NTNU
Norwegian University of
Science and Technology

PRODUCTION OPTIMIZATION OF CONTRAST AGENT SUBSTANCE

MODELING, DYNAMIC OPTIMIZATION & CONTROL

Master Thesis

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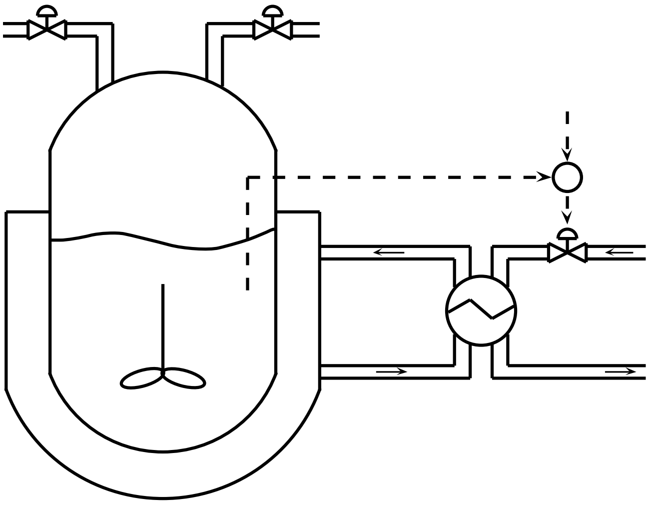
Author:
Henrik Tuvnes

Supervisors:
Professor Sigurd Skogestad
Phd fellow Håkon Dahl-Olsen



Norwegian University of Science and Technology
Department of Chemical Engineering

PROJECT DESCRIPTION

Motivation

The main substance for contrast agent synthesis is produced by GE Healthcare at Lindesnes in a line of batch process steps. Several of these sub-processes have to be optimized in order to maximize the throughput and economic gain of the process. This work will focus on the batch reactor step where the main substance for contrast agents is synthesized. It is believed that this batch reactor has potential for optimization, and it is desirable to increase the conversion and selectivity through maximized reactor utilization and optimal regulation.

Tasks

The work will include:

- A short literature study on dynamic optimization and control with focus on batch reactor processes.
- An industrial case study on the batch reactor step in the production line of contrast agent substance at GE Healthcare, including:
- Modeling of the process step using existing process information and measurements.
- Use the model developed for dynamic optimization. The optimization shall be made independent from current practice of running the process.
- Look at feedback control solutions for handling disturbances and process variability.
- Comments and discussion based on the results.

Assignment given: 30. January 2009

Supervisor: Professor Sigurd Skogestad (Department of Chemical Engineering)
Co-supervisor: PhD Fellow Håkon Dahl-Olsen (Department of Chemical Engineering)
External supervisor: Ole-Martin Hoyland (GE Healthcare AS, Lindesnes)

ABSTRACT

The main substance in GE Healthcares contrast agent production is produced at Lindesnes in a line of batch process steps. This thesis focuses on the batch reactor step where it is desirable to maximize the selectivity and conversion by maximized reactor utilization and optimal control.

In this thesis a model of the batch reactor step at Lindesnes was developed using existing process information, previous projects and general process insight. The model parameters were estimated from measurements of several batch runs. This model was used for dynamic optimization of the operating procedure, where the objective was to maximize the conversion and selectivity at the end of the batch run. A sensitivity analysis was made regarding model uncertainties and process disturbances. On-line feedback control as a strategy for handling these model uncertainties and disturbances was analyzed. The emphasis was on finding optimal variables to control.

The model obtained is considered to be a good representation of the batch reactor around the operating region where the data was obtained. It is argued that there is some uncertainty in the temperature dependency of the model, and that the model should be validated outside the region of operation from where it is obtained. From dynamic optimization it is shown that the batch reactor step has potential for improved performance by changing the operating procedure and conditions from what is done in current practice. Increased reactor temperature and an optimal reactant input profile throughout the batch can theoretically result in a 0.8 % increase in the yield and 23 % reduction in the amount of waste and main reactant at the end of the batch. The optimal achievable performance is considered to be most sensitive to model errors related to the temperature dependency.

If accurate on-line measurements can become available, simple on-line feedback control is a good alternative to re-optimization strategies for handling disturbances and process variability in this system. It is found that the pH in the solution should be controlled to maximum by addition of NaOH throughout the batch for optimal performance. And that the product (DROH) or the main reactant (D) are the optimal unconstrained variables for on-line feedback control. Controlling one of them to the optimal reference trajectory by input of the RCl reactant, yield a minimal loss from the truly optimal performance (when re-optimizing) for every disturbance considered.

PREFACE

This thesis took place at the Department of Chemical Engineering at NTNU in cooperation with GE Healthcare AS, Lindesnes.

I want to thank my supervisors Professor Sigurd Skogestad and Ph.D. fellow Håkon Dahl-Olsen for guidance, support and motivation during this work.

I also want to thank Professor Magne Hillestad for giving me a flying start with process data gathering and modeling issues. Ole Martin Hoyland at GE Healthcare is also acknowledge for being readily available for questions and discussions.

A special thanks is given to the guys at the cybernetics office for discussions and good times.

Declaration of Compliance

I hereby declare that this is an independent work in compliance with the exam regulations of the Norwegian University of Science and Technology.

Signature:

June 25, 2009

CONTENTS

LIST OF FIGURES

NOMENCLATURE

$\rightharpoonup$	Irreversible reaction
$\bar{\ }$	Average value of a variable
$\rightleftharpoons$	Equilibrium reaction
σ	Standard deviation of a variable
θ_i	Estimated model parameter i
$^{\text{meas}}$	Measured value from data
$^{\text{ref}}$	Reference value
$^{\text{set}}$	Set point
$^{\text{sim}}$	Simulated value
$^{\text{tot}}$	Total (e.g. total mass m^{tot})
$C_{i,0}$	Initial concentration of species i, [kmol/m^3]
C_i	Concentration of species i, [kmol/m^3]
G_i	Measurement gain
J	Objective function
$J_{\text{opt}}(d)$	J when re-optimizing with the disturbance
$J_c(c,d)$	J when tracking c with disturbance
K_i	Equilibrium constant or reaction rate pre-exponent of reaction i
L	$J_{\text{opt}}(d) - J_c(c,d)$, loss from optimality
$N_{i,0}$	Initial moles of species i, [kmol]
N_i	Moles of species i, [kmol]
R	Universal gas constant [kJ/kmol,K]
r_i	Rate of reaction i, [kmol/h]
R_{xy}	Sample correlation coefficient
t	Time, continuous
c	Time varying reference trajectory
d	Disturbance
DoF	Degree of freedom
T	Temperature in reactor
tf	Final time
U	Accumulated input
u	Input
V	Volume of reactor
x	State
y	Output

CHAPTER 1

INTRODUCTION

As an introduction, this chapter describes the motivation for the initiation of the project and the goals and challenges that are tried met and overcome. Also included is some background information on batch production and the production line of the main contrast agent substance at GE Healthcare. To get an overview of this work, the document structure is also described. In this thesis, it is assumed that the reader has elementary knowledge within differential calculus and optimization theory, linear algebra and control theory.

1.1 Secrecy Agreement

Due to possible sensitive information and a secrecy agreement with GE Healthcare; the name of some of the chemical components in the process are camouflaged with pseudonyms. Data that can be used to identify the properties of these chemical components are not published. Concentration measurements from the data set are only published through the unit [kmol]. Without the knowledge of the chemical structure of the components or their physical properties, the published data cannot be used to trace back to the real chemical species and their concentrations in the real process. As is in compliance with the secrecy agreement made between the author and GE Healthcare, Lindesnes.

1.2 Document Structure

This report consists of 6 chapters in a natural order of appearance. With introduction and a brief overview of some of the issues and techniques used in dynamic optimization of industrial batch processes as the first two chapters. This put the industrial case study in an academic framework. The following three chapters describes the industrial case study where the reactor step at GE Healthcare is modeled, optimized mathematically and analyzed for good on-line feedback control solutions, as a measure for handling process variability and disturbances. In these three chapters, a short summary of the results is made at the end. An overall summary with conclusive remarks and suggestions for further work is given as the last chapter.

1.3 Batch Production

Batch production in the chemical industry can be characterized by completing sub tasks sequentially in a production line toward the final product. Batch processes are typically used for small scale operations of expensive products such as in the pharmaceutical and the specialty chemical industry, for processes that are difficult to convert to continuous operation and small flexible plants close to the consumer [Fog06], [BSH06]. Batch process units are flexible in the sense that the same unit often can be used for multiple tasks, and that the thermodynamic variables; pressure and temperature easily can be manipulated to accommodate a relatively large area of operating regions. Additional flexibility is available in semi-batch processes where the feed rate can be manipulated throughout the batch. In the following ”semi batch process” is included in the term batch process.

1.4 Production Line at GE Healthcare

A production line of the main substance in GE Healthcares contrast agent production is located in Lindesnes. This factory synthesize a chemical component used in GE Healthcares production of contrast agents. The production line of this chemical compound consists of the main batch process steps shown in Figure (1.1).

The synthesis step is the focus in this thesis. It consists of a set of reactions (desired and un-desired) carried out in a batch reactor system, visualized in Figure (1.1), that will be described in detail in Chapter (3). A short summary of this step is given next.

The synthesis step is semi-batch process where the reactants are mainly added initially to the batch. Solid reactants are first dissolved by a solvent in the reactor as a preparation step. The reactions are then initiated by adding the reactant RCl. 93 % of this reactant is added initially, and the remaining reactant is added after 2 hours. Throughout the reaction time, additional reactants (RCl and NaOH) can be added to the batch to compensate for deviations from reference values of certain measurements taken. The magnitude of these extra inputs are calculated from previous experience and look-up tables [GEH]. Energy is transferred through a heat exchanger jacket that is coupled to a cooling and heating cycle. The reactor

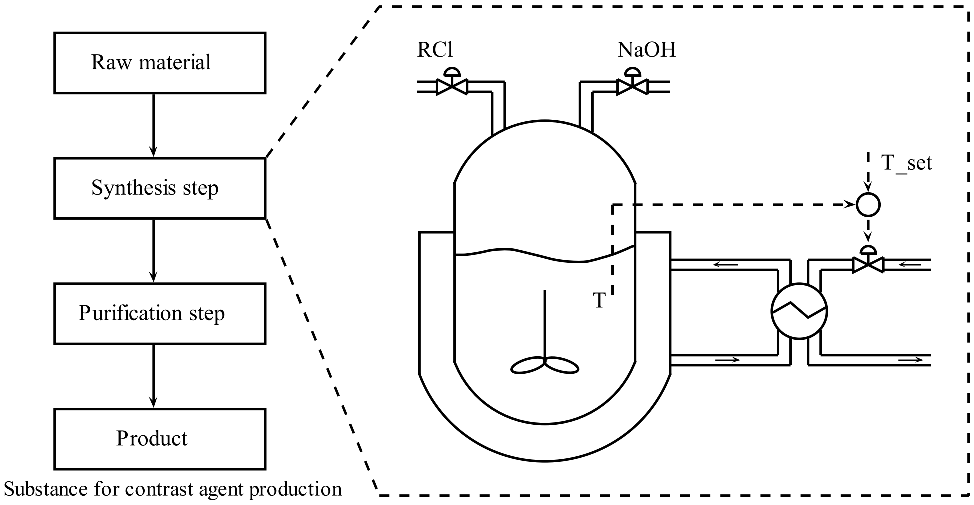


Figure 1.1: Production line and flow chart of the synthesis step at GE Healthcare, Lindesnes factories.

temperature is set constant after the initial addition of the reactants by a temperature feedback controller, coupled to the cooling and heating cycle, Figure (1.1). The batch reactor is run for 24 hours.

The purification step involves ion-exchange, up-concentration and water removal, crystallization and filtration. The product from this production line at Lindesnes is the main substance for further synthesis of the contrast agents produced by GE Healthcare Bio-Sciences.

1.5 Motivation

In industry, detailed models of batch processes are seldom available and the majority of these processes are run based on modified recipes developed in the laboratory [BSR01]. The laboratory recipes are modified to accommodate the different operating conditions in large scale production. The modification is often based on accumulated experience and trial and error [BSH06]. These modified recipes can be sub optimal and there can be economic potential in optimizing the operating procedure based on a deterministic large scale model of the process. For industrial batch processes with available measurements during runs, corrective action to compensate for deviations from some performance reference is often operator dependent and made based on accumulated experience and look-up tables. Thus, in addition to optimize the operating procedure open-loop it is desirable to use the model for on-line control or optimization as a measure for handling process disturbances and variability.

Regarding the batch reactor step in the production line at GE Healthcare at Lindesnes, the process is operated based on accumulated experience, and manual corrective actions are made based on a look-up table when deviation from references occur [GEH]. It is believed that this batch reactor step has potential for dynamic optimization of the operating procedure, for maximizing the product conversion and selectivity. In order to mathematically optimize the process, a deterministic model is needed. And if measurements are readily available, a model of the process can also be used for on-line feedback control or optimization solutions, as a measure for handling process variability and disturbances instead of using manual and operator dependent decisions.

1.6 Project Scope and Emphasis

To put the case study in an academic framework, a literature study within the field of dynamic optimization of industrial batch processes is performed. The study is narrowed down to include theory that is relevant for the GE Healthcare case study performed in later chapters.

The work will aim at develop a deterministic model of the component balance in the batch reaction process using existing process information, insight and measurements.

A detailed model of the energy transfer in the system is not included in this work. In the actual process there are reactor temperature measurements readily available and a lower level temperature feedback control loop is able to keep the temperature around a desired set point with an acceptable response time. The temperature measurements are used as inputs to the system when the model (reaction rates) parameters are estimated. Also, in assuming first order dynamics (with a reasonable time constant) from the temperature set point to the reactor temperature, the energy transfer need not be modeled in more detail to optimize the chemical performance in this process.

An open loop dynamic optimization study is performed on the batch reactor step based on the developed model of the process and the available optimization degrees of freedom. The optimization is made independent from current practice of running the process.

Regarding relevant disturbances and model uncertainties; on-line feedback control solutions are analyzed.The emphasis is on finding good variables to control.

The goal of this thesis is to mathematically model and optimize the batch process step at GE Healthcare off-line, and find good theoretical solutions for disturbance handling, since implementation and testing on the real process is not an option during this thesis. Also, the model developed is based on available data collected from previous batch runs and general knowledge of the process. No laboratory analysis or experiments are performed. Thus, the outcome of this thesis is strictly theoretical and includes possibilities for process optimization and theoretical good solutions for disturbance handling.

CHAPTER 2

DYNAMIC OPTIMIZATION AND CONTROL OF BATCH PROCESSES

This section gives an overview of the field of dynamic optimization of industrial batch processes and techniques for handling disturbances and process variability. The emphasis is on the case where a fairly good model of the system and on-line measurements are available, as is the case in the later case study. An overview is given on overall (high level) control strategies for disturbance and uncertainty handling, with selection of good output variables for on-line feedback control as the emphasis.

Batch processes are time varying in nature as opposed to steady state of continuous processes. The material goes from an unprocessed initial state at t_0 and end up at a final state at t_f as processed product. Batch optimization is thus different from optimization of continuous processes. In continuous steady state processes the optimization is performed by identifying constant set points for variables that optimize an objective function (economic). Control or optimal control is implemented on these variables on-line to minimize the loss from the optimal behavior when disturbances occur. In batch optimization we generally seek optimal input profiles that optimize an objective function expressing the desired performance of the batch [BSH06]. As with continuous processes, on-line control can be implemented to minimize the loss that occur when disturbances are present, if on-line measurements are available. Since batch processes are inherently repetitive, batch to batch or run to run optimization can be done if measurements from previous batches are available (this run to run optimization is implemented in a feedback fashion).

The distinction between the terms ”optimization” and ”control” is in this thesis, regarding batch production, separated by considering the operational objectives on different timescales. The term ”optimization” is used for off-line calculation of optimal operation of the current batch and the successive other batches. The term ”control” is used within a batch run for reducing the loss from optimal operation when disturbances are present. This can be done by various techniques such as simple PID feedback control or in some optimal fashion by on-line estimation and optimization (batch MPC).

There are many insightful papers written in the field of dynamic optimization of batch processes, e.g. [BSH06], [BSR01] and [TAR94].

2.1 Challenges

There are several challenges regarding dynamic optimization and control of industrial batch reactors. Solving the posted optimization problem is usually not a challenge in itself, many algorithms are available and widely documented in the literature [NW99]. The challenges of optimal operation of batch reactors are mainly within modeling, process monitoring and control [Bon98].

Modeling

In order to improve an existing process using dynamic optimization techniques a good representation of the system is required in form of a process model. There are a variety of model types available in the literature, but the focus here will be on first principle state space models and estimated parameters. The advantage of using first principle models versus empirical models for dynamic optimization are that first principle models often extrapolate better outside the nominal operating region, where the data was obtained [TAR94].

In the industry these models are rarely available due to costly development compared to the potential benefit from them [TAR94]. There are several challenges regarding obtaining a good deterministic model of a batch reactor. The most pronounced problems are related to lack of process insight such as unknown side reactions, reaction stoichiometry and kinetics and process disturbances. If the kinetic and stoichiometric parameters are not obtained in the laboratory, these parameters can be estimated by fitting data to the model e.g. by least square algorithms. Unfortunately the data set often lack variability in the measured inputs, that excite the measured outputs, since the process is tried run similar each time (near identical runs). This low input variability yield uncertainty in the estimated parameters. If measurements are available, run time (on-line) or run end (off-line) re-estimation techniques may be used to update the process model parameters [LPSB97].

Process Monitoring and Control

Because of the characteristics of batch processes there are several challenges related to process monitoring and control. The most pronounced characteristics and their implication are stated below.

- Time varying and non-linear system. The states in batch reactor systems can change significantly during the operation [Bon98]. In addition, model equations (such as the the reaction rates) are often non-linear which make controller design more difficult than steady state systems. However, there are solution available to these problems in the literature and the reader is referred to [Ber96] for an overview.
- Few measurements with time delay. On-line composition measurements are rear in batch processing [Bon98]. Off-line composition measurements, such as High-Performance Liquid Chromatography (HPLC) measurements, are often time consuming and introduce a significant time delay. High quality composition measurements are typically available at the end of the batch run [BSR01].
- Irreversible behavior. Many chemical reactions are irreversible and thus it may be impossible to correct an off spec product. Also, the ability to influence the reaction usually decrease with time [Bon98].

