach is straightforward to implement, it tends to be slow due to the fact that this feasible path method requires repeated and expensive solution of the differential equations. Furthermore, the quality of the solution is strongly dependent on the parameterization of the control profile (Logsdon and Biegler, 1989).

The most computationally intensive part of the sequential approach is the step where the dynamic equations are integrated accurately, even when the decision variables are far from the optimal solution. In the simultaneous approach, an approximation of the system equations is introduced in order to explicitly avoid integration of the dynamic equations. Thus, the optimization is carried out in the full space of discretized inputs and states. In general, the differential equations are satisfied only at the *solution* of the optimization problem (Vassiliadis *et al.*, 1994) and so this method is called the “infeasible path” approach. This approach has been used in several batch applications (Cuthrell and Biegler, 1989; Eaton and Rawlings, 1989; Ruppen *et al.*, 1995). In this approach there is a trade-off between approximation and optimization (Srinivasan *et al.*, 1995). It could turn out that a less accurate approximation of the integration gives a better cost. Thus, the solution obtained could correspond to an inadequate state approximation. Improvement of the integration accuracy requires either introducing accuracy as a constraint or increasing the number of collocation points. When the system is stiff, a very large number of decision variables is needed which leads to a large-scale optimization problem (Terwiesch, 1994).

Both the sequential as well as simultaneous approaches converge to a *local* optima. Determination of the global optimum is a non-trivial problem and from a practical perspective, one generally tries out a variety of initial conditions and picks out the solution with the best objective function as the global optimum. An alternative approach based on dynamic programming has been developed by Luus and Rosen (1991). In this approach, a piecewise constant control policy is found by employing dynamic programming in an iterative fashion using contraction of the region over which allowable values of the control are taken. This has been applied in a variety of batch applications (Luus, 1993a; Luus, 1993b). However, computational complexity increases substantially for this approach as the problem dimension becomes large (Bryson and Ho, 1975).

### 2.4 Indirect Optimization Methods

Using calculus of variations, the problem of minimizing a scalar cost function eq. (7) subject to the dynamic constraints eq. (8) can be reformulated as minimizing the Hamiltonian  $H$  which leads to

a class of indirect optimization methods (Bryson and Ho, 1975). This reformulation leads to the following Euler-Lagrange equations:

Minimize the Hamiltonian

$$H(x, \lambda, u) = \lambda^T f(x, u) + \mu_1^T (Pu - b) + \mu_2^T (Qx - c) \quad (9)$$

subject to:

$$\begin{aligned} \dot{x} &= f(x, u); & x(0) &= x_0 \\ \dot{\lambda}^T &= -\lambda^T \frac{\partial f}{\partial x} - \mu_2^T Q; & \lambda(t_f) &= \frac{\partial \phi}{\partial x} \Big|_{t=t_f} \end{aligned} \quad (10)$$

where  $\lambda(t) \neq 0$  is the  $n$ -vector of adjoint states and the vectors  $\mu_1$  and  $\mu_2$  are the Kuhn-Tucker parameters of dimension  $p$  and  $q$  respectively. When any constraint is active, the corresponding Lagrange multiplier is positive and when a constraint is not active, the corresponding Lagrange multiplier is equal to zero (Maurer, 1977; Gill *et al.*, 1981; Fletcher, 1991). Thus,  $\mu_1^T (Pu - b)$  and  $\mu_2^T (Qx - c)$  are always equal to zero. The necessary condition for optimality of  $H$  is given by the following  $m$  relations:

$$H_u = \lambda^T \frac{\partial f}{\partial u} + \mu_1^T P = 0 \quad (11)$$

which implies that  $x$ ,  $u$ ,  $\lambda$ ,  $\mu_1$  and  $\mu_2$  exist such that the following expressions hold:

$$\begin{aligned} \dot{x} &= f(x, u) \\ x(0) &= x_0 \\ \dot{\lambda}^T &= -\lambda^T \frac{\partial f}{\partial x} - \mu_2^T Q \\ \lambda(t_f) &= \frac{\partial \phi}{\partial x} \Big|_{t=t_f} \\ \lambda^T \frac{\partial f}{\partial u} + \mu_1^T P &= 0 \\ \mu_1^T (Pu - b) &= 0 \\ \mu_2^T (Qx - c) &= 0 \\ \mu_1 &\geq 0 \\ \mu_2 &\geq 0 \end{aligned} \quad (12)$$

The formulation represented by eq. (12) provides an indirect method for solving for the optimal inputs. One can see that to solve eq. (12) for the optimal inputs  $u_i$ , one needs to integrate the state equations ( $\dot{x} = f(x, u)$ ) forward in time and the adjoint equations ( $\dot{\lambda}^T = -\lambda^T \frac{\partial f}{\partial x} - \mu_2^T Q$ ) backwards in time. Thus, a *two-point* boundary value problem needs to be solved numerically for the inputs  $u_i$ . A variety of numerical methods have been utilized for solving this two point boundary value problem. For instance, the shooting method was utilized for the optimization of batch polymerization (Hicks *et al.*, 1969; Chen and Jeng, 1978), and for determining the optimal operating policy in batch antibiotic fermentation (Lim *et al.*, 1986; Parulekar, 1992).

There are several difficulties associated with the numerical solution of the problem formulated via the variational approach. In the shooting method, the initial conditions of the adjoint states are guessed and both the system state equations and the adjoint state equations are integrated forward in time. The values of the adjoint states obtained at the final time are compared with the known terminal conditions of the adjoint states. The initial conditions of the adjoints states are iteratively updated till the terminal conditions of the adjoint states match. However, this method can have stability problems when the adjoint equations are integrated forwards in time.

Furthermore, unless good initial guesses for the adjoint states are available (which is rarely the case), it is computationally expensive to find the optimal solution. The gradient method is slow to converge close to the optimum and a large number of decision variables may be necessary to parameterize the inputs. The solution via the variational approach depends on *necessary* conditions of optimality. These are *sufficient* conditions of optimality only when the objective function is convex and the dynamic and static constraints are linear. In most practical situations, it is uncertain if the solution that satisfies the necessary conditions of optimality is a local or a global optimum and one resorts to heuristic arguments to determine if the nature of the local optimum.

