Integrated Batch Process Development based on Mixed-Logic Dynamic Optimization

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The image on the cover is the painting "Fábrica de Horta del Ebro" (1909) painted by Pablo Picasso (1881 – 1973). It was extracted from google.com/images.

To my family

"Even the longest journey must begin where you stand."

Lao Tzu (604 BC – 531 BC)

Foreword

This has been a long journey. As at the end of many trips, I feel comforted by the achieved targets, confident for persevering in spite of hurdles, grateful for the opportune walking sticks, and realized with the accomplishments. Undoubtedly, this has been the most arduous challenge of my career.

I graduated as a Chemical Engineer in 2006 and as a MSc in Environmental Technology in 2007 at Universitat Autònoma de Barcelona (UAB). After a short period of experimental research at UAB, I enrolled in 2008 in the Chemical Process Engineering program at Universitat Politècnica de Catalunya (UPC-BarcelonaTech) to undertake my doctoral studies. From then on, my PhD work has been developed in the CEPIMA Research Group under Prof. Antonio Espuña's supervision and in collaboration with the Process Systems Engineering (AVT.PT) Research Group at RWTH Aachen University, which I had the opportunity to visit in three occasions, headed by Prof. Wolfgang Marquardt.

When I first met Prof. emer. Luis Puigjaner –founder of CEPIMA Research Group and my first contact there– and Prof. Antonio Espuña –the group leader at present and my thesis advisor– they proposed me to extend my expertise in Chemical and Environmental Engineering toward a new field of work to me, as it was the complex machinery of Decision Support Systems for Batch Process Management. From every perspective I found it an extremely appealing field of work. It was also a challenging opportunity to complement my previous background and gather experience in Process Systems Engineering (PSE), one of my professional interests. So began the journey. And I soon shared Prof. Espuña's devotion and enthusiasm for the optimization of batch processes and for the integration of decision levels, which have distinguished this research in many ways.

After intense studying of topics like top-tier modeling and optimization tools in Operations Research and the formulation of state-of-the-art problems of PSE, I finally defined the objectives of my work. Eureka, I would focus on batch process optimization with structural decisions and using dynamic performance models. From my inquiries I had concluded that this was a very stimulating and rather unexplored problem from a practical point of view, especially if we considered processes with several stages whose processing route was not fixed beforehand. The contact with AVT.PT Research Group at RWTH Aachen University and the inspiring conversations with Prof. Marquardt were priceless in this regard. Through the collaboration with Kathrin Frankl which I deeply appreciate, I acquainted with the PhD work by Jan Oldenburg, which has been a huge influence to my approach combining Dynamic Optimization (DO), discrete-continuous hybrid models, and Generalized Disjunctive Programming (GDP) in the so-called Mixed-Logic Dynamic Optimization (MLDO) problems.

This PhD thesis bets for integration assuredly. Numerous degrees of freedom in Batch Process Development are here optimized simultaneously. The advantages are undeniable: to avoid suboptimal solutions and to guarantee a better utilization of batch plants systematically. However, it became totally understandable to me why many experts prefer the more manageable *divide and conquer* strategies, which solve problems like batch process synthesis, plant allocation, and plant design sequentially or iteratively. The reason is that the resulting integrated optimization problem may become of scandalous complexity from a mathematical point of view. In fact, the most difficult part in the realization of this work has been to understand, deal with, and bring to fruition the search procedures and solvers that should optimize the MLDO problems, once formulated. I humbly recognize that this was an unfamiliar field to me, where I have had to dedicate many hours and a great effort. In the end, and thanks to the excellent MINLP solvers that are currently available in the market, the problems posed have come to be solved through the integrative approach here proposed, what has permitted to carry out interesting analyses of the influence of different decisions in Batch Process Development. In this regard, I feel appealed by this quote by Picaso: *"The chief enemy of creativity is 'good' sense"*. Despite PSE community is rightly directed toward the integration in the decision-making, the *'good' sense* would request smaller steps toward such integration. Nevertheless, and looking backwards, the accomplishments obtained through the eager approach here presented are extremely encouraging.

The credit of making a success of this journey is definitely of the many opportune walking sticks and the many traveling companions that I have found. First of all, I would like to thank Prof. Antonio Espuña for this professional challenge, for the confidence in my expertise and support in my work, and for his critical observations and comments that have helped this study to make a qualitative jump forward. I am also grateful to Prof. Luis Puigjaner and Prof. Moisès Graells for making possible that I joined CEPIMA Research Group. I want to express my immense gratitude toward Prof. Wolfgang Marquardt, for opening the door for me in his group. The matters discussed with him were really constructive and have contributed to set the basis for this work. Additionally, I want to thank the support and inspiration found in my colleagues from Barcelona and Aachen, where I have met great professionals and lasting friends. I feel privileged for having participated with them in research projects and life experience. Especially, I want to mention Kathrin Frankl for our collaboration along these years. I also appreciate the great labor of the administrative support in the Chemical Engineering Department at UPC-BarcelonaTech and in the AVT.PT chair at RWTH Aachen University. To my families Moreno, Benito, Libreros, and Rojas, I dedicate this thesis. Them, and my friends, thanks for the unquestioning support and love these many years. A special recognition has to be given to Mónica Sorín. Thanks for this parallel journey to learn about myself and my road companions. Finally, I want to thank Nicolás Rojas, my husband, because he is my motor, my compass, my water, my map in every journey.

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Marta Moreno
Cerdanyola del Vallés, January 5th 2014

Contents

Resum

La indústria de productes químics especials es basa en la fabricació discontinua, ja que permet adaptar de forma freqüent els sistemes de producció en funció de les fluctuacions de mercat. Per ser líder al sector, són necessàries eines de suport a la decisió que ajudin a l'àgil desenvolupament i implementació de nous processos. A més, aquests han de ser competitius per garantir la seva viabilitat a llarg termini. Altres peces clau per una operació eficient són l'ús de plantes flexibles així com l'estudi dels fenòmens fisicoquímics. Aquesta tesis aborda justament el desenvolupament sistemàtic de processos químics discontinus que siguin eficients, econòmicament competitius i ecològics, per contribuir a la seva ràpida introducció en els sistemes de producció, tant en escenaris de plantes existents com des de les bases. En concret, es planteja la resolució simultània de la síntesi conceptual d'esquemes de procés i l'assignació d'equips, tenint en compte el disseny de la planta.

Amb aquest objectiu, es proposa una metodologia de solució basada en optimització, on les alternatives estructurals es representen en una Xarxa d'Estats i Equips (SEN per les sigles en anglès) que es formula mitjançant un problema d'Optimització Dinàmica Mixta-Lògica (MLDO per les sigles en anglès) que es resol minimitzant una funció objectiu. La solidesa de la metodologia proposada rau en la estratègia de modelat del problema MLDO, que integra els diferents tipus de decisions en un sol model d'optimització. En concret, es consideren: (i) la combinació d'alternatives de síntesi i assignació d'equips, (ii) models de procés i trajectòries de control dinàmics, (iii) esdeveniments discrets associats al canvi de fase i operació, (iv) informació quantitativa i qualitativa, (v) sincronització de transferències de material en tasques consecutives, i (vi) elements de processat discontinus i semi-continus.

Existeixen diverses estratègies per resoldre el problema MLDO resultant. En aquesta tesi es proposa en primer lloc un mètode determinístic directe-simultani, on el model mixt-lògic es transforma en un mixt-enter. Aquest es discretitza al seu torn de forma completa per obtenir un problema de Programació No-Lineal Mixta-Entera (MINLP per les sigles en anglès) el qual es pot resoldre utilitzant algoritmes d'optimització convencionals. A més, es presenten un Algoritme Genètic Diferencial (DGA per les sigles en anglès) i un mètode híbrid. Totes dues estratègies esdevenen alternatives de cerca amb l'objectiu de mantenir la bondat de la solució i millorar l'eficàcia de computació per tractar problemes de dimensió industrial.

La metodologia de solució proposada s'aplica al desenvolupament de processos discontinus en escenaris de plantes existents, tenint en compte les restriccions físiques dels equips. Un primer exemple aborda la manufactura de productes químics basada en un sistema de reaccions competitives. Concretament, es desenvolupa i millora el procés de producció implementat en una xarxa de reactors considerant diferents escenaris econòmics, criteris de decisió, i modificacions de planta. En un segon exemple, s'optimitza el procés foto-Fenton per ser executat en una planta pilot per eliminar contaminants emergents.

Buscant integrar el desenvolupament de procés i el disseny de plantes flexibles en escenaris de base, es presenta una formulació estocàstica en dues etapes per a optimitzar el benefici esperat d'acord a diversos escenaris de demanda. Per gestionar la complexitat d'aquest problema es proposa la utilització d'una heurística. Com a exemple, es planteja el disseny d'una planta de base on implementar l'anterior sistema de reaccions competitives. Decisions com les trajectòries dinàmiques de control o la configuració d'equips permeten adaptar la recepta màster en funció de la demanda. Un darrer exemple defineix el procés de producció de fibra acrílica, il·lustrant decisions com la selecció de tasques, tecnologia, reactius o reutilització de dissolvents.

Resumen

La industria productos químicos especiales se basa en la fabricación discontinua, la cual permite la adaptación frecuente de los sistemas de producción en función de las fluctuaciones de mercado. Para ser líder en el sector, son necesarias herramientas de soporte a la decisión que contribuyan al ágil desarrollo e implementación de nuevos procesos. Además, éstos deben ser competitivos para garantizar su viabilidad a largo plazo. Otras piezas clave para una operación eficiente son la utilización de plantas flexibles y el estudio de los fenómenos fisicoquímicos. Esta tesis aborda justamente el desarrollo sistemático de procesos químicos discontinuos que sean eficientes, económicamente competitivos y ecológicos, para contribuir a su rápida introducción en los sistemas de producción, ya sea en escenarios de plantas existentes o desde las bases. En particular, se plantea la resolución simultánea de la síntesis conceptual de esquemas de proceso y la asignación de equipos, teniendo en cuenta además el diseño de planta.

Con este fin, se propone una metodología de solución basada en optimización, donde todas las alternativas estructurales se representan en una Red de Estados y Equipos (SEN por sus siglas en inglés) que se formula mediante un problema de Optimización Dinámica Mixta-Lógica (MLDO por sus siglas en inglés) que se resuelve minimizando una función objetivo. La solidez de la metodología propuesta reside en la estrategia de modelado del problema MLDO, que integra los diferentes tipos de decisiones en un solo modelo de optimización. En concreto, se consideran: (i) la combinación de alternativas de síntesis y asignación de equipos, (ii) modelos de proceso y trayectorias de control dinámicos, (iii) eventos discretos asociados al cambio de fase y operación, (iv) información cuantitativa y cualitativa, (v) sincronización de la transferencia de material en tareas consecutivas, y (vi) elementos de procesado discontinuos y semi-continuos.

Existen diversas estrategias para resolver el problema MLDO resultante. En esta tesis se propone en primer lugar un método determinístico directo-simultáneo, donde el problema mixto-lógico se reformula en un mixto-entero. A su vez, éste se discretiza de forma completa para obtener un problema de Programación No-Lineal Mixta-Entera (MINLP por sus siglas en inglés) el cual se puede resolver mediante algoritmos de optimización convencionales. Además, se presentan un Algoritmo Genético Diferencial (DGA por sus siglas en inglés) y un método híbrido. Ambas estrategias se plantean como alternativas de búsqueda con objeto de mantener la bondad de la solución y mejorar la eficacia de computación para tratar problemas de dimensión industrial.

La metodología de solución propuesta se aplica al desarrollo de procesos discontinuos en escenarios con plantas existentes, teniendo en cuenta las restricciones físicas de los equipos. Un primer ejemplo aborda la fabricación de productos químicos basada en un sistema de reacciones competitivas. En concreto, se desarrolla y mejora el proceso de producción a implementar en una red de reactores considerando diferentes escenarios económicos, criterios de decisión, y modificaciones de planta. En un segundo ejemplo, se optimiza el proceso foto-Fenton a ser ejecutado en una planta piloto para eliminar contaminantes emergentes.

Persiguiendo la integración del desarrollo de proceso con el diseño de plantas flexibles en escenarios base, se presenta asimismo una formulación estocástica en dos etapas para optimizar el beneficio esperado de acuerdo a varios escenarios de demanda. Para manejar la complejidad de dicho problema se propone la utilización de una heurística. Como ejemplo, se plantea el diseño de una planta de base para implementar el anterior sistema de reacciones competitivas, donde decisiones como las trayectorias dinámicas de control o la configuración de equipos permiten adaptar la receta máster en función de la demandas. Por último, se presenta un ejemplo donde se define el proceso de producción de fibra acrílica, ilustrando decisiones como la selección de tareas, alternativas tecnológicas, reactivos químicos o la reutilización de disolventes.

Summary

Specialty chemicals industry relies on batch manufacturing, since it requires the frequent adaptation of production systems to market fluctuations. To be first in the market, batch industry requires decision-support systems for the rapid development and implementation of chemical processes. Moreover, such processes should be competitive to ensure their long-term viability. The use of general-purpose and flexible plants and the consideration of physicochemical insights to define an efficient operation are also cornerstones for the success of specialty chemical industries. This thesis tackles precisely the systematic development of batch processes that are efficient, economically competitive, and environmentally friendly, to assist their agile introduction into production systems in grassroots and retrofit scenarios. Synthesis of conceptual processing schemes and plant allocation sub-problems are solved simultaneously, taking into account the plant design.

With this purpose, an optimization-based approach is proposed, where all structural alternatives are represented in a State-Equipment Network (SEN) superstructure, following formulated into a Mixed-Logic Dynamic Optimization (MLDO) problem to be solved minimizing an objective function. Essentially, the strength of the proposed methodology lies in the modeling strategy which combines the different kinds of decisions of the integrated problem in a unique MLDO model. Accordingly, it considers: (i) combination of synthesis and allocation alternatives, (ii) dynamic process performance models and dynamic control variable profiles, (iii) discrete events associated to transitions of batch phases and operations, (iv) quantitative and qualitative information, (v) material transference synchronization to ensure batch integrity between unit procedures, and (vi) batch and semi-continuous processing elements.

Different strategies can be used to solve the resulting MLDO problem. In this thesis, a deterministic direct-simultaneous approach is first proposed. The mixed-logic model is reformulated into a mixed-integer one, which is fully-discretized to provide a Mixed-Integer Non-Linear Programming (MINLP) that is optimized using conventional solvers. Then, a Differential Genetic Algorithm (DGA) and a hybrid approach are presented. The purpose of these evolutionary strategies is to pose solution alternatives that keep solution goodness while seek for the improvement of computational efficiency to handle industrial-size problems.

The optimization-based approach is applied in retrofit scenarios to solve simultaneous process synthesis and plant allocation taking into account the physical restrictions of existing plant elements. The production of specialty chemicals based on a competitive reaction system in an existing reactor network is first defined through process development and improvement according to different economic scenarios, decision criteria, and plant modifications. Additionally, a photo-Fenton process is optimized to eliminate an emergent wastewater pollutant in a given pilot plant, pursuing the minimization of processing time and cost.

Batch process development in grassroots scenarios is also proven to be a problem of utmost importance to deal with uncertainty in future markets. Seeking for plant flexibility in several demand scenarios, the expected profit is optimized through a two-stage stochastic formulation that includes simultaneous plant design, process synthesis, and plant allocation decisions. A heuristic solution algorithm is used to handle the problem complexity. A grassroots plant design is defined to implement the previous competitive reaction system, where decisions like the feed-forward trajectories or operating modes allow the adaptation of master recipes to different demands. A final example defines an acrylic fiber production process, illustrating decisions like the selection of tasks, technological alternatives, chemicals, and solvent reuse.