2.2 Opportunities

There are also characteristics in batch processing that make life easier.

- On-line measurements. On-line spectroscopy measurement, such as Near Infrared Spectroscopy (NIR), are availible for industrial use [BSR01], but require accurate and comprehensive calibration.
- Slow process dynamics. The dynamics of many batch processes are slow and thus enough time is available to process measurements, re-estimate model parameters and implement corrective action and run optimization algorithms on-line [Bon98].
- Repeating runs. Batch operations are repeated run after run and information from previous runs can be used to enhance the performance of the next batch through control and optimization in a run to run feedback fashion [BSH06].

2.3 Optimization Objectives

The goal for optimization of industrial processes is generally to increase the economics of the process. The economic objectives can be transformed into technical objectives such as increase the productivity and the quality of the product, decrease the energy consumption of the process and maintain safe operation. Increased productivity can be achieved by increasing the amount of product per batch run and increasing the number of batches per shift. Increased quality can reduce costly separation, and can be achieved by minimizing the waste product of the process. The quality issue is often very important, especially in the pharmaceutical industry, since it can turn the whole batch into waste if the quality is under a certain limit [Bon98]. Thus, there are often output constraints related to the quality of the product at the end of the batch. Constraints regarding safety can also be present to ensure safe operation.

These technical objectives can be stated mathematically in an objective functional, J, that is a measure of the performance of the process. A typical and general continuous objective functional is given in Equation (2.1). Henceforth the term: "objective function" is used for convenience.

$$J = S(\mathbf{x}(t_f)) + \int_{t_0}^{t_f} L(t, \mathbf{x}(t)), \mathbf{u}(t))dt \tag{2.1}$$

Where S is a function related to the performance at the final batch time (t_f), and L is a function that include the objectives that are accumulated throughout the batch such as: time, input usage (**u**) and certain states (**x**). Where the variables in boldface indicate vector notation.

And with the process constraints written as sets of inequalities:

$$\mathbf{c}(\mathbf{x}(t), \mathbf{u}(t)) \le 0 \tag{2.2}$$

$$\mathbf{d}(\mathbf{x}(t_f)) \le 0 \tag{2.3}$$

Where **d** represent the constraints at the final time (run end constraints) and **c** represent the constraints during the operation (run time constraints).

2.4 Problem Formulation

Given a mathematical model of the system on continuous state space form:

$$\dot{\mathbf{x}}(t) = \mathbf{f}(\mathbf{x}(t), \mathbf{u}(t)), \qquad \mathbf{x}(0) = \mathbf{x}_0 \tag{2.4}$$

$$\mathbf{y}(t) = \mathbf{g}(\mathbf{x}(t)) \tag{2.5}$$

Where **x** is the state space with the initial conditions $\mathbf{x}_0$, **y** are the outputs, **u** are the process inputs and **f** and **g** are sets of linear and non linear functions.

The problem consist of minimizing or maximizing the objective function (J) subject to the model and the set of constraints by using the available inputs and parameters **u** (decision variables). The final batch time (t_f) can also be included as a decision variable. Equations (2.6) to (2.10) show the standard formulation of the optimization problem where t is omitted in the notation.

$$\min_{\mathbf{u}} J \tag{2.6}$$

subject to:

$$\dot{\mathbf{x}} = \mathbf{f}(\mathbf{x}, \mathbf{u}), \qquad \mathbf{x}(0) = \mathbf{x}_0 \tag{2.7}$$

$$\mathbf{y} = \mathbf{g}(\mathbf{x}) \tag{2.8}$$

$$\mathbf{c}(\mathbf{x}, \mathbf{y}, \mathbf{u}) \leq 0 \tag{2.9}$$

$$\mathbf{d}(\mathbf{x}, \mathbf{y}) \leq 0 \tag{2.10}$$

There are various techniques and algorithms available in the literature for solving these types of optimization problems, and the methods that can be used are dependent on the system and the problem formulated. An overview of the available methods are, in this thesis, considered to be out of scope and the reader is referred to [NW99] and [Nai03] for information regarding the solution of these optimization problems. The optimization algorithm used for solving the specific optimization problem in the industrial case study presented in Chapter (4) is given in Section 2.5.

2.5 Obtaining the Optimal Solution

The dynamic optimization problem regarding the case study, posted in Section (4.3), was solved using gPROMS™, a process modeling and optimization software. gPROMS solve the problem by using the internal dynamic optimization solver *CVP-SS*. *CVP* refer to ”Control Vector Parameterization”, which indicate that the solver (in gPROMS) require the decision variables (inputs) to be parameterized as stepwise linear or constant over a specified number of intervals [Ent08]. *SS* refer to a “single shooting algorithm“. ”Single shooting algorithms“ integrate the system, with the values of the decision variable obtained from the optimization algorithm at the current iterate, ones over the entire specified time horizon. From this integration the time variation of the state variables, current objective function value and value of constraints are obtained. Based on this information, the optimization algorithm decides on new decision variable values that are used in the next iterate. This procedure is repeated until convergence is achieved [Ent08].

The system is integrated using the internal solver *DASOLV*. *DASOLVE* uses a variable step length and backward differentiation formulae algorithm [Ent08].

For deciding on the decision variable values at the next iterate, the dynamic optimization solver *CVS-SS* utilize the non linear program (NLP) solver *SRQPD*. The

SRQPD solver use a sequential quadratic programming (SQP) method and a line search strategy for the solution of the nonlinear programming (NLP) problem. The general idea of the SQP method is to, at the current iterate, approximate the NLP problem as a quadric programming subproblem [NW99]. The challenge is to select an appropriate design of the quadric approximation where it is a good representation of the NLP [NW99]. The quadric programming problem is solved and the parameter values of the next iterate is obtained. There are a variety of methods for solving quadric programming problems and the reader is referred to [NW99].

Regarding convergence of the algorithm to the global optimum, this can only be guaranteed if the optimization problem posted is convex. This is unfortunately often not the case in engineering problems.

2.6 Nominal Open-loop Optimal Solution

Solving the optimization problem stated in Section (2.4) give the nominal optimal input trajectory **u***, when implemented open-loop, that optimize the objective function, J, without the presence of model inaccuracy (model-plant mismatch) or unknown disturbances during the process. Unfortunately, model-plant mismatch and unknown disturbances will always be present.

There are especially large uncertainty and variability in batch process environments, and implementation of the nominal solution open-loop is rarely appropriate in industry. However, the nominal solution is still useful for qualitative insight in the shape of the optimal profiles (how the process should be run for optimality) and for determine the physical limits of the system [Bon98]. Also, there are ways of reducing the uncertainty and variability, if measurements are available, by on-line control (require run time measurements) and or run to run based optimization (require run end measurements). A brief overview of some of these methods is given in next.

2.7 Strategies for Handling Disturbances and Uncertainties

If measurements are available during or after the batch run, some form of on-line or iterative (batch to batch) correction or re-optimization scheme can be implemented on the process in a feedback fashion. The type of strategy that should be used depends on the batch control objectives. That is, whether the objective is at the end of the batch (run end) or during the batch (run time) or both. Other aspects that influence the choice of strategy is the characteristics of the batch system (Section (2.1) and (2.2)), number of measurements and the delay in analyzing them. Some of the available strategies are briefly given below, classified according to when the measurements are available (during or after the batch). For an overview of the available strategies the reader is referred to [Bon98], [BSR01] and [BSH06].

On-line Measurements Available

On-line corrections can be made as measurements are available throughout the batch run, and deviation with respect to a reference or objective is present.

Simple Feedback Control on output variables using available inputs, visualized in Figure (2.1). A time-varying controller can be used, e.g. a time varying LQG or PID. The key challenge here is to identify good output variables to control, variables that when controlled to references give acceptable loss from optimality during disturbances and uncertainty. Selection of these are discussed in more detail in Section (2.8). This method require relatively many on-line measurements during the batch and a fairly good model of the system for calculating, off-line, the nominal optimal reference trajectories and the time-varying controller parameters. The advantage of this strategy is that acceptable performance can be achieved by tracking the selected references without the need for re-optimization [SP05]. In addition it is relatively easy to implement.

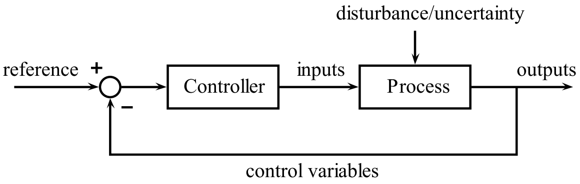


Figure 2.1: Feedback block diagram

On-line optimization (repeated optimization, batch MPC). Based on a model and the on-line measurements, the current and future inputs that minimize an objective function are calculated. This strategy requires an accurate model of the

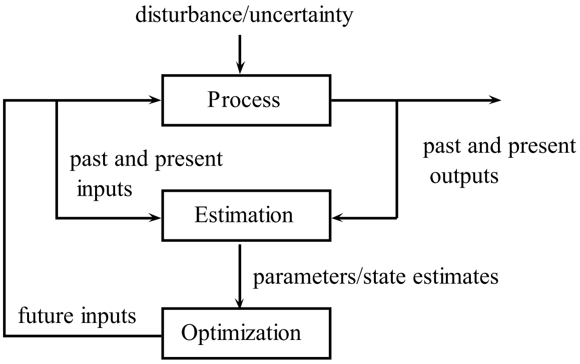


Figure 2.2: General structure of an on-line batch optimization system, [LPSB97]

system. The model used can also be updated by re-estimating the model parameters as measurements are made available before running the optimal control algorithm, visualized in Figure (2.2). A challenge here is that the estimation part require relatively large variations in the inputs to cover the parameters to be estimated, which often does not correspond to the optimal input profiles [BSH06].

Only Run-end Measurements Available

Run to run simple feedback. Parameters (π) that characterize the inputs profiles can be updated toward the optimal solution by successive runs. The run time input profiles (**u**) are parameterized with respect to the parameter value (π). The parameters are calculated based on run end measurements of the current and previous runs in a feedback fashion [BSR01]. A discrete run to run control law where j is the current batch index and K is the controller gain is shown in Equation (2.11).

$$\pi_{j+1} = \pi_j + K\left(y_{\text{ref}} - y_j\right) \tag{2.11}$$

Run to run optimization. Iterative improvement of subsequent batches to obtain the optimal operation over few batches. Model parameters are re-estimated based on previous runs and a re-optimized open-loop solution is implemented to the next batch. As with on-line optimization this strategy suffers from a conflict between the requirement of a good estimation and optimal inputs (persistency of excitation).

2.8 Selection of On-line Feedback Control Variables

In the industrial case study presented in the following chapters, the emphasis and goal is to find good theoretical solutions off-line, since no test runs can be made on the real process during this work. The chosen strategy for handling disturbances and model uncertainties in the case study is “simple feedback control” and selection of good output variables for reference tracking (“self-optimizing control“).

Self-optimizing control

Self-optimizing control is when acceptable operation (acceptable loss in the objective function J) can be achieved using pre-calculated set points, c, for the controlled variables y (without the need for re-optimizing when disturbances occur) [Sko00].

This definition is for steady state processes, but can be extended to time varying un-steady state systems by changing: “... the pre-calculated set points c ...” to “... the pre-calculated reference trajectories c(i)...”.

The selection begins with determining the optimal operation (result of the nominal optimization problem) and the available degrees of freedoms (inputs u). In the case where the optimal values of variables are at constraints, these variables should be controlled at their constraints (“active constraint control” [Sko00]) for optimal operation, and implementation is relatively easy. If there are degrees of freedom left, control of unconstrained variables is the next step. The problem of selecting good unconstrained variables for control is discussed next, and the discussion is limited to the case where only one degree of freedom is left (SISO).

[Sko00] present requirements for a good unconstrained variable to control:

1. It should be easy to measure and control accurately. Small implementation error.
2. The optimal value (trajectory) should be insensitive to disturbances. Small optimal variation.
3. It should be sensitive to changes in the manipulated variable (u). The input-output gain should be large.

For steady state problems there are various methods for evaluating the candidate output variables in the search for the self-optimizing control variable. These methods are presented in [SP05]. For non-linear and time varying systems there are absence of such methods in the literature, but there are ongoing research regarding this [DOSS08].

Direct Evaluation of Loss

One simple, but time consuming method that can be used, also for non-steady state systems, is the brute force method: ”Direct evaluation of loss” [SP05]. This method is applicable if the candidate control variables (y) and the possible disturbances (d) are small in numbers.

Let the loss (L) be defined as the difference in the objective function, J, for the two cases: $J_{\text{opt}}(d)$ and $J_c(u,d)$.

$$L = J_{\text{opt}}(d) - J_c(u,d) \tag{2.12}$$

Where $J_{\text{opt}}(d) \triangleq J(u_{\text{opt}}(d), d)$ is the result of re-optimizing the problem with the known disturbance present in the optimization problem. And $J_c(u,d)$ is the result when tracking a nominal optimal reference trajectory (c) using simple feedback control with the disturbance present.

The loss is then evaluated for all the candidate controlled variables over the possible disturbances. The controlled variable with smallest worst case or average value of the loss over all the disturbances is then preferred [SP05].

Figure (2.3) show the objective function value for an increasing disturbance. The re-optimized case, $J_{\text{opt}(d)}$, is the truly optimal performance in the presence of the

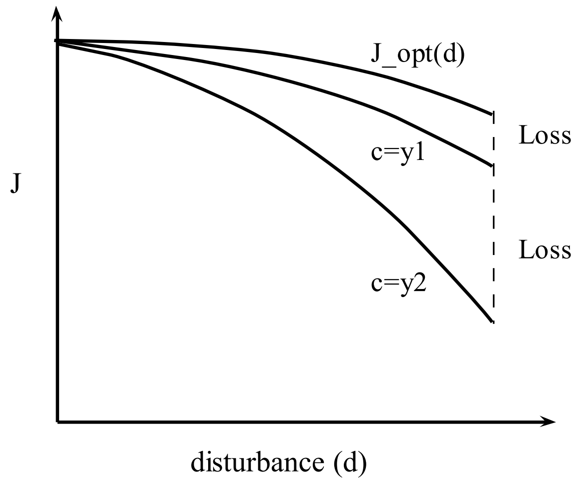


Figure 2.3: Loss in performance when tracking variables (y) to references (c) instead of re-optimizing ($J_{\mathrm{opt}}(d)$) when disturbances (d) are present. Here y1 is a better variable to control than y2. The figure illustrates the case where the objective is to maximize the objective function (J).

disturbance. When controlling a variable y to the nominal optimal reference trajectory, during this disturbance, a loss occur. The objective in self-optimizing control is to select the variable y that minimize this loss for every possible disturbance. In the figure, y1 is a better variable to control than y2 for this disturbance.

CHAPTER 3

INDUSTRIAL CASE STUDY MODELING AND PARAMETER ESTIMATION

The synthesis step is an important step in GE Healthcares production line of contrast agents. It is a semi batch alkylation reaction where the reactants are mainly added initially to the batch. Throughout the batch run, small additional amount of reactants are added to the batch to compensate for deviations from reference values of certain measurements taken. The magnitude of these extra inputs are calculated from previous experience in look-up tables [GEH]. The reactor temperature is set constant after the initial addition of the reactants by a temperature feedback controller coupled to a reactor jacket and a cooling and heating cycle. The simplified batch process diagram is shown in Figure (3.1).

The goals in this chapter is to develop and obtain a model of the batch system. This model can then be used for optimization of the process inputs. Also, it is desirable to use the model of the process for process control purposes. That is, calculations of inputs can be made from the model and deviations from an optimal or desired output trajectory, given that such output measurements are readily available.

In this chapter a model of the batch system is developed from first principles and parameter estimations from batch data of several batches. The reaction model structure is based on elementary chemical reaction engineering and work done by Cybernetica AS and discussions with Professor Magne Hillestad at the Department of Chemical Engineering at NTNU. The model structure is slightly altered and the reaction rate parameters are obtained by non-linear parameter estimation with measurements from several batches.

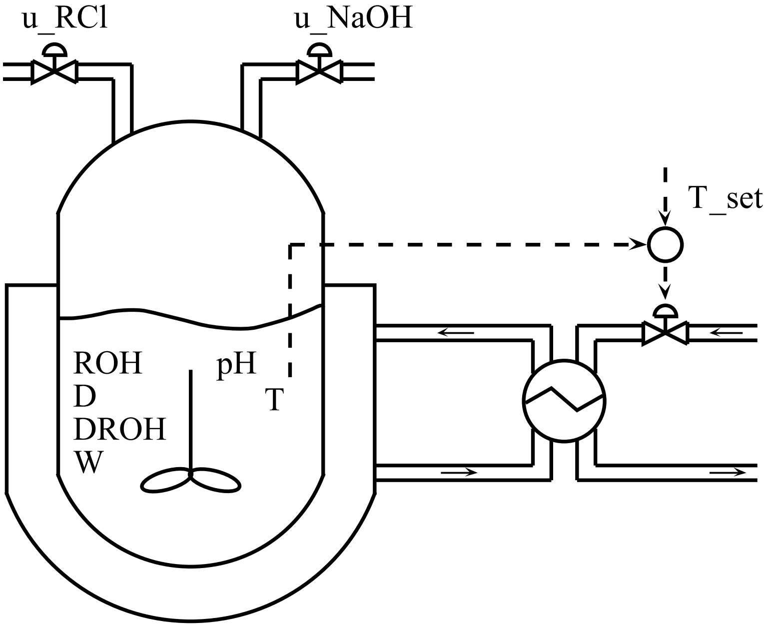


Figure 3.1: Simplified batch process diagram

3.1 Challenges

- No experiments on reaction mechanism and kinetics was available and very little is known on these issues.
- There are few output measurements during the batch. Concentrations of two species and the pH in the solution are measured three times during a batch run.
- The data set includes temperature and reactant input measurements from several batch runs. However, since it is desirable to run each batch similarly (near identical runs), these data lack variability in the inputs that excite responses in the measured outputs of the process. This makes parameter estimation difficult and can result in uncertain parameters.

3.2 Current Practice and Procedure

This section describe the current practice and procedure in running the alkylation batch in more detail. The abbreviations of the system species are given and described in Table (3.1)[1].