### 3 COMPUTATION OF OPTIMAL OPERATING POLICY

It is seen from the previous section that while the *formulation* of the end-point optimization problem is straight-forward, the numerical calculation of the optimal inputs is a difficult computational problem. In this section, the solution *structure* of the end-point optimization problem represented by eq. (2) and eq. (3) is analyzed. It is shown that the optimal solution can be divided into several time intervals depending on the values taken by the input vector. In some time intervals, the input vector is on its constraint values while in other time intervals it is in the interior of its constraints. While the optimal solution is in general discontinuous, the solution in *each* interval is analytic. Expressions in the form of state feedback will be derived for the inputs in each interval. These analytical expressions can be used to develop an efficient parameterization of the input to compute the optimal solution by iterating on the switching times.

#### 3.1 Model Reduction

The concentrations  $C_B$ ,  $C_C$  and  $C_D$  can be written in terms of the concentration  $C_A$  and volume  $V$  as follows:

$$\begin{aligned}
 C_B &= \frac{\frac{\nu_2}{\nu_1}(C_A \cdot V - C_{A0} \cdot V_0)}{V} \\
 &\quad + \frac{(\frac{\nu_2}{\nu_1}C_{AF} - C_{BF})(V_0 - V)}{V} + \frac{C_{B0} \cdot V_0}{V} \\
 C_C &= \frac{\frac{\nu_3}{\nu_1}C_{AF}(V - V_0) + \frac{\nu_3}{\nu_1}C_{A0} \cdot V_0 - \frac{\nu_3}{\nu_1}C_A \cdot V}{V} \\
 C_D &= \frac{\frac{\nu_4}{\nu_1}C_{AF}(V - V_0) + \frac{\nu_4}{\nu_1}C_{A0} \cdot V_0 - \frac{\nu_4}{\nu_1}C_A \cdot V}{V}
 \end{aligned} \tag{13}$$

Thus, there are only two independent variables,  $C_A$  and  $V$ . Defining

$$\begin{aligned}
 x_1 &= C_A \cdot V \\
 x_2 &= V
 \end{aligned} \tag{14}$$

the system represented by eq. (2) and eq. (3) can be written as follows:

Minimize the function

$$J = \phi(x_1(t_f), x_2(t_f)) \tag{15}$$

subject to the dynamic constraints:

$$\frac{d}{dt} \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} -r'_A(x_1, x_2, T) \cdot x_2 + C_{AF}F \\ F \end{bmatrix} \tag{16}$$

The input constraints are represented as:

$$\begin{bmatrix} -1 & 0 \\ 1 & 0 \\ 0 & -1 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} F \\ T \end{bmatrix} - \begin{bmatrix} -F_{min} \\ F_{max} \\ -T_{min} \\ T_{max} \end{bmatrix} \leq \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \quad (17)$$

and the state constraints are represented by:

$$\begin{bmatrix} -1 & 0 \\ 1 & 0 \\ 0 & -1 \\ 0 & 1 \end{bmatrix} \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} - \begin{bmatrix} -x_{1min} \\ x_{1max} \\ -x_{2min} \\ x_{2max} \end{bmatrix} \leq \begin{bmatrix} 0 \\ 0 \\ 0 \\ 0 \end{bmatrix} \quad (18)$$

where  $r'_A$  is the reaction rate with respect to species  $A$  written in terms of the new variables  $x_1$  and  $x_2$ . The objective is to find the optimal volumetric feed rate,  $F$ , and the optimal temperature,  $T$ , that optimizes the objective function given by eq. (15).

### 3.2 Development of Analytical Expressions

The optimal solution can be divided into the following types of intervals:

1. Solution in the interior of the static constraints
2. Solution on a static constraint

We first develop analytical expressions for the optimal feed rate and the optimal temperature in the *interior* of state and input constraints. Then we will consider the effect of constraints.

#### Solution in the interior of the static constraints

**Theorem 1:** For the optimization problem posed by eq. (15) and eq. (16), in the absence of state and input constraints, the optimal feed rate,  $u$ , takes a value in the interior of the constraints such that the dynamic system represented by eq. (16) stays on a surface  $L$  described by:

$$L(x_1, x_2) = C_{AF}x_2 \frac{\partial r'_A}{\partial x_1} + r'_A + x_2 \frac{\partial r'_A}{\partial x_2} = 0 \quad (19)$$

The optimal temperature,  $T$ , is in the interior of the constraints and can be calculated from:

$$\frac{\partial r'_A}{\partial T} = 0 \quad (20)$$

**Proof:** Application of calculus of variations to eq. (15) and eq. (16) results in the minimization of the Hamiltonian:

$$H = \lambda_1(-r'_A x_2 + C_{AF}F) + \lambda_2 F \quad (21)$$

subject to

$$\frac{d}{dt} \begin{bmatrix} x_1 \\ x_2 \end{bmatrix} = \begin{bmatrix} -r'_A(x_1, x_2, T) \cdot x_2 + C_{AF}F \\ u \end{bmatrix} \quad (22)$$

with

$$\begin{bmatrix} x_1(0) \\ x_2(0) \end{bmatrix} = \begin{bmatrix} x_{10} \\ x_{20} \end{bmatrix} \quad (23)$$

and

$$\frac{d}{dt} \begin{bmatrix} \lambda_1 \\ \lambda_2 \end{bmatrix} = \begin{bmatrix} \lambda_1 x_2 \frac{\partial r'_A}{\partial x_1} \\ \lambda_1 r'_A + \lambda_1 x_2 \frac{\partial r'_A}{\partial x_2} \end{bmatrix} \quad (24)$$

with

$$\begin{bmatrix} \lambda_1(t_f) \\ \lambda_2(t_f) \end{bmatrix} = \begin{bmatrix} \frac{\partial \phi}{\partial x_1} |_{t=t_f} \\ \frac{\partial \phi}{\partial x_2} |_{t=t_f} \end{bmatrix} \quad (25)$$

In the absence of constraints, the first order necessary condition for optimality with respect to  $F$  is

$$H_F = \lambda_1 C_{AF} + \lambda_2 = 0 \quad (26)$$

Since eq. (26) is independent of  $F$ , we differentiate eq. (26) once with respect to time and equate it to zero. This results in

$$\lambda_1 (C_{AF} x_2 \frac{\partial r'_A}{\partial x_1} + r'_A + x_2 \frac{\partial r'_A}{\partial x_2}) = 0 \quad (27)$$

Since  $\lambda_1 \neq 0$ , we have

$$C_{AF} x_2 \frac{\partial r'_A}{\partial x_1} + r'_A + x_2 \frac{\partial r'_A}{\partial x_2} = 0 \quad (28)$$

which is the same as eq. (19). This implies that when the input and state constraints are not active, the input  $u$  takes a value that keeps the system on the surface described by eq. (28).