Notation

Acronyms

AI	Artificial Intelligence
AIBN	azobisisobutyronitrile
AN	acrylonitrile
AOP	Advanced Oxidation Process
AP	Augmented Penalty
B&B	Branch-and-Bound
CHR	Convex-Hull Relaxation
CNF	Conjunctive Normal Form
DAE	Differential-Algebraic Equations
DGA	Differential Genetic Algorithm
DMF	dimethylformamide
DNF	Disjunctive Normal Form
DO	Dynamic Optimization
DOE	design of experiments
DOF	degrees of freedom
DP	Dynamic Programming
EHS	Environment Health and Safety
EPC	end-point constraint
GA	Genetic Algorithm
GBD	Generalized Benders Decomposition
GDP	Generalized Disjunctive Programming
GMP	Good Manufacturing Practices
HAZOP	Hazard and Operability Analysis
HEN	heat exchanger network
HS	Harmony Search
IFS	initial feasible solution
KPI	key performance indicator
LCIA	Life Cycle Impact Assessment
MIDO	Mixed-Integer Dynamic Optimization
MILP	Mixed-Integer Linear Programming

MINLP	Mixed-Integer Non-Linear Programming
MLD	Mixed-Logic Dynamical
MLDO	Mixed-Logic Dynamic Optimization
MO	multi-objective
MP	Mathematical Programming
mSTN	Maximal State-Task Network
NCO	necessary conditions of optimality
NLP	Non-Linear Programming
OA	Outer Approximation
OC	Optimal Control
PC	path constraint
PCT	Paracetamol
PSE	Process Systems Engineering
PWC	piecewise constant
RFDL	Recipe Formal Definition Language
RTN	Resource-Task Network
SA	Simulated Annealing
SEN	State-Equipment Network
SO	single-objective
SQP	Sequential Quadratic Programming
STN	State-Task Network
TOC	Total Organic Carbon
TS	Tabu Search
VA	vinyl acetate

General sets

ID	Set of disjunctive terms

General variables

$z_k(t)$	Differential process variables in mathematical stage k
$y_k(t)$	Algebraic process variables in mathematical stage k
$u_k^{dyn}(t)$	Dynamic control variables in mathematical stage k
u^{stat}	Time-invariant or static continuous control variables
u^{int}	Integer control variables
u^{Bool}	Logical or Booleans decisions
u^{bin}	Binary decisions
γ	Algebraic time-invariant variables
p	Process parameters

General functions

A	Matrix of the semi-explicit DAE system of differentiation index 1 at most
f	DAE system

g	Path constraints
g^e	End-point constraints
h	Algebraic equations evaluated at the final time
l	Set of relations that define initial conditions
m	Stage-to-stage continuity between consecutive mathematical stages
f^d	DAE system in disjunctive equations
g^d	Path constraints in disjunctive equations
$g^{d,e}$	End-point constraints in disjunctive equations
h^d	Algebraic equations evaluated at the final time in disjunctive equations
l^d	Set of relations that define initial conditions in disjunctive equations
m^d	Stage-to-stage continuity between consecutive mathematical stages in disjunctive equations
B^d	Equations system to define bypass stages in disjunctive equations
Ω	Logical propositions
Φ	Objective function

Problem sets

Λ_i	Set of technological specifications in task $i \in PS$
$\Lambda_j \subseteq \Lambda_i$	Set of technological specification of unit $j \in U$ in task $i \in PS$, $\|\Lambda_j\|=1$, $\forall j \in U$
Ψ_i	Set of configurations in task $i \in PS$
C	Set of chemical compounds involved in the process
$C_j^s \subseteq C$	Subset of potential reactants, solvents, or catalysts in unit $j \in U$ subject to be selected
$D_{i,\psi} \subseteq U_i$	Subset of batch units U_i in task $i \in PS$ whose input flow rate is a control variable in configuration $\psi \in \Psi_i$. It is defined such that $\|D_{i,\psi}\| = DOF_{i,\psi} - \|U_i\|$, where $\|U_i\|$ represents DOF removed by output flow rates
$I_j \subseteq K_j$	Set of input stages for unit $j \in U$ at Level 1
J	Set of all existing and potential equipment pieces, $J = U \cup T \cup Sp \cup Mx$
$J_i \subseteq J$	Set of equipment pieces within potential task $i \in PS$,
K_j	Set of stages for unit $j \in U$ at Level 1
L	Set of potential stages at Level 0, $L=\{1,...,L^{\max}\}$
$L^a \subseteq L$	Set of active stages at Level 0
$L_j^0 \subseteq L$	Set of stages at Level 0 where unit $j \in U$ can start its operation,$L_j^0=\{1, \|K_{j'}\|-\|O_{j'}\|+1 \mid j' \neq j, j' \in U\}$
$M_j^{in} \subseteq M_j$	Set of input pipelines to unit $j \in U$ at Level 1
$M_j^{out} \subseteq M_j$	Set of output pipelines from unit $j \in U$ at Level 1
M_j	Set of pipelines for unit $j \in U$ at Level 1
Mx	Set of existing and potential mixers
N	Set of pipelines at Level 0
$N_{i,\psi}^0 \subseteq N$	Set of pipelines at Level 0 whose flow rate is restricted to zero in configuration $\psi \in \Psi_i$ of task $i \in PS$
$N_i^b \subseteq N_i$	Bypass pipeline for process stage $i \in PS$, $\|N_i^b\|=1$
$N_i^f \subseteq N$	Set of pipelines at Level 0 for task $i \in PS$ whose flow rate is fixed by the preceding task, $\|N_i^f\|=1$ except for process stages preceded by a buffer $j \in T$

$N^r \subseteq N$	Set of pipelines at Level 0 for recirculation
$N_i^{in} \subseteq N_i$	Subset of input pipelines to process stage $i \in PS$
$N_j^{in} \subset N$	Set of input pipelines to equipment $j \in J$ at Level 0
$N_j^{out} \subset N$	Set of output pipelines from equipment $j \in J$ at Level 0
$N_i \subseteq N$	Set of pipelines at Level 0 for task $i \in PS$
$O_j \subseteq K_j$	Set of output stages for unit $j \in U$ at Level 1
$P \subset C$	Subset of desired products
PS	Set of potential process stages or tasks
Q	Set of ordered positions that can be assumed by unit procedures of $j \in U$, $Q = \{1, ..., \|U\|\}$
Sp	Set of existing and potential splitters
T	Set of existing and potential storage tanks
$T_n^r \subseteq T$	Buffer tank for potential recirculation of flow $n \in N^r$, $\|T_n^r\| = 1, \forall n \in N^r$
U	Set of existing and potential batch units

Problem parameters

Dem_p	Demand of product $p \in P$
$DOF_{i,\psi}$	Degrees of freedom with regard to the flow rates at Level 0 at process stage $i \in PS$, according to each configuration $\psi \in \Psi_i$
$l_{j,q}^0$	Starting stage of unit $j \in U$ when the task-unit Boolean $W_{j,q}$ is $true$, $l_{j,q}^0 = q$-th element of the ascending sort of L_j^0 of unit $j \in U$
$L^{\max}$	Maximum number of stages at Level 0,
$p_{j,c}$	Values for the set of process parameters p_j in unit $j \in U$ when potential chemical alternative $c \in C_j^s$ is selected

Problem variables

$Batch_p$	Production size associated to each batch of product $p \in P$
$F_{m,k}^j$	Flow rate for every input or output pipeline $m \in M_j^{in} \cup M_j^{out}$ and stage $k \in K_j$ of unit $j \in U$ at Level 1
$F_{n,l}$	Flow rate for every pipeline $n \in N$ and stage $l \in L$ at Level 0
int_k^j	Internal control variable for every stage $k \in K_j$ of unit $j \in U$ at Level 1 and $k \in L$ of unit $j \in J \backslash U$ at Level 0
NB_p	Number of batches of product $p \in P$
R_n	Recirculation Boolean to indicate whether intermediate flow in pipeline $n \in N^r$ is recirculated ($R_n = true$) or not ($R_n = false$)
r_n	Recirculation binary to indicate whether intermediate flow in pipeline $n \in N^r$ is recirculated ($r_n = 1$) or not ($r_n = 0$)
S_c^j	Chemical compound Boolean to indicate whether reactant, solvent, or catalyst $c \in C_j^s$ is selected in unit $j \in U$ ($S_c^j = true$) or not ($S_c^j = false$)
s_c^j	Chemical compound binary to indicate whether reactant, solvent, or catalyst $c \in C_j^s$ is selected in unit $j \in U$ ($s_c^j = 1$) or not ($s_c^j = 0$)
$Shortfall_p$	Unaccomplished demand of product $p \in P$
$Size^j$	Capacity of unit $j \in U \cup T$

T^f	Total time at Level 0
t^s	Starting time in at Level 0
t^{end}	Final time at Level 0
$t^{j,end}$	Final time of unit $j \in U$ at Level 1
$T^{j,f}$	Total time of unit $j \in U$ model at Level 1
$t^{j,s}$	Starting time of unit $j \in U$ at Level 1
t_k^j	Duration of stage $k \in K_j$ of unit $j \in U$ at Level 1
t_l	Duration of stage $l \in L$ at Level 0
$v_k^j(t)$	Volume of material in batch unit $j \in U$ at stage $k \in K_j$ or in storage tank $j \in T$ at stage $k \in L$
V_λ^j	Technology Boolean to indicate whether technological specification $\lambda \in \Lambda_j$ for processing unit $j \in U$ is selected (V_λ^j=$true$) or not (V_λ^j=$false$)
v_λ^j	Technology binary to indicate whether technological specification $\lambda \in \Lambda_j$ for processing unit $j \in U$ is selected (v_λ^j=1) or not (v_λ^j=0)
$W_{j,q}$	Task-unit assignment Boolean to indicate whether unit procedure order $q \in Q$ is assigned to unit $j \in U$ ($W_{j,q}^i$=$true$) or not ($W_{j,q}^i$=$false$)
$w_{j,q}$	Task-unit assignment binary to indicate whether unit procedure order $q \in Q$ is assigned to unit $j \in U$ ($w_{j,q}^i$=1) or not ($w_{j,q}^i$=0)
X_ψ^i	Configuration Boolean to indicate whether alternative $\psi \in \Psi_i$ of process stage $i \in PS$ is selected (X_ψ^i=$true$) or not (X_ψ^i=$false$)
x_ψ^i	Configuration binary to indicate whether alternative $\psi \in \Psi_i$ of process stage $i \in PS$ is selected (x_ψ^i=1) or not (x_ψ^i=0)
$x_{c,m,k}^j$	Flow composition of compound $c \in C$ for every input or output pipeline $m \in M_j^{in} \cup M_j^{out}$ and stage $k \in K_j$ of unit $j \in U$ at Level 1
$x_{c,n,l}$	Flow composition of compound $c \in C$ for every pipeline $n \in N$ and stage $l \in L$ at Level 0
y_j	Equipment binary to indicate whether processing or storage unit $j \in U \cup T$ is selected (y_j=1) or not (y_j=0)
Y_j	Equipment Boolean to indicate whether processing or storage unit $j \in U \cup T$ is selected (Y_j=$true$) or not (Y_j=$false$)
Z_i	Process stage Boolean to indicate whether process stage $i \in PS$ is selected (Z_i=$true$) or not (Z_i=$false$)
z_i	Process stage binary to indicate whether process stage $i \in PS$ is selected (z_i=1) or not (z_i=0)

Index of terms

For the sake of consistency, the terms used in this thesis are defined according to the Standard S88 (ANSI/ISA-88) and complemented by the terminology at the PSE research community devoted to batch processing.
[1] Definition extracted from the Standard S88 (ANSI/ISA-88).

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Chapter 1

Introduction

"A drug is not just its active component, but a system with three interacting elements; medically active ingredient, formulation additives, and delivery vehicle. The efficacy of a drug deteriorates precipitously if the highly active ingredient cannot be delivered to the cells effectively, or its dissolution into the blood stream is hampered by poorly selected excipients. Furthermore, a drug is a part of a therapeutic process, which involves a series of operations with specific time schedules and quantitative dosages."

Stephanopoulos & Reklaitis (2011, p. 4273)

Since the 1990s, several authors in the area of Process Systems Engineering (PSE) have underlined the challenges of solving the problem of batch process development (Rippin, 1983b, Reklaitis, 1990, Rippin, 1993, Allgor et al., 1996, Stephanopoulos et al., 1999, Stephanopoulos & Reklaitis, 2011), and such has been the topic of various relevant doctoral dissertations (Allgor, 1997, Ahmad, 1997, Ali, 1999, Cavin, 2003, Papaeconomou, 2005). All of them claimed the importance of developing processes that allow the implementation of competitive and efficient production lines in batch plants. However, the research in this area found some difficulties, namely a problem complexity that demands high modeling and optimization efforts, the presence of other alternatives to improve batch manufacturing like the enhancement of plant design and short-term scheduling strategies, the mistrust on the expected benefits extent, and the need of modeling and optimization tools which were not mature yet. For all these reasons, cautious efforts have been dedicated to this problem in comparison to other areas of study of PSE. Generally, the whole problem has been addressed through *divide and conquer* strategies, entailing the successive solution of independent sub-problems and losing a significant part of the interaction among the decisions made. So in this sense, there are still many open frontiers and challenges to pose the batch process development as a promising problem, as it will be exposed in this chapter.

1.1 Batch process development for value growth in chemical plants

1.1.1 Batch industry

Chemical industry is characterized by an increasing complexity due to highly competitive production scenarios, globalization and emerging markets, and a volatile economic situation. As a result, there is an ubiquitous need for continuous process improvement on the one hand, in order to preserve firm's value in the production of commodity chemicals. On the other, continuous process development is required to propitiate the production of new specialty chemicals and thus increase the firm's value (Grossmann, 2004). Particularly, the economic opportunities of being the first in the market were presented as very attractive in the 1990s (Puigjaner, 1999) and still are. Thus, the ability to discover new products and be fast to market becomes something crucial for chemical enterprises to remain competitive (Bayer et al., 2001, Grossmann & Biegler, 2004). In addition to requiring fast process development, new production lines should also be sustainable during the production period in order to ensure their long-term viability and acceptance; therefore, it is also necessary to design effective and efficient processes to be economically profitable, environmentally benign, and safe (Stephanopoulos et al., 1999, Grossmann, 2004, Grossmann & Guillén-Gosálbez, 2010, Kravanja, 2010). Moreover, rapidly changing market environments involve uncertainty in product demands, cancellations, and returns, in raw material availability, in prices of chemicals, and in environmental parameters. This variability hampers strictly accurate forecasts, which should be replaced by plausible future scenarios.

In this context, batch plants, whose principal claim is their inherent flexibility and adaptability, are capable of giving an agile response, satisfying the demand of a variety of products according to changing and tight market requirements. In particular, batch systems enhance the distinction between process and plant and the possibility that each equipment piece can be used to execute different production procedures. This practical distinction constitutes the key point for versatility of batch plants, usually referred to as an operations-centered perspective (Stephanopoulos & Reklaitis, 2011) in opposition to the equipment-centered view of continuous processes. This way, the competence of batch plants to select, reorder, and adapt equipment units and the procedures they perform should be highlighted, enabling the processing requirements for each particular product to be fulfilled.

1.1.2 Batch process development

Once a new product has been discovered and its production opportunity has been recognized, the development of its production process is a planning activity that may be decomposed into two principal sub-problems: the synthesis of conceptual processing schemes and the allocation of manufacturing facilities (Rippin, 1983b, Stephanopoulos et al., 1999, Stephanopoulos & Reklaitis, 2011), typically solved sequentially as shown in Figure 1.1. This Figure also summarizes the decisions related to each sub-problem.

The process synthesis problem is defined as the selection of the topology of a process in order to convert a set of raw materials into a desired set of products (Rudd et al., 1973), with decisions ranging from reaction pathways to the selection of unitary operations. In batch process development, reaction mechanisms may be assumed, since they are generally available from previous product development activities. This way, the relevance of process synthesis sub-problem is mostly associated to the definition of processing paths for product manufacturing. Assuming the reaction mechanisms, the **synthesis of conceptual processing schemes**, as defined by Stephanopoulos et al. (1999), focuses on the definition of: (i) the unitary operations, *e.g.* reaction, separation, heat exchange, and their technological specification, (ii) their sequence and splitting or merging in process stages, which are typically known as tasks, (iii) the chemical components involved, *e.g.* reagent, solvent, catalyst, (iv) the batch operations and phases, and (v) the processing conditions, defined by reference trajectories of control variables. The outcome is the so-called task network or *process model*, according to the Standard S88 (ANSI/ISA-88) for batch process management. Typically, the selection of waste treatment options is a downstream activity solved subsequently, even though unitary operations and technologies for waste treatment have an impact on global process design targets and should be addressed in parallel to process synthesis.

The **allocation of manufacturing facilities** sub-problem defines how to implement the process into a particular plant, involving decisions on: (i) the type of campaign, its sequence and coordination, (ii) the equipment pieces selection and interconnection, (iii) the batch sizes, (iv) the cycle times, and (v) the specification of unit procedures according to the task definition in the process model, taking into account the physical plant constraints (Reklaitis, 1990, Rippin, 1983b, 1993, Barbosa-Póvoa, 2007). The goal is to allocate the tasks and processing conditions defined in the synthesis step to particular equipment pieces (Stephanopoulos et al., 1999). The resulting strategy for carrying out a process task at each equipment item is termed procedure and the set of unit procedures that detail the allocation of the entire process in a physical plant composes the so-called

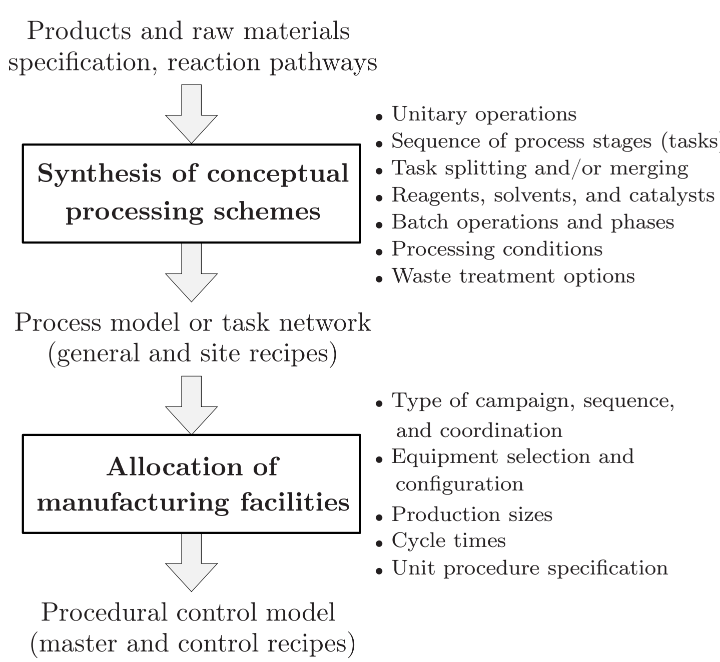


Figure 1.1: Sub-problems in batch process development and decisions made in each case (adapted from Stephanopoulos et al., 1999). The terminology is defined in consonance to the Standard S88 (ANSI/ISA-88) for batch process management.

procedural control model, according to the Standard S88 (ANSI/ISA-88).