---

[1] The real name of some chemical components are not given due to a secrecy agreement with GE Healthcare

Table 3.1: Abbreviations of the batch system species

Abbreviations	
MeOH	Solvent
NaOH	Reactant and manipulated variable 1
RCL	Reactant (alkyl-chloride) and manipulated variable 2
ROH	Intermediate product and reactant
D	Main reactant 3
D^-	Ionic reactant 3
DROH	Product
W	Waste product

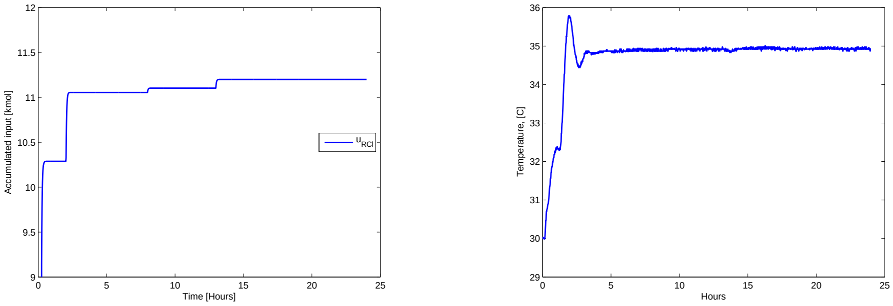
Process Inputs and Initial Conditions

All of the D reactant is mixed with NaOH and the solvent MeOH, to dissolve the solid D in the liquid solution. This dissolution step require a temperature around 40-45 $^\circ C$ and can take up to 20 hours. This thesis focuses on the reaction step after the dissolution of D and assumes that all D is dissolved. The reaction is initialized with the addition of RCl (an alkyl-chloride), which is divided into four stages. Initially approximately 93% of the total addition of RCl is added within the first hour of the batch. After two hours the remaining 7% is added. This discontinuous addition is done to prevent low pH initially [GEH]. After 6.5 hours, measurements of pH, waste product and D concentration are taken and after 8 hours, when the results are available, a decision is made on whether to add additional RCl or NaOH to the batch or not. This decision and the amount of extra reactants are made based on previous experience and a look-up table. After 11 hours, new measurements are taken and the same procedure as above is performed at 13 hours. The batch is typically run for 24-26 hours, based on the final measurements at 24 hours.

The temperature in the reactor is initially $30^\circ C$ and increase about $5^\circ C$ because of the addition of RCl to the solution. After the initial addition of RCl, the temperature is controlled to $35^\circ C$ throughout the reaction by a temperature controller coupled to a cooling and heating cycle. The temperature in the reactor is considered as an input (or measured disturbance) to the system in this chapter, as the temperature is measured every minute.

The volume is not stated in this report due to a confidentiality agreement with GE Healthcare. The reactor volume is set constant in the model since the additional inputs to the batch at 8 and 13 hours are small in magnitude compared to the initial reactor volume.

Each batch has its unique input history and this has been taken into account when fitting the model to the data. An example of the input profiles for a specific batch is given in Figure (3.2).



(a) Accumulated RCl input profile

(b) Temperature profile

Figure 3.2: The inputs of batch #16

Measurements

In addition to the temperature measurements, there are only a few measurements available during each batch. Measurements of D and W concentration are performed three times during the reaction respectively at 6.5 hours, 11 hours and 24 hours. The pH in the solution is measured at 6.5 and 11 hours.

The concentration measurements are made from a HPLC (High Performance Liquid Chromatography) instrument. A detailed description of this instrument is considered to be out of scope. The instrument give the measured output in the unit: area percentage $[m^2\%]$ ($\in [0,100]$). In order to compare measurements with simulations this unit need to be converted to [kmol], by Equation (3.1).

$$y_D\left[m^2\%\right] = G_D\left[\frac{m^2\%}{\text{kmol}}\right] x_4\,[\text{kmol}] \tag{3.1}$$

$$y_W\left[m^2\%\right] = G_W\left[\frac{m^2\%}{\text{kmol}}\right] x_6\,[\text{kmol}] \tag{3.2}$$

The gains G_W and G_D are calculated based on calibration data and not stated in the report due to the confidentiality agreement with GE Healthcare. The units of the measured concentrations in [kmol] is henceforth used in the report, and are based on $[m^2\%]$ from the data set.

There are on-line NIR (Near Infrared Spectroscopy) concentration measurements available on the process for the two species, D and W. This instrument need calibration data from other sources (HPLC) and this is performed rarely. Considering the current uncertainty in them, the NIR data is not used as an input in the parameter estimation problem later. However, if calibrated properly and periodically, these on-line measurements can be used for process control purposes.

The Data Set

The data set consists of 30 batches with temperature and reactant input data and concentration measurements as given in Section (3.2). In order to investigate the quality of the data set with respect to model fitting a statistical analysis was performed and given in Appendix (A). This analysis indicates that un-measured disturbances are the main reason for the batch to batch variations in the data set. This is also backed up by discussions with GE Healthcare. The temperature profiles in the data set vary mostly within the first 5 hours of the runs and effect the measured outputs mainly at 6.5 hours. It is shown that it is small to medium correlation between the average temperature in the reactor within the first 5 hours and the D and W concentration measurements at time 6.5 hours. This indicate that there will be some degree of uncertainty in the estimated activation energy parameters in the model obtained later. This was expected due to the small difference in the temperature profiles from batch to batch.

Batch Objectives

There are a couple of objectives present at the end of the batch run. These objectives are present to ensure a certain quality and conversion of the final product.

- Amount of waste (W) less than 0.10 [kmol].
- Amount of reactant 3 (D) less than 0.23 [kmol].

3.3 Model

The model for the alkylation process is based on a project between Cybernetica AS and GE Healthcare and personal communication with representatives from the two companies. It is a first principle model based on elementary chemical reaction engineering [Fog06]. The model is slightly altered and the unknown kinetic parameters are re-estimated from 30 batches using non-linear least squares, described in Section (3.4).

Assumptions

- Constant reactor volume.
- Semi-batch reactor, addition of reactants as manipulated variables.
- First order reactions with respect to each component, second order overall reaction order.
- Liquid phase only. Perfect mixing.

- Temperature dependent reaction rates. Pressure independent system.

Reactions

Initially reactant D is mixed with reactant NaOH to dissolve solid D into liquid phase D^-. The preparation reaction can be described as:

$$NaOH \rightharpoonup Na^+ + OH^- \tag{3.3}$$

$$D \overset{K_D}{\rightleftharpoons} D^- + H^+ \tag{3.4}$$

Where K_D is the equilibrium constant for the dissociation, which is assumed to be constant. Instead of introducing a temperature dependent equilibrium constant $K_D(T)$, the temperature dependency is introduced with the reaction rate constant $K_1(T)$ in Reaction (3.5).

The alkylation reaction is then initiated by adding the reactant RCl. RCl first undergo a substitution reaction in the alkaline environment, described by the Reaction (3.5). This is assumed to be a fast reaction [GEH].

$$RCl + OH^- \overset{r_1}{\rightleftharpoons} ROH + H^+ + Cl^- \tag{3.5}$$

Where r_1 is the temperature dependent reaction rate for Reaction (3.5). This is assumed to be a equilibrium reaction pushed mainly to the right, where K_{-1} is the reaction rate constant for the reverse reaction. Assuming that the strong electrolytes NaOH, HCl and NaCl are completely dissociated in the solution. And that the aqueous acid-base equilibrium is present with K_w as the equilibrium constant.

$$H_2O \overset{K_w}{\rightleftharpoons} OH^- + H^+ \tag{3.6}$$

The alkylation reactants are D^- and ROH, which gives the alkylated product (DROH) and alkylated waste products (W). Where r_{w1} and and r_{w2} describe the rate of over-alkylated and wrongly-alkylated product respectively. Also, H^+ must be a part of the reaction, since the main product (DROH) and waste (W) products are not ions.

$$ROH + D^- + H^+ \overset{r_P}{\rightharpoonup} DROH \tag{3.7}$$

$$ROH + DROH \overset{r_{W1}}{\rightharpoonup} W \tag{3.8}$$

$$ROH + D^- + H^+ \overset{r_{W2}}{\rightharpoonup} W \tag{3.9}$$

Equations

$$\frac{dV}{dt} = 0 \tag{3.10}$$

$$\frac{dN_{\mathrm{RCl}}}{dt} = -r_1 V + u_{\mathrm{RCl}} \tag{3.11}$$

$$\frac{dN_{\mathrm{NaOH}}}{dt} = -r_1 V + u_{\mathrm{NaOH}} \tag{3.12}$$

$$r_1 = K_1(T) C_{\mathrm{RCl}} C_{\mathrm{OH^-}} - K_{-1} C_{\mathrm{ROH}} \tag{3.13}$$

$$\tag{3.14}$$

$$C_{\mathrm{i}} = \frac{N_{\mathrm{i}}}{V} \tag{3.15}$$

Where i is the i'th component.

$$\frac{dN_{\mathrm{ROH}}}{dt} = (r_1 - r_P - r_{w1} - r_{w2})V \tag{3.16}$$

$$\frac{dN_{\mathrm{D^{tot}}}}{dt} = -(r_P + r_{w2})V \tag{3.17}$$

$$\frac{dN_{\mathrm{DROH}}}{dt} = (r_P - r_{w1})V \tag{3.18}$$

$$\frac{dN_{\mathrm{W}}}{dt} = (r_{w1} + r_{w2})V \tag{3.19}$$

$$r_P = K_P(T) C_{\mathrm{ROH}} C_{\mathrm{D^-}} \tag{3.20}$$

$$r_{w1} = K_{w1}(T) C_{\mathrm{ROH}} C_{\mathrm{DROH}} \tag{3.21}$$

$$r_{w2} = K_{w2}(T) C_{\mathrm{ROH}} C_{\mathrm{D^-}} \tag{3.22}$$

From the equilibrium reaction (3.4) the total concentration of D is:

$$C_{\mathrm{D}}^{\mathrm{tot}} = C_{\mathrm{D}} + C_{\mathrm{D^-}} \tag{3.23}$$

Assuming equilibrium, the equilibrium constant is given approximately as:

$$K_{\mathrm{D}} = \frac{C_{\mathrm{H^+}} C_{\mathrm{D^-}}}{C_{\mathrm{D}}} \tag{3.24}$$

The water dissociation equilibrium:

$$K_{\mathrm{w}} = C_{\mathrm{H^+}} C_{\mathrm{OH^-}} \tag{3.25}$$

Combining yields:

$$\frac{C_{\mathrm{D^-}}}{C_{\mathrm{D}}} = \frac{K_{\mathrm{D}}}{K_{\mathrm{w}}} C_{\mathrm{OH^-}} \tag{3.26}$$

Inserting Equation (3.23) into Equation (3.26) and defining $K_r = \frac{K_{\mathrm{D}}}{K_{\mathrm{w}}}$ yields:

$$C_{\mathrm{D^-}} = \frac{K_r C_{\mathrm{OH^-}}}{1 + K_r C_{\mathrm{OH^-}}} C_{\mathrm{D}}^{\mathrm{tot}} \tag{3.27}$$

The concentration of OH^- in the solution will be as given in Equation (3.28), where C_{NaOH} is the amount of OH^- left after Reaction (3.5).

$$C_{\mathrm{OH}^-} = C_{\mathrm{NaOH}} - C_{\mathrm{D}^-} \tag{3.28}$$

Inserting Equation (3.27)into Equation (3.28) result in a second order polynomial with the realistic solution given in Equation (3.29).

$$C_{\mathrm{OH}^-} = -\frac{1 + K_r\left(C_{\mathrm{D}}^{\mathrm{tot}} - C_{\mathrm{NaOH}}\right)}{2K_r} + \sqrt{\left(\frac{1 + K_r\left(C_{\mathrm{D}}^{\mathrm{tot}} - C_{\mathrm{NaOH}}\right)}{2K_r}\right)^2 + \frac{C_{\mathrm{NaOH}}}{K_r}} \tag{3.29}$$

And the pH in the solution:

$$\mathrm{pH} = 14 + \log_{10}\left(C_{\mathrm{OH}^-}\right) \tag{3.30}$$

The reaction rates are assumed to be temperature dependent with respect to a reference temperature.

$$K_1(T) = k_1^{\mathrm{ref}} \exp\left[-\gamma_1\left(\frac{T^{\mathrm{ref}}}{T} - 1\right)\right] \tag{3.31}$$

$$K_{-1} = k_{-1}^{\mathrm{ref}} \tag{3.32}$$

$$K_r = k_r^{\mathrm{ref}} \tag{3.33}$$

$$K_P(T) = k_P^{\mathrm{ref}} \exp\left[-\gamma_P\left(\frac{T^{\mathrm{ref}}}{T} - 1\right)\right] \tag{3.34}$$

$$K_{w1}(T) = k_{w1}^{\mathrm{ref}} \exp\left[-\gamma_w\left(\frac{T^{\mathrm{ref}}}{T} - 1\right)\right] \tag{3.35}$$

$$K_{w2}(T) = k_{w2}^{\mathrm{ref}} \exp\left[-\gamma_w\left(\frac{T^{\mathrm{ref}}}{T} - 1\right)\right] \tag{3.36}$$

$$\tag{3.37}$$

Where:

$$\gamma_i = \frac{E_{A,i}}{RT^{\mathrm{ref}}} \tag{3.38}$$

$$T^{\mathrm{ref}} = 308.15[K] \tag{3.39}$$

$$\tag{3.40}$$

And $E_{A,i}$ is the activation energy for the respective reactions i. T^{ref} is chosen to be 35 °C which is the temperature set point in all the batches in the data set.

Energy Transfer

The energy transfer in the system is not modeled, since the reactor temperature is measured every minute for each batch run in the data set and used as an input to the simulations and estimations. The energy is transferred through a jacket around the reactor. A combined cooling and heating system deliver ice-water and steam to heat exchangers with flows coupled to the jacket, as seen i Figure (3.1). A temperature feedback control loop keep the reactor temperature at a pre-defined set point T_{set} of 35 °C after about 5 hours.

Inputs

The inputs of the reactants (u_{RCl} and u_{NaOH}) [kmol/h] are modeled as first order equations with a time constant τ_u, equal for the two inputs, as seen in Equation (3.41).

$$u = \frac{F - U}{\tau_u}, \qquad \tau_u = 0.05[\text{h}] \tag{3.41}$$

Where F is the amount of measured input [kmol] and U is the calculated accumulated input given by Equation (3.42).

$$\frac{d\text{U}}{dt} = u, \qquad U(0) = 0 \tag{3.42}$$

Integration and Sampling Time

The process is simulated (model is integrated) using “Forward Euler” with a sampling time of 1 minute. The input measurements of the accumulated input F and the temperature T is available every minute in data set.

Compact Model Summary

The model can be stated in a compact format shown in Table (3.2). Where x_i is the amount of species i in [kmol], and i = [1:RCl 2:NaOH 3:ROH 4:D 5:DROH 6:W]

The model in Table (3.2) is henceforth written on state space vector form:

$$\dot{\mathbf{x}} = \mathbf{f}(\theta, \mathbf{x}, \mathbf{u}) \tag{3.43}$$

$$\mathbf{y} = \mathbf{g}(\theta, \mathbf{x}) \tag{3.44}$$

Where **x** is the state space, **y** are the outputs, **u** are the inputs included temperature, θ are the unknown parameters and **g** and **f** are sets of linear and non-linear functions.

3.4 Parameter Estimation

The unknown parameters to be estimated from the data are:

$$\theta = \begin{bmatrix} k_1^{\text{ref}} & k_{-1}^{\text{ref}} & k_r^{\text{ref}} & k_p^{\text{ref}} & k_{w1}^{\text{ref}} & k_{w2}^{\text{ref}} & \gamma_1 & \gamma_p & \gamma_w \end{bmatrix} \tag{3.45}$$

Table 3.2: Compact model summary

State space model	
$\dot{x}_1 = -a_1 x_1 \bar{x}_2 + a_5 x_3 + u_1$,	$\bar{x}_2 = \left[-\frac{1+K_r(x_4/V - x_2/V)}{2K_r} + \sqrt{\left(\frac{1+K_r(x_4/V - x_2/V)}{2K_r}\right)^2 + \frac{x_2/V}{K_r}} \right] V$
$\dot{x}_2 = -a_1 x_1 \bar{x}_2 + a_5 x_3 + u_2$,	$a_1 = V^{-1} k_1^{\text{ref}} \exp\left[-\gamma_1 \left(\frac{T^{\text{ref}}}{T} - 1\right)\right]$
$\dot{x}_3 = a_1 x_1 \bar{x}_2 - a_2 x_3 \bar{x}_4 - a_3 x_3 x_5$	$a_5 = k_{-1}^{\text{ref}}$
$-a_4 x_3 \bar{x}_4 - a_5 x_3$,	$a_2 = V^{-1} k_p^{\text{ref}} \exp\left[-\gamma_p \left(\frac{T^{\text{ref}}}{T} - 1\right)\right]$
$\dot{x}_4 = -a_2 x_3 \bar{x}_4 - a_4 x_3 \bar{x}_4$,	$a_3 = V^{-1} k_{w1}^{\text{ref}} \exp\left[-\gamma_w \left(\frac{T^{\text{ref}}}{T} - 1\right)\right]$
$\dot{x}_5 = a_2 x_3 \bar{x}_4 - a_3 x_3 x_5$,	$a_4 = V^{-1} k_{w2}^{\text{ref}} \exp\left[-\gamma_w \left(\frac{T^{\text{ref}}}{T} - 1\right)\right]$
$\dot{x}_6 = a_4 x_3 \bar{x}_4 + a_3 x_3 x_5$,	$\bar{x}_4 = \frac{K_r \bar{x}_2}{V + K_r \bar{x}_2} x_4$
$y_4 = c_4 x_4$,	$c_4 = G_D$
$y_6 = c_6 x_6$,	$c_6 = G_W$
$y_2 = 14 + \log_{10}\left(\frac{\bar{x}_2}{V}\right)$,	$K_r = k_r^{\text{ref}}$

These 9 parameters are estimated from 8 measurements in each batch over a total of 30 batches. The estimation problem is formulated as a least square problem:

$$\min_{\theta} f(\theta) \tag{3.46}$$

Subject to the model:

$$\dot{\mathbf{x}} = \mathbf{f}(\theta, \mathbf{x}, \mathbf{u}) \tag{3.47}$$

$$\mathbf{y} = \mathbf{g}(\theta, \mathbf{x}) \tag{3.48}$$

Where θ is the set of scaled unknown parameters to be estimated. The parameters are scaled in the algorithm to range from 1 to 10 to ensure a properly scaled system.