In the absence of constraints, the first order necessary condition with respect to  $T$  is

$$H_T = -\lambda_1 x_2 \frac{\partial r'_A}{\partial T} = 0 \quad (29)$$

Since  $\lambda_1 \neq 0$ , we have

$$\frac{\partial r'_A}{\partial T} = 0 \quad (30)$$

This implies that when the input and state constraints are not active, the input  $T$  takes a value is obtained from the state feedback eq. (30).  $\diamond$

If we differentiate the surface described by eq. (19) with respect to time, we get an expression which is a function of  $F$ . Thus, the problem of keeping system (16) on the surface represented by eq. (19) is a regulation problem has a relative degree of one (Isidori, 1989). This is a standard regulation problem for which there are a variety of controller design methods (Isidori, 1989). Note that if one takes the jacket dynamics into account, the computation of the flow rate in the jacket is a regulation problem of relative degree two.

### Solution on a static constraint

There are two types of static constraints in this problem: (1) input constraints and (2) state constraints. If the input,  $F$ , is on its constraint value for part of the optimal solution, then  $F = F_{min}$  or  $F = F_{max}$ . If the input,  $T$ , is on its constraint value for part of the optimal solution, then  $T = T_{min}$  or  $T = T_{max}$ .

The problem formulation represented by eq. (15) - eq. (18) indicates that there are two independent states:  $x_1$ , the amount of species  $A$  and  $x_2$ , the reactor volume. If state constraints are active for part of the optimal solution, there are two possible cases:

1. One state constraint is active while the other is inactive
2. Both state constraints are active

#### One state constraint is active

Suppose the volume constraint is active ( $x_2 = x_{2min}$  or  $x_2 = x_{2max}$ ). Clearly, this indicates that the optimal flow rate has to be zero to enforce this constraint. The optimal temperature is in the interior of the constraints and can be calculated from eq. (20).

Suppose the volume constraint is not active but  $x_1$ , the amount of species  $A$ , is at a constraint. Thus

$$x_1 = c \quad (31)$$

where  $c = x_{1min}$  or  $c = x_{1max}$ . Taking the time derivative of eq. (31) and substituting eq. (16), we get:

$$-r'_A(c, x_2, T).x_2 + C_{AF}F = 0 \quad (32)$$

Expression (32) provides an algebraic relation between the inputs,  $u$  and  $T$ , and the volume,  $x_2$ . Furthermore, expression (20) provides a relation between the input  $T$  and the volume  $x_2$ . The optimal inputs may be computed by solving these equations simultaneously and utilizing the equation  $u = \frac{dx_2}{dt}$ . If this leads to an infeasible solution, clearly the optimal solution cannot have one active state constraint.

#### Both state constraints are active

In this situation, both inputs are utilized to keep the two states on their constraint values. For instance,  $x_2 = x_{2min}$  or  $x_2 = x_{2max}$  clearly indicates that  $u = 0$ . In addition, if  $x_1 = x_{1min}$  or  $x_1 = x_{1max}$  then differentiating this constraint equation with respect to time results in

$$r'_A(x_1, x_2, T) = 0 \quad (33)$$

The above algebraic expression can be solved for  $T$  as a function of the states  $x_1$  and  $x_2$ . Since the states are on their constraint values, the optimal input  $T$  can be easily computed.

## 4 SPECIAL CASES

Note that the analytical expressions developed in the previous section do not depend on the objective function  $J$ . Thus, the above results provide analytical expressions for the inputs in all possible

intervals that *might* occur rather than the intervals that *actually* occur in a specific application. Physical compromises and tradeoffs *intrinsic* to the system result in inputs at values in the interior of their constraint values. In this section the *structure* of the optimal solution, when the reaction involved is elementary in nature, is analyzed. It is shown that the optimal solution proposed by Theorem 1 can be simplified considerably. Both irreversible as well as reversible reactions are considered.

#### 4.1 Irreversible Elementary Reaction

If the reaction represented by eq. (1) is an irreversible elementary reaction, the reaction rate may be represented by:

$$r_A = kC_A^a C_B^b \quad (34)$$

where  $k$  is given by

$$k = k_0 \exp\left(-\frac{E}{RT}\right) \quad (35)$$

Theorem 2: For *elementary irreversible* reactions of the form of eq. (34), the optimal temperature is on its constraints. In addition, the optimal feed rate is given by

$$F = \frac{Vr_A}{C_{AF} - C_A} \quad (36)$$

when the surface expression given by eq. (28) is satisfied.

Proof: Substituting for  $C_A$  and  $C_B$  in terms of  $x_1$  and  $x_2$  by using eq. (13) and eq. (14) to get the expression for  $r'_A$  and then utilizing eq. (20), results in the following expression:

$$\frac{\partial k}{\partial T} = 0 \quad (37)$$

Substituting for  $k$  in terms of  $T$  from eq. (35):

$$\frac{E}{RT^2} k_0 \exp\left(-\frac{E}{RT}\right) = 0 \quad (38)$$

which implies that there is no  $T$  in the *interior* of  $T_{min}$  and  $T_{max}$  where eq. (38) is satisfied. This implies that the optimal temperature is on a constraint value.

If the reaction rate expression is of the form of (34), then the surface defined by eq. (19) results in:

$$C_A = \frac{a}{a+b-1} C_{AF} \quad (39)$$

To obtain the expression for optimal flow rate, eq. (39) can be differentiated once with respect to time. This results in the following

$$\frac{dC_A}{dt} = 0 \quad (40)$$

Combining eq. (3) and (40), expression (36) can be obtained for optimal flow rate of component A.