In the allocation of manufacturing facilities, the number of products and the degree of similarity of their process models involve different degree of complexity in the equipment structures (Barbosa-Póvoa, 2007, Maravelias, 2012). Particularly, *single-product* plants address the production of an only product following a unique production path. *Multi-product* plants embrace the production of several products, assuming that all products follow the same production route. Finally, *multipurpose* plants are general-purpose facilities where a variety of products may be produced through arbitrary equipment sequences and locations, sharing the available equipment and resources.

Additionally, two possible scenarios exist in the allocation problem: the grassroots and the retrofit. Figure 1.2 presents the process development sub-problems in relation to the enterprise, product, and plant activities in both situations using the concept of lifecycle. This is understood as the sequence of phases spanning the design, creation, use, and decommissioning of an artifact, referred to the aforesaid enterprise, product, process, or plant (Marquardt et al., 2000). The grassroots scenario involves that an enterprise constructs a new plant, after having developed a product and having defined the process models for a portfolio of products to be produced and commercialized (Figure 1.2a). In the retrofit case, the same pattern is followed, with the difference that an existing plant is now adapted to incorporate the newly defined process models (Figure 1.2b). In batch industry for specialty products manufacturing, the latter scenario is the most common situation, since the product lifecycle is often much shorter than the plant one; hence, new products should be introduced repeatedly in existing plants, requiring new or modified process models each time (Allgor, 1997). Several actions can be taken therein: (i) the modification of processing conditions, (ii) the adaptation of equipment structure by changing the piping connections, (iii) the re-sizing of equipment pieces, or (iv) the installation of additional processing units (Grossmann et al., 1987). In the end, in most cases the viability of a new production line is vinculated to the fast and efficient incorporation of the corresponding process into an existing plant, rather than to the design of a new manufacturing facility (Allgor et al., 1996).

The information regarding the process definition is gathered in recipes, which suffer a series of modifications along the batch process development and product manufacturing activities. Particularly, the Standard S88 (ANSI/ISA-88) differentiates four different recipe categories according to their degree of completion: general, site, master, and control recipes. The *general recipe* defines product-specific processing information, independently to the particular equipment items where the process is going to be implemented. The *site recipe* additionally has into account the conditions found at a particular manufacturing location. Being independent to specific equipment items, general and site recipes are related to the process model, obtained in the synthesis of conceptual processing schemes. Following, the information of the general or the site recipe information is targeted to a set of equipment elements in the *master recipe*, which takes into account the allocation of manufacturing facilities and is thus associated to the procedural control model. Afterwards, during the product manufacturing activities, the information of the master recipe is adapted within the *control recipe* to produce a particular batch of product. All in all, the integrated solution of batch process development sub-problems, involving the synthesis of processing schemes and the allocation of production plants, is equivalent to the definition of master recipes to define the implementation of new or modified production lines in a batch plant.

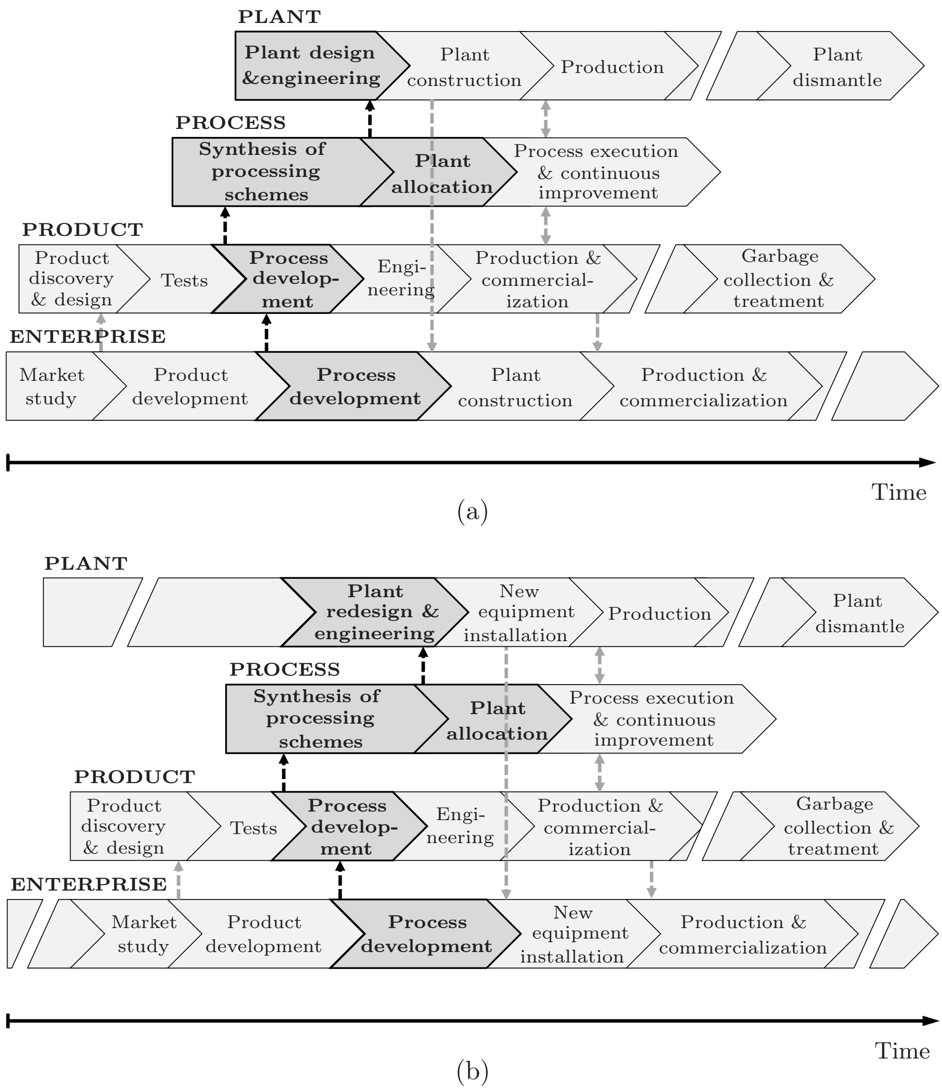


Figure 1.2: Lifecycles in an enterprise: (a) grassroots scenario and (b) retrofit scenario (adapted from Marquardt et al., 2000).

1.1.3 Challenges in batch process development

Rapid process development. Nowadays batch manufacturing is devoted to specialty chemicals industry, which requires the frequent adaptation of production facilities to market fluctuations and to discoveries of new chemical products. This way, new products should be introduced frequently in manufacturing systems, requiring the development of production processes and the specification of master recipes to be used in the production stage. Hence, a first challenge in batch process development is the use of rational and systematic approaches and the rapid time-to-market execution of the process lifecycle steps, until the new product is introduced into the production system. This is a pivotal element for chemical producers to meet economic leverage and keep competitive in a market-place with growing globalization (Puigjaner, 1999, Stephanopoulos et al., 1999).

Development of competitive and sustainable processes. The synthesis of processing schemes is a potential area to improve process performance, as well as an increasingly important field of activity in academia and industry (Kravanja, 2010, Li & Kraslawski, 2004, Rippin, 1993). For example, in the case of continuous industry, savings of 35% in net present cost and 50% in energy consumption have been reported using systematic process synthesis methodologies (Douglas, 1988). Moreover, Stephanopoulos & Reklaitis (2011) noted that rough estimations of the added value or lost opportunity –understood as the benefit margin that can be obtained through the production of a particular product– decrease by several orders of magnitude along the chain of activities in a product lifecycle, namely: (i) the product discovery, design and testing, (ii) the process development, (iii) the engineering design, (iv) the product manufacturing, and (v) the commercialization. End-of-pipe process retrofit may require huger investments and operating costs than equivalent process design at early stages. Thus, a second challenge is the development of competitive and sustainable processing schemes to improve reference production targets for future manufacturing activities (Stephanopoulos & Reklaitis, 2011, Stephanopoulos et al., 1999, Allgor et al., 1996, Allgor, 1997).

Plant flexibility. Due to the need of batch plants to be reconfigured and adapted in front of changing market scenarios along their lifecycle, a third challenge is to account for external uncertainty during the design of batch plants. General and flexible facilities that conduct most of the processes in the company's port folio with small investments are prized (Allgor, 1997). For that, driving factors in batch plant design should be the maximization of future flexibility at minimum investment cost, accounting for uncertainty in product demands, in raw material availability, in prices of chemicals, and in environmental parameters in the design problem. The objective is to define versatile systems which can ensure the manageable response to changes in the business environment, the increase of decisions accuracy, the adaptation of master recipes, and the improvement of process performance.

Insights into process performance. Finally, significant benefits can be brought by coordinating batch tasks through plant design, planning, and scheduling, but Rippin (1993) pointed out that a further determinant of success is the design and operation of the individual units that carry out each of the batch tasks. The performance of unit procedures is determined by the physicochemical properties of the system. Moreover, the degree of completion of each process stage has an effect over the state variables of the material being transferred to the next task, which in turn may require the adaptation of its processing conditions depending on the input states. Such interactions between process performance in upstream and downstream tasks have been identified in many chemical processes and come out into trade-offs in global objective functions and performance indicators. Barrera & Evans (1989, p. 49) specified that there are three types of trade-offs related to process performance: (1) cycle time versus intensity of processing within each individual unit, (2) the effect of upstream tasks performance over downstream stages, and (3) investment or total rental costs versus operational costs associated to the processing rate of the system. Therefore, deciding on operating procedures has a high probability of affecting synthesis decisions and inversely. This way, the solution of synthesis and allocation sub-problems in batch process development should be embraced together, seeking for a holistic treatment of process development and recipe optimization. In particular, integrated approaches that combine structural and processing conditions ensure fully functional and optimally operated process plants in both nominal regimes and changing frameworks (Shobrys & Shobrys, 2002). Overall, the integration of process development sub-problems becomes a further challenge to avoid suboptimal solutions in grassroots designs and to adapt existing equipment guaranteeing an improved plant utilization in retrofit scenarios.

1.2 Use of fixed and approximated recipes

Despite the challenges in batch process development sub-problems and their integrated solution, fixed processing recipes are typically employed in batch industries, based on nominal conditions and tests in the laboratory or pilot plant (Rippin, 1993, Romero, 2003, Srinivasan et al., 2003). Specifically, laboratory recipes used during the product development activities are scaled-up to provide the first piece of information related to the process synthesis. Usually, these recipes are not further improved by synthesizing industrial-scale processing schemes. On the contrary, the allocation sub-problem is addressed with fixed predefined recipes or very simple approximated models of the tasks involved (Reklaitis, 1990). For instance, tasks are extensively described by fixed time and size factor models (Robinson & Loonkar, 1972, Biegler et al., 1997), where the time is a predefined parameter and the capacity requirements are calculated as a function of the batch size.

However, decisions made at the batch process development sub-problems –*i.e.* the task selection, the definition of reference trajectories for control variables, or the selection of chemical compounds involved– affect the efficiency of the process for several reasons (Allgor, 1997). First, actions derived from fixed or approximated recipe parameters reduce the possibilities of further improvements of processing times, conditions, and tasks sequence. Second, existing equipment may be forced to operate in extreme or suboptimal conditions, since procedures that were suitable in the laboratory have to be implemented to the industrial scale, which may be equipped with different specifications. Moreover, the direct implementation may not be feasible. Finally, the objectives in bench scale experiments also differ from those of full-scale manufacture. On the whole, the process information generated from the original product synthesis during the product discovery, product design, and product synthesis activities should only serve as the starting point for process design rather than a completing process definition.

Until now, batch process development and recipe optimization has received limited academic and industrial attention and is more concerned about the allocation of predefined process tasks to appropriate equipment items and about the sequencing of operations (Reklaitis, 1990, Stephanopoulos et al., 1999, Rippin, 1993, Allgor, 1997). Published work in batch plants design and scheduling of batch plants has grown exponentially –for an extensive review on process design, the interested reader is referred to Reklaitis (1990) for the period up to 1990 and Barbosa-Póvoa (2007) for the period from 1990 to 2007. On the contrary, in the area of synthesis and design of batch processes, only a few researchers have examined methods to incorporate recipe modifications during the development of a batch process, as Allgor (1997) and Papaeconomou (2005) underlined. This happens even though the effort should be more dedicated to the process design for new chemicals production to be implemented in existing batch sites, instead of the definition of especially designed plants for a given portfolio of products (Rippin, 1993, Cavin, 2003). The evolution experienced by these areas in the last decades is presented in Figure 1.3, according to the number of publications in a series of review papers (Stephanopoulos et al., 1999, Allgor, 1997, Barbosa-Póvoa, 2007).

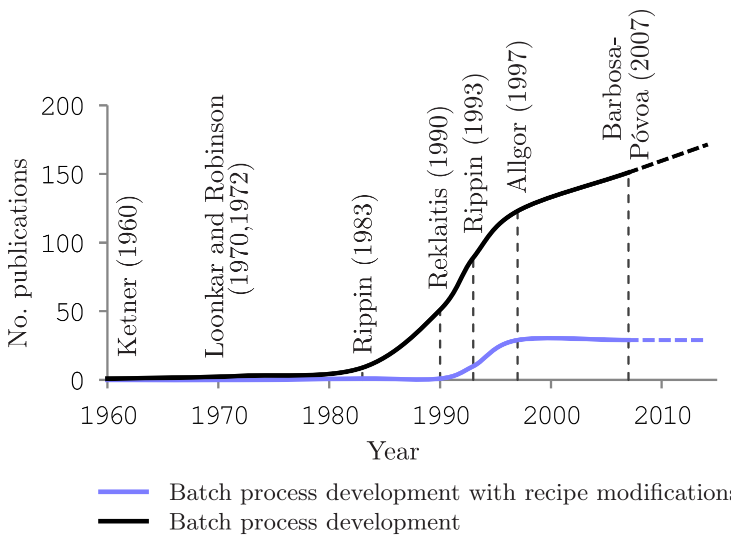


Figure 1.3: Evolution of the number of publications dedicated to batch process development (dark line) and particular works that consider modifications of the process model and the recipe (light line). Dotted lines represent a prediction, according to the examined review papers. Data sources: Stephanopoulos et al. (1999), Allgor (1997), and Barbosa-Póvoa (2007).

1.2.1 Complexity of batch process development

The main reason for the use of fixed recipes is the high mathematical and computational complexity for modeling and solving the process synthesis and allocation sub-problems: First, the batch nature of the process involves not only a combinatorial assessment to match equipment and task networks (Allgor, 1997, Gani & Papaeconomou, 2006), but also an evolution of processing conditions along time in each process stage, requiring dynamic models to represent process performance instead of steady-state ones and dynamic profiles of control variables instead of continuous set-points (Barton et al., 1998, Srinivasan et al., 2003). Moreover, the operation of batch processes is featured by discrete events that determine the transitions between batch operations and phases (Barton et al., 1998). Qualitative information should be also covered in the optimization model, involving decisions like task selection, sequence, and splitting, equipment assignments, or chemicals selections, among others. Finally, batch integrity should be ensured in all processing path alternatives by synchronizing material transference between batch and semi-continuous plant elements, as a function of the processing scheme and the task performance.

As a result of the evident problem complexity, there is reluctance on the expected results, despite being aware of the need and incentives associated to the coordination and integration of the synthesis of processing schemes and plant allocation sub-problems. Specifically, there is a sensible concern about the importance of verifying whether the potential benefits will justify and outweigh the effort and time required to generate and solve such complex models, before embarking on a scheme to establish or maintain an optimal profile (Rippin, 1993, Allgor, 1997). Overall, the possible variation of task performance is presented not only as an important problem, but also as a difficult one.

Concurrently, big efforts by PSE community have been required to succeed in the development of detailed modeling capabilities and optimization techniques, which can be applied to solve batch plant design and scheduling problems with dynamic profiles and a high number of discontinuous variables combined into task-unit superstructures. In the 1990s, such tools were immature and further development was still required (Puigjaner, 1999, Allgor, 1997). As a result, the modeling load and computational difficulties to solve such complex systems limited dramatically the research in the direction of batch synthesis and operation problems when they were initially posed (Rippin, 1993, Stephanopoulos et al., 1999, Allgor, 1997, Ahmad, 1997, Ali, 1999).

1.3 Process synthesis and allocation in academy

Due to the abovementioned difficulties to solve batch process development, most academic studies kept faithful to the natural decomposition into process synthesis and allocation sequence, seeking for a problem simplification. Nevertheless, integrative attempts have been also addressed. An overview of the available literature is presented in this section and extended in Chapter 2.