The objective function $f(\theta)$ is defined as:

$$f(\theta) = ||\mathbf{R}(\theta)||_2^2 \tag{3.49}$$

Where **R** is a stacked vector of scaled residuals between the measurements in the data set and the corresponding simulated outputs, Equation (3.48), for all batches and all defined outputs **y**. The difference between simulated and measured outputs are scaled with the average value of the measurement as shown in Equation (3.53). All the measurements in every batch, $\mathbf{B}_i$ are weighted equal.

$$\mathbf{R} = \begin{bmatrix} \mathbf{B}_1 \\ \vdots \\ \mathbf{B}_{30} \end{bmatrix} \tag{3.50}$$

Where 30 is the total number of batches in the dataset and $\mathbf{B}_i$ includes all the output measurements in batch i, where $i = 1,2,...,30$. In each batch $\mathbf{B}_i$ there are specific time instants, j , where the measurements are taken. $\mathbf{Y}_{j,i}$ include all the output measurements at time instant j, where $j = 1,2,3$ and correspond to the time instants 6.5, 11 and 24 hours respectively.

$$\mathbf{B}_i^\top = \begin{bmatrix} \mathbf{Y}_1 & \mathbf{Y}_2 & \mathbf{Y}_3 \end{bmatrix}_i \tag{3.51}$$

$\mathbf{Y}_{j,i}$ is a vector of the scaled difference (residual) between the measurements from the data set and corresponding simulated output for time instant j and batch number i.

$$\mathbf{Y}^\top{}_{j,i} = \mathbf{S}_j \begin{bmatrix} y_1^{\text{sim}} - y_1^{\text{meas}} \\ \vdots \\ y_3^{\text{sim}} - y_3^{\text{meas}} \end{bmatrix}_{j,i} \tag{3.52}$$

Where $K = 1,2,3$ and correspond to D, W and pH measurements respectively. The scaling, $\mathbf{S}$, is defined as:

$$\mathbf{S}_j = \begin{bmatrix} \bar{y}_1^{\text{meas}} & \mathbf{0} & \\ & \ddots & \\ \mathbf{0} & & \bar{y}_3^{\text{meas}} \end{bmatrix}_j^{-1} \tag{3.53}$$

Where $\bar{y}_k^{\text{meas}}$ is the average of the measured variable k, over all of the batches at time instant j.

The resulting estimated parameters are given in Table (3.3).

Table 3.3: Value and description of the estimated parameters

Estimated parameters				
i	θ_i	Value	Description	
1	k_1^{ref}:	412.10	$[\text{m}^3/\text{kmol}\cdot\text{h}]$	Pre-exponential (frequency) reference factor
2	k_{-1}^{ref}:	0.070453	$[1/\text{h}]$	Pre-exponential (frequency) reference factor
3	k_r^{ref}:	1871.9	$[\text{m}^3/\text{kmol}\cdot\text{h}]$	Equilibrium constant at reference temperature
4	k_p^{ref}:	0.99222	$[\text{m}^3/\text{kmol}\cdot\text{h}]$	Pre-exponential (frequency) reference factor
5	k_{w1}^{ref}:	$1.7574\cdot10^{-3}$	$[\text{m}^3/\text{kmol}\cdot\text{h}]$	Pre-exponential (frequency) reference factor
6	k_{w2}^{ref}:	$3.6804\cdot10^{-3}$	$[\text{m}^3/\text{kmol}\cdot\text{h}]$	Pre-exponential (frequency) reference factor
6	γ_1:	43.67	$[-]$	Dimensionless activation energy
8	γ_p:	26.17	$[-]$	Dimensionless activation energy
9	γ_w:	17.98	$[-]$	Dimensionless activation energy

3.5 Obtaining the Parameters

Because possible non-convex optimization problems require a good initial starting point for converging to a reasonable solution and the relatively large amount of parameters, the estimation was divided into 5 steps. First the parameters was estimated by only considering the first batch in the data set, this was done in order to get a correct dynamic behavior of the system before running the algorithm. This initial basis of the parameters was obtained by trial and error and comparing by plotting the measured values with the simulated values for the first batch in the data set.

When a proper dynamic behavior was obtained, this initial guess was used in the estimation algorithm for the first batch. This gave a better basis for estimating the parameters over all the 30 batches.

From the two steps above it was clear that the parameters related to the waste generation was naturally separated from the others in magnitude. The waste reaction rates are small in magnitude compared to the product reaction rate and does not effect the dynamic behavior of the product or the main reactant to a large extend. Thus the reaction rate parameters for the main product and reactants were estimated first over all the batches in the data set. When a good fit was obtained, these values were used and set constant when the parameters related to the waste generation was estimated. When a good fit was obtained in the waste generation parameters, all the parameters was re-estimated with their respective initial values obtained from the previous steps.

Algorithm

The objective function is calculated by simulating the system with the estimated parameters and calculating the scaled difference (residual) between the simulated values and the measurements available in the data set. The optimization problem is solved using MATLAB™ (a technical computing and programming software) with the internal function *lsqnonlin* in the *Optimization Toolbox*™ [Mat09]. The *lsqnonlin* function solve the posted optimization problem by minimizing the non-linear residual objective function **R** over a space of parameters θ of the function, **R**.

The method used in *lsqnonlin* is the Levenberg-Marquardt (LM) method [Mar63], and is popular for solving non-linear least squares problem. As with other non-linear least squares algorithm (Gauss-Newton method), the LM method exploit the least squares structure of the posted problem to save computational time, by using an approximation for the Hessian: $\nabla^2 f(\theta) \approx J(\theta)^\top J(\theta)$, where J is here the Jacobian: $J(\theta) = \left[\frac{\partial R_j}{\partial \theta_i}\right]_{i=1,2,\dots,n}^{j=1,2\dots,m}$ [NW99]. The LM method uses a trust region strategy for deciding the search direction of the current iterate[NW99]. For each iteration, the sub-problem in Equation (3.54) is solved to obtain the search direction p. This is done by restating Equation (3.54) as a linear least squares problem.

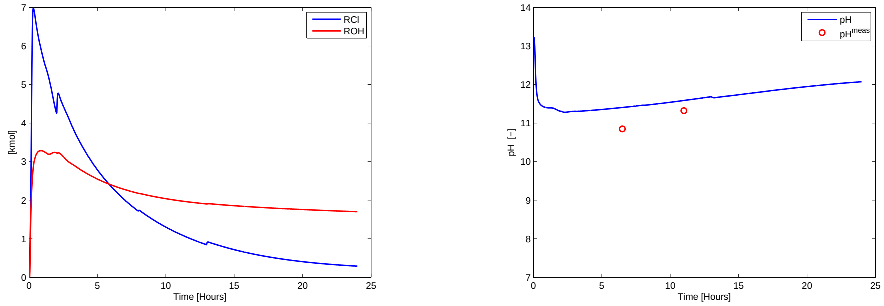
$$\left[J(\theta)^\top J(\theta) + \lambda I\right] p = -J(\theta)^\top R(\theta) \tag{3.54}$$

The positive scalar λ decides the magnitude and direction of p. When p is found the new iterate is at: $\theta_{k+1} = \theta_k + p$. For finding λ the reader is referred to [NW99].

When using the estimation algorithm, the integration solver had finer resolution than the optimization algorithm to avoid smoothness problems.

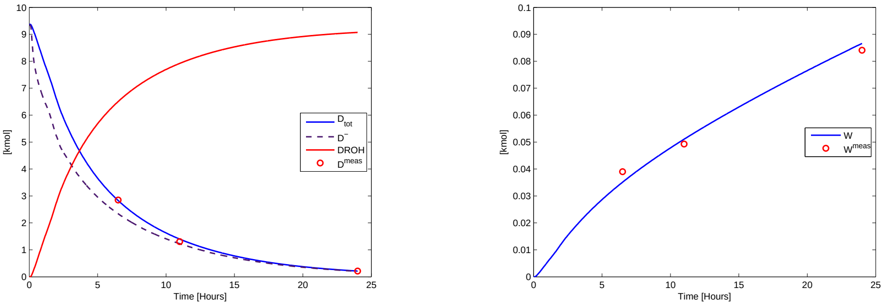
3.6 Result and Model Validation

Figure (3.3) show one of the simulated batches with the parameters obtained from the estimation. Figure (3.3) show that the dynamics of the waste (W) and the reactant (D) are captured good throughout the batch run in the model, for this batch. Figure (B.1) in Appendix (B) shows plots of the measured versus the simulated values, of the measured states, for all the batches considered in the data set.



(a) Reactant RCl (blue) and intermediate product ROH (red)

(b) pH



(c) Reactant D (blue), D^- (broken dark blue line) and product DROH (red)

(d) Waste product (W)

Figure 3.3: Simulation of batch # 16 with the estimated parameters. The circles are the measurements during the batch. The inputs are shown in Figure (3.2).

Appendix (B) show that the overall trends of the W and D states are captured in the model, but smaller variations between the batches (batch to batch variation) are not. This can be explained by the small measured variation in the inputs of the process. And that un-measured disturbances are probably the main reason for batch to batch output variations, [GEH].

Table (B.1) show that the batch to batch estimation is best at the first measurements of W and D at 6.5 hours and decrease with time. This is because up to 5 hours the batch temperatures varies the most, and this is the measured input that excite the outputs the most.

The pH measurements shown in Figure (3.3) and in Figure ((B.1)) is somewhat misleading. The trend of simulated pH, is approximately 0.5 pH units above the average pH in the data set. However, the pH at GE Healthcare is measured on a diluted sample (1 part sample and 3 parts distilled water) to ensure good conductivity. The reported pH is not corrected for the dilution made [GEH], and they accept the resulting systematic error in their pH measurements. A measured pH of approximately 11 in the diluted sample (1:3) is in the concentrated solution, based on the equilibrium constant of the alkaline solution, 0.2 to 0.5 pH units higher than measured. And thus closer to what is obtained in the simulations. The pH estimation in the model is thus considered to be a good approximation of the real pH in the solution.

3.7 Summary and Discussion

Based on the good estimation of the dynamics of the states (W and D) throughout the batches, and the fairly good correlation of the measurements and the simulated outputs where the temperature variation is largest (from 0 to 5 hours); the model and the parameters are consider to be accurate enough for dynamic optimization of the batch process. However, there exist some uncertainty in the temperature dependency in the model (the estimated arrhenius activation parameters, γ). The estimated model parameters should therefore be verified in the laboratory. Or, by running some batches with more variation in the temperature and measured inputs and re-estimate the model parameters. This should also be performed to ensure that the parameters are accurate also outside the region of operation from where they are obtained (temperatures around 30 to 35 °C).

CHAPTER

4

INDUSTRIAL CASE STUDY DYNAMIC OPTIMIZATION

In the past, before 1986, the alkylation reaction was run three times more dilute in a batch reactor for 48 hours. The conversion and selectivity achieved was relatively good, sometimes measured as low as 0.10 [kmol] main reactant (D) and 0.07 [kmol] waste product (W) at the end of the batch. In the present, the reaction time is reduced to 24 hours and the concentration is approximately three times higher. It is now difficult to obtain a main reactant amount lower than 0.17 [kmol] without exceeding 0.10 [kmol] waste. [GEH]

Considering the higher selectivity in the past, it is believed that this production step has potential for optimization. The optimization in this case means increasing the selectivity and conversion at the end of the reaction without extending the reaction time or the degree of dilution.

From the model obtained in Section (3.3) with the parameters in Table (3.3) we want to optimize the outputs at the end of the batch.

4.1 Optimization Degrees of Freedom

The current practice of running the batch is to add the reactants initially and control the process with extra additions of RCl and NaOH after 8 and 13 hours. The initial addition of NaOH with the solvent (MeOH) is necessary to ensure dissolution of the main reactant (D), as discussed in Section (3.2). The input profile of NaOH should then not be included as an input variable in the optimization, but remain fixed as an initial condition. Additional input of NaOH throughout the batch can however be used as a control input, Section (5). The addition of RCl initiates the reaction, and the input profile of RCl is chosen to be a manipulated variable in the optimization problem.

The reactor temperature set point is also included as an optimization degree of freedom. A lower level feedback control loop keep the reactor temperature at a set point T_{set}. It is assumed that the temperature in the system can be described by first order dynamics with a time constant τ_T, as seen in Equation (4.1)

$$\dot{T} = \frac{T_{\text{set}} - T}{\tau_T}, \qquad \tau_T = 0.5[h], \qquad T_0 = 30[^\circ C] \tag{4.1}$$

The degrees of freedom in the optimization is then the input profile of RCl ($\mathbf{u}_{\text{RCl}}$) and the reactor temperature set point profile ($\mathbf{T}_{\text{set}}$) given to the lower level temperature controller . The optimization inputs are parameterized by piecewise constant intervals of length 0.5 hours with 48 intervals in total. The performance enhancement in using smaller intervals is neglectable as the main reaction rates are relatively slow.

4.2 Input Constraints

- The maximum reactor temperature set point is set at 45 °C, to ensure realistic performance.

- The total amount of accumulated input of RCl is set at a high limit of 11.23 [kmol], which is the average total amount of added RCl for a run in current practice.

4.3 Objective Function

Given a fixed final batch time of 24 hours and fixed initial conditions we want to maximize the selectivity (S) and the conversion (χ) at the end of the batch. The product between the selectivity and the conversion is the yield (Y) of the reaction, and a suitable objective for this process is to maximize the yield which is defined in Equation (4.2).

$$Y = \chi S = \left(\frac{\mathrm{N}_{\mathrm{D},t_0} - \mathrm{N}_{\mathrm{D},t_f}}{\mathrm{N}_{\mathrm{D},t_0}}\right)\left(\frac{\mathrm{N}_{\mathrm{DROH},t_f}}{\mathrm{N}_{\mathrm{D},t_0} - \mathrm{N}_{\mathrm{D},t_f}}\right) = \frac{\mathrm{N}_{\mathrm{DROH},t_f}}{\mathrm{N}_{\mathrm{D},t_0}} \tag{4.2}$$

When the initial amount of main reactant (D) is fixed at 9.37 [kmol], maximizing the yield is equal to maximizing the amount of final product (DROH), or equivalently minimizing the sum of main reactant and waste (W). Since we have a high limit constraint on the amount of waste we would also like to have the waste in the objective function. We could alternatively have maximized the yield, with endpoint constraint on the waste, but to avoid feasibility problems in the optimization algorithm, the waste is included in the objective function rather than have endpoint constraints on any of the outputs. This also gives freedom in deciding the relative amounts of waste and main reactant at the end of the batch time.

The endpoint optimization problem is then formulated as:

$$\max_{\mathbf{u}_{\text{RCl}},\mathbf{T}_{\text{set}}} J \tag{4.3}$$

Where the objective function is written on linear Mayer form that only depend on the states at the final batch time (t_f):

$$J = 1.105 \cdot N_{\text{DROH},t_f} - 11.789 \cdot N_{\text{W},t_f} \tag{4.4}$$

Where N_{DROH,t_f} and N_{W,t_f} are the amount of product (DROH) and waste (W) in [kmol] at the final batch time. The amount of product is weighted by a factor of 10 and the waste a factor of 1. The weights on the outputs in the objective function are scaled (Equation(4.5)) with their average final values over all the batches in the data set. The final values of the outputs are obtained by simulating the batches in the data set with the model obtained in Section (3). This is henceforth referred to as “current practice” simulation.

$$J = \frac{10}{\bar{N}^{\text{sim}}_{\text{DROH,tf}}} \cdot N_{\text{DROH},t_f} - \frac{1}{\bar{N}^{\text{sim}}_{\text{W,tf}}} \cdot N_{\text{W},t_f} \tag{4.5}$$

The objective function is maximized subject to the model equations and the input constraints:

$$\dot{\mathbf{x}} = \mathbf{f}(\theta, \mathbf{x}, \mathbf{u}) \tag{4.6}$$

$$\mathbf{y} = \mathbf{g}(\theta, \mathbf{x}) \tag{4.7}$$

$$\int_{t_0}^{t_f} u_{\text{RCl}}\, dt \leq 11.23[\text{kmol}] \tag{4.8}$$

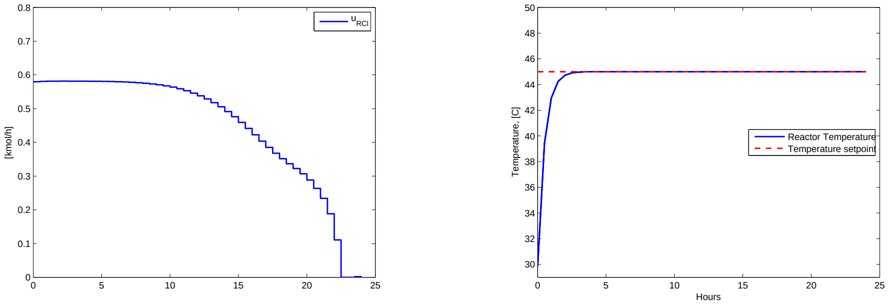
$$T_{\text{set}} \leq 45^\circ C \tag{4.9}$$

The solution was obtained using gPROMS™ with the methods described in Chapter (2.5).

4.4 Results

The nominal optimal solution is a constant reactor temperature set point of 45 °C ($T_{\text{set}} = 45°\text{C}$), which is at the maximum constraint. And the optimal RCl input profile ($\mathbf{u}_{\text{RCl}}$), shown in Figure (4.1). The optimal rate of RCl reactant addition is constant at 0.58 [kmol/h] from start to approximately 10 hours, where it start to decrease and reach zero at around 22 hours.

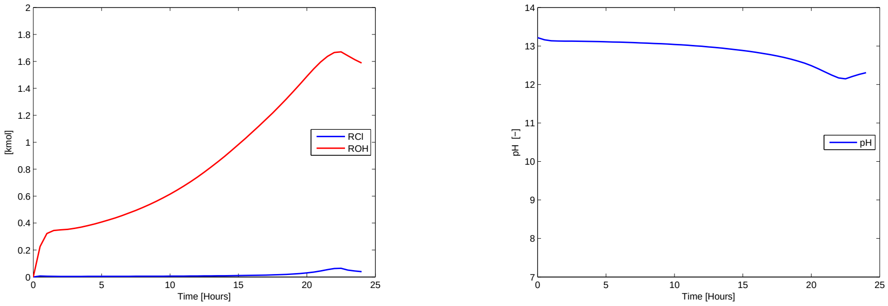
The results from the optimization are shown in Table (4.1) and show an increase in the yield by 0.8 %, which is mainly due to an increase in the conversion. The



(a) Optimal RCl input profile (kmol/h). The total RCl usage is 10.87 (kmol).