This implies that, in case of a semi-batch reactor with a single elementary irreversible reaction, the optimal flow rate is given by eq. (36) if the surface condition given by eq. (28) is satisfied, and the optimal flow rate is on a constraint ( $F_{min}$  or  $F_{max}$ ) if the condition given by equation (28) is violated.

The above theorem is significant in the sense that if we know *a priori* that the optimal solution is on the constraints, it significantly reduces the computational burden of calculating the optimal inputs.

## 4.2 Reversible Elementary Reaction

If the reaction represented by eq. (1) is a reversible elementary reaction, the reaction rate may be represented by:

$$r_A = k_1 C_A^a C_B^b - k_2 C_C^c C_D^d \quad (41)$$

where  $k_1$  and  $k_2$  are given by

$$k_1 = k_{10} \exp\left(-\frac{E_1}{RT}\right) \quad (42)$$

$$k_2 = k_{20} \exp\left(-\frac{E_2}{RT}\right) \quad (43)$$

Theorem 3: For elementary reversible reactions of the form of eq. (41), the optimal feed rate is given by:

$$F = V r_A \left[ \frac{ac_1 k_1 C_A^{a-1} C_B^b + \frac{b^2}{a} c_1 k_1 C_A^a C_B^{b-1} + \frac{c^2}{a} c_2 k_1 C_C^{c-1} C_D^d + \frac{d^2}{a} c_2 k_2 C_C^c C_D^{d-1}}{ac_1 k_1 C_A^{a-1} C_B^b C_{AF} - ac_1 k_1 C_A^a C_B^b - bc_1 k_1 C_A^a C_B^b + cc_2 k_2 C_C^c C_D^d + dc_2 k_2 C_C^c C_D^d} \right] \quad (44)$$

In addition, the optimal temperature is given by:

$$T = \frac{E_1 - E_2}{R \left( \ln \left[ \frac{k_{10} E_1 C_A^a C_B^b}{k_{20} E_2 C_C^c C_D^d} \right] \right)} \quad (45)$$

Proof: If the rate expression is of the form given by eq. (41), the surface given by eq. (19) results in

$$(a + b - a C_{AF} - 1) \cdot k_1 C_A^a C_B^b = (c + d - 1) \cdot k_2 C_C^c C_D^d \quad (46)$$

To obtain the expression for optimal flow rate, the above equation can be differentiated once with respect to time. This results in the following:

$$c_1 k_1 \left[ a C_A^{a-1} C_B^b \frac{dC_A}{dt} + b C_A^a C_B^{b-1} \frac{dC_B}{dt} \right] - c_2 k_2 \left[ c C_C^{c-1} C_D^d \frac{dC_C}{dt} + d C_C^c C_D^{d-1} \frac{dC_D}{dt} \right] = 0 \quad (47)$$

where  $c_1$  and  $c_2$  are constants defined as follows:

$$c_1 = a + b - a C_{AF} - 1 \quad (48)$$

$$c_2 = c + d - 1 \quad (49)$$

Combining eq. (3) with the above equations, expression (44) can be obtained for flow rate of component  $A$ . This implies that, in case of a semi-batch reactor with single elementary reversible reaction, the optimal flow rate is given by eq. (44) if the corresponding surface condition is satisfied, and the optimal flow rate is on a constraint ( $F_{min}$  or  $F_{max}$ ) if the surface condition is violated.

The necessary condition for optimal temperature can be found out similarly by using eq. (41) through (43) in eq. (37).

This implies that the unconstrained optimal temperature for a single elementary reversible reaction is given by eq. (45). When the temperature value given by this expression is not in the interior of the temperature constraint values, the optimal temperature will be on the constraint ( $T_{min}$  or  $T_{max}$ ).

### 4.3 Implementation Issues

In the previous section, it was shown that the optimal input profile consists of two types of time intervals, *i.e.*, time intervals where the inputs are on their constraints and time intervals where the inputs take values between their bounds for which analytical expressions are available in terms of the system states. For the end-point optimization problem described by eq. (15) and eq. (16), the optimal flow rate starts with  $F$  at a constraint value,  $F_{min}$  or  $F_{max}$ . The flow rate switches to a value between the upper and lower constraints when the system states satisfy the surface condition given by eq. (19). This flow rate continues till the reactor is full (*i.e.* the volume constraint is hit) or until the system hits another state constraint (*e.g.* a maximum concentration) and the reactor operates in batch mode till the final time is reached. The optimal temperature profile is on a constraint if eq. (20) results in a temperature that is greater than  $T_{max}$  or less than  $T_{min}$ . Otherwise, eq. (20) determines the optimal temperature profile. Thus, the *structure* of the optimal solution (sequence of time intervals) is known *a priori*. To compute the switching times for the optimal flow rate, it may be necessary to do numerical iteration where the switching times are guessed and iteratively refined till there is no further improvement in the objective function.

In the calculation of the analytical expressions (19) and (20), the objective function represented by eq. (15) does not appear. Thus, the solution is actually optimal for a whole *class* of objective functions. Furthermore, the expressions (19) and (20) are developed using necessary (rather than sufficient) conditions of optimality. Whether the solution is actually optimal for a particular objective function is typically found via heuristic arguments. For instance whether the objective is to *minimize* the product or *maximize* the product, the flow rate calculated from the analytical expression given by eq. (19) is the same. However, it is intuitively obvious that the flow rate that *minimizes* the product amount would be if the reactant flow is on the lower constraint ( $F_{min} = 0$ ).

The optimization approach described in this section depends on an accurate model of the process. In reality, there will be uncertainties in model parameters as well as variations in initial conditions from batch to batch. In this situation, open-loop implementation of the optimal strategy will lead to sub-optimal performance. On-line measurements taken during the batch process can be effectively used to adjust the operating strategy under the presence of uncertainty. In measurement-based optimization method, several state variables of the process are measured on-line. The measurements are incorporated into the analytical expressions represented by eq. (19) and eq. (20) and new input profiles are computed. The updated input profiles obtained from the optimization algorithm are then sent to the actual process in closed-loop. The procedure for this strategy is given below:

1. Find the solution of optimization problem using the process model with nominal parameters.

2. Implement the nominal solution on the process for a portion of the batch time.
3. Measure the state variables from the process on-line.
4. Compute new values of the inputs  $F$  and  $T$  by utilizing the measurement values in expressions (19) and (20).
5. Implement the resulting input profiles on the process.
6. Go to step 3 and repeat the process until the final time is reached.