1.3.1 Decomposed problems

The *synthesis of batch processing schemes* was first addressed in the mid 1990s. It was strongly incentivized by changing market requirements, which entailed the frequent adaptation of product portfolios in batch plants as well as the development of the corresponding batch processes. At that moment, the synthesis of continuous processes was already a strengthened area of study, provided with several complementary solution approaches. Namely knowledge-based, optimization-based, and combined methodologies had been developed, which served as a base for batch problems. For instance, the synthesis of batch processing schemes was solved in some contribution by disregarding the subsequent allocation of equipment items (Linninger et al., 1994, 1995, 1996, Ahmad, 1997, Barton et al., 1999, Ali, 1999, Sharif et al., 2000, Papaeconomou et al., 2002, 2003a,b, Papaeconomou, 2005), whilst other studies used sequential decision-making procedures to include allocation decisions (Iribarren, 1985, Iribarren et al., 1994, Cavin, 2003, Cavin et al., 2004, 2005, Mosat et al., 2007, 2008).

Research in the allocation of manufacturing facilities sub-problem included a thoughtful study of the *optimal operation of individual units*. In particular, since the early works by Denbigh (1958) and Aris (1960) the field of Optimal Control (OC), also referred to as Dynamic Optimization (DO), was applied to define batch unit performance by optimizing dynamic profiles of control variables. In the 1980s and 1990s, several solution approaches were developed (see the reviews by Binder et al., 2001, Srinivasan et al., 2003, Schlegel, 2004), converting DO for batch unit optimization in a popular area of research in the academic context due to its applicability and excellent results. As for the decision variables considered, later works also optimized the batch phase durations (Vassiliadis et al., 1994), as well as structural decisions like the number of trays in distillation columns (Oldenburg et al., 2003, Jain et al., 2013). In the latter case, the use of integer or logical variables was required to formulate the structural decisions, resulting in Mixed-Integer (MIDO) or Mixed-Logic (MLDO) problems, respectively.

Additionally, the *design of single-product, multiproduct, and multipurpose batch plants* became a relevant problem, dealing with the allocation of equipment items to particular process tasks, among other decisions like the equipment sizing and operational decisions, *e.g.* processing mode, batch size, storage tank location, or unit duplication. The solution of these problems attracted much interest since the mid 1980s, becoming a consolidated area of research. A detailed framework of this field of study is presented in the reviews by Reklaitis (1990) and Barbosa-Póvoa (2007). It is frequent in batch plant design that the use of fixed or approximated recipes hinders the adaptation to global targets of recipe parameters, *e.g.* adaptation of set-points, reference trajectories for control variables, processing times and volumes, and chemicals involved, among others decisions. For instance, the most widespread assumption to represent recipe modifications in batch plant design problems has been the definition of processing times and sizes for each task either as fixed parameters or as a function of batch sizes (Robinson & Loonkar, 1972, Biegler et al., 1997), which are still used at present literature (Barbosa-Póvoa, 2007). As a result, processing times and overall performance can be only accommodated through operational decisions.

1.3.2 Integrated problems

The combination of process synthesis and allocation of manufacturing facilities has been also reported in several works, tackling this formidable problem with different degrees of integration and from different perspectives. For that purpose, most contributions pose solution strategies that reduce the complexity of the integrated problem, for instance applying an iterative assessment of structural and performance decisions, replacing Differential-Algebraic Equations (DAE) systems representing the dynamic process behavior by approximated algebraic equations, or pre-specifying particular decisions.

The interactions between decisions associated to *batch process synthesis* and to *equipment allocation* have been addressed using iterative and simultaneous solution approaches. Charalambides et al. (1995, 1996) and Sharif et al. (1999) used a simultaneous approach, applying DO and MIDO formulations in sequenced process stages to optimize the reference trajectories of control variables. However, it was necessary to assume predefined process structure and task-unit assignment in order to accomplish their purpose. Another suggested approach was to approximate the dynamic process behavior in batch tasks to algebraic models. Such model simplification permitted to consider decisions like the task-unit assignment and operating procedures –*e.g.* operating mode in parallel in-phase or out-of phase– as degrees of freedom. Particularly, Allgor, Barton, et. al (1997, 1999, 1999a) proposed the use of the so-called *screening models* to provide rigorous lower bounds in minimization problems. Iribarren et al. (2004) used *posynomial functions*, which related size factors to certain operating parameters through a symbolic rearrangement of process equations. Going a step further, Allgor & Barton (1999b) developed an iterative solution approach based on their prior contributions, to additionally include the dynamic behavior of batch process tasks and define the feed-forward trajectory of control variables. Besides, Linninger and Chakraborty (1999, 2002, 2003) solved simultaneously the selection of waste treatment paths for pharmaceutical industry effluents, their task-unit assignment, and the definition of constant set-points for processing conditions, taking into account capacity constraints.

Additionally, the *synthesis of new processing schemes in retrofit scenarios* concerns inherently the integration of process synthesis and allocation sub-problems, since process models can not be defined unaware of physical restrictions of the plants where the process should be implemented. Several contributions have addressed this problem, paying a special attention to the introduction of sustainable targets in new process development (Halim & Srinivasan, 2006, 2008, Simon et al., 2008, Carvalho et al., 2009, Bumann et al., 2011, Halim et al., 2011, Banimostafa et al., 2011, 2012).

Finally, several studies have been carried out regarding the incorporation of *recipe modifications in batch plant design*, allowing the adaptation of recipe parameters according to global production targets during the allocation of manufacturing facilities, instead of assuming fixed recipes. This way, several contribution replaced the widespread fixed time and size factor model (Robinson & Loonkar, 1972, Biegler et al., 1997) by more detailed recipe representations that allowed further degrees of freedom. In particular, most relevant proposals were: (i) the determination of residence times in semi-continuous units (Knopf et al., 1982), (ii) the use of time and size factor models (Espuña & Puigjaner, 1989, Modi & Karimi, 1989), (iii) the approximation of process behavior to algebraic performance models (Tricoire, 1992, Salomone & Iribarren, 1992, Montagna et al., 1994, Asenjo et al., 2000, Pinto et al., 2001), (iv) the iterative use of approximated and detailed models to solve structural and performance decisions (Barrera & Evans, 1989, Salomone et al., 1994, 1997), and (v) the use of detailed dynamic performance models in the plant design problem (Bhatia & Biegler, 1996, Corsano et al., 2004, 2006, 2007).

Considering the effect that every process stage has on downstream tasks, due to their connection via outflows and inflows, synchronization between consecutive tasks should be accounted for in the model. However, previous works do not include in their formulations material transfer operations or the consideration of dynamics in process variables therein, and the only related constraints are the fulfillment of material and energy balances with transition states represented in a unique temporal point in each transfer operation. Indeed, it is only in the context of scheduling and plant design that some studies explicitly address equipment synchronization (Furman et al., 2007, Ferrer-Nadal et al., 2008a), although dynamic transferring states are dismissed because dynamic models are not used in the formulations.

1.4 Industrial application of process synthesis and allocation

In industrial practice, synthesis of continuous processes using hierarchical decision tools penetrated with a very positive impact and contributions nothing less than spectacular around the 1980s (Stephanopoulos & Reklaitis, 2011). The extension of posterior research on batch process development into production facilities has also taken some steps, relying principally on hierarchical and decomposition approaches combined with process simulation. For instance, the batch process simulator *BATCHES* was commercialized by the software supplier Batch Process Technologies, Inc. in the mid 1980s, followed by the *SuperPro Designer*, developed by Intelligen, Inc. Following, Stephanopoulos and co-workers developed a program to address batch process synthesis (Linninger et al., 1994), the *Batch-Design-Kit*, acquired by the software supplier Hyprotech Ltd. in 1997. Contemporary, the firm Aspen Technology, Inc. developed the recipe-based modeling technology *Batch Plus*, later upgraded to *Aspen Batch Process Developer*. Overall, commercial software for batch process simulation are available to support screening strategies for the evaluation of batch processing alternatives in industry.

However, the use of general flow-sheeting capabilities for batch processes still requires further work to be established successfully, especially regarding the use of optimization-based approaches. This is an essential step for ensuring reasonable development and pay-back times, while exploiting the full potential of PSE tools (Klatt & Marquardt, 2009). In general, the difficulties to apply batch process development methodologies in industrial practice are explained by the following limitations from the practitioner's point of view (Klatt & Marquardt, 2009): (i) the lack of robust and user-friendly optimization-based environments, despite the availability of well-established software for batch process simulation, (ii) the difficulties to quantify the benefit obtained with proposed methods and solutions, (iii) the difficulties to model and simulate solids and biotechnological processes, (iv) the lack of efficient formulations for middle- and large-scale applications, and (v) the need of reliable model equations and parameters, which are frequently unavailable.

1.5 Thesis overview

This thesis tackles the fast development of batch processes that are efficient, economically competitive, and environmentally friendly, as well as their agile introduction into production systems, by solving simultaneous process synthesis and plant allocation in grassroots and retrofit scenarios. Thus optimum master recipes are provided.

1.5.1 Motivation

Several elements motivate this complex and demanding problem. First, the challenges associated to the evaluation of processing trade-offs are more important at early decision-making in the process lifecycle, when added value of production benefits provides a greater leverage. Second, recent advances in modeling and optimization tools raise the question whether it is possible their application to integrated batch process development, extending their original use solving other problems in PSE. For instance, Mathematical Programming (MP) and DO have been successfully applied to scheduling and design of batch plants, synthesis of continuous processes, and optimization of individual unit operation. These advances are complemented by efforts in the characterization of physicochemical parameters and equations for a variety of processes. Last but not less important, few examples are available in the literature that provide a quantification of the expected benefit in solving simultaneous process synthesis and allocation, crucial to determine whether it is worth the effort and dedication to solve this of problem.

1.5.2 Objectives

For all these reasons, the principal goal of this thesis is to present a systematic and rigorous modeling strategy that is capable of integrating in a unique optimization model the different kind of decisions in the synthesis of batch conceptual processing schemes and allocation of equipment items sub-problems, assuming single-product campaigns, in both retrofit and grassroots scenarios. The specific objectives are:

- To identify the general problem specification and the degrees of freedom of the two principal sub-problems in batch process development –*i.e.* synthesis and allocation–, as well as to provide a compromised terminology that reflects the PSE literature and the Standard S88 (ANSI/ISA-88) concepts for batch processing;

- To develop a modeling strategy to solve the problem of simultaneous synthesis of processing schemes and allocation of manufacturing facilities using an optimization-based approach;
- To evaluate whether current available model-based tools and approaches allow this problem to be solved, concentrating in new developments of logic-based modeling and MP solvers for mixed-integer and non-linear formulations;
- To apply the modeling strategy to the development of new processes in retrofit scenarios, taking into account the restrictions of the existing plant;
- To apply the modeling strategy to the design of flexible plants in grassroots scenarios, considering simultaneously process synthesis and allocation degrees of freedom;
- To provide a tool for analyzing processing interactions for multiple scenarios and performance indicators in the decision-making process, meeting an equilibrium for trade-offs between: (i) profit and time within each individual unit, (ii) the performance of subsequent tasks, and (iii) different weights in global objective functions, *e.g.* investment and operational costs;
- To evaluate the interactions between structural decisions of batch process synthesis and dynamic profiles of operating procedures, while considering physical plant decisions and/or restrictions;
- To study the influence of synchronizing material transfer stages through dynamic profiles.

1.5.3 Scope

The approach to solve integrated batch process development that is proposed in this thesis is focused on the modeling aspect, under the premise that the appropriate formulation of the optimization model is a crucial step in the solution approach. Complementary, deterministic, stochastic, and hybrid solution procedures are proposed. In this regard, the goal is to provide suitable solution methodologies to obtain quantitative solutions, paving the way to further research for the development of robust solution tools and software that could be offered to industrial practice. The optimization model obtained is large in size and complex in type of variables and mathematical functions. Thus, a thorough study of optimization approaches is required to render robust solution strategies to deal with the mathematical implications of this formidable problem and to avoid case-specific model analysis and evaluation. This is out of the scope of this work.

In addition, before a direct application in industry could be suggested, two other issues should be considered. First, in practice reliable physicochemical parameters and correlations required in the optimization model are not always available or with an appropriated level of detail. Therefore, it will be necessary to deal with internal uncertainties regarding process parameters, to simplify the process models in order that they become manageable, and to validate those models with experimental data from pilot or production plants. These activities, which are also out of the scope of this contribution, should complement the process development practice. Second, corporative changes in batch industries are required in order that integrated solution of process synthesis and allocation is likely to be applied. Chemical enterprises use to be composed of differentiated departments to carry out the process synthesis, engineering, and plant operation, which could be even located at different sites. To integrate batch process synthesis and allocation, a close interconnection of working divisions is mandatory, as seen in trending organizations of some top-tier companies.

Regarding the decision-making, process control decisions are partially addressed in this thesis, since the feed-forward trajectories of control variables are optimized. However, the assessment and analysis of the indicators of the control system performance, emphasizing controllability and stability, are not included in objective functions or optimization model restrictions. Therefore, the strict problem of simultaneous process design and control is not covered. Moreover, the optimization of master recipes is tackled through process development as a planning activity. Thus, on-line or real-time applications during the manufacturing stage are considered out of the scope of this work both at the process control and at the scheduling decision levels. Finally, internal process disturbances and model uncertainties are not taken into account in the formulation; on the contrary, production adaptability is covered by optimizing operation policies according to different scenarios, economic contexts, and driving factors, and plant flexibility is uniquely addressed according to external uncertainty, like demand variation.

1.5.4 Optimization-based approach

An optimization-based approach is proposed to solve the simultaneous synthesis of batch processing schemes and allocation of manufacturing facilities, accounting for equipment decisions or restrictions. Some authors have explicitly dissuaded the use of optimization-based approaches, where all the decisions are integrated in a superstructure. For example, Klatt & Marquardt (2009) considered that *"it is very unlikely that a single integrated problem formulation can be found which on the one hand covers all possible alternatives in a superstructure and is still computationally tractable on the other hand."* On the contrary, other kind of approaches have been recommended, as for example the systematic decomposition of the problem, where a gradual refinement of the design specifications can be combined with an increasing level of detail in the model (Marquardt et al., 2008).

Despite the attractive of *divide and conquer* strategies, a significant part of the interaction among the decisions made is lost. In contrast, an integrative model-based approach that combines all the alternatives for process synthesis and allocation in a unique formulation should precisely allow a rigorous and quantitative balancing of the process trade-offs, considering all the degrees of freedom involved in the problem, and is therefore proposed in this thesis. The core idea is to enhance numerical solution properties by using advanced modeling strategies, which have provided promising results in other PSE applications. Specifically, the objective is to prove that the integrated problem is tractable, even though huge computational efforts may be required. In addition, the obtaining of quantitative results systematically from a unique model is pursued, in order to compare optimum solutions in different economic and demand scenarios or for various production policies.

The modeling strategy proposed relies on the combination of DO and mixed-logic modeling, and on the synchronization of material transfer stages in equipment and task sequences. *Mixed-logic modeling* tools are used to combine the quantitative and qualitative information in the formulation, and has been previously applied to similar problems in the context of continuous process synthesis (Raman & Grossmann, 1993, Türkay & Grossmann, 1996b, Grossmann & Guillén-Gosálbez, 2010, Khor et al., 2011) and scheduling of batch processes (Lee & Grossmann, 2000, Castro & Grossmann, 2012). As for *DO*, it has been proved to be a powerful tool to handle dynamic models and to optimize dynamic reference trajectories of control variables (Srinivasan et al., 2003, Biegler & Grossmann, 2004). DO has been used in combination to mixed-integer and mixed-logic formulations to incorporate structural decisions, with contributions in the context of simultaneous design and control (Bansal et al., 2002a,b), scheduling of continuous processes with grade transitions (Prata et al., 2008), and design of individual batch units with structural decisions (Oldenburg et al., 2003, Jain et al., 2013). Finally, the *synchronization* between tasks is included in the model to incorporate the effect of upstream and downstream process stages, which are connected via outflows and inflows (Furman et al., 2007, Ferrer-Nadal et al., 2008a). To the author's knowledge, the combination of these modeling issues has not hitherto been applied in the context of batch process development.

Process synthesis decisions subject to be considered in this approach are: (i) the selection of process stages and splitting into subtasks, (ii) the technological specification of unit procedures, (iii) the selection of chemicals involved, (iv) the recirculation of intermediate flows, (v) the reference trajectories of control variables, (vi) the duration of batch phases composing each task, and (vii) the material transfer synchronization between tasks. The allocation of equipment items may include: (i) the task-unit assignment, (ii) the equipment configuration –*i.e.* operating mode in single, series, or parallel operation, and (iii) the location of storage tanks. Additionally, equipment capacities are related either to free decision variables in grassroots scenarios, or to model constraints of existing units in the retrofit case. Finally, the objective function can be composed of economic contributions, like the amortization of new investments, the equipment occupation expenses, reflecting cleaning, maintenance, and labor expenses, the various processing and utility costs, the raw material costs, the waste treatment costs, and the economic impact of product quality, as well as ecological or environmental decision criteria. Overall, the main contribution of this thesis is to provide a modeling framework that permits the simultaneous optimization of all the abovementioned decision variables which, despite the existing interactions, are typically addressed separately.