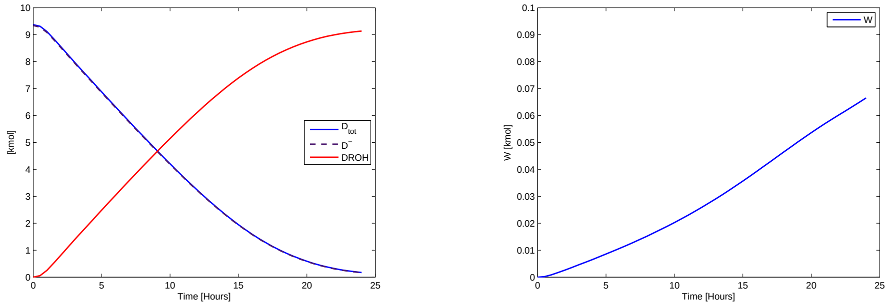
(b) Optimal temperature set point (red broken line) and resulting temperature trajectory (blue line).

Figure 4.1: The optimal inputs of the optimized batch.



(a) Reactant RCl (blue) and intermediate product ROH (red)

(b) pH



(c) Reactant D (blue), D^- (broken dark blue line) and product DROH (red)

(d) Waste product (W)

Figure 4.2: Simulation of the batch with the optimal inputs shown in Figure (4.1).

Table 4.1: Result of optimization and comparison with average current practice.

Case	**D** [kmol]	**W** [kmol]	**DROH** [kmol]	**J**, (4.4)	**Yield** [%],(4.2)
Current practice	0.223	0.0859	9.06	9.00	96.7
Optimized batch	0.171	0.0656	9.13	9.32	97.5

amount of waste (W) and main reactant (D) at the end of the batch has been reduced by 23 % from what is achieved in current practice simulations, and must be considered to be a very good result. Also, the total RCl input usage is 10.87 [kmol]. This is 3.2 % less than the average of what is used in current practice. The output trajectories of the optimized batch procedure is shown in Figure (4.2).

Physical Interpretation

To help explain the resulting optimal operation, the essence in the rate equations for the product and the waste is shown:

$$\frac{d}{\mathrm{dt}}[\mathrm{DROH}] = k_p(\gamma_p)[\mathrm{D}^-][\mathrm{ROH}] - k_{w1}(\gamma_w)[\mathrm{DROH}][\mathrm{ROH}] \tag{4.10}$$

$$\frac{d}{\mathrm{dt}}[\mathrm{W}] = k_{w2}(\gamma_w)[\mathrm{D}^-][\mathrm{ROH}] + k_{w1}(\gamma_w)[\mathrm{DROH}][\mathrm{ROH}] \tag{4.11}$$

The reason for why the temperature in the reactor should be maximized is evident from the temperature dependency of the model equations, Table (3.2), and the obtained parameters, Table (3.3). The rate of product formation has a larger temperature dependency than the waste generation rate, defined from the obtained arrhenius activation energy parameters of the waste (γ_w) and the product (γ_p), where $\gamma_p > \gamma_w$. The reference temperature is set at 35 °C and a temperature above this will increase the rate of product formation more than the increase in rate of waste formation.

However, this increase in temperature should only be done with the obtained optimal input profile shown in Figure (4.1 a), and not all RCl added initially as is current practice. This is because when adding all RCl initially, the amount of product reach maximum relatively fast (faster with a higher temperature) and the second term in the waste generation equation gets large (the waste generation is dependent on the product concentration, over-alkylated product). The input rate of RCl is such that the amount of waste generated from DROH is reduced, but still give a high conversion at the end of the batch.

The reason for why the total accumulated input of RCl is not on the constraint of 11.23 [kmol] is probably due to the increase in reaction rates with a higher reactor temperature, and thus excess RCl is not needed to ensure fast reactions. Also, since RCl react with OH^- to produce ROH relatively fast, the pH in the solution is considerably decreased at start when all RCl is added initially. With the optimal RCl input profile in Figure (4.1), the pH in the solution is kept higher than what is achieved in current practice (Figure (3.3 b)). A high pH keep the equilibrium reaction: $D \overset{K_D}{\rightleftharpoons} D^- + H^+$ far to the right (as seen in Figure (4.2 c)) and ensure faster reaction rates.

Based on the result that not all of the available RCl is needed to optimize the batch process, it is of economic intrest to find out how much total RCl reactant that is needed and still be within the batch objectives stated in Section (3.2). This analysis is given in Appendix (C). And it is shown that the total amount of RCl input required is 14.6 % of what is used on average in current practice. The resulting conversion and selectivity is also better than what is achieved in current practice. However, considering uncertainties in the model and variability in the real process, the minimum RCl input implementation is probably not a robust one.

4.5 Disturbances and Model Uncertainties

The optimal operation obtained in Section (4.4) is when assuming a perfect model and no disturbances during a run. In practice, disturbances will allways be present and the model obtained is not a perfect representation of the real system, discussed in Section (3.6).

Disturbances that can be present in the real process that are considered here are, [GEH]:

- Error in the measured initial amount of reactant NaOH.
- Reactant and solvent quality (NaOH, D, RCl). Change of feed-stock and recycled solvent. The quality of reactants and solvents can degrade the reaction rates in the system.
- Implementation errors. Wrong input and temperature profiles from the control system.
- Model parameter uncertainties.

In order to analyze the sensitivity the optimization has for model-plant mismatch and various disturbances, the disturbances and uncertainties have to be modeled. The chosen values for the disturbances are considered to be the worst case independent modeling error and disturbances that can be present in the system.

In addition to represent model-plant mismatch (model uncertainty), the errors in the reaction rate parameters can be view as reactant and solvent quality disturbances that slows the rate of reaction. The chosen parameters are the reaction rate pre-exponents (K) and the arrhenius activation energies (γ) for the product and the waste generation and the equilibrium constant (Kr). +20% means that the parameter has been increased by 20% in magnitude from the original estimated parameter, -20% is a 20 % decrease. - 10 % NaOH means that the initial amount of NaOH is 90% of the nominal value.

Regarding implementation errors; three cases are considered. The input profile of RCl is reduced by 10 %. That is, at every control time step, the added RCl is 10 % lower than it should be from the nominal optimal feed profile in Figure (4.1). Also, a case where the added RCl is 10 % more than the nominal optimal is considered. Error in the temperature set point is considered by letting the temperature set point be constant at T=35°C (the set point used in current practice) instead of the optimal at 45°C (alternative interpretation: the reaction rate dependency is set to zero).

In the following, the model uncertainties and the implementation errors are included in the collective name: “disturbances“.

4.6 Sensitivity Analysis for Various Disturbances

In this section an analysis of the nominal optimized batch implemented open loop, $J_{\text{open-loop}}$ is performed with various disturbances and compared with the performance of the system when re-optimizing the inputs with the disturbances present, $J_{\text{opt}}(d)$. The result will give an indication on the sensitivity of the nominal optimized batch in the presence of disturbances and uncertainty. Also, the result will indicate what type of disturbance that degrades the achievable performance of the system most. The disturbances analyzed are the ones considered in Section (4.5).

The results from the sensitivity analysis show that even for relatively large parametric uncertainties in the model, that the loss: $L = J_{\text{open-loop}}(d) - J_{\text{opt}}(d)$ is small, which means that the nominal optimal input profile is close to the optimal for these disturbances. Or in other words: the open loop implementation is relatively insensitive to model parameter errors.

For the last three disturbances (implementation errors) the loss from optimal behavior is relatively large, and strategies for reducing the loss should be considered. The largest loss, and one of the two cases that lead to worse performance than what is achieved in current practice, is when the temperature set point is decreased from 45 to 35 °C , this can be explained by the temperature dependency on the reaction rates and that the improved performance (compared to current practice) is mainly achieved by increasing the temperature. The second worst disturbance is the error in the initial amount of NaOH by 10 %, and the performance is considered to be very dependent on the pH in the solution. This loss can potentially be minimized easily by measurement of the solution pH and feedback correction by adding more NaOH. Also, the disturbance where the nominal optimal RCl input is reduced by 10 % yield a relatively large loss.

The optimal performance that is theoretically achievable is most sensitive to disturbances regarding the temperature and temperature dependency of the reac-

Table 4.2: Sensitivity analysis for various disturbances. When re-optimizing, the input $\mathbf{T}_{\text{set}}$ is always constant at 45 °C exept for the * case: Which alter the relative size of the Arrhenius parameters, $\gamma_w > \gamma_p$, and thus alter $\mathbf{T}_{\text{set}}$ when re-optimizing. Here, the objective function is given with three significant figures for the purpose of visualization.

Disturbance	$J_{\textbf{open-loop}}(d)$	$J_{\textbf{opt}}(d)$	**Loss**
- 10% NaOH	8.939	9.204	0.2650
- 20% K_p	9.098	9.102	0.0040
+ 20% K_{w1} + 20% K_{w2}	9.152	9.153	0.0010
- 90% K_r	9.247	9.281	0.0340
- 20% γ_p	9.162	9.164	0.0020
+ 20% γ_w	9.220	9.221	0.0010
* - 20% γ_p + 20% γ_w	9.052	9.064	0.0120
- 10% u_{RCl}	9.147	9.303	0.1560
+ 10% u_{RCl}	9.238	9.318	0.0800
T_{set}=35°C	8.779	9.016	0.2370

tion rates in the model. The temperature dependency parameters in the model (estimated from multiple batches) are also unfortunately the parameters that are considered to be most uncertain, as discussed in Section (3.6).

Evaluating the performance for all possible disturbances is not possible, and disturbances that are not considered here may be present in the real process. However, the disturbances evaluated here are considered to be the worst case disturbances that could potentially degrade the performance of the system considerably.

Considering the model uncertainty, un-modeled disturbances and variability in the real process, implementation of the nominal optimal solution open-loop is probably not appropriate in industry without laboratory analyses and verification of the obtained model. However, the nominal solution is still useful for qualitative insight in how the process should be run and for determine the physical limits of the system.

Also, the nominal optimal solution with on-line feedback control as a measure for handling disturbance and variability is considered to be of potential in this case. The problem then consists of finding good output variables to control. This will be the focus in the next chapter.

4.7 Summary

In this chapter it is shown that the batch reactor step indeed has potential for improved performance by changing the operating procedure and conditions from what is done in current practice. Increased reactor temperature and a continuous addition of the RCl reactant throughout the batch can theoretically result in a 0.8 % increase in the yield and 23 % reduction of both the waste and the main reactant amount at the end of the batch.

This best case result is when assuming that the model obtained in Chapter (3) is a perfect representation of the real system and no disturbances are present. This is not the case regarding the real batch process at GE Healthcare.

Thus, a sensitivity analysis of the optimization regarding disturbances and model uncertainties was made, and it is shown that the nominal optimal operating procedure is relatively insensitive to model uncertainties, but more sensitive to implementation errors. Also, the optimal achievable performance of the batch is very dependent on the reaction rate temperature parameters, and these should be verified.

CHAPTER 5

INDUSTRIAL CASE STUDY SELECTION OF CONTROLLED VARIABLES

To this chapter we have fixed a model of the batch and obtained optimal open-loop input profiles assuming a perfect model of the system with no disturbances present. Reality is much harsher than ideal behavior and in this chapter we want to, in the presence of the worst case model uncertainties and disturbances defined in Section (4.5), close the loop by controlling good output variables on-line to the pre-calculated set point trajectories obtained in Section (4.4). In this thesis ”good output variables” to control is the self-optimizing variables defined in Section (2.8) [SP05].

This strategy for handling disturbances and uncertainty is relatively easy to implement in practice and a good alternative to batch MPC and advanced re-estimation strategies given that these ”self-optimizing” variables exist, can be measured and controlled. Thus, the goal in this chapter is to find these output variables that when controlled close to the optimal trajectory, lead to acceptable loss for any disturbance that may occur.

In order to implement feedback control we need available inputs, measurements and a feedback control law. Since the performance of this batch is only dependent on the final state, the performance of the feedback control law itself is not considered of great importance in this thesis. The important thing is that it can track the chosen output variable to the reference trajectory fairly good in simulations and that it is stable.

5.1 Degree of Freedom Analysis

The nominal (without disturbances) optimal input trajectories of the batch are obtained in Chapter (4). Where T^{set} should be held constant at 45 °C and the input profile $\mathbf{u}_{RCl}$ is shown in Figure (4.1 a). Since the temperature should be held at the maximum bound for optimality, the temperature set point is lost as a control DoF.

The remaining control DoF is additional feed of RCl and negative RCl input. Negative RCl input is realized by adding the negative RCl input to the nominal optimal input profile, $u_{\text{RCl}}(i) = u_{\text{RCL}}^{\text{optimal}}(i) + u_{\text{RCl}}^{\text{control}}(i)$, thus $u_{\text{RCl}}^{\text{control}}(i)$ should be less than $u_{\text{RCl}}^{\text{optimal}}(i)$ in the negative direction to ensure a realistic implementation. Additional input of NaOH beyond the initial addition is also an available degree of freedom. Negative u_{NaOH} is unrealistic and u_{NaOH} is restricted to be positive.

As in Section (4.1) the control horizon is parameterized into 48 intervals. Thus the degrees of freedom are:

$$\mathbf{u}_i = \begin{bmatrix} 1: u_{\text{RCl}} \\ 2: u_{\text{NaOH}} \end{bmatrix}_i \qquad i = 1, 2, ..., 48 \tag{5.1}$$

With the constraints:

$$u_{\text{RCl}}^{\text{control}}(i) \leq 0.5[\text{kmol/h}] \tag{5.2}$$

$$-u_{\text{RCl}}^{\text{control}}(i) \leq u_{\text{RCl}}^{\text{opt}}[\text{kmol/h}] \tag{5.3}$$

$$u_{\text{NaOH}}(i) \leq 0.5[\text{kmol/h}] \tag{5.4}$$

$$u_{\text{NaOH}}(i) \geq 0[\text{kmol/h}] \tag{5.5}$$

With these two inputs, we can at best control two chosen variables.

5.2 Candidate Controlled Variables

In this chapter we assume that all the outputs ($\mathbf{y}$) can be measured with a sampling time of 0.5 hours, even though on-line measurements are currently only available for W and D [1]. The pH is only measured three times during the batch in current practice, but on-line pH measurements can be made available with investments. RCl is not considered an output variable because it is rapidly converted to ROH in excess of OH^-. The candidate control variables (outputs) are then:

$$\mathbf{y}_i = \begin{bmatrix} 1: N_{\text{ROH}} \\ 2: N_{\text{D}} \\ 3: N_{\text{W}} \\ 4: N_{\text{DROH}} \\ 5: \text{pH} \end{bmatrix}_i \tag{5.6}$$

---

[1] Currently there are NIR measurements of W and D available every hour, as discussed in Section (3.2)

5.3 Control of pH

From discussions with GE Healthcare and by looking at the model equations it is realized that the pH in the solution has an effect on the reaction rates in the system. For large pH, the OH^- concentration is high and the reaction rates are high. This is also seen by the optimal operation of the batch versus current practice, where the pH in the optimized batch is higher throughout the batch run. Therefore this pH effect was analyzed further by re-optimizing the system with u_{NaOH} as an additional optimization degree of freedom.

From this analysis, given in Appendix (D), it was found that it is optimal to maximize the pH in the solution throughout the batch. Also, this extra optimization DoF did not effect the optimal u_{RCl} input profile or the temperature set point T_{set}, see Appendix (D).

Thus the new optimal operation can be implemented by including feedback on the pH using u_{NaOH} and choose the set point at the maximum pH possible (“active constraint control“ [Sko00] , and discussed in Section (2.8)). The maximum pH in the solution is here set to be at 13.2, as it is the initial pH in the solution. The pH feedback control strategy is visualized in Figure (5.1). This feedback implementation is more robust than implementing the open-loop optimal u_{NaOH} profile, when disturbances are considered.

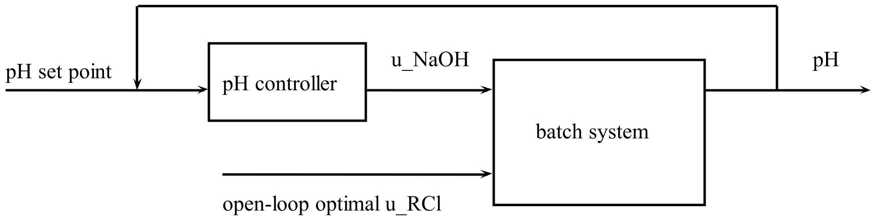


Figure 5.1: pH feedback control structure. Included in the batch system is the temperature feedback control loop.

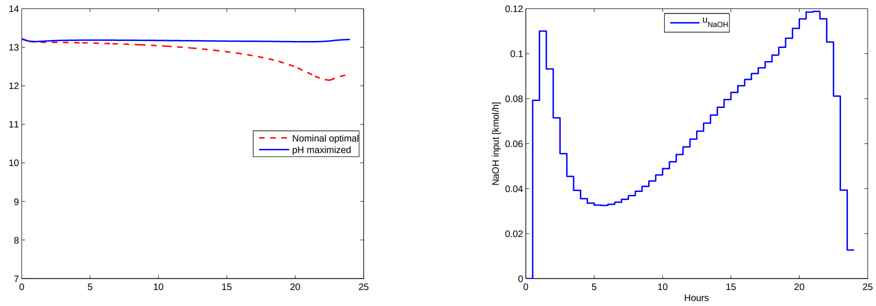
The control law used is a simple proportional controller, shown in Equation (5.7). With the controller gain, K_{pH}, tuned manually by simulations to obtain acceptable performance.

$$u_{\mathrm{NaOH}}(i)[\mathrm{kmol/h}] = -K_{\mathrm{pH}}\left(\mathrm{pH}(i) - 13.2\right), \qquad K_{\mathrm{pH}} = 2 \tag{5.7}$$

The result with pH controlled to the maximum by feedback using u_{NaOH} without disturbances present is given in Figure (5.2) and Table (5.1). And show that the objective function is increased slightly (from 9.32 to 9.33). This may not seem as much, but later when we analyze the performance with the disturbances present (Table (5.3)) controlling the pH has a considerable effect. The performance is enhanced (compared to not controlling pH) for every disturbance considered. In the following, u_{NaOH} is lost as a control degree of freedom, since its job is to maximize pH. The remaining available control degree of freedom is then u_{RCl} with its

Table 5.1: Results of optimization with constant pH=13.2 and comparison with current practice without disturbances.