## 5 ILLUSTRATIVE EXAMPLES

In this section, the methodology described in this work is illustrated via simulation of several batch reactor examples.

### 5.1 Example 1

Methyl acetate synthesis by esterification of acetic acid with methanol and the backward reaction, the hydrolysis of methyl acetate is considered.



This is an elementary reversible reaction and the reaction rate is given by Yu *et al.*, [2004]:

$$r_A = k_{10} \exp \left[ -\frac{E_1}{RT} \right] C_A C_B - k_{20} \exp \left[ -\frac{E_2}{RT} \right] C_C C_D \quad (51)$$

where

$$\begin{aligned} A &: CH_3COOH \\ B &: CH_3OH \\ C &: CH_3COOCH_3 \\ D &: H_2O \end{aligned}$$

The reaction parameters and conditions are included in Table 1. The objective of the optimization problem is to find the acetic acid feeding policy that corresponds to the maximum amount of methyl acetate produced inside the reactor.

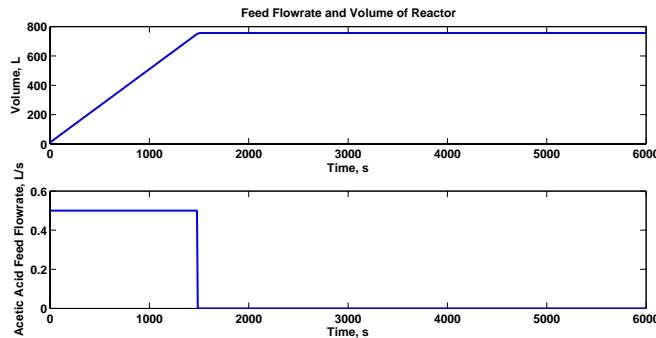
The condition for optimal flow rate in the interior to the constraints is given by eq. (44) which simplifies to  $k_2 C_c C_d = 0$ . Clearly, this condition is infeasible, indicating that the optimal flow rate of acetic acid is always on a constraint for this example. Hence, acetic acid is fed to the reactor at maximum flow rate until it hits the volume constraint after 1475 s, and after this time, the flow rate is reduced to zero. The optimal flow rate and volume of the reactor are given in Figure 1. One can see from Figure 1 that the volume of the reactor hits the maximum bound of 750 after 1475 s and the flow rate of acetic acid is cut to zero in order to maintain the reactor volume on the maximum bound.

In addition, one can make use of eq. (45) to determine the optimal reaction temperature corresponding to the optimal solution in the interior of the constraints. If eq. (45) results in a temperature that is in the interior of temperature constraints, that temperature corresponds to

Table 1: Reaction Parameters and Conditions for Example 1

Parameter	Value	Units
Minimum temperature ( $T_{Min}$ )	325	$K$
Maximum temperature ( $T_{Max}$ )	373	$K$
Simulation time $t$	6000	$s$
Frequency factor for forward reaction $k_10$	$1.29 \times 10^4$	$(L/mol.s)$
Frequency factor for backward reaction $k_20$	$8.82 \times 10^3$	$(L/mol.s)$
Activation energy for forward reaction $E_1$	$44.3 \times 10^3$	$(J/mol)$
Activation energy for backward reaction $E_2$	$50.3 \times 10^3$	$(J/mol)$
Concentration of acetic acid in feed $C_{AF}$	1	$(mol/L)$
Initial reactor volume $V_0$	10	$L$
Initial concentration of A in the reactor ( $C_{A0}$ )	0	$(mol/L)$
Initial concentration of B in the reactor ( $C_{B0}$ )	10	$(mol/L)$
Initial concentration of C in the reactor ( $C_{C0}$ )	0	$(mol/L)$
Initial concentration of D in the reactor ( $C_{D0}$ )	0	$(mol/L)$
Maximum volumetric flow rate of feed ( $F_{0,Max}$ )	0.5	$(L/s)$
Minimum volumetric flow rate of feed ( $F_{0,Min}$ )	0	$(L/s)$
Maximum reactor volume ( $V_{Max}$ )	750	$L$

Figure 1: Optimal Flowrate of Reactant



optimal temperature. If at any time, the temperature resulting from eq. (45) is not in the interior of temperature constraints, it indicates that the optimal temperature is on the constraint. The optimal temperature profile corresponding to the esterification example considered is shown in Figure 2. The amount of methyl acetate obtained by maintaining the temperature profile given in Figure 2 and the flow rate profile given in Figure 1 is 98.3 mol. The concentration profiles of reactants and products corresponding to these optimal inputs are shown in Figure 3.

## 5.2 Example 2

The production of baker's yeast in a fed-batch reactor is considered. The reaction is of the type  $X \rightarrow S$  and the dynamic model and parameters for this example are obtained from Menawat *et al.* [1987]. The dynamic model for fed-batch reactor consists of the material balance on the biomass  $X$ , substrate  $S$ , and the overall volume  $V$  of the system. This model is equivalent to the reaction

Figure 2: Optimal Temperature Profile

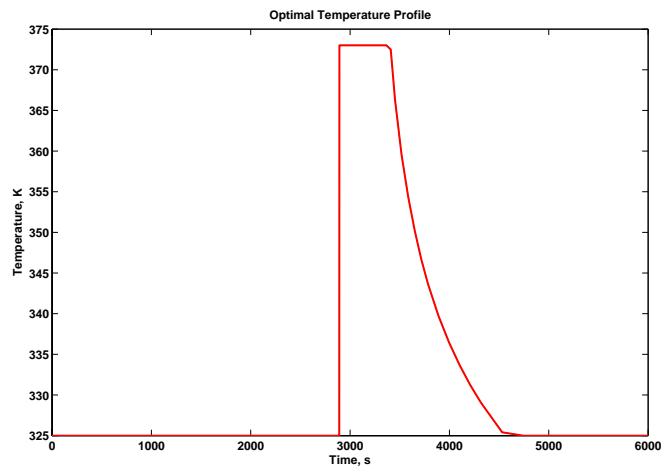
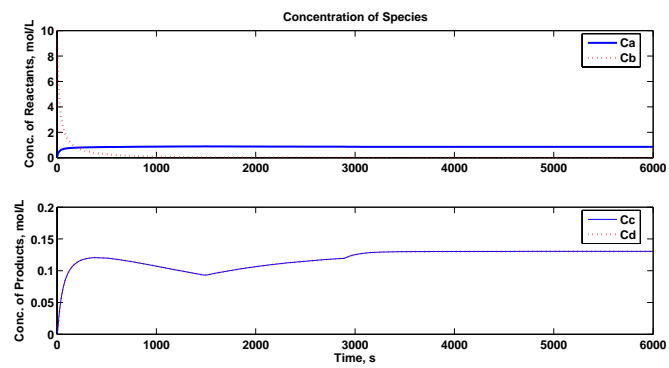