Generally, optimization-based approaches that include synthesis decisions are developed in three steps: the representation of a superstructure with all processing alternatives, the formulation of such superstructure to construct the optimization model, and its solution (Grossmann & Guillén-Gosálbez, 2010). The proposed modeling framework and solution approach are developed accounting for these steps, as following detailed. First, the equipment diagram of the existing or potential plant serves as a base to the process superstructure, in order to facilitate the incorporation of physical plant restrictions and decisions. Particularly, the State-Equipment Network (SEN) representation (Smith & Pantelides, 1995) is used. Second, the superstructure is mathematically formulated using MLDO. In particular, the formulation is composed of disjunctive equations to relate the structural and allocation decisions and multistage models to represent process performance in each process stage, which may be composed by a series of bath operations or phases. The combination of logic modeling and multistage models had been previously addressed by Oldenburg & Marquardt (2008), who referred to this optimization problem as disjunctive multistage modeling. In their case, the formulation was applied to the design of individual batch units with structural decisions, which is extended in this thesis to cover the new requirements of batch process development. Specifically, the following key features characterize the formulation:

(i) Single-stage and multistage models are combined to represent continuous and batch processing elements; and
(ii) The superstructure is divided in modeling levels, which allow time overlapping of operating procedures in batch units, whose processing order is not known beforehand;

(iii) Flow rates and compositions are synchronized in material transfer operations and phases.

Third, the resulting MLDO model is reformulated into a MIDO one and solved using deterministic, stochastic, or hybrid optimization methods.

1.5.5 Overview of chapters

The rest of this thesis is structured as follows.

Chapter 2 reviews the state-of-the-art of batch process development, focusing on the following research topics: the synthesis of conceptual processing schemes, the allocation of manufacturing facilities, their integration at different degrees, and the parallelism between process development and operational problems –*i.e.* short-term scheduling and process coordination.

Chapter 3 presents the general problem statement of the integrated batch process development tackled in this thesis. Moreover, the modeling requirements to address the simultaneous consideration of synthesis of processing schemes, plant allocation, and plant design are exposed. Next, the modeling strategy based on MLDO is developed.

In Chapter 4, the state-of-the-art solution approaches to solve the MLDO problem are reviewed and three particular strategies are proposed. On the one hand, a deterministic direct-simultaneous approach is presented, which is used to solve the different examples along this thesis. It is based on the MLDO reformulation into a MIDO problem, the full-discretization of process and control variables to obtain a Mixed-Integer Non-Linear Programming (MINLP) problem, and its solution through commercial solvers. On the other, two alternative methods are introduced as a first step to pursue the solution of industrial-size problems: the Differential Genetic Algorithm (DGA) and its combination with the previous direct-simultaneous approach in a hybrid optimization algorithm.

Then, Chapter 5 tackles the development of new processes to be introduced in existing plants, whose equipment restrictions are considered in the optimization model. The production of specialty chemicals based on a competitive reaction system in an existing reactor network is first defined through process development and improvement according to different economic scenarios, decision criteria, and plant modifications. Additionally, the development of a photo-Fenton process to be implemented in an existing pilot plant is optimized, pursuing the minimization of processing time and cost to eliminate an emergent wastewater pollutant.

Besides, Chapter 6 focuses on the application of the proposed approach to simultaneous process development and flexible plant design. In particular, the expected profit in several demand scenarios is maximized using a two-stage stochastic formulation of the optimization problem. Moreover, the previous solution strategies to solve the MLDO problem are combined with a heuristic algorithm to enable the plant design under uncertainty, while accounting for process synthesis and allocation decisions. A grassroots plant design is defined to implement the previous competitive reaction system, where decisions like the feed-forward trajectories or operating modes allow the adaptation of master recipes to different demand scenarios. An industrial-size case study for acrylic fiber production is also presented, illustrating synthesis decisions like the selection of process stages, technological alternatives, and chemicals, in a grassroots scenario.

Finally, Chapter 7 summarizes the contributions of this thesis and exposes the further research directions that can be followed on the basis of the results obtained.

Chapter 2

State-of-the-art: batch process development

"If I had an hour to save the world, I would spend 59 minutes defining the problem and one minute finding solutions."
Albert Einstein (1879 – 1955)

In this chapter, the problem of batch process development is defined and contextualized. Academic contributions are reviewed, considering relevant advances for solving the *synthesis of conceptual processing schemes* and the *allocation of manufacturing facilities*, as well as for addressing their *integration* at different degrees. Special attention is paid to optimization-based approaches. The overview also presents the parallelism between process development and process management activities during the manufacturing stage, like *short-term scheduling* and *process coordination*. Moreover, the use of a heterogeneous terminology is identified in this area of research. For the sake of clarity, the definitions presented in Chapter 1 are here used, being consistent to the Standard S88 (ANSI/ISA-88). Overall, the goal is to provide a complete perspective of the batch process development problem which allows to state the problem solved in following chapters of this thesis.

2.1 Overview of batch process development

The problem of batch process development is defined as a planning activity that entirely involves all decisions from the selection of best molecule to the optimal coordination of operations for the manufacturing of a range of other products (Stephanopoulos et al., 1999). It may be decomposed in two sub-problems, namely *the synthesis of conceptual processing schemes and waste treatment options*, and *the allocation of manufacturing facilities* (Rippin, 1983b, Stephanopoulos et al., 1999, Stephanopoulos & Reklaitis, 2011) as shown in previous chapter (Figure 1.1, p. 3) and they are typically solved sequentially.

Several challenges are associated to the problem of batch process development. First, the added value has a greater relevance at early process development stages (Stephanopoulos & Reklaitis, 2011, Allgor et al., 1996). For example, master recipe information, which is detailed during process development, is the basis for operational decisions made during product manufacturing activities. In addition, the rapid process development using rational and systematic approaches is fundamental for chemical producers to be agile introducing the production of new chemicals and keep competitive in the market-place (Puigjaner, 1999, Stephanopoulos et al., 1999). Moreover, global targets are strongly influenced by processing conditions that determine task performance within the process network (Rippin, 1993), establishing several trade-offs that are often reflected in economic outcomes (Barrera & Evans, 1989). All these challenges encourage the research on process development, seeking to avoid the overuse of fixed and approximated recipes obtained from experimental procedures utilized in the preliminary product design (Rippin, 1993, Romero, 2003, Srinivasan et al., 2003).

Additionally, in the particular case of batch processes, an emphasis on the integration of process synthesis and plant allocation sub-problems should be placed, since process and plant are defined as independent items therein. New processes should be defined frequently to refresh the products' portfolio in batch facilities (Barrera & Evans, 1989). In these situations, the definition of process task networks with no consideration of the plant constraints leads to suboptimal solutions. So does the allocation of equipment items with no adjustment of tasks and processing conditions.

2.2 Synthesis of conceptual processing schemes

According to Rudd et al. (1973), process synthesis deals with the selection of the topology of a process in order to convert a set of raw material into a desired set of products. Such problem involves decisions ranging from chemical reaction paths to complete process flow sheet definition. Assuming th reaction mechanism, batch process synthesis can be understood as the synthesis of a processing scheme or a general process recipe by selecting process operations and their interconnections to transform a set of raw materials into the final product (Stephanopoulos et al., 1999). Overall, the problem statement of the synthesis problem can be formulated as follows:

> *Given the specification of raw materials and products and reaction mechanisms, determine: (a) the unitary operations, (b) their splitting or merging in process stages –or tasks–, (c) their sequence, (d) the chemical components involved –e.g. reagent, solvents, catalysts–, and (e) the processing conditions, such that the process model or task network of the process is obtained.*

In his doctoral dissertation about the synthesis of batch processes for producing pharmaceuticals and specialty chemicals, Ali (1999) refines the definition of the process synthesis problem by assuming information that is typically available from the chemist's recipe in previous laboratory steps (Ali, 1999, p. 46):

> *Given the chemist's recipe which includes: (a) chemical reactions, (b) laboratory processing steps, (c) their operating conditions, (d) raw materials, (e) product specifications including intermediate product specifications, (f) additional materials used –e.g. solvents, catalysts, and non-reacting quench materials–, (g) physical property information, and (h) notes on operations, determine the process model which consists of the optimal set of: (a) process stages, (b) their relative ordering, and (c) their processing conditions, such that production costs are minimized.*

This author also refers the development of the task network as the core of process synthesis stage of the batch process development, and defines three elements constituting this problem, namely the task selection, the task ordering, and the processing conditions selection (Ali, 1999).

The synthesis of conceptual processing schemes is a potential area to improve process performance through the development of effective and efficient processes (Rippin, 1993) and has become an increasingly important field of activity in academia and industry (Li & Kraslawski, 2004, Kravanja, 2010). For instance, savings of 35% in net present cost and 50% in energy consumption are reported using systematic process synthesis methodologies (Douglas, 1988). In addition, seeking for a holistic treatment of the process systems problem, traditional conceptual synthesis, which is focused on deciding processing unit types and their interconnection, is pursued to embrace other disciplines, like environmental impact assessment, supply chain design, process intensification, or simultaneous product and process design, among others (Li & Kraslawski, 2004).

2.2.1 Brief overview of process synthesis history

As Stephanopoulos & Reklaitis (2011) trace in their exhaustive overview of PSE, the two pioneering textbooks of Rudd and collaborators in the late 1960s –*i.e. Strategy of Process Engineering* (Rudd & Watson, 1968) and *Process Synthesis* (Rudd et al., 1973)– marked the beginnings of a synthesis perspective in chemical process engineering, which was able to complement and equilibrate the simulation and analysis culture that was present up to that moment. Both perspectives are presented in Figure 2.1. From then on, academic research developed systematic process synthesis ideas, which provided process engineers with methodologies to invent new processing systems, rather than simply analyze existing ones. Particularly, the rise in energy costs in the 1970s incentivized a great deal this area of study (Nishida et al., 1981, Liu et al., 2011), whose early pivotal developments were collected in several reviews (Hendry et al., 1973, Hlavacek, 1978, Stephanopoulos, 1980, Nishida et al., 1981).

Almost thirty years later, Grossmann & Daichendt (1996) noticed that two different approaches to represent process synthesis problem had been developed and established, namely Douglas' hierarchical decomposition (Douglas, 1985, 1988) and Grossmann's Mathematical Programming (MP) (Grossmann, 1990, Grossmann et al., 1999). Rippin (1990) pointed out that both approaches were concerned with different aspects

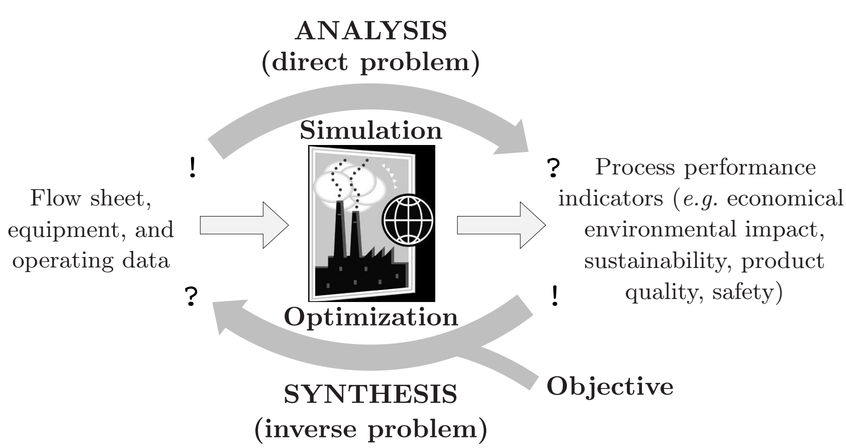


Figure 2.1: Analysis and synthesis perspectives in PSE (adapted from Klatt & Marquardt (2009)).

of design and could be regarded as complementary. Historically, they were categorized as knowledge-based and optimization-based respectively, and numerous investigations and contributions were developed regarding both methodologies and their combination, emphasizing applications to continuous process design. Moreover, most of the research was concentrated on the study of subsystems (Grossmann & Daichendt, 1996, Stephanopoulos & Reklaitis, 2011) like: (i) energy management systems, *e.g.* heat exchanger networks (HEN) and power system networks, (ii) separation systems, *e.g.* distillation sequences, (iii) mass exchange networks, (iv) reactor networks, (v) integrated networks of separation and energetic systems, and (vi) biochemical processes. The advances in this period were reflected in various text-books, like the ones by Biegler et al. (1997) and by Seider et al. (1999). More titles are provided in Stephanopoulos & Reklaitis' review (2011).

Regarding batch process synthesis, prior tools developed for continuous processes could not be directly applied. The nature of batch process involved different modeling assumptions. For example, among other issues, conditions encountered in the batch process could vary widely from the beginning of the process stage to the end. Additionally, optimal trajectories of feed-forward control variables are commonly time-dependent instead of constant set-points. Finally, each task would be composed by several operations and batch phases, which required the representation of discrete events and the switching conditions for operation or phase transitions (Rippin, 1983b). In the mid 1990s, several works directed their attention to this problem, strongly incentivized by changing market requirements, which entailed the frequent adaptation of product portfolios in batch plants and, consequently, the development of new batch processes to be implemented. However, the modeling requirements described above converted the synthesis of batch processing schemes in a complex problem, and the necessary computational tools were still not available. Therefore, the research on batch process development evolved toward process allocation, namely the optimization of batch individual units and the design of batch plants where predefined process models were assumed in most cases.

In the last decade, the increasing awareness of the necessary incorporation of sustainability aspects in the decision-making process was captured in the field of process synthesis (Grossmann & Guillén-Gosálbez, 2010). Particularly, this is posed to be a problem of paramount importance for sustainable production and consumption (Kravanja, 2010, Grossmann & Guillén-Gosálbez, 2010). The economic impact of environmental, safety, and social targets evaluation in process and plant design is much lower at early stages of product and process lifecycles (Stephanopoulos et al., 1999, Diwekar & Shastri, 2011). Additionally, Gwehenberger & Narodoslawsky (2008) pointed out that ecological process synthesis would become prominent tools for the chemical engineer in the 21st century, beyond the optimization of process operation for economic purposes. To that end, the chemical industry needs to undergo dramatic changes. This way, traditional decision-making would have to be redirected to consider the synthesis of processing schemes in early process development steps, with the simultaneous attainment of multiple objectives, rather than being concentrated on the evaluation of processing alternatives based on economic criteria like cost minimization or profitability maximization (Li & Kraslawski, 2004, Kravanja, 2010, Grossmann & Guillén-Gosálbez, 2010, Diwekar & Shastri, 2011).

As for the industrial impact of process synthesis, the advances in last fifty years cannot be overestimated (Stephanopoulos & Reklaitis, 2011). Nevertheless, it is worth noting that industrial practice for batch process synthesis has been dominated by knowledge-based approaches relying in engineer's experience and analytical tools like simulation. Despite the ubiquitous optimization in PSE research in last two decades, algorithmic and numerical methods for process synthesis have not received sufficient attention in the industrial environment, even though optimization-based synthesis methodologies could lead to considerable economical improvements in process development and manufacturing activities (Klatt & Marquardt, 2009).

2.2.2 Knowledge-based approaches

Knowledge-based approaches were the basis of the earliest attempts to obtain systematic procedures to solve process synthesis. They are also referred to as sequential or conceptual approaches (Henao & Maravelias, 2011) and rely on process engineer's knowledge to decompose the problem according to the natural decision hierarchy. In particular, engineers' experience is incorporated into the solution strategy establishing heuristic rules and procedures to generate process flow sheets and to refine sequentially the design specifications. This way, conceptual design of processing schemes can be created or invented starting from barren process information (Stephanopoulos & Reklaitis, 2011).

First contributions to knowledge-based approaches

After the pioneer textbooks by Rudd and collaborators (Rudd & Watson, 1968, Rudd et al., 1973), various complimentary contributions arouse to address the synthesis of continuous processes. For example, King (1971) discussed the selection of alternative separation systems and presented a categorization of separation system alternatives and selection procedures based on priorities and heuristics. Siirola (Siirola, 1970, Siirola & Rudd, 1971) carried out a research on computer-aided synthesis of chemical process designs using systematic approaches, which were based on Means-Ends Analysis and were implemented in the computer program AIDES. Mahalec & Motard (1977) proposed the computer system BALTAZAR upon the concepts in AIDES and the use of rules to iteratively modify and improve the design from a base case.

Douglas (1985, 1988) presented the most representative knowledge-based contribution, the so-called hierarchical approach, where the synthesis problem was divided into five decision levels: (1) batch versus continuous, (2) input-output structure of the flow sheet, (3) recycle structure and reactor considerations, (4) separation systems, and (5) heat exchanger network. The methodology included the use of heuristics, short-cut design procedures, and physical insights, as well as the evaluation of economic potential at each decision level, to sentence the convenience of taking a particular solution and justify further efforts. This approach was implemented in the computer programs PIP and *ConceptDesigner* by Kirkwood et al. (1988) and Han et al. (1995) respectively. Finally, some authors proposed heuristic procedures based on thermodynamic insights. One of the first proposals was the method by Jaksland et al. (1995) to solve separation system networks. Summarizing, these are some of the initial contributions for continuous processes, which represented the basis for subsequent works on batch process synthesis.