Case	**D** [kmol]	**W** [kmol]	**DROH** [kmol]	**J**, (4.4)	**Yield** [%],(4.2)
Current practice	0.223	0.0859	9.06	9.00	96.7
Optimized batch	0.171	0.0656	9.13	9.32	97.5
Optimized with pH max	0.159	0.0659	9.15	9.33	97.6



(a) Blue: pH held constant at 13.2, Red: Nominal pH profile.

(b) Input usage of NaOH.

Figure 5.2: New optimal operation without disturbances, where the pH is maximized using additional input of NaOH, u_{NaOH}. Total accumulated $U_{\text{NaOH}} = 1.62$ [kmol], and correspond to 12.6 % of the total NaOH usage (initial condition + U_{NaOH}). Optimal u_{RCl} and T_{set} profiles is the same as in Figure (4.1).

constraints given in Section (5.1), and can at best be used to control one of the remaining outputs.

5.4 Input – Output Analysis

In order to find the effect (directions and magnitude) u_{RCl} has on the outputs throughout the batch, an analysis of the the input – output relation of the system is performed with respect to additional usage of u_{RCl} throughout the batch.

Here, since the performance of the system only depend on the final state and the process is non-linear and time-varying, the time varying process input-output gain, $\mathbf{G}(i)$ is defined as:

$$\mathbf{G}(i) = \frac{\Delta \mathbf{y}_i}{\Delta u_{\text{RCl}}(i)} \tag{5.8}$$

$$\Delta \mathbf{y}_i = \mathbf{y}_i - \mathbf{y}_{\text{opt}} \tag{5.9}$$

Where $\Delta \mathbf{y}_i$ is the deviation in the outputs (simulated with square pulse - nominal optimal reference) at the final time step, for an additional square pulse in the RCl input, $\Delta u_{\mathrm{RCl}}(i)$, during control time step i. The control and test horizon is parameterized into 48 intervals, thus i=1,2,...,48.

The procedure is visualized in Figure (5.3). To obtain $G(i)$ for all the outputs, the process is simulated 48 times with an additional square pulse in the input, Δu_i, of amplitude 1 [kmol/h] and duration of 0.5 hours at time step i. Or in other words, for an extra addition of 0.5 [kmol] RCl at control time step i, how does this effect the outputs at the final batch time step. This is done for each control interval, i, and $\Delta \mathbf{y}_i = \mathbf{y}_{\mathrm{opt}} - \mathbf{y}_i$ and $\mathbf{G}(i) = \frac{\Delta \mathbf{y}_i}{\Delta \mathbf{u}_i}$ is calculated.

It should be noted that this analysis is performed with the nominal optimal u_{RCl} input profile and the pulse as an addition. The pH controller is turned off (no input of u_{NaOH}).

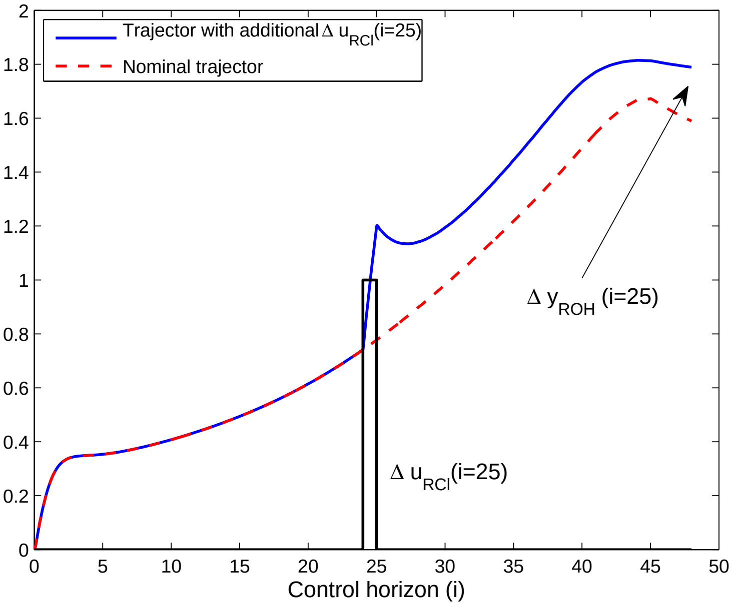
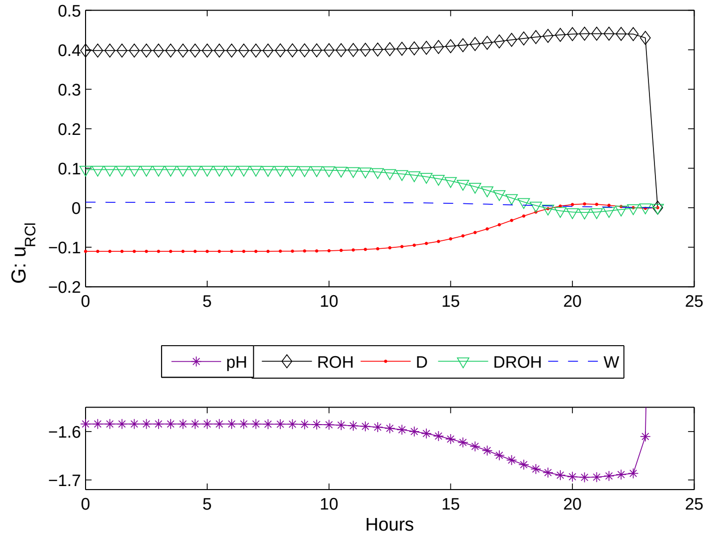


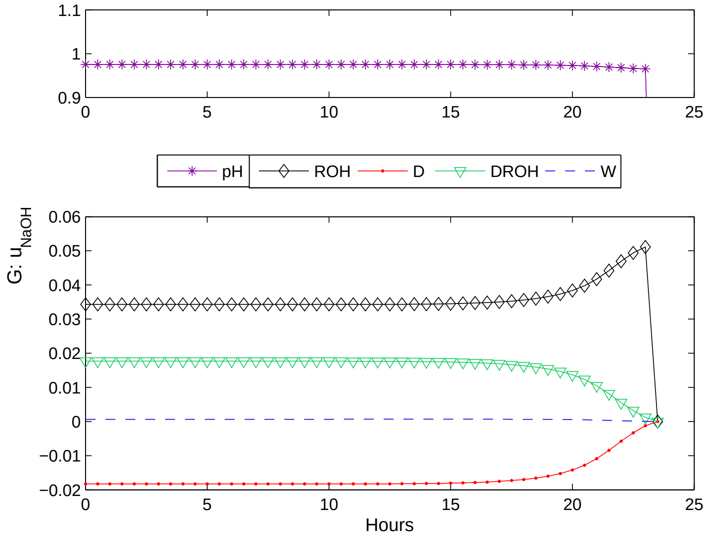
Figure 5.3: Visualization of the gain calculation example for the ROH state.

Example:
At control time step i=25 (12 to 12.5 hours), and an extra square puls of total magnitude 1.0 [kmol] in RCl, $\Delta u_{\mathrm{RCl}}(i=25) = 1.0$ [kmol]. Regarding the output ROH [kmol]: simulations obtain a final ROH amount of 1.79 [kmol]. The nominal value from simulations in Section (4.1) gave a ROH amount of 1.59 [kmol].
Thus, $\Delta y_{\mathrm{ROH}(i=25)} = 0.20$ and $G_{(\mathrm{ROH})(i=25)} = \frac{0.20}{0.5}\frac{[\mathrm{kmol}]}{[\mathrm{kmol}]} = 0.40$.

This gain analysis is also performed regarding pulses in the u_{NaOH} input and responses in the outputs. The resulting gains are shown in Figure (5.4). These gains are not scaled for the purpose of a more intuitive visualization. For u_{RCl} the gains and their signs (±) are relatively constant for the first part of the process. From 15 to 24 hours the gains decrease and change sign for the outputs D and DROH. This show that the ability to influence these variables decrease at the end of the batch. Regarding the u_{NaOH} input, the gains are approximately a factor of 10 smaller in magnitude than for u_{RCl}, except for the pH output. Based on this analysis, the magnitude of interaction (by using u_{NaOH} to control pH) is considered to be small and it seems that a simple decentralized control structure can give acceptable performance.



(a) Process gain of u_{RCl} to $\mathbf{y}$



(b) Process gain of u_{NaOH} to $\mathbf{y}$

Figure 5.4: Effect of square pulses in input at control interval i to the outputs ($\mathbf{y}$) at the final batch time.

Tracking Controller

From the above section, it was argued that a decentralized control structure will probably give acceptable performance. This control structure is visualized in Figure (5.5) where the pairing is: control pH with u_{NaOH} and one of the other output candidates with u_{RCl}. The pH control loop is already closed and configured, and the remaining task is to close the other.

The goal of this section is not to come up with an optimal control law, but merely to use a control law that is capable of tracking one of the output references by using the available u_{RCl}.

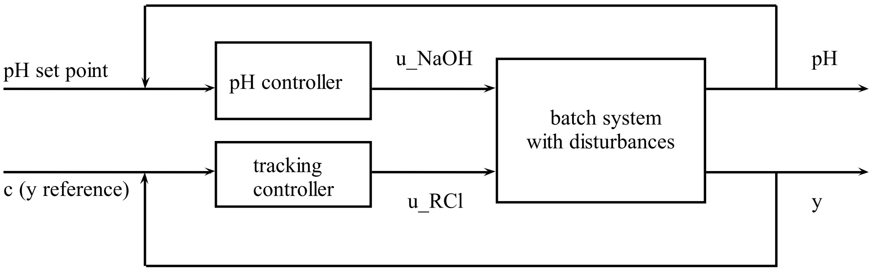


Figure 5.5: Decentralized pH and reference tracking control structure. Included in the batch system is the temperature feedback control loop.

For simplicity a time varying proportional controller, Equation (5.10), is used for tracking the chosen output reference trajectory, since the system characteristics are time-varying. For simplicity, and in order to capture the system gain characteristic shown in Figure (5.4), the controller gains have the inverse characteristics of the gain $\mathbf{G}(i)$, but scaled (tuned) to ensure tracking capabilities for all the disturbances.

$$u_{\text{RCl}}(i) = u_{\text{RCl}}^{\text{opt}}(i) - K_y(i)\left(y(i) - y_{\text{ref}}\right) \tag{5.10}$$

Where i is the i'th control interval and y(i) is the choosen output to track. $K_y(i)$ is defined as:

$$K_y(i) = \frac{P_y}{G_y(i)} \tag{5.11}$$

The tuning parameter P_y used are shown in Table (5.2) and tuned manualy, from simulations, to be able to track the chosen outputs fairly good for all the disturbances. Since the system is not scaled the tuning parameters range over a large interval, especially for the waste (W) state.

This procedure (gain calculation and controller design) for tracking time-varying trajectories is not standard procedure and can not be implemented on the real batch process. Real implementation requires far more robust procedures. But nevertheless the objective here is only to be able to track the reference fairly good in simulations so that a comparison of the theoretical performance of the system while tracking different output variables can be made for various disturbances.

Table 5.2: Tracking controller parameters

Output	ROH	D	DROH	W
P	15	10	10	50000

As an example of the tracking performance with the chosen control law, plots of the candidate controlled variable with and without the tracking controller on is shown in Figure (5.6) and the corresponding input profiles are shown in Figure (5.7). This example is for the disturbance: $T_{\text{set}} = 35°\text{C}$ (implementation error on the temperature set point). And is the disturbance where it is most difficult to track the references, because of the relatively bad performance of the system at low temperatures. For completeness, and as a check for that the chosen controlled variable is tracked fairly good, plots are made for every disturbance and chosen controlled variable and the corresponding input usage of u_{RCl} and u_{NaOH}. These plots can be found on the attached CD in Appendix (E).

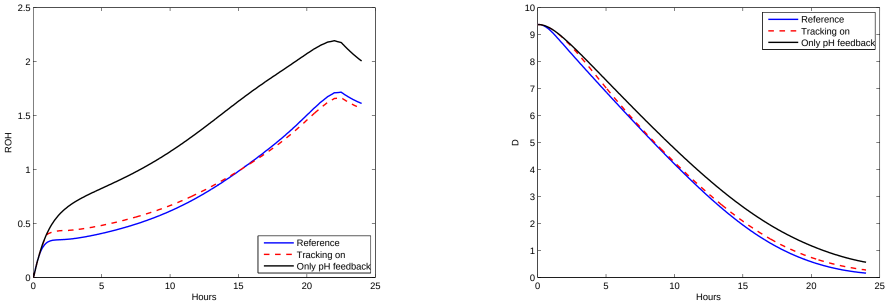
The plots show that the controlled variables are tracked fairly good for every disturbance, except for the waste (W) state for disturbances that deteriorate the system performance to a large extent (such as error in the temperature set point). Also, the tracking is not perfect and better tracking could be achieved with a more advanced control law, e.g. with included integral action. However, for large disturbances in the model equations it is inherently difficult to track the nominal optimal output profiles at the end of the batch, because of the reduced reaction rates (physical limits). The ability to influence the system decrease with time, as shown in Figure (5.4). The pH is controlled to the set point very good for every disturbance, and it is concluded that the decentralized control structure works well.

5.5 Selection of Controlled Variable

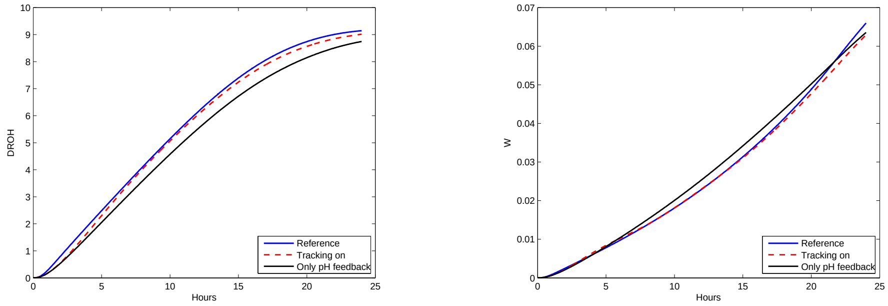
We want to find the output variable when controlled close to the nominal optimal pre-calculated reference trajectory, lead to acceptable loss (L, Equation (5.12) for every possible disturbances. Or in other words; find the variables (y), when controlled to references (c) lead to the optimal adjustment of the manipulated variable (u_{RCl}) for all disturbances. The disturbances considered here are the ones discussed in Section (4.5). Since the system is non-linear and time varying a simple, but somewhat time consuming method is used: “the direct evaluation of loss” discussed in Section (2.8).

$$L = J_{\text{opt}}(d) - J_c(c, d) \tag{5.12}$$

Where $J_{\text{opt}}(d)$ is the result of re-optimizing the problem with the known disturbance present and pH feedback implemented. The scheme is visualized in Figure (5.8) And $J_c(c, d)$ is the result of tracking the nominal (without disturbance) op-



(a) ROH (b) D



(c) DROH (d) W

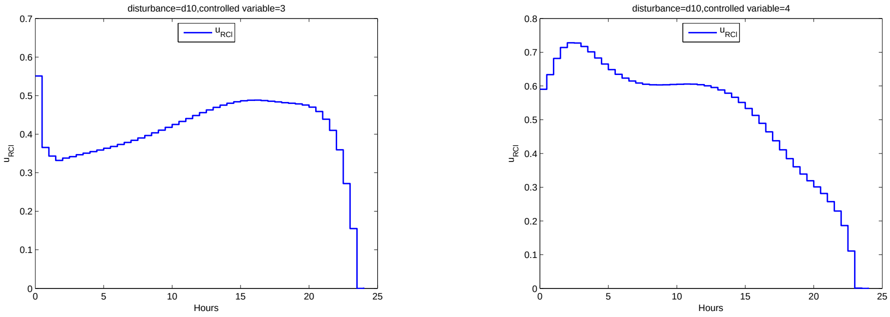
Figure 5.6: Controlled variables tracked to references with disturbance in the temperature set point: $T_{\text{set}} = 35°\text{C}$. These four plots are four different simulations. For each sub figure only the variable that is tracked is shown, the other states of the system deviate from the nominal optimal reference. The corresponding input usage u_{RCl} for each simulation is shown in Figure (5.7).

timal pre-calculated output references ($c = y_{\text{ref}}$) using simple feedback with the disturbance present, visualized in Figure (5.5).

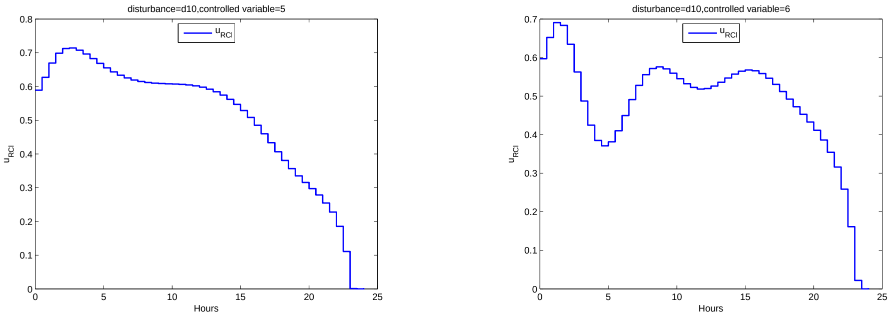
The loss is evaluated for all the candidate control variables (y) over the considered disturbances. The controlled variable with smallest average value of the loss over all the disturbances is then preferred controlled.

5.6 Results

Table (5.3) show the resulting objective function (J) by tracking each candidate control variable for every disturbance. The last column shows the result by reoptimizing the problem. The first column “only pH control” is the result when controlling pH and using the nominal optimal u_{RCl} input profile (tracking controller off), Figure (5.1). And show that improved performance can be achieved by keeping the pH in the solution at the maximum compared to when the nominal



(a) Controlled variable: ROH (b) Controlled variable: D



(c) Controlled variable: DROH (d) Controlled variable: W

Figure 5.7: Corresponding input usage u_{RCl} when tracking the trajectories shown in Figure (5.6).