Figure 3: Concentration of Reactants and Products



$S \rightarrow X$ . If we define  $x_1$  as the amount of substrate and  $x_2$  as the reactor volume, the model developed by Menawat *et al.* [1987] can be reduced to the following equations:

$$\begin{aligned}\frac{dx_1}{dt} &= -\mu x_2 + C_{SF}F \\ \frac{dx_2}{dt} &= F\end{aligned}\quad (52)$$

The substrate concentration  $S$  is given by

$$S = \frac{x_1}{x_2} \quad (53)$$

Furthermore, the biomass  $X$  can be computed from the following algebraic expression:

$$X = Y_{X/S} \left[ \frac{V_0}{x_2} S_0 - \frac{x_1}{x_2} + C_{SF} - \frac{V_0}{x_2} C_{SF} + \frac{V_0}{x_2} \cdot \frac{X_0}{Y_{X/S}} \right] \quad (54)$$

and

$$\mu = \frac{\mu_m k_2 S X}{Y_{X/S} \cdot (S^2 + (k_1 + k_2)S + k_1 k_2)} \quad (55)$$

The description and numerical values of model parameters and initial conditions are given in Table 2. The objective of optimization is to find the substrate feeding policy that corresponds to the maximum amount of biomass at the end of the batch reaction.

The necessary condition for optimal substrate flow rate, equivalent to eq. (19), is

$$C_{SF} x_2 \frac{\partial \mu}{\partial x_1} + \mu + x_2 \frac{\partial \mu}{\partial x_2} = 0 \quad (56)$$

When the appropriate expressions are substituted for each term of the above equation, the following surface equation is obtained for the bio-reactor.

$$X S^3 - C_{SF} X S^2 - k_1 k_2 X S + C_{SF} k_1 k_2 X = 0 \quad (57)$$

The only feasible solution to the surface condition given by eq. (57) is

$$S = \sqrt{k_1 k_2} \quad (58)$$

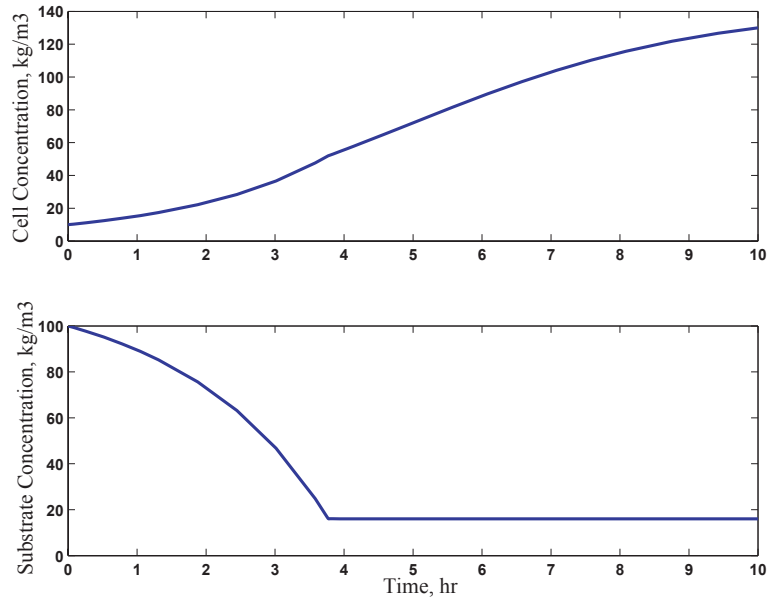
This is consistent with the results obtained by Menawat *et al.*, [1987]. To obtain the expression for optimal flow rate, eq. (58) can be differentiated once with respect to time. Simplification of the expression obtained results in the following expression for optimal flow rate of substrate.

$$F = \frac{\mu X V}{Y_{X/S} (C_{AF} - S)} \quad (59)$$

This implies that, for the fed-batch reactor considered, the optimal flow rate is given by eq. (59) if the surface condition given by eq. (58) is satisfied, and the optimal flow rate is on a constraint ( $F_{min}$  or  $F_{max}$ ) if the condition given by eq. (58) is violated.

Simulations are conducted using the parameters and reaction conditions given in Table 2. It can be seen that the condition given by eq. (58) corresponds to a substrate concentration of  $15.81 \text{ kg/m}^3$ . Since the initial substrate concentration inside the reactor is  $100 \text{ kg/m}^3$ , no substrate is fed until

Figure 4: Substrate and Biomass Concentrations



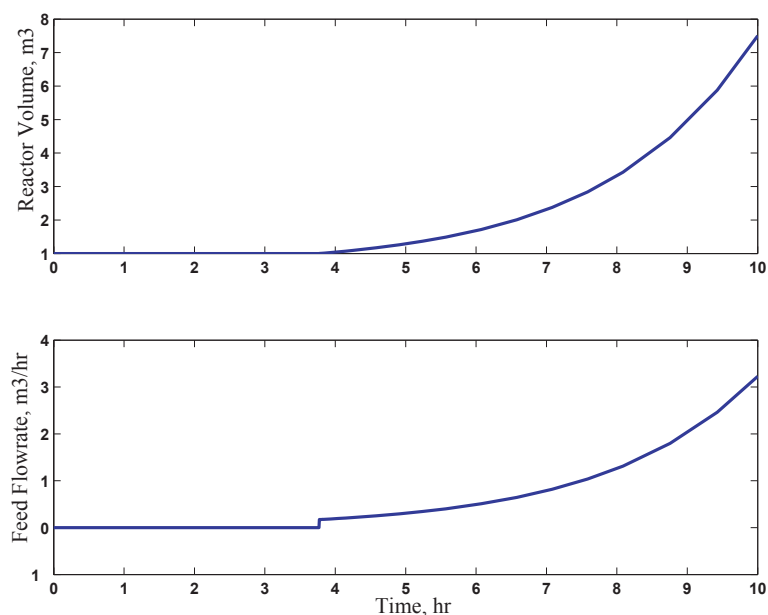
the substrate concentration inside the reactor drops to  $15.81 \text{ kg/m}^3$  after  $3.8 \text{ h}$ . At this point, the substrate feed rate is adjusted according to eq. (59) to maintain the substrate concentration at  $15.81 \text{ kg/m}^3$ . It can be seen from Figure 4 that the substrate concentration remains constant at  $15.81 \text{ kg/m}^3$  after  $3.8 \text{ h}$  while the cell mass concentration continues to increase. The input profile used to maintain the substrate concentration and the corresponding increase in the reactor volume are shown in Figure 5.