Knowledge-based approaches for batch process synthesis

The first systematic procedure for batch process synthesis was proposed by Iribarren (1985) based on Douglas' hierarchical approach. Essentially, the methodology was composed of three steps: (1) single-product preliminary design, (2) single-product structural optimization, including plant allocation with decisions on storage tanks and parallel units, and (3) evaluation of flow sheet alternatives for multi-product requirements. Later, Iribarren et al. (1994) presented a heuristic approach that was focused on batch tasks merging in processing units whenever it was possible, with the purpose of reducing the annualized capital costs by compacting the processing schemes and required facility investments. The solution procedure pursued a reduction in the number of alternatives that had to be evaluated to find a good design in order to economize the computational load. Another hierarchical approach was proposed by Linninger et al. (1994, 1995, 1996), which included the selection of treatment options in the synthesis of batch processing schemes. Particularly, the solution assessment was measured in terms of economic and ecological impact, through the evaluation of material balances, regulations compliance in all process streams, and treatment costs associated to the selected technology. This methodology was implemented in the computer toolkit *BatchDesign-Kit* (Linninger et al., 1994).

Going a step further, Papaeconomou and coworkers (Papaeconomou et al., 2002, 2003a,b, Papaeconomou, 2005) proposed a heuristic approach to define sequences of batch reaction and separation tasks for the conversion of raw materials into purified final products. The approach was distinguished by the great level of detail provided in the definition of the task sequence. Despite, the effect of task processing conditions in the design of batch plants had been studied earlier (Barrera & Evans, 1989), this work was relevant because the definition of batch process models included processing conditions and operation transitions of each task. Moreover, the process was synthesized starting from bare information. In particular, rule-based solution procedures were used, whose algorithms were derived from process knowledge and thermodynamic insights –*e.g.* kinetic models or phase diagrams–, providing feasible and efficient solutions without requiring significant computational efforts.

The increasing concern for sustainable production and consumption in the last years additionally motivated the development of heuristic and decomposition approaches for batch process synthesis. Several contributions were proposed, pursuing the incorporation of sustainable targets in newly defined processes or in process already implemented in existing plants whose development had been carried out without accounting for sustainable concerns. For instance, Halim & Srinivasan (2006) proposed a systematic methodology for waste minimization in batch processes, which was based on the use of heuristic procedures with cause-and-effect relations and guidewords –*e.g.* larger pressure or smaller temperature– to diagnose waste sources and generate waste minimization alternatives. Other studies have addressed the retrofit of batch processes for sustainable designs through a general framework based on path flow decomposition of the process flow sheet and indicator-based identification of retrofit potential (Simon et al., 2008, Carvalho et al., 2009, Bumann et al., 2011, Banimostafa et al., 2011, 2012), which had been originally developed for continuous processes (Uerdingen et al., 2003, 2005, Carvalho et al., 2008). Most of them included modifications in the process recipe. Further details on batch process development in retrofit scenarios are provided in Chapter 5.

Overall, knowledge-based approaches reduce the problem complexity through its decomposition and sequential solution and provide good designs (Henao & Maravelias, 2011). Nevertheless, knowledge-based approaches cannot lead to rigorous optimal solutions because the full interaction between decisions made in different solution steps is disregarded and the improvement of synthesis alternatives relies on heuristics (Grossmann & Daichendt, 1996, Yeomans & Grossmann, 1999). This limitation can be partially mitigated by combining a gradual refinement of design decisions with an increasing level of modeling detail (Marquardt et al., 2008) or with the combination of these approaches with optimization-based tools.

2.2.3 Optimization-based approaches

Optimization-based approaches based on analytical and numerical methods lead to systematic solution strategies through a formal mathematical representation of the process synthesis problem. In particular, all processing alternatives are first organized in a *superstructure*, which is later formulated into a Mathematical Programming (MP) problem to be finally optimized according to the decision criteria (Grossmann & Guillén-Gosálbez, 2010). Therein, the superstructure should represent all topological alternatives for the process, including the combination of process stages and their interconnection.

First contributions to optimization-based approaches

The first algorithmic method to solve process synthesis was based on branch and bound search (Lee et al., 1970), whereas the selection of the optimal configuration from a given superstructure was first formulated by Umeda et al. (1972) and by Ichikawa & Fan (1973) as a Non-Linear Programming (NLP) problem using continuous variables. Later, Papoulias & Grossmann (1983c), Grossmann (1985) realized that the use of integer variables was required to represent the qualitative information associated to structural decisions in the synthesis problem, and proposed Mixed-Integer Linear Programming (MILP) formulations of the process synthesis problem. This way, integer variables could indicate the selection or not of a process stage or connection. However, linear equations were unable to capture fully the nonlinear behaviour of connecting items –*i.e.* mixers and splitters– and unitary operations –*e.g.* reaction, separation, heat exchange– in the processing flow sheet.

By that time, the Generalized Benders Decomposition (GBD) algorithm (Geoffrion, 1972) was already developed to solve Mixed-Integer Non-Linear Programming (MINLP) problems; however, its application to process synthesis had not been considered up to that moment. It was the extension of GBD into the Outer Approximation (OA) algorithm (Duran & Grossmann, 1986a) what triggered the use of MINLP formulations for process synthesis. Particularly, the development and refinement of the OA algorithm (Duran & Grossmann, 1986a,b, Kocis & Grossmann, 1987, 1988, 1989a,b, Viswanathan & Grossmann, 1990), as well as its implementation in the MINLP solver DICOPT within the modeling system GAMS (Brooke et al., 1988), were crucial advances for solving MINLP for process synthesis (Grossmann & Daichendt, 1996) and other PSE problems –*e.g.* design and scheduling of batch plants. Additionally, the computer program PROSYN was developed (Kravanja & Grossmann, 1990, 1994), where the solution procedure associated to the OA algorithm was implemented, exploiting the structure of the flow sheet to improve the solution approach efficiency (Kocis & Grossmann, 1989a).

The review papers by Floudas & Grossmann (1994), Grossmann & Daichendt (1996) and Grossmann et al. (1999) summarized the early advances that took place in MP approach to process synthesis and design. There, the combinatorial explosion in solution procedures and the outcome of local optima were identified as initial limitations, to be overcome through several approaches: (i) the integration of logics in mixed-integer optimization, using Generalized Disjunctive Programming (GDP) formulation to reduce the combinatorial search, (ii) the global optimization of NLP models, (iii) the rigorous preliminary screening for MINLP models, and (iv) the formulation of superstructures.

As a result, a number of optimization algorithms emerged to tackle global optimum solutions (Floudas, 2000), mostly based on Branch-and-Bound (B&B) schemes. In particular, the MINLP solver BARON (Sahinidis, 1996, Tawarmalani & Sahinidis, 2004) implemented in the modeling system GAMS acquired a great acceptance. Other global solution strategies have been also proposed (Floudas & Gounaris, 2009), such as the algorithm for optimizing bilevel MINLP programs presented by Mitsos (2010). Regarding the systematic generation of superstructures, procedures had been reported for synthesis of subsystems –*e.g.* HEN (Yee & Grossmann, 1990). However, such systematization resulted more complex for general processes. The first proposal for the synthesis of continuous processes was the axiomatic approach by Friedler et al. (1993). Later, Yeomans & Grossmann (1999) presented a systematic framework based on different superstructure and the use of logics to formulate the optimization problem as a GDP. The problem of design under uncertainty was also addressed (Acevedo & Pistikopoulos, 1998).

Numerous contributions applying MP for synthesis of continuous processes were developed in early optimization-based approaches for process synthesis. Moreover, most of the reported work had concentrated in developing ad hoc models for specific types of subsystems, like: reactor network synthesis (Achenie & Biegler, 1988, 1990, Balakrishna & Biegler, 1992, 1996, Kokossis & Floudas, 1991, 1994, Lakshmanan & Biegler, 1996a,b, Schweiger & Floudas, 1999a,b), separation network sequences (King, 1971, Papadopoulos & Linke, 2009), HEN (Linnhoff & Eastwood, 1997, Papoulias & Grossmann, 1983b, Yee & Grossmann, 1990), utility systems (Papoulias & Grossmann, 1983a), or combinations of unitary operations (Kocis & Grossmann, 1988, Balakrishna & Biegler, 1993). It should be noted that many of these contributions developed systematic optimization-based methods for process synthesis based on thermodynamic insights. For instance, Linnhoff & Eastwood (1997) pioneered pinch technology for the synthesis of HEN. Balakrishna & Biegler (1993) modeled reaction-separation networks according to a species-dependent residence time distribution function, which were integrated with an energy targeting formulation. The reader is referred to Grossmann & Daichendt (1996), Yeomans & Grossmann (1999), and Grossmann & Guillén-Gosálbez (2010) for a thoughtful overview of ad hoc contributions.

Optimization-based approaches for batch process synthesis

The first issue to be addressed in order to apply optimization-based approaches to batch process synthesis is the representation of the different elements that compose the procedural model or recipe in the superstructure, bearing in mind the differentiation between process and plant associated to batch processing. Researchers solving batch process synthesis, plant design, and scheduling problems developed various representations of the task network, in consonance to the mathematical modeling strategy used to formulate the problem. First, Kondili et al. (1993) proposed the State-Task Network (STN) representation, which included the process tasks and material states defined in the recipe, with the limitation of not considering explicitly the equipment units and their interconnection. The STN representation was extended by Barbosa-Póvoa & Macchietto (1994a) in the so-called maximal State-Task Network (mSTN), in order to represent simultaneously the design and operational characteristics of the problem. At the same time, Pantelides (1994) introduced the Resource-Task Network (RTN), where processing units, storage tanks, materials, and utilities were treated as resources that were either consumed/occupied or generated/released at each task. Finally, Smith & Pantelides (1995) proposed the State-Equipment Network (SEN) representation, where equipment units and states of transfer material were involved and tasks were not included into the superstructure, unless they were deduced from pre-specified equipment-task assignments. Currently, these representations are still used.

Regarding the problem formulation and solution, Barton et al. (1998) encouraged the natural extension of Dynamic Optimization (DO) formulation from solving individual process stages to address the design of processing sequences to define an entire batch process. DO problems, also known as Optimal Control problems, were based on optimization models that included differential equations to represent process dynamics along time. The authors also noted that the introduction of integer decisions in DO problems was also required in order to represent the structural alternatives from the process superstructure and thus include synthesis decisions in the problem. As a result, Mixed-Integer Dynamic Optimization (MIDO) formulations were obtained. Additionally, Barton et al. (1998) anticipated the need of including discontinuities in DO and MIDO problems in order to represent discontinuities in physical properties inherent to batch processes, as well as discrete events inherent to operating procedures, resulting in hybrid discrete/continuous models.

Accordingly, Charalambides et al. (1995, 1996) defined the task network with STN representation and captured the dynamic aspects of batch processes by using DO. The optimization problem was composed of multistage models, where each mathematical stage corresponded to a process stage as well. The trade-off between processing intensities was tackled through the optimization of the dynamic profiles of the control variables at the different tasks. However, being the first attempt to apply Dynamic Optimization techniques in processes synthesis, the problem was simplified by assuming the process structure. The considered network was composed of one reaction, one mixing, and one distillation task with recycle, at their periodic steady state. The reactor cooling water and the distillation reflux ratio were defined as control variables. The optimization problem sought to establish the recipe characteristics, the sizing of the equipment items utilized, and the operating policy of each task to meet the required product specifications, by maximizing the total net revenue.

Sharif et al. (1999) solved a similar problem which also included integer variables in the optimization model to account for discrete equipment sizes together with the optimization of dynamic profiles for the control variables. Therefore, a MIDO problem was obtained. Nevertheless, integer variables were not included for structural decisions in the process synthesis problem, since the task sequence and structural decisions were also predefined in this case.

In contrast, Iribarren et al. (2004) considered more structural decisions associated to the synthesis problem, but simplifying the representation of the batch process performance by using algebraic approximations. In particular *time and size factor models* were used to represent the process behavior in tasks as a function of the process synthesis decisions taken. Particularly, the synthesis of multiproduct and multi-host protein production processes was solved using a MINLP formulation based on a SEN representation that also included semi-continuous operation. The work was based on the earlier studies by Montagna et al. (2000), Asenjo et al. (2000), and Pinto et al. (2001) to design multiproduct batch plants for protein production. These prior contributions were spread by Iribarren et al. (2004) to include structural decisions associated to process synthesis alternatives, namely the selection between several possible hosts, the selection of downstream separation and purification alternatives, and the operating mode following either a parallel in-phase configuration or an out-of-phase one. Plant design and scheduling decisions were also included –*i.e.* the unit size and the processing order of each product within the product portfolio. However, the simplification of the batch process performance with algebraic equations involves a significant loss of information regarding the feasibility of the actual process and the improvement potential.

Finally, optimization-based approaches have been also extended to solve specific batch process subsystems. This is the case of batch HEN, where several contributions are found since the early research by Vaselenak et al. (1986). In particular, continuous approaches had to be adapted to incorporate concepts like the indirect and direct heat transfer to differentiate heat transference using or not heat storage, respectively. The former case allows heat exchange between tasks at different times. A contextualization of the batch HEN is presented by Liu et al. (2011). Besides, optimization-based approaches have been also proposed to solve mass exchange networks (Foo et al., 2005b), utility systems (Foo et al., 2004), and water recovery networks (Foo et al., 2005a).

Optimization-based methodologies can be very effective because a large number of process alternatives are considered simultaneously (Henao & Maravelias, 2011). In particular, the use of a unique optimization model where the task network and process behaviour are formulated permits to incorporate the simultaneous solution of different kinds of synthesis decisions, like the task sequence or the processing conditions (Grossmann & Daichendt, 1996, Henao & Maravelias, 2011). This way, process trade-offs and interactions between capital equipment expenses and processing costs can be evaluated (Barrera & Evans, 1989). Despite this problem goes in hand with mathematical complexity, the solution of process synthesis has strongly motivated chemical engineers to develop MINLP algorithms. For instance, solution methods like the OA (Duran & Grossmann, 1986a) and the branch-and-reduce global solver BARON (Sahinidis, 1996, Tawarmalani & Sahinidis, 2004) have been developed, leading great advances in the field of Mathematical Programming and Operations Research.

Currently, optimization-based approaches to address simultaneous decision-making is quite affordable in the case of continuous processes. However, for batch processes it becomes a much formidable problem to be solved, due to the dynamic behavior and higher combinatorial complexities to couple process and equipment. In fact, a fragile equilibrium exists between simple models that allow computationally tractable optimizations and rigorous models that provide realistic optima. Additionally, the optimality of the solution can be only guaranteed with respect to the alternatives considered a priori (Grossmann, 1985). Thus, the systematic generation of synthesis alternatives to be included in the superstructure is an aspect that requires further study in optimization-based approaches. Due to the problem complexity and the need of an initial task network superstructure, the application of optimization-based approaches to the synthesis of conceptual batch processing schemes is subject to the combination of MP and DO techniques with the use of heuristic and decomposition approaches.

2.2.4 Combined approaches

Giving response to the abovementioned limitations of knowledge- and optimiza- tion-based approaches for process synthesis, several attempts have been presented in the literature to exploit their complementary capabilities:

1. Algebraic and numerical methods provide the missing quantification in knowledge-based approaches, and thus the **optimality objective** of the resulting processing schemes (Stephanopoulos & Reklaitis, 2011). For instance, several authors incorporated the optimization of either specific tasks (Sharif et al., 2000) or specific solutions of the task sequence (Fonyó & Mizsey, 1990, Mizsey & Fonyó, 1990, Daichendt & Grossmann, 1997, Kravanja & Grossmann, 1997, Bedenik et al., 2004) in some step of hierarchical decomposition approaches.

2. Heuristics can be used to attenuate the mathematical complexity of optimization-based approaches. In this regard, the most relevant proposal was the use of **mixed-logic modeling**, which allowed the incorporation of heuristics and previous knowledge about the process into the optimization problem, formulated through logical propositions (Raman & Grossmann, 1991, 1992, 1993, 1994, Viswanathan & Grossmann, 1994, Floudas & Grossmann, 1994, Türkay & Grossmann, 1996b). This way, the combinatorial size of the optimization problem is reduced by eliminating regions of the search space within the MILP or MINLP problems.
3. **Two-staged methodologies** were posed, where decomposition strategies were used to systematize the generation of superstructures to be afterwards optimized using MP methods (Daichendt & Grossmann, 1994a,b, Ali, 1999, Linninger & Chakraborty, 1999, Chakraborty & Linninger, 2002, 2003, Cavin, 2003).
4. Knowledge-based tools based on **thermodynamic insights** were also used to define processing sequences in optimization problems (Ahmad, 1997, Allgor, 1997, Allgor et al., 1999, Allgor & Barton, 1999a, Barton et al., 1999).
5. **Iterative procedures** to support the solution of MIDO problems have been developed too, solving separately the structural decisions in the synthesis problem and the process performance (Allgor & Barton, 1999b).

First contributions to combined approaches

The possibility to mathematically formulate heuristic rules and available process knowledge was one of the most important advances in algorithmic and numerical strategies for process synthesis, which stimulated considerably this area of research. In particular, the introduction of logical relations in the formulation allowed to reduce the size of the optimization problem. Balas (1985), who pioneered the Disjunctive Programming methodology to introduce logics in mathematical modeling, cited in his work the synthesis problem between the areas of application. Few later, several contributions (Raman & Grossmann, 1991, 1993, Floudas & Grossmann, 1994, Grossmann & Daichendt, 1996, Grossmann et al., 1999) posed logic-base modeling as a challenging alternative for continuous process synthesis, which could limit the combinatorial explosion in MP approaches. Disjunctive Programming problems, generalized as Generalized Disjunctive Programming (GDP), allowed to capture both qualitative and quantitative parts of the problem by using Boolean variables, logical disjunctions, and algebraic equations (Vecchietti & Grossmann, 2000, Grossmann & Westerberg, 2000). This way, available process knowledge, system restrictions, and heuristics could be formulated through logical propositions (Raman & Grossmann, 1994, Türkay & Grossmann, 1996a).