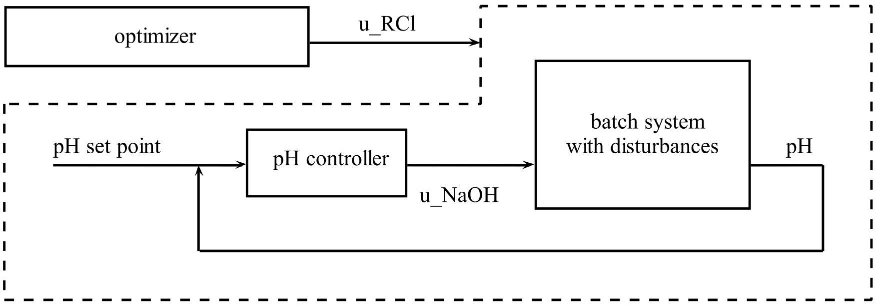


Figure 5.8: Re-optimizing with the disturbance present and internal pH feedback control loop.

open-loop solution is implemented, Table 4.2, for every disturbance considered.

Table 5.3: Performance with constant pH set point at 13.2 and one extra controlled output (c=y). Numbers in boldface indicate the highest objective function value with the given disturbance, and thus the best controlled variable.

Disturbance	only pH control	c = ROH	c = D	c = DROH	c = W	$J_{\mathbf{opt}}(d)$
- 10% NaOH	**9.327**	**9.327**	**9.327**	**9.327**	**9.327**	9.328
- 20% K_p	9.114	9.069	**9.119**	**9.119**	8.991	9.120
+ 20% K_{w1} + 20% K_{w2}	**9.158**	**9.158**	**9.158**	**9.158**	9.078	9.160
- 90% K_r	9.309	9.308	**9.310**	**9.310**	9.309	9.310
- 20% γ_p	9.175	9.151	**9.178**	**9.178**	9.110	9.179
+ 20% γ_w	**9.227**	**9.227**	**9.227**	**9.227**	9.196	9.228
- 20% γ_p + 20% γ_w*	**9.064**	9.047	9.063	9.063	8.887	9.099
- 10% u_{RCl}	9.150	**9.326**	9.317	9.314	9.323	9.310
+ 10% u_{RCl}	9.219	**9.327**	9.323	9.322	9.326	9.327
T_{set}=35°C	8.913	8.117	**9.070**	9.069	8.790	9.070

Regarding (the scheme shown in Figure (5.5)) tracking references (c=y) by changing the input profile u_{RCl}, little or no improvement can be made compared to only controlling pH when considering the first 7 disturbances in the table. These disturbances are related to the model equations and the open loop implementation is close to optimal, as noted in Section 4.6. However, for the last 3 disturbances (implementation errors) improvements are made.

There is little improvement that can be made by re-optimization compared to when controlling D or DROH. Also, the re-optimization strategy is worse than the feedback scheme for implementation error in u_{RCl} (- 10%). This is because of the constraint in the optimization problem on the total amount of RCl available, which the feedback strategy does not have. This indicates that on-line feedback control on the right variable is a good alternative to re-optimization strategies in this system.

From Table (5.3) the best variable for feedback control in addition to maximize the pH is the product concentration (DROH) or the main reactant concentration (D). Controlling either of these two variables lead to acceptable loss for every disturbance considered here. These two variables are considered to be the “self-optimizing” variables in the system and should be controlled.

To show this more intuitively plots are made of the objective function values for the disturbance (d): $T_{\mathrm{set}} = 45° - d$ (implementation error in the temperature set point). Here, as the disturbance increase, the performance deteriorates as expected. However, tracking the nominal optimal trajectory of either DROH or D (red line) result in a minimal loss compared to the truly optimal (black line) (by re-optimization). Also, tracking ROH (pink line) is worse than when only controlling pH and using the nominal u_{RCl} open-loop profile.

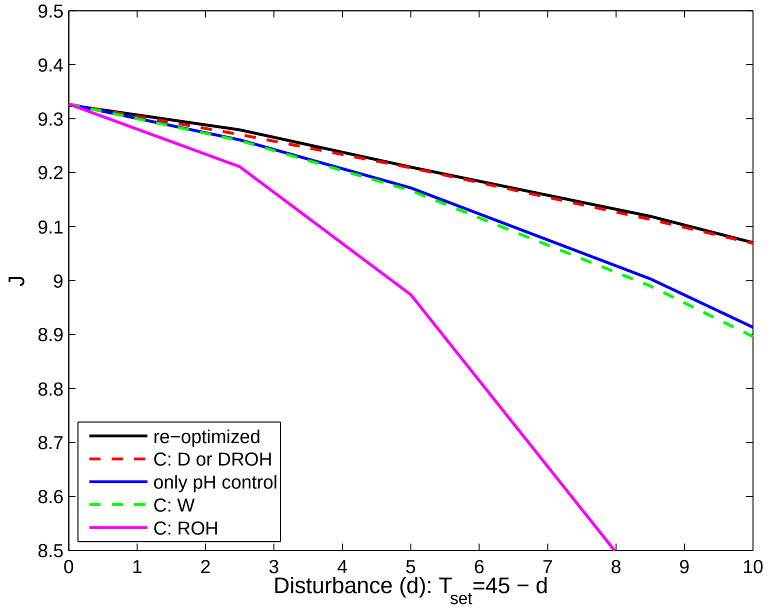
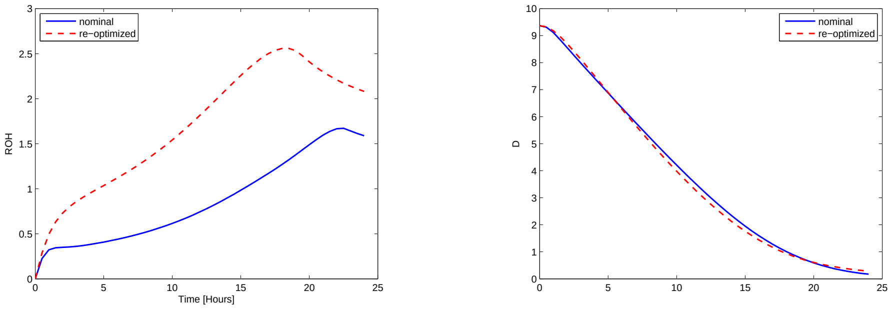


Figure 5.9: Visualization of the performance (objective function) when tracking alternative variables. For this disturbance (increasing implementation error in the temperature setpoint), DROH and D(red broken line) are the best variables to track and are self optimizing variables. Black line: re-optimized. Blue line: tracking controller off. Green (broken) and pink line correspond to tracking the W and ROH outputs respectively.

The reason for why D and DROH is the self optimizing variables in this system can be explained from the requirements of a good variable for control, given in Section (2.8).

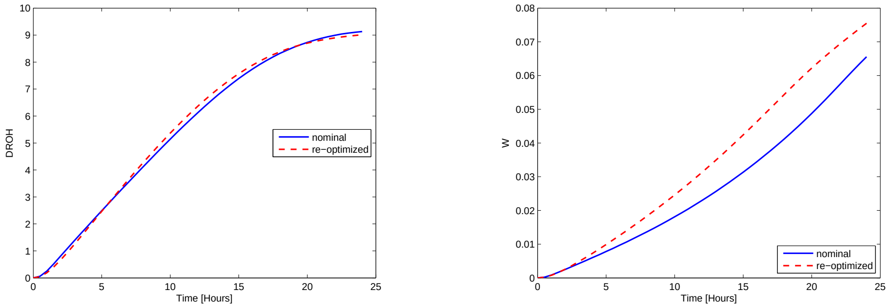
- The D and DROH variables are relatively sensitive to changes in the manipulated variable u_{RCl}. This is shown in the input-output analysis in Figure (5.4).

- For D and DROH, the optimal trajectory is insensitive to disturbances (the optimal variation is small). This is shown in Figure (5.10) for the temperature set point disturbance, but is the general characteristic of D and DROH for all the considered disturbances. The optimal ROH and W trajectories vary significantly, and their optimal variation is generally large.



(a) ROH

(b) D



(c) DROH

(d) W

Figure 5.10: Blue line: nominal optimal trajectories without disturbance. Red (broken) line: optimal output trajectories for the $T_{\mathrm{set}} = 35$ disturbance (implementation error in the temperature set point). For DROH and D, the optimal variation for this disturbance is small. For W and ROH it is large.

5.7 Summary

In this chapter we have found that the pH in the solution should be controlled to maximum (active constraint control) throughout the batch by using the available NaOH input, u_{NaOH}. This yield a nominal (without disturbances) performance that is better than what was obtained in Chapter (4), when no extra NaOH was added to the batch. Also, controlling the pH reduce the loss in performance that occur when the considered disturbances are present.

It is also shown that the remaining degree of freedom u_{RCl} should be used to control one of the self-optimizing variables: D or DROH. Controlling one of them to the optimal trajectory, found when maximizing the pH, yield a minimal loss from the truly optimal performance (re-optimized) for every disturbance considered in this thesis.

In the real batch process, on-line (NIR) measurements of the main reactant (D) are available every hour. And GE Healthcare, Lindesnes is currently testing a system with on-line pH measurements on another batch process. Thus, if accurate pH and NIR measurements can be readily available for this batch, the feedback control strategy for handling disturbances is of great potential and a good alternative to re-optimization strategies such as Batch MPC.

CHAPTER 6

CONCLUSION

Model

In this thesis a model of the batch reactor step at GE Healthcare is obtained by using existing process information, previous projects and general process insight. The model parameters are estimated from measurements of several batch runs. The model obtained is considered to be a good representation of the batch reactor around the operating region where the data was available. However, there exists some uncertainty in the temperature dependency of the reaction rates, because of low variability in the batch to batch temperature profiles in the data set. These parameters should therefore be validated or re-estimated by experiments with more variability in the reactor temperature. And as a check for that the parameters are accurate outside the region of operation from where they are estimated (temperatures around 30 to 35 ° C).

Optimization

Based on the model developed it is shown that the batch reactor step indeed has potential for improved performance by changing the operating procedure and conditions from what is done in current practice. Increased reactor temperature and a continuous addition of the RCl reactant throughout the batch can theoretically result in 0.8 % increase in the yield and 23 % reduction of both the waste (W) and the main reactant (D) amount at the end of the batch.

This best case result is when assuming that the model obtained is a perfect representation of the real system and no disturbances are present. This is not the case regarding the real batch process at GE Healthcare. However, the nominal solution is still useful for qualitative insight in how the process should be run and for determine the physical limits of the system.

An analysis of the sensitivity the optimization has for model errors and disturbances is made. From the sensitivity analysis it is shown that the optimal achievable performance (re-optimized batch with disturbance implemented) is mainly dependent on the temperature parameters estimated. And implicate that the temperature dependency in the model indeed need verification.

When implementing the nominal optimal operating procedure open loop there is a loss in performance compared to when the operating procedure is re-optimized when disturbances are present. It is shown in Table (4.2) that this loss is small for the model errors considered, but larger for implementation errors and error in the initial conditions of NaOH. And indicate that the optimal operating procedure is relatively insensitive to model uncertainties, but sensitive to implementation errors.

Control

In this thesis it is found that the pH in the solution should be controlled to maximum (active constraint control) throughout the batch by using the available NaOH input, u_{NaOH}. This yield a nominal performance that is better than what was obtained in Chapter (4). Also, controlling the pH reduce the loss in performance that occur when the considered disturbances are present.

It is also shown that the remaining degree of freedom u_{RCl} should be used to control one of the self-optimizing variables: D or DROH. Controlling one of them to the new optimal trajectory (resulting from controlling pH to maximum), yield a minimal loss from the truly optimal performance (when re-optimizing) for every disturbance considered. Given that accurate on-line measurements of pH and D or DROH can become readily available: on-line feedback control is a good alternative to re-optimization strategies in this system for handling disturbances and variability.

Further Work

For further work on this process, it is suggested that the model structure and parameters are validated in experiments or laboratory. This can be performed by running batches with more variability in the measured inputs (temperature and reactant inputs) and validate or re-estimate the parameters. However, considering the risk of yielding an off spec batch compared to the potential benefit from it, this is most likely not acceptable.

Another "safe" method would be to gradually alter the operating procedure toward the optimal. E.g. by increasing the temperature set point 1 °C each batch in addition to adding the RCl reactant more gradually in the beginning of the batch.

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APPENDIX A

DATA ANALYSIS

A statistical analysis of the data set has been performed to investigate the quality and usefulness of the data set regarding the identification of a batch model. The correlations between the variables are also analyzed in order to better understand the batch process.

There are five measured inputs in the data set (the temperature profile, initial added reactant 1 (RCl) and 2 (NaOH) and additional input of reactant 2 (RCL) at 8 and 13 hours. Regarding the temperature profile; only the first five hours of the batch is considered. This is the interval where the temperature vary the most between the batches, because the temperature after 5 hours is set constant at 35 ° in all the batches by the temperature controller, Figure (3.2 b). Additional input of reactant 1 (NaOH) at 8 and 13 hours is not considered in this analysis since this event only occur in one of the batches in the data set. There are eight measured outputs in the data set (three measurements of two of the concentrations and two measurements of the pH in the solution during the batch run). The data set consists of 30 batches (n=30) with their respective measured inputs and outputs.

In order to estimate model parameters from the data, we want large variation in the inputs that excite consistent variations in the measured outputs. The mean and standard deviation of the measured inputs and outputs are given in Table (A.1).

An estimate of the correlation between two variables, **x** and **y**, can be expressed by the *Sample Correlation Coefficient*, R_{xy}, given in Equation A.1, [RN88].

$$R_{xy} = \frac{n\mathbf{x}\mathbf{y}^\top - \mathbf{x1}\mathbf{y1}}{\sqrt{n\mathbf{x}\mathbf{x}^\top - (\mathbf{x1})^2}\sqrt{n\mathbf{y}\mathbf{y}^\top - \left(\mathbf{y1}\right)^2}} \tag{A.1}$$

Where n is the size of the sample row vectors, and **1** is a column vector with ones of size n.

This correlation will indicate only the degree of *linear* relation between the variables. Thus, for each correlation calculation a **x** vs **y** plot is made as a check for non-linear correlations and ”outliers” in the data set. These plots are not given in the report, but are made available on the CD attached. However, no non-linear relation or “outliers“ was found. Also, correlation does not imply causality and care have to be made when assigning correlations between the variables. E.g. if it apparently is a correlation between A and B, this may be due to a third variable C that correlates to A and B.

Table A.1: Description of inputs (x) and outputs (y)

Variable	Average	σ	Description
x1	33.87 [K]	0.274	Average reactor temperature the first 5 hours
x2	11.223 [kmol]	0.0136	Initial amount of reactant 1 (NaOH)
x3	11.054 [kmol]	0.0081	Initial amount of reactant 2 (RCl)
x4	0.0350 [kmol]	0.0337	Amount of extra reactant 2 (RCl) added at t=8 hour
x5	0.1432 [kmol]	0.0681	Amount of extra reactant 2 (RCl) added at t=13 hour
y1	2.8794 [kmol]	0.1301	Measured amount of reactant 3 (D) at t=6.5 hours
y2	1.3256 [kmol]	0.1485	Measured amount of reactant 3 (D) at t=11 hours
y3	0.2298 [kmol]	0.0258	Measured amount of reactant 3 (D) at t=24 hours
y4	0.0370 [kmol]	0.0019	Measured amount of waste product (W) at t=6.5 hours
y5	0.0497 [kmol]	0.0033	Measured amount of waste product (W) at t=11 hours
y6	0.0857 [kmol]	0.0038	Measured amount of waste product (W) at t=24 hours
y7	10.996 [-]	0.182	Measured pH at t=6.5 hours
y8	11.074 [-]	0.160	Measured pH at t=11 hours

Where the standard deviation of the sample σ is defined as:

$$\sigma = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(x_i - \bar{x})^2} \tag{A.2}$$

The sample correlation coefficient between the input and output variables (**x**,**y**) is given in Table (A.2).

From Table (A.1) and (A.2) one can make out some indications on the system and the variables:

- The variation in the inputs x2 and x3 from batch to batch are very small compared to the mean, and will most likely have neglectable effect on the outputs.
- The variation in the inputs x1, x4 and x5 are relatively large compared to the mean, and will most likely have an noticeable effect on the outputs.
- x1 show a small to medium correlation (0.30) with y1 and y4 and indicate that the reaction rates are temperature dependent, but that a larger varia-

Table A.2: The Sample Correlation coefficients, R_{xy} between the variables

	y1	y2	y3	y4	y5	y6	y7	y8	x1	x2	x3	x4
y2	**0.81**	-	-	-	-	-	-	-	-	-	-	-
y3	-0.23	-0.15	-	-	-	-	-	-	-	-	-	-
y4	**-0.49**	-0.33	-0.06	-	-	-	-	-	-	-	-	-
y5	**-0.71**	**-0.87**	0.14	0.22	-	-	-	-	-	-	-	-
y6	0.20	0.17	**-0.81**	0.02	-0.06	-	-	-	-	-	-	-
y7	-0.22	-0.32	0.09	0.07	0.27	-0.11	-	-	-	-	-	-
y8	-0.25	-0.36	-0.21	0.20	0.25	0.01	**0.52**	-	-	-	-	-
x1	-0.35	0.003	0.30	0.31	0.006	-0.24	-0.13	-0.25	-	-	-	-
x2	-0.15	-0.22	-0.06	-0.06	0.23	0.02	0.005	0.12	0.04	-	-	-
x3	0.22	0.20	0.07	-0.39	-0.19	-0.17	-0.11	-0.09	0.24	-0.003	-	-
x4	**-0.79**	**-0.70**	0.31	0.23	**0.64**	-0.19	0.33	0.12	0.14	0.19	-0.22	-
x5	**-0.70**	**-0.96**	0.17	0.27	**0.83**	-0.20	0.40	**0.47**	-0.18	0.23	-0.23	**0.61**

tion in the temperature profile would be preferable in order to estimate the temperature dependence on the reaction rate parameters more accurately.