The effect of uncertainty in  $k_2$  is summarized in Table 3. The simulation set in which the parameter  $k_2$  is at its nominal value (no uncertainty) is indicated in bold font. The maximum deviation from the optimal solution is 40% which indicates that the uncertainty in the parameter  $k_2$  has a significant effect on the accuracy of the optimal solution. Thus, open-loop implementation in the presence of uncertainty in  $k_2$  could lead to significant loss in product (and hence profit).

Table 2: Reaction Conditions for Example 2

Parameter	Value	Units
Simulation time $t$	10	$h$
Specific growth rate ( $\mu_m$ )	0.5	$(h^{-1})$
Haldane-Monod parameter $k_1$	0.5	$(\text{kg}/\text{m}^3)$
Haldane-Monod parameter $k_2$	500	$(\text{kg}/\text{m}^3)$
Yield coefficient ( $Y_{XS}$ )	0.5	$(\text{kgcell}/\text{kgsubstrate})$
Concentration of substrate in feed ( $C_{SF}$ )	300	$(\text{kg}/\text{m}^3)$
Initial reactor volume $V_0$	1	$\text{m}^3$
Initial concentration of substrate ( $C_{S0}$ )	100	$(\text{kg}/\text{m}^3)$
Initial concentration of cell mass ( $C_{X0}$ )	10	$(\text{kg}/\text{m}^3)$
Maximum reactor volume ( $V_{Max}$ )	10	$\text{m}^3$

Figure 5: Optimal Flowrate and Volume



The measurement-based optimization strategy is applied to the baker's yeast fermentation problem. In this simulation study, the measured variable is the concentration of substrate. This algorithm is implemented for the fermentation for various extents of uncertainty in the parameter  $k_2$ . The results are summarized in Table 4. The second column of the table indicates the substrate concentration in the reactor at the switching time,  $t_{switch}$ . It should be noted that the switching time for all the runs is the same. The percentage deviation of the amount obtained in closed-loop from the optimal solution is zero for all extents of uncertainty, indicating that the measurement-based optimization handles the uncertainty in the parameter  $k_2$  effectively.

## 6 CONCLUSIONS

In this paper, the structure of the optimal solution for the end-point optimization in a semi-batch reactor with a single reaction is analyzed. It is shown that the optimal solution can be divided into different intervals depending on whether the static constraints are active or not. In each interval, the optimal solution can be computed analytically. Parametric uncertainty is handled via closed-loop implementation of the optimal strategy. This methodology is illustrated via two simulation examples.

## ACKNOWLEDGMENTS

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Table 3. Effect of Uncertainty in  $k_2$  on Nominal Solution

Uncertainty		$S \sqrt{k_1 k_2}$ (kg/m <sup>3</sup> )		t_switch (hr)		Objective J (kg of Biomass)		% Deviation
%	$k_2$	Open-Loop	Optimal	Open-Loop	Optimal	Open-Loop	Optimal	
+50	750	15.81	19.36	3.77	3.55	1001.5	1082.5	7
+40	700	15.81	18.71	3.77	3.58	1000.8	1065.8	6
+30	650	15.81	18.03	3.77	3.62	1000.0	1048.7	5
+20	600	15.81	17.32	3.77	3.67	996.8	1025.4	3
+10	550	15.81	16.58	3.77	3.72	989.9	1002.9	1
<b>0</b>	<b>500</b>	<b>15.81</b>	<b>15.81</b>	<b>3.77</b>	<b>3.77</b>	<b>973.4</b>	<b>973.4</b>	<b>0</b>
-10	450	15.81	15.00	3.77	3.84	923.6	945.1	2
-20	400	15.81	14.14	3.77	3.92	836.6	907.1	8
-30	350	15.81	13.23	3.77	4.02	717.2	858.3	16
-40	300	15.81	12.25	3.77	4.15	575.6	802.5	28
-50	250	15.81	11.18	3.77	4.33	430.5	735.8	41

Table 4. Effect of Uncertainty in  $k_2$  on Closed-Loop Optimization

Uncertainty		$S \sqrt{k_1 k_2}$ (kg/m <sup>3</sup> )		t_switch (hr)		Objective J (kg of Biomass)		% Deviation
%	$k_2$	Closed loop	Optimal	Closed loop	Optimal	Closed loop	Optimal	
+50	750	15.81	19.36	3.77	3.55	1080.1	1082.5	0
+40	700	15.81	18.71	3.77	3.58	1064.2	1065.8	0
+30	650	15.81	18.03	3.77	3.62	1044.1	1048.7	0
+20	600	15.81	17.32	3.77	3.67	1026.1	1027.4	0
+10	550	15.81	16.58	3.77	3.72	998.1	1002.9	0
<b>0</b>	<b>500</b>	<b>15.81</b>	<b>15.81</b>	<b>3.77</b>	<b>3.77</b>	<b>973.4</b>	<b>973.4</b>	<b>0</b>
-10	450	15.81	15.00	3.77	3.84	940.4	945.1	0
-20	400	15.81	14.14	3.77	3.92	902.8	907.1	0
-30	350	15.81	13.23	3.77	4.02	858.1	858.3	0
-40	300	15.81	12.25	3.77	4.15	800.7	802.5	0
-50	250	15.81	11.18	3.77	4.33	731.2	735.8	0