First publications (Raman & Grossmann, 1991, 1992, 1993, 1994) relied on linearly approximated models of process stages. Later, Viswanathan & Grossmann (1994) contributed to the development of symbolic logic and optimization techniques for process synthesis, and Floudas & Grossmann (1994) worked on the development of logic-based modeling and global optimization tools. Additionally, Türkay & Grossmann (1996b) proposed a new logic-based OA solution method, which was an adaptation of the OA algorithm by Duran & Grossmann (1986a) where logical reasoning was incorporated in the search procedure, based on the previous works by Raman & Grossmann (1991, 1992, 1993, 1994).

The combination of hierarchical decomposition and Mathematical Programming techniques was also addressed in several contributions synthesizing of continuous processes (Fonyó & Mizsey, 1990, Mizsey & Fonyó, 1990, Daichendt & Grossmann, 1997, Kravanja & Grossmann, 1997, Bedenik et al., 2004). Most of the reported strategies were based on the simplification of MINLP problems by postulating the superstructure of the flow sheet alternatives at different levels of representation. Then, each level was modeled with a specific level of aggregation or complexity and the entire flow sheet was optimized according to the corresponding set of modeling assumptions. Overall, bounding strategies and the progressive increase in the detail level of process models were common tools in search strategies. For example, the multilevel search tree defined by Daichendt & Grossmann (1997) ranges from a high level of abstraction to a detailed flow sheet definition: (1) input-output level, (2) reaction level, (3) separation level, and (4) heat-integration level.

Finally, a two-staged methodology to generate superstructures that should be later optimized was proposed by Daichendt & Grossmann (1994a). This combined method was based on a preliminary screening to identify challenging solutions throught the use of aggregated models. Next, reduced MINLP models were formulated, containing only the best alternatives found in the preliminary screening. The application of the proposed search strategy was illustrated for a heat-integrated distillation columns network and a HEN (Daichendt & Grossmann, 1994b).

Combined approaches for batch process synthesis

The formulation of a unique optimization model to find global optimal solutions with regard to all the elements of the batch process development was a complex activity, especially with the computational tools that were available when this problem was first posed (Ali, 1999). This motivated the use of combined approaches to solve such problem. As a result, superstructure formulations and MP tools were initially combined with problem decomposition strategies (Sharif et al., 2000, Cavin, 2003), base-case development (Ali, 1999), automatic generation of superstructures (Ali, 1999, Linninger & Chakraborty, 1999, Chakraborty & Linninger, 2002, 2003, Cavin, 2003), knowledge-based targeting procedures (Allgor, 1997, Allgor et al., 1999, Allgor & Barton, 1999a), and the use of iterative solution loops (Ahmad, 1997, Barton et al., 1999, Allgor & Barton, 1999b), as following detailed.

Ahmad (1997) and Barton et al. (1999) first proposed an iterative approach to synthesize batch solvent recovery routes, using a targeting procedure based on thermodynamic insights. In particular, they developed the notion of **solvent recovery targeting** for multi-component systems. This method predicted the correct distillation sequence of pure components and azeotrope cuts for a given stream composition. To do so, the iterative solution approach was composed of rigorous simulations, targeting of the attainable solvent recovery that predicts the limiting behavior, and engineer intervention to suggest design modifications if the maximum recovery obtained is not acceptable. Next, the solvent recovery targeting was involved in NLP formulations to address the synthesis of batch processes with integrated solvent recovery and recycling in pharmaceutical and specialty chemical industries. In this case, all feasible distillation sequences were evaluated simultaneously based on prior thermodynamic considerations. The environmental impact was minimized, posing the solvent recovery problem as a pollution prevention challenge. Additionally, this approach was applied to single-product and multiproduct problems where the solvent use was integrated across parallel processes. Processing conditions, like solvent-reagent ratio or flow rates, were also considered as degrees of freedom. However, the representation of transient behavior of batch processes through targeting expressions hinders the definition of batch operation improvement in compromised solutions.

A similar targeting approach was proposed by Allgor and coworkers. In this case, the problem was based on STN representation and was formulated as a MIDO problem that included integer variables for structural decisions in process synthesis. The process performance was also represented by algebraic approximations, the so-called **screening models** (Allgor, 1997, Allgor et al., 1999, Allgor & Barton, 1999a). These provided rigorous global lower bounds in cost minimization problems, thus allowing to screen and remove unworthy alternatives in the superstructure without eliminating the global solution. For that, the screening models were derived from domain-specific knowledge, based on physical insights specific for each unitary operation. The drawback of the method is that the solution to this problem cannot be implemented directly, but only provides the screening of structural alternatives to identify best candidates, as well as a reliable target of the objective function. According to the authors, the obtained structural solutions should be followed by the detailed design of the actual process, for instance by using DO. Allgor & Barton (1999b) integrated this further step in the process synthesis problem by using an iterative approach. Specifically, structural decisions of the processing network and equipment assignment were complemented with the solution dynamic trajectories of the control variables, using an iterative targeting procedure. This way, the optimization problem was decomposed into sub-problems providing rigorous upper and lower bounds on the objective. Screening models were used for calculating the rigorous global lower bounds in the master problem, while the primal problem provided upper bounds by solving DO sub-problems.

A **hierarchical approach** composed of different levels of abstraction combined with MP was described by Sharif et al. (2000). This work was similar to the abovementioned work by Daichendt & Grossmann (1997) in the context of continuous processes. In this case, the decomposition levels were: (i) abstract process design, (ii) conceptual process design, (iii) concrete process design and mapping to equipment, and (iv) plant design. The contribution was focused on solving the abstract level, thus determining the performance of abstract process stages termed cells using DO. Further process development steps rendering plant allocation and design problems were not conceived.

At the same time, Ali (1999) suggested a **two-staged solution approach** systematizing the generation and formulation of superstructures which were following optimized. The outstanding feature of their methods was that it pursued to reduce the optimization model generated and to limit the search space of alternatives, in order that mathematical complexity was attenuated. To generate the optimization superstructure, a method based on Means-Ends Analysis and Non-Monotonic Planning is used, providing a base case design and the search space of feasible alternatives. The problem was then formulated as a reduced MINLP that could be solved through conventional MINLP solution strategies. Processing conditions in process stages were considered as degrees of freedom in that step. The approach was applied to the problem of batch process synthesis for the production of pharmaceuticals and specialty chemicals.

A **two-staged problem procedure** including superstructure generation and optimization was also proposed by Linninger & Chakraborty (1999) to address the synthesis and optimization of batch waste treatment flow sheets in the pharmaceutical industry. In the first step, an informed search heuristic method based on linear planning theory was used to systematically synthesize structural alternatives which were then included in the superstructure. Following, MP tools were used to formulate the superstructure and select the optimal flow sheet and its operating parameters. In particular, process availability, plant capacity, and regional regulatory limits for pollutant disposal were included in the formulation in order to take into account site-specific constraints in a plant-wide optimum process design. Path consistency was ensured in the optimization model by using logical propositions formulated as algebraic equations. The goal was to minimize the cost associated to the different treatment alternatives while satisfying a set of modeling constraints representing environmental concerns. Later, the methodology was further extended to incorporate multi-objective optimization to balance economic and ecological targets in the objective function (Chakraborty & Linninger, 2002) and to address the synthesis of optimal plant-wide waste treatment policies under uncertainty (Chakraborty & Linninger, 2003).

Cavin (2003) **decomposed** the problem of batch process synthesis in two components which should be combined eventually: (1) waste treatment path selection and (2) allocation of existing plants to tasks. Basically, the goal was to select waste treatment paths that could reduce environmental impact in either new or existing batch plants, also taking into account widespread economic objectives. For that, structural decisions were considered. Processing conditions within the process recipe were not optimized; however, the predefined temperatures and pressures for each stage of the recipe had to satisfy the physically feasible range in the unit selected during the allocation problem. Regarding the solution approach, the waste treatment path selection was addressed through an **iterative method** on the one hand (Cavin, 2003). On the other, the allocation problem solution was solved through a **two-staged approach** composed of the automatic generation of superstructures (Cavin, 2003) and its corresponding multi-objective optimization, which was addressed through a stochastic optimization method, the Tabu Search (TS), in posterior contributions (Cavin et al., 2004, 2005). In broad terms, the objective of was focused on the design of the single most efficient batch process to produce a single product in a multi-purpose facility.

Mosat et al. (2007, 2008) proposed a combined solution approach to introduce new processes in grassroots and retrofitted multipurpose batch plants assuming pre-defined process recipes, based on the prior by Cavin et al. (2004, 2005). This time, **multi-objective optimization** was used to enhance productivity and robustness, using the TS solution method. The approach newly incorporated the concept of *superequipment*, referred to generalized processing elements that could substitute any unit from the buy list and that were transformed into real equipment in the end. This strategy was used to simplify the combinatorial problem. Moreover, **heuristics** were incorporated into the optimization problem to represent information like: (i) the suitability of equipment classes to perform particular process stages, (ii) design specifications, (iii) scale-up rules for each process stage, or (iv) *superequipment* rules, among others.

Finally, Halim & Srinivasan (2008) extended their previous knowledge-based approach (Halim & Srinivasan, 2006) to **combine heuristic and optimization** tools for systematic waste minimization in batch processes, including the generation and evaluation of design alternatives. Process simulation through material and energy balances was incorporated in the methodology, as well as the evaluation of energy utilization, the synthesis of recycle networks, and the use of multi-objective optimization solved using Simulated Annealing (SA). Equipment flow sheet was assumed to be given, since the methodology was mostly developed for the process synthesis in retrofit scenarios.

To sum up, the great advantage of combined approaches was that they render practical optimization procedures where structural and processing decisions are defined. However, most of the works still simplify either the representation and definition of the process performance –*e.g.* using algebraic model approximations for batch process stages– or the associated degrees of freedom –*e.g.* optimizing constant profiles of the control variables or assuming a predefined value.

Besides, solution strategies that used abovementioned logic-based GDP formulations to introduce heuristics and process knowledge in optimization models for batch process synthesis were expected. For example, the works by Linninger and Chakraborty (1999, 2002, 2003) included logical rules in the superstructure formulation. However, in the case of batch processes, dynamic behavior should be also represented. Formulations that included dynamic equations in mixed-logic models have been applied to other problems of PSE. For example, one of the first steps in this context was Mixed-Logic Dynamical (MLD) optimization by (Bemporad & Morari, 1999) to solve model predictive control problems. Therein, lineal or linearized equations were used to represent the time-dependent interdependence between physical laws, logical rules, and operating constraints, and logical decisions were represented by integers. Later, mixed-logic modeling with process dynamics were applied to scheduling problems in continuous processes with grade transitions (Nyström et al., 2005, 2006, Prata et al., 2008), design of individual batch units (Oldenburg et al., 2002, 2003), and simultaneous design and control (Bansal et al., 2002a,b). In the contributions by Oldenburg et al. (2003) and by Prata et al. (2008), not only logical rules but also Booleans and disjunctive equations were used, together with dynamic non-linear equations. This modeling approach is referred to as Mixed-Logic Dynamic Optimization (MLDO) (Oldenburg et al., 2003). However, to the author's knowledge, there are no available references yet in the context of batch process synthesis.

2.3 Allocation of manufacturing facilities

The problem of allocating batch manufacturing facilities consists of the assignment of process stages, which have been selected for producing a desired product and compose the process model, to specific physical equipment items in a new or existing plant (Stephanopoulos & Reklaitis, 2011). It is the major activity of production scheduling and is usually addressed in operational decision-making during the manufacturing stage, as it is the case of the short-term scheduling reviewed by Méndez et al. (2006). However, the allocation problem has to be considered during batch process development as well, in order to match process model elements to particular equipment pieces (Stephanopoulos et al., 1999). Moreover, the introduction of modifications in the process recipe in this step eases the solution of this problem. Answering the following questions posed by Stephanopoulos et al. (1999, p. S981) has a long-term and deep impact on the process under development:

- Do we have the necessary equipment to realize this process?
- Among several production facilities and their corresponding equipment items, which are the best for allocating this process?
- Can we identify the main advantages and drawbacks of assigning this process to a given production facility?
- For a given equipment inventory in a production plant, which is the attainable scale of production?

In summary, the problem statement for the allocation of manufacturing facilities during process development reads as follows:

> *Given: (a) the tasks and their sequence, and (b) the processing conditions defined in the synthesis step, subject to: (a) the physical plant constraints, determine: (a) the type of campaign, its sequence, and coordination, (b) the equipment pieces selection and interconnection, (c) the production sizes, (d) the cycle times, and (e) the task adaptation to physical plant, such that the objective function is optimized.*

Different challenges arise from this statement according to the size and complexity of the system considered. In particular, Rippin (1983b) mentions the following systems:

1. Operation of individual units;
2. Operation of a sequence of equipment items; and
3. Design of a single-product, a multiproduct, or a multipurpose plant.

The allocation of manufacturing facilities is required in grassroots and retrofit scenarios. In the former case, new equipment items are designed to fulfill the specific processing requirements. In the latter case, available existing equipment should be adapted and plant modifications can be done, like the consideration of expanding the capacity of particular items or installing new connections pipelines, processing units, or storage items. In order to make possible the use of existing units, the feasibility of each solution should be evaluated with regard to physical restrictions imposed by operating constraints, capacities, and available connections.

Following, research contributions to the optimization of individual units and the design of batch plants problems are reviewed, being two predominant areas in academy due to the challenges associated to optimize the design and operation of batch systems.

2.3.1 Optimization of individual batch units

The optimization of individual units for batch process operation is a pivotal problem in batch process development. The degree of completion of each task is determined by the corresponding processing conditions and times (Rippin, 1993) and at the same time, has an effect on operating costs, environmental impact, and safety indicators. Moreover, the process performance of each task affects to the state properties of material transferred to subsequent process stages. Rippin (1983b) examined the role of individual unit performance in the context of batch process development underlining the following features:

- The conditions encountered in the batch process may vary widely from the beginning of the process stage to the end, unlike the case of continuous processes where the operation occurs in the neighborhood of steady-state conditions.
- Besides, the equipment units that execute the sequence of process stages have to process different products, hence the adaptability to accommodate the different processing conditions and requirements for a variety tasks is mandatory.
- Moreover, optimal trajectories of feed-forward control variables may be time-dependent instead of constant set-points.
- Finally, each task may be composed by several batch operations and phases which require the definition of switching conditions that determine operation or phase transitions.

As a result, the optimization of batch unit operation is more complex than the analogous continuous problem, and has become a challenging problem regularly addressed in the literature. Overall, optimizing the operation of individual process stages corresponds to the well-known open-loop control problem. Therein, the feed-forward control profiles to meet a processing objective are defined, even though stability and controllability indicators are generally not taken into account. The problem may be stated as follows (Rippin, 1983b):

> *Given: (a) the kinetics and reactions taking place and (b) upper and lower constraints for process and control variables, and assuming that: (a) the reactor is homogeneous and the control variables –e.g. temperature or feed addition rate– can be freely chosen at any time, determine: (a) the optimal profiles for batch reactors, such that the objective function is optimized.*

To solve this problem, the availability of reliable mathematical models representing the process behavior are crucial. Rippin (1993) also indicated that *"the possibility of improving batch reactor performance by time profiles of temperature or feed addition rate is entirely dependent on the kinetics occurring in the reactor, with a further dependence on the objective function used"*. This way, first-principle or point measurements at different times of the batch should be used to define the required process models. However, the obtaining of accurate models may encounter some difficulties, especially in the case of complex kinetics or intermediates that cannot be measured (Rippin, 1983b, Moreno-Benito et al., 2013). In addition, dynamic models are required to fully represent the batch process behaviour, covering a wide range of processing conditions, which will change along the time. Finally, to complete the procedural model, discrete events and switching conditions associated to operation or phase transitions should be also accounted for. A clarifying survey of hybrid models to represent problems with continuous variables and discrete events is presented by Cruse et al. (2006). Three problem categories are defined according to their degree of complexity, namely: (i) single-stage models composed essentially by DAE systems, (ii) multistage models with explicit discontinuities with predefined phase transitions, and (iii) general discrete-continuous hybrid models with implicit discontinuities to define stage transitions as a function of process variables. Particularly, the formal mathematical description of hybrid models had been generalized by Barton & Pantelides (1994).

Optimization-based approaches

In the early 1960s, Denbigh (1958) and Aris (1960) demonstrated that the optimization of temperature profiles could improve the operation in tubular reactors. Hence, the interest for systematic studies on temperature profiles grew, and numerous investigators undertook the analogous problem of optimizing feed-forward trajectories of control variables along time in batch reactors. Optimal Control (OC) techniques, which had been developed in the 1950s for aerospace applications, were adopted to solve this problem (Pollard & Sargent, 1970, Sargent & Sullivan, 1979). OC consists of the optimization of dynamic systems according to an objective function by adjusting the profiles of control variables along time and are also referred to as Dynamic Optimization (DO) problems.