- x4 show a strong correlation with y1, y2 and y5. The x4–y1 correlation is explained by the fact that the operators will add RCl after 8 hours (x4) if the measurement of D after 6 hours (y1) is low. Also, y1 correlates naturally to y2 (low amount of D at t=6.5 corresponds to low amount of D at t=11 hours). However, the correlation is not 1 and this can be due to the correction made by x1.
- The same thing applies for the x5 – y2 correlations. The x5–y2 correlation is explained by the fact that the operators will add RCl after 13 hours (x5) if the measurement of D after 11 hours (y2) is low.
- The relatively strong correlation between y1–y4, y2–y5, y3–y6 (between measured reactant and waste product at times 6.5, 11 and 24 hours) indicate that it is suitable to model the rate of waste (W) generation as a strong function of the reactant (D) concentration (W is wrongly alkylated or over alkylated D)

APPENDIX

B

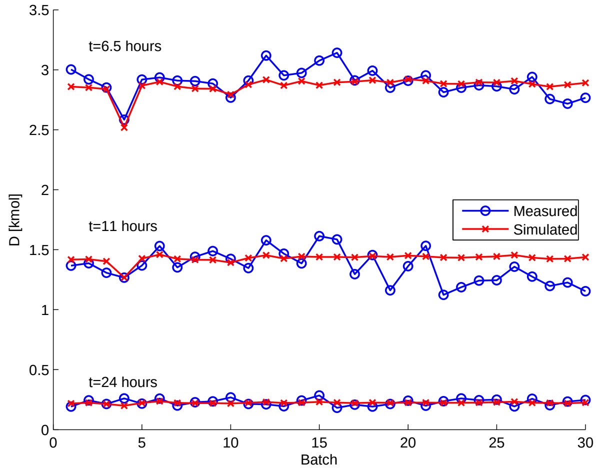
MODEL VALIDATION AND ACCURACY

This section compares the simulated model and the measurements of the batches in the data set. The validity and accuracy of the obtained model is analyzed and discussed.

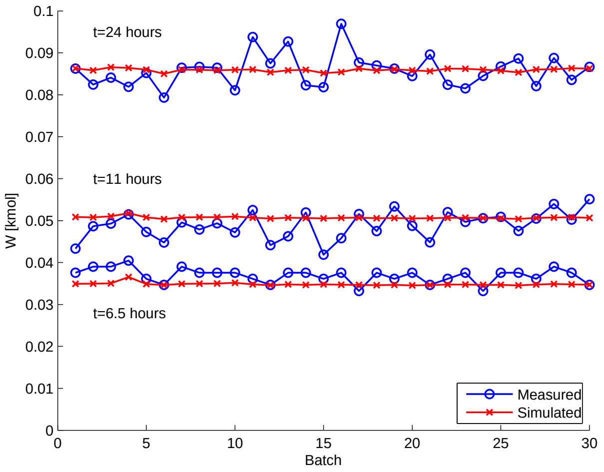
Simulations of the batches and comparison with the measurements show that the dynamics of the batch process is captured good for the two measured states (D and W) in the model (the simulated outputs at the three time steps lies approximately at the average value of the corresponding measurements), see Figure (3.3) and Figure (B.1) . This indicates that the model structure and the estimates of the reaction rate parameters are fairly good for these two states.

The trend of simulated pH, is approximately 0.5 pH units above the average pH in the data set. However, the pH at GE Healthcare is measured on a diluted sample (1 part sample and 3 parts distilled water) to ensure good conductivity. The reported pH is not corrected for the dilution made [GEH], and they accept the resulting systematic error in their pH measurements. A measured pH of approximately 11 in the diluted sample (1:3) is in the concentrated solution, based on the equilibrium constant of the alkaline solution, 0.2 to 0.5 pH units higher than measured. And thus closer to what is obtained in the simulations. The pH estimation in the model is thus considered to be a good approximation of the real pH in the solution. The dynamics of the un-measured states (RCl, ROH and DROH) cannot be verified, without measurements.

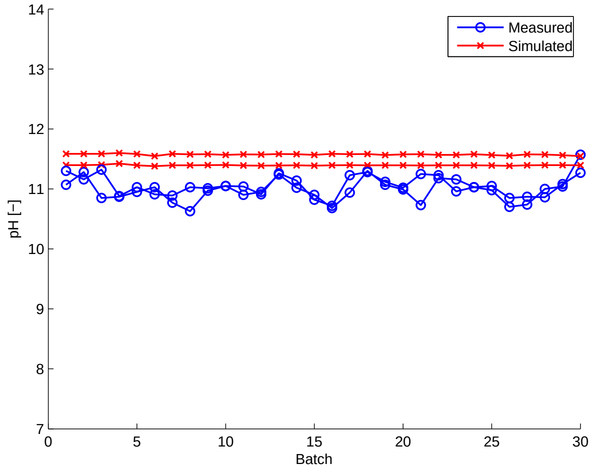
Regarding the estimated reaction rate activation energies (γ), it probably exist relatively large uncertainties in them, especially for the waste generation equations. The batch temperatures in the data set varies mostly within the first 5 hours, but the variation is still relatively small and the temperature after 5 hours is at the setpoint of 35 °C in all the batches. It would be favorable, regarding estimation accuracy, with larger variations in the batch temperatures over the entire batch



(a) D: Reactant 3



(b) W: Waste product



(c) pH

Figure B.1: Comparison between simulated and measured values for the batches in the data set. Red: simulated, blue: measurement in the data set runs. Batch number 4, which is captured relatively good, is also the batch with the largest deviation (from the average) in the temperature profile the first 5 hours.

The batch to batch comparison shown in Figure (B.1) indicates that the variation between the batches is not captured well in the model. This can be explained by the small variance in the input parameters of the process, as seen in Table (A.1). And un-measured disturbances, such as reactant and solvent quality and error in the measurement of the initial amount of the reactants, are probably the main reason for batch to batch output variations, [GEH].

Table (B.1) indicates the performance of the model. The performance index is chosen to be: The scaled root mean square error (rms), defined in Equation (B.1), which give an indication of how close the measurements are to the simulated outputs over all the batches. And the R_{xy} value, which indicate the batch to batch correlation of the measurements and the simulated outputs. That is, how correlated the direction and magnitude of the simulated outputs (x) and measurements (y) are over the batches. R_{xy} is defined in Equation (A.1).

Table B.1: The root mean square (rms) and the sample correlation coefficient, R_{xy} between measured and simulated variables for the 30 batches

	$D_{t=6.5}$	$D_{t=11}$	$D_{t=24}$	$W_{t=6.5}$	$W_{t=11}$	$W_{t=24}$
R_{xy}	0.59	0.17	-0.04	0.55	0.21	-0.13
rms	0.026	0.090	0.105	0.061	0.059	0.035

$$\text{rms} = \sqrt{\frac{1}{30}\sum_{i=1}^{30}\frac{\left(y_i^{\text{meas}} - y_i^{\text{sim}}\right)^2}{\bar{y}^{\text{meas}}}} \tag{B.1}$$

Where y is the amount of the species D and W at a given time and i is the batch number. The scaling factor is choosen to be the average of the measured values over all the 30 batches.

Table (B.1) show that the batch to batch estimation is best at the first measurements of W and D at 6.5 hours (with R_{xy} around 0.6) and decrease with time. This is because up to 5 hours the batch temperatures varies the most, and this is the measured input that excite the outputs the most.

Based on the good estimation of the dynamics of the states (W and D) throughout a batch, and the fairly good correlation of the measurements and the simulated outputs where the temperature variation is largest (0 to 5 hours); the model and the parameters are consider to be accurate enough, at least for academic purpose, for dynamic optimization of the batch process. The estimated model parameters should however be verified in the laboratory. Or, by running some batches with more variation in the temperature and measured inputs and re-estimate the model parameters.

APPENDIX C

MINIMAL RCL INPUT USAGE

Optimization of the throughput and purity of a system is not the only way to increase the economic performance of a process. If less reactant (raw material) can be used and still result in acceptable performance (be within the purity and yield limit), money can be made by using less. It is therefore interesting to find out how much total RCl input is needed and still be within the performance criteria of the batch (output constraints).

The output constraints (with some back-off) are here: Final (tf) amount of waste (W, x_6) less than 0.08 [kmol] and amount of reactant 3 (D, x_4) less than 0.20 [kmol].

The endpoint optimization problem is then formulated as:

$$\min_{\mathbf{u}_{\mathrm{RCl}},\mathbf{T}_{\mathrm{set}}} J \tag{C.1}$$

Where the objective functional J is given as:

$$J = U_{\mathrm{RCl}}(\mathrm{tf}) \tag{C.2}$$

Where U_{RCl} is the accumulated input u_{RCl} usage:

$$\dot{U}_{\mathrm{RCl}} = u_{\mathrm{RCl}}, \qquad U_{\mathrm{RCl}}(0) = 0 \tag{C.3}$$

Subject to the model equations and the input and output constraints:

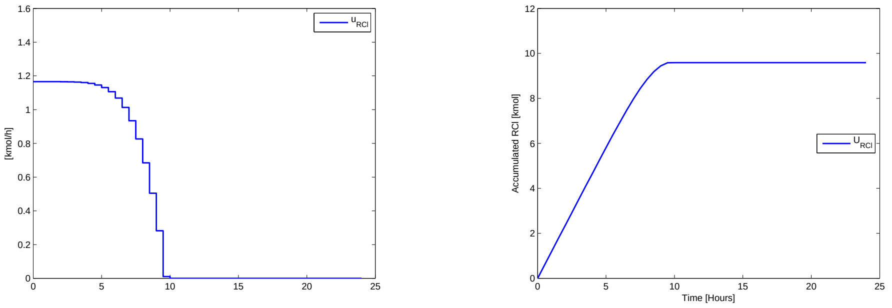
$$\dot{\mathbf{x}} = \mathbf{f}(\theta, \mathbf{x}, \mathbf{u}) \tag{C.4}$$

$$\mathbf{y} = \mathbf{g}(\theta, \mathbf{x}) \tag{C.5}$$

$$x_4(\mathrm{tf}) \leq 0.20 \tag{C.6}$$

$$x_6(\mathrm{tf}) \leq 0.08 \tag{C.7}$$

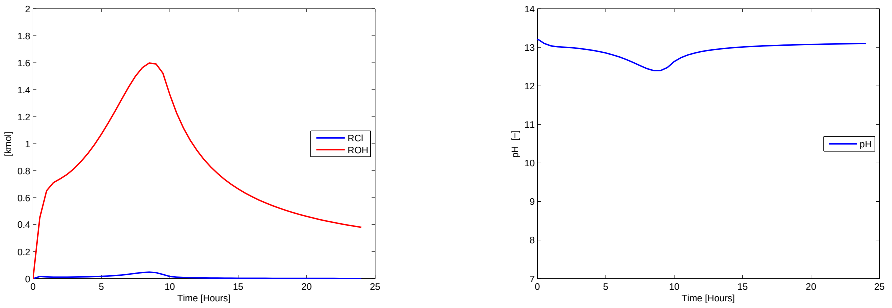
$$T_{\mathrm{set}} \leq 45^\circ C \tag{C.8}$$



(a) Minimum reactant input trajectory, u_{RCl}

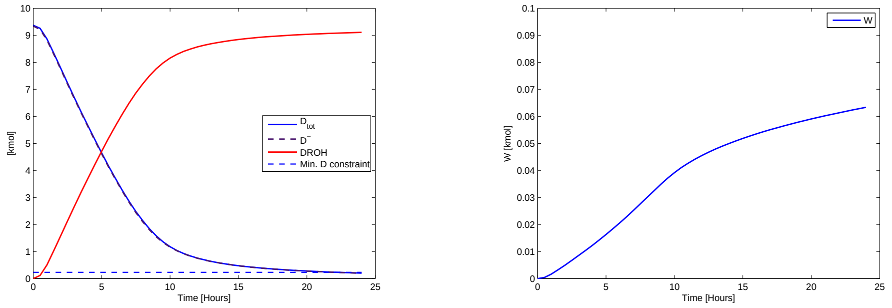
(b) Accumulated u_{RCl} =9.59 (kmol)

Figure C.1: The optimal input profile that minimize the required usage of u_{RCl}. A reduction in RCl usage of 14.6 % from what is used at current practice. The input rate is at start 1.2 [kmol/h] and decrease to zero at 10 hours. The temperature set point is constant at 45°C throughout the process.



(a) Reactant RCl (blue) and intermediate product ROH (red)

(b) pH



(c) Reactant D (blue), D^- (broken dark blue line) and product DROH (red)

(d) Waste product (W)

Figure C.2: Simulation of the batch with the inputs given in Figure (C.1).

The result is a reduction in the total RCl usage of 14.6 % compared to what is used in current practice. Also, even though the main reactant D is at the backed-off limit, the performance in terms of yield and selectivity is better than what is achieved in current practice. Thus, the economics of the process can be increased by whatever the cost of 14.6 % of the total RCl is per batch. However, this result is when a perfect model with no disturbances present is assumed. Because the main reactant D is at the backed-off limit and considering uncertainties in the model and variability in the real process, this implementation is probably not a robust one. Nevertheless, it is an interesting result.

Table C.1: Optimization result at end of batch with minimal RCl usage as the optimization objective.

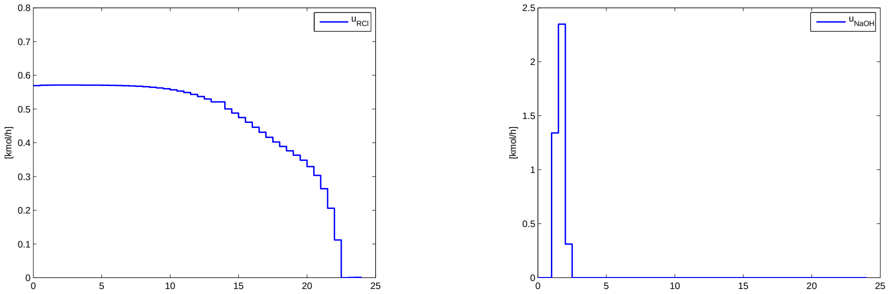
D [kmol]	**W** [kmol]	**DROH** [kmol]	**J**, (4.4)	**Yield** [%],(4.2)
0.20	0.0633	9.11	9.316	97.2

APPENDIX D

INCLUDING NAOH INPUT AS A DOF IN THE OPTIMIZATION PROBLEM

The model equations indicate that high pH increase the performance of the system. And that additional use of NaOH can enhance the performance of the batch beyond the nominal optimal operation obtained in Section (4.4) (where NaOH was not included as an optimization input). Because of this, a case is investigated to find out how introduction of u_{NaOH}, as an extra optimization degree of freedom (DoF), effect the optimal solution. And if u_{NaOH} effect the profiles of the other available optimization inputs.

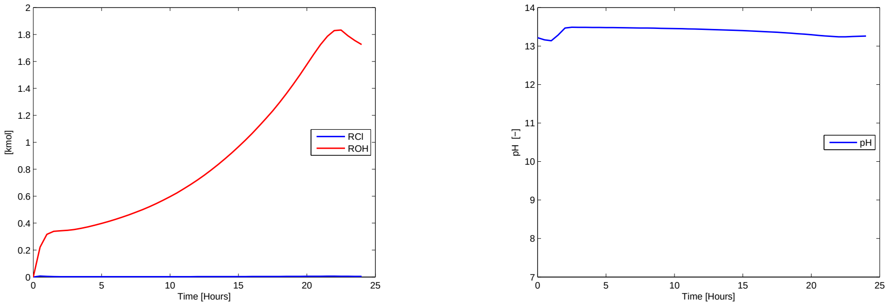
The extra optimization degree of freedom comes in as additional input of NaOH throughout the batch. The parameterization is the same as for the u_{RCl} and $\mathrm{T}_{\mathrm{set}}$ inputs. But, with a high bound on the total accumulated u_{NaOH} at 2 [kmol] in order to ensure realistic simulations of the pH in the batch.



(a) Optimal RCl reactant input trajectory

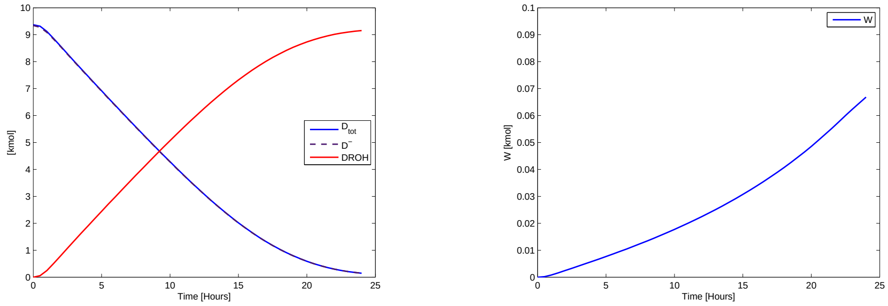
(b) Optimal NaOH reactant input trajectory

Figure D.1: The optimal inputs with u_{NaOH} included as a optimization DoF



(a) Reactant RCl (blue) and intermediate product ROH (red)

(b) pH



(c) Reactant D (blue), D^- (broken dark blue line) and product DROH (red)

(d) Waste product (W)

Figure D.2: Simulation of the batch with the inputs given in Figure (D.1)

Table D.1: Optimization result at end of batch with u_{NaOH} as an additional DoF

D [kmol]	**W** [kmol]	**DROH** [kmol]	**J**, (4.4)	**Yield** [%],(4.2)
0.149	0.0668	9.154	9.33	97.7

The results show that introducing additional input of NaOH in the optimization problem increased the optimal objective function to 9.33. This is slightly better than the nominal optimal operation obtained in Section (4.4), with an objective function of 9.32. However, the introduction of u_{NaOH} as an extra optimization DoF did not effect the other optimal inputs: (u_{RCl} and T_{set}). As seen in Figure (D.1 a), the optimal input trajectory of u_{RCl} is the same as in Figure (4.1). The optimal temperature set point is also the same (constant at 45 [°C]) throughout the batch. The optimal input of u_{NaOH} is such that the pH is maximized. Thus this optimal performance (when NaOH is also included) is obtained by maximizing the pH in the solution. This can also be achieved by using u_{NaOH} to control the pH at the maximum possible value (constraint) by simple feedback control.

APPENDIX E

ATTACHED CD

Attached on the last page is a compact disc with the work performed. Including Matlab files and plots, gPROMS model and various results referred to in the report.

The CD is only attached the version that is given to the Institute of Chemical Engineering (NTNU) and GE Healthcare AS.

Folder Structure and Information on the CD

What	Location	Information
Matlab model	../model/matlab/	estimation and simulation
gPROMS model	../model/gPROMS/	optimization
Correlation plots	../plots/correlation/	plots of correlation coefficients
Tracking plots	../plots/tracking/	plots of tracking states