## References

- [1] Biegler, L. T., Grossmann, I. E., and Westerburg, A. W., *Systematic Methods of Chemical Process Design*, Prentice-Hall PTR, Upper Saddle River, New Jersey 07458 (1999).
- [2] Bryson, A. E. and Ho, Y. C., *Applied Optimal Control*, Hemisphere, Washington DC, 1975.
- [3] Chen, S. A. and Jeng, W. F., "Minimum End Time Policies for Batchwise Radical Chain Polymerization," *Chem. Eng. Sci.*, **33**, 735-745 (1978).
- [4] Cuthrell, J. E. and Biegler, L. T., "Simultaneous-optimization and solution methods for batch reactor control profiles," *AIChE J.*, **13**, 49-62 (1989).
- [5] Eaton, J. W. and Rawlings, J. B., "Feedback-control of chemical processes using online optimization techniques," *Comp. Chem. Engng.*, **14**, 469-479 (1990).
- [6] Edgar, T. F. and Himmelblau, D. M., *Optimization of Chemical Processes*, McGraw-Hill, New York, 1988.
- [7] Fletcher, R., —em Practical Methods of Optimization, Wiley, Chichester, 1991.
- [8] Fogler, H. S., *Elements of Chemical Reaction Engineering*, 3rd ed., Prentice-Hall PTR, Upper Saddle River, New Jersey 07458, 1999.
- [9] Gill, P.E., Murray, W., and Wright, M.H., *Practical Optimization*, Academic Press, London, 1981.
- [10] Hasabe, S., and Hashimoto, I., "Present Status of Batch Process Systems Engineering in Japan," *NATO Adv. Studies Inst.*, Antalya, Turkey, 1992.
- [11] Hicks, J. and Mohan, A. and Ray, W. H., "The Optimal Control of Polymerization Reactors," *Can. J. Chem. Engng.*, **47**, 590-599 (1969).
- [12] Isidori, A., *Nonlinear Control Systems*, Springer-Verlag, Berlin, 1989.
- [13] Lim, H. C., Tayeb, Y. J., Modak, J. M. and Bonte, P., "Computational Algorithms for Optimal Feed Rates for a Class of Fed-Batch Fermentation: Numerical Results for Penicillin and Cell Mass Production," *Biotech. Bioengng.*, **28** (9), 1408-1420 (1986).
- [14] Logsdon, J. S. and Biegler, L. T., "Accurate solution of differential algebraic optimization problems," *Ind. Eng. Chem. Res.*, **28**(11), 1628-1639 (1989).
- [15] Luus, R., "Optimization of fed-batch fermenters by iterative dynamic-programming," *Biotech. Bioengng.*, **41**, 599-602 (1993a).
- [16] Luus, R., "Application of iterative dynamic-programming to very high-dimensional systems," *Hungarian J. Ind Chem.* 21(4), 243-250, (1993b)
- [17] Luus, R., and Rosen, O., "Application of dynamic-programming to final-state constrained optimal-control problems," *Ind. Eng. Chem. Res.*, **30**, 1525-1530(1991).
- [18] Maurer H., "On optimal control problems with bounded state variables and control appearing linearly," *SIAM J. Control Optimization*, **15**(3), 345-350 (1977).

- [19] Menawat, A., Mutharasan, R., and Coughanowr, D.R., "Singular Optimal Control Strategy for a Fed-Batch Bioreactor: Numerical approach, *AIChE Journal*, **33**(5), 776-783 (1987).
- [20] Mujtaba, I. M. and Macchietto, S., "Efficient optimization of batch distillation with chemical reaction using polynomial curve fitting techniques," *Ind. Eng. Chem. Res.*, **36**(6), 2287-2295 (1997).
- [21] Palanki, S., "Optimal Operation of Batch Reactors," in *Recent Developments in Optimization and Optimal Control in Chemical Engineering*, Ed. R. Luus, 37/661 (2), 179-193, Research Signpost, Trivandrum, 2002.
- [22] Palanki, S., Kravaris, C., and Wang, H. Y., "Synthesis of State Feedback Laws for End-Point Optimization in Batch Processes," *Chem. Eng. Sci.*, Vol. 48, No. 1, 135-152 (1993).
- [23] Parulekar, S. J., "Analytical optimization of some single-cycle and repeated fed-batch fermentations," *Chem. Eng. Sci.*, 47 (15-16), 4077-4097 (1992)
- [24] Ruppen, D., Benthack, C. and Bonvin, D., "Optimization of batch reactor operation under parametric uncertainty - Computational aspects," *J. Process Control*, **5**(4), 235-240 (1995).
- [25] Sorensen, E., Macchietto, S. and Stuart, G. and Skogestad, S., "Optimal control and on-line operation of reactive batch distillation," *Comp. Chem. Engng.*, **20**(12), 1491-1498 (1996).
- [26] Soroush, M., and Kravaris, C., "Optimal Design and Operation of Batch Reactors 2: A Case Study," *Ind. Eng. Chem. Res.*, 32 (5), 882-893 (1993).
- [27] Srinivasan, B., Myszkowski, P. and Bonvin, D., "A Multi-Criteria Approach to Dynamic Optimization," *Proc. ACC*, 3, 1767-1771 (1995).
- [28] Terwiesch, P., *Dynamic Optimization of Batch Process Operations with Imperfect Modeling*, Ph.D Thesis 10857, Swiss Federal Institute of Technology (ETHZ), Switzerland, 1994.
- [29] Vassiliadis, V. S., Sargent, R. W. H. and Pantelides, C. C., "Solution of a class of multistage dynamic optimization problems .1. Problems without path constraints," *Ind. Eng. Chem. Res.*, **33**(9), 2111-2122 (1994).
- [30] Xaumier, F., Le Lan, M., Cabassud, M., and Casamatta, G., "Experimental Application of Nonlinear Model Predictive Control: Temperature Control of an Industrial Semi-Batch Pilot-Plant Reactor," *J. Process Control*, 12, 6, 687-693 (2002)
- [31] Yu, W., Hidajat, K., and Ray, A.K., "Determination of adsorption and kinetic parameters for methyl acetate esterification and hydrolysis reaction catalyzed by Amberlyst 15", *Applied Catalysis A: General*, **260**, 2, 191-205 (2004).