Since then, numerous DO solution strategies have been developed. In the 1980s and 1990s, important advances in analytical and numerical techniques took place. For instance, Dynamic Programming (DP) was developed based on Hamilton-Jacobi-Bellman formulation that transformed the original problem into a system of partial differential equations (Bellman, 1957), which was extended to include path constraints on state and control variables (Luus, 1990). Several works have further dedicated to the application of DP to batch and semi-batch reactor optimization since then (Rosen & Luus, 1992, Luus, 1994, Bojkov & Luus, 1996, Guntern et al., 1998, Luus & Okongwu, 1999, Luus, 2006, 2009). Alternative solution methods were proposed. In particular, necessary conditions of optimality derived from Pontryagin's formulation were the basis for indirect methods (Bryson & Ho, 1975). Moreover, the conversion of the time-continuous optimization problem into a finite-dimensional nonlinear programming problem by discretization gave place to various direct methods, classified as sequential (Sargent & Sullivan, 1978, Kraft, 1985), simultaneous (Neuman & Sen, 1973, Tsang et al., 1975, Biegler, 1984), and hybrid (Bock & Plitt, 1984, Bock et al., 2000). A comprehensive review of the different solution approaches is provided by Binder et al. (2001), Srinivasan et al. (2003) and Schlegel (2004).

In the last two decades, DO has acquired a great popularity in the academic context. In general, dynamic models with detailed kinetics and mass and energy balances have been used to optimize the operation of unitary operations. For example, many contributions were dedicated to batch or semi-batch reactors (Cuthrell & Biegler, 1989, Garcia et al., 1995, Lehtonen et al., 1997, Ishikawa et al., 1997, Bonvin, 1998, Luus & Okongwu, 1999, Ubrich et al., 1999, Abel et al., 2000, Aziz & Mujtaba, 2002, Srinivasan & Bonvin, 2003, Zhang & Smith, 2004, Sun et al., 2007), batch distillation columns (Hansen & Jørgensen, 1986, Christensen & Jørgensen, 1987, Diwekar et al., 1989, Logsdon et al., 1990, Sundaram & Evans, 1993, Diwekar, 1995, Mujtaba & Macchietto, 1996, Sharif et al., 1998, Kim, 1999, Oldenburg et al., 2002, 2003, Low & Sørensen, 2005, Cruse et al., 2006, Barakat & Sørensen, 2008) and reactive distillation columns (Sørensen et al., 1996), among others. In these works, frequent decision variables are the dynamic profiles for the selected control variables and the batch phase durations in Multistage Dynamic Optimization problems (Vassiliadis et al., 1994).

Superstructure formulation based on mixed-integer and mixed-logic modeling were also applied to account for structural decisions, leading to MIDO or MLDO problems respectively. This way, design and operation decisions such as the equipment configuration, the number of trays in distillation columns, or the input location were considered simultaneously to optimal control variable profiles. (Sundaram & Evans, 1993, Diwekar, 1995, Mujtaba & Macchietto, 1996, Sharif et al., 1998, Oldenburg et al., 2002, 2003, Low & Sørensen, 2005, Cruse et al., 2006, Barakat & Sørensen, 2008). MIDO and MLDO formulations were also motivated by their application in integrated design and control problems, as it is the case of Mohideen et al. (1996a,b, 1997) and Bemporad & Morari (1999). The state-of-the-art of MIDO and MLDO modeling and solution approaches is further detailed in Chapters 3 and 4. In conclusion, many advances in modeling capabilities and optimization techniques for dynamic processes were driven, which permitted the widespread application of detailed modeling and optimization-based approaches to define the operation of individual batch units in the academic context.

Regarding the industrial application, only a few attempts have been done to displace the use of fixed recipes and apply the abovementioned optimization-based approaches, even though the potential gains of optimization are significant. Habitually, process is periodically adjusted using heuristics gained from experience, which may lead to slight improvements from batch to batch. According to Srinivasan et al. (2003) and Schlegel (2004), the bottlenecks that limit industrial acceptance of DO are: (i) the lack of reliable models and measurements, (ii) the difficulties to interpret the optimal solution unless the objective function represent a physical variable or parameter, (iii) the need to link optimization tools with the actual measurement-based information that is commonly available, and (iv) the lack of robustness and efficiency of the solution techniques.

2.3.2 Design of single-product, multiproduct, and multipurpose plants

The design of batch plants is a consolidated problem that has attracted much research interest since the mid 1980s (Rippin, 1993), when an exponential grow of related contributions occurred due to a renewed interest in batch production (Puigjaner, 1999). Batch plant design consists of the development of a processing facility for the production of a desired product portfolio (Ali, 1999). In essence, this problem tackles the definition of operational decisions, the assignment of process stages to appropriated equipment items, and the equipment sizing (Rippin, 1983b). Moreover, it is required that the scheduling is anticipated in the design stage (Birewar & Grossmann, 1989); hence, scheduling constraints regarding equipment allocation, as well as batching, timing, and task sequence in process items, are mostly included in batch plant design formulations. The objective is to define a system that can assimilate and coordinate the process models for the various products to be manufactured.

A detailed framework of the batch plant design problem is presented in the reviews by Reklaitis (1990) and Barbosa-Póvoa (2007). Particularly, the following decisions are given to compose this problem:

- Definition of the processing network, *i.e.* process recipe for each product;
- Selection of operating strategy for organizing the manufacturing process, *i.e.* single-product, multiproduct, or multipurpose batch plants;
- Allocation of equipment items to tasks and synthesis of equipment configuration, considering the following operating modes: parallel units in-phase or out-of-phase, one unit assigned to multiple tasks, serial units assigned to one task, or intermediate storages; and
- Equipment sizing.

In this context, (Barbosa-Póvoa, 2007) provided a thorough problem statement for the generic optimal design problem of batch plants, which included plant allocation and assumed given process recipes:

> *Given: (a) the product recipes describing the production of one or more products over a single or multiple campaign structures, (b) all possible equipment units to be installed in the plant and their suitability to perform the different operational tasks, (c) the time horizon, (d) the resource utilisation along the time horizon, (e) the inventory availability for each material involved, (f) the product demands and raw material delivers along the time horizon, (g) the storage policies, and (h) the operating and capital cost data, determine: (a) the optimal plant configuration –i.e. number, type, and capacity of equipment items and their connectivity and (b) the process schedule making use of the selected resources to achieve the required production –i.e. timing, storage policies, batch sizes, amounts transferred and task-equipment allocation, such that a plant performance objective is optimized.*

First contributions

Early works on batch plant design were focused on the minimization of capital costs associated to equipment investment in single-product plants, subject to a set of production requirements and fixed recipes. Ketner (1960) presented the first contribution, where this problem was addressed by selecting the optimal equipment sizes. The research on that field was later resumed by Loonkar & Robinson (1970) solving a similar problem. Since then, subsequent research incorporated progressively more complex decision-making: the design of multiproduct (Robinson & Loonkar, 1972, Grossmann & Sargent, 1979) and multipurpose plants (Mauderli & Rippin, 1979, Suhami & Mah, 1982), the evaluation of uncertainty in the production demands and the solution of flexible design (Reinhart & Rippin, 1986, Wellons & Reklaitis, 1989, Shah & Pantelides, 1992), the use of parallel units and discrete equipment sizes (Sparrow et al., 1975), the use of intermediate storage (Takamatsu et al., 1979, Yeh & Reklaitis, 1987), the retrofit problem (Vaselenak et al., 1987), and the consideration of processing costs in addition to equipment investment

(Barbosa-Póvoa & Macchietto, 1994a). For an extended overview of batch plant design progress in the last sixty years, the reader is referred to the reviews by Reklaitis (1990), Rippin (1993), Allgor (1997, Appendix D), and Barbosa-Póvoa (2007).

Recipe definition in batch plant design

Ideally, best allocation solutions should be specified according to physical and chemical phenomena in process stages to match the process model to the master recipe to be implemented in a particular plant. However, it is frequent in batch plant design that the use of fixed or approximated recipes hinders the adaptation of recipe parameters like set-points and reference trajectories for control variables according to the global targets. The most common modeling assumptions with regard to process recipes in batch plant design problems are: (i) constant processing time and size, (ii) constant time and size factor model, where capacity requirements are defined as a function of the batch size (Robinson & Loonkar, 1972, Biegler et al., 1997, Ravemark & Rippin, 1998), and (iii) time and size factor model, where time is also a function of the batch size (Espuña & Puigjaner, 1989, Modi & Karimi, 1989). Therefore, processing times and overall performance can be only accommodated through operational decisions such as the operating mode, batch size, storage tank location, or unit duplication. Thus, the assumptions defining fixed and approximated recipes are a huge limitation in the allocation of manufacturing facilities in batch process development.

Allocation decisions in batch plant design

The outstanding decisions in batch plant design related to the allocation of equipment items to process stages are essentially: the equipment sizing, the task merging and splitting, the use of parallel units, and the use of intermediate storage. These have an impact on the control recipe and, particularly, on the duration of process stages, cycle times, and processing rates (Rippin, 1983b, Reklaitis, 1990). For instance, the **cycle time**, understood as the interval between the production of successive batches, is limited by the duration of the various process stages. Disparities in the time scales of different tasks can be settled through the use of out-of-phase parallel units, where batches can be fed alternatively from more rapid tasks to debottleneck slow process stages and raise the global processing rate. In contrast, parallel units working in-phase may be used to increase the **batch size** and avoid the underuse of equipment items that allocate preceding and subsequent process stages, what has an effect over the global plant capacity. Another example is the assignment of one single unit to **multiple tasks**, in order to reduce the number of equipment items to be purchased. Finally, intermediate storage tanks allow the division of the task network into **segments** with different cycle times. For that, it is necessary that batch integrity is not mandatory and that intermediates and products are sufficiently stable to be stored up to the next cycle time before being transferred for further processing.

Material transference synchronization

Synchronization is understood as the overlapping of tasks in different processing or storage units during a material transference operation between consecutive tasks. In the context of scheduling and design of batch plants, several works address material transfer operations in multiproduct (Kim et al., 1996, Ha et al., 2000, Castro & Grossmann, 2005) and multipurpose plants (Heo et al., 2003, Ferrer-Nadal et al., 2007, Furman et al., 2007, Ferrer-Nadal et al., 2008a, Castro & Novais, 2008). However, their main objective is eluding physically inconsistent allocation solutions (Ferrer-Nadal et al., 2008a), rather than a thoughtful evaluation of transfer durations and transfer profiles. Thus, these works deal with the fulfillment of material and energy balances with a unique material state point in each transfer operation.

2.4 Integration in the decision-making

Several contributions made an effort to integrate completely or partially the abovementioned sub-problems. Particularly, the combined batch process synthesis and plant allocation is here highlighted, as well as the modification of process recipes during the batch plant design. Additionally, the synthesis of new processing schemes to be implemented in existing plants should evolve inherently the integration of batch process development, since the synthesis problem should not be defined unaware of physical restrictions of the existing plant in order to calculate feasible solutions. The research related to this last problem is reviewed in Chapter 5. Finally, the highest degree of integration is accomplished through the simultaneous process and plant optimization. In this case, process synthesis and plant allocation are accompanied by plant design decisions, such as equipment sizing. That is a formidable problem, whose contributions are detailed in Chapter 6.

Regarding the solution strategy, let us note that works here categorized as integrated problems are those that define decision variables typically associated to different subproblems, either these degrees of freedom are solved simultaneously, iteratively, or sequentially. In fact, decomposition and sequential approaches have headed historically the integrated batch process development. In contrast, the application of optimization-based strategies has been hindered by the complexity of its modeling and optimization steps, despite their asset characteristics for the simultaneous evaluation of process development trade-offs formulated in a unique model. In particular, the batch nature of the process involves not only a the need of combinatorial evaluation to match equipment and task networks (Gani & Papaeconomou, 2006, Allgor, 1997), but also the use of dynamic models instead of steady-state ones (Srinivasan et al., 2003, Allgor, 1997), as well as dynamic profiles of control variables instead of continuous set-points and the representation of discrete events associated to operation and phase transitions. As a result, the use of complementary optimization-based approaches and heuristics or problem decomposition is prioritized to solve the abovementioned decision-making integration in batch process development.

2.4.1 Integrated synthesis of batch processing schemes and plant allocation

Some of the works carrying out batch process synthesis previously reviewed included task-equipment assignment and other decisions related to the allocation of manufacturing facilities. These works are detailed in Table 2.1.

Iribarren (1985) and Iribarren et al. (1994) first proposed decomposition approaches for process development involving process and plant design solved sequentially. First, conceptual processing schemes were synthesized. Next, allocation decisions were addressed, namely the optimal location of storage tanks and the number of units in parallel in each stage to satisfy plant scheduling constraints in single-product and multiproduct

Reference	Solution approach	Synthesis decisions	Allocation decisions	Application
Iribarren (1985)	Hierarchical decomposition	Flow sheet, *e.g.* batch vs. continuous, recycle vs. series	Storage tank location, No. parallel units, task sequence at each unit	Single-product and multiproduct problems
Iribarren et al. (1994)	Heuristic procedure	Process decision variables, batch vs. continuous	Task merging at each unit	butadiene sulfone production system
Charalambides et al. (1995, 1996)	Simultaneous NLP: multistage DO with DAE	Dynamic profiles of control variables	Equipment sizing, predefined task sequence and allocation	Reaction-separation systems
Allgor, Barton, et al. (1997, 1999, 1999a)	Simultaneous MINLP: screening models (based on physical insights) to simplify MIDO problems	Process structure, task sequence, solvent candidates	Task-unit assignment	Reaction-distillation systems
Allgor & Barton (1999b)	Combined approach to solve MIDO: iterative MILP and NLP sub-problems, screening models (based on physical insights)	Process structure, task sequence, solvent candidates, dynamic profiles of control variables	Task-unit assignment	Reaction-distillation systems
Sharif et al. (1999)	MIDO (OA/AP solution method)	Dynamic profiles of control variables	Equipment sizing with discrete values, predefined task sequence and allocation	Batch single-product process design
Linninger & Chakraborty (1999)	Two-step approach: superstructure generation and optimization	Chemicals reuse, recycle, and recovery options, treatment selection	Task-unit assignment, capacity constraints	Pharmaceutical waste management, multiproduct systems
Chakraborty & Linninger (2002, 2003)	Two-step approach: superstructure generation and MO optimization	Treatment paths selection, adjustment of processing conditions	Task-unit assignment, capacity constraints	

Table 2.1: Integrated synthesis of batch processing schemes and plant allocation.

Reference	Solution approach	Synthesis decisions	Allocation decisions	Application
Cavin (2003), Cavin et al. (2004, 2005), Mosat et al. (2007, 2008)	Two-step approach: superstructure generation and MO optimization (TS solution method)	Waste treatment path	Task-unit assignment, operating mode (*i.e.* series or parallel), predefined processing conditions, equipment operating constraints	Process and waste treatment, retrofit scenarios
Iribarren et al. (2004)	Simultaneous MINLP: time and size factors dependent on synthesis decisions	Host, separation and purification alternatives	Operating mode (*i.e.* parallel in-phase or out-of-phase), product processing order, unit sizing	Multiproduct and multi-host protein production
Halim & Srinivasan (2006, 2008)	Heuristic approach: cause-and-effect relations and guidewords (Batch-ENVOPExpert); combination with MO optimization	Task sequence, task alternatives, chemicals, processing conditions	Operation and control definition, storage and unit sizing	Systematic waste minimization, grassroots and retrofit scenarios
Simon et al. (2008)	Hierarchical approach: path flow decomposition and indicator-based assessment, with dynamic indicators	Unitary operations, occupation times, dynamic profiles of control variables	Batch sizing, task-unit assignment, task merging or splitting, operating mode (*i.e.* parallel), equipment sizing, buffer tanks location	Single-product process improvement, retrofit scenarios
Carvalho et al. (2009)	Heuristic approach: path flow decomposition, indicator-based assessment, and sensitivity analysis, with indicators based on thermodynamic insights	Task alternatives, task sequence, recycling options, solvent, processing conditions	Equipment sizing	Sustainable water management and insulin production, grassroots and retrofit scenarios

Table 2.1 (cont.): Integrated synthesis of batch processing schemes and plant allocation.

Reference	Solution approach	Synthesis decisions	Allocation decisions	Application
Halim et al. (2011)	Combined approach: guidewords, path flow decomposition, indicator-based assessment, and stochastic optimization (combined Batch-ENVOPExpert and SustainPro)	Task alternatives, task sequence, flow sheet structure, chemicals, processing conditions	Operation definition, storage and unit sizing	Waste minimization: acetone process, methanol and DME production, grassroots and retrofit scenarios
Bumann et al. (2011)	Heuristic approach: path flow decomposition, indicator-based assessment, and sensitivity analysis with DAE	Time-invariant processing conditions (Process Operation Parameters, POPs), flow sheet structures (Process Layout Settings, PLSs)	Unit occupancy and pseudo-residence time	Economic and ecological single-product process improvement, retrofit scenarios
Banimostafa et al. (2011, 2012)	Heuristic approach: path flow decomposition and indicator-based assessment	Solvent, recovery options, processing conditions	Time/volume debottlenecking	Economic and ecological pharmaceutical process improvement, retrofit scenarios

Table 2.1 (cont.): Integrated synthesis of batch processing schemes and plant allocation.

campaigns. Later, the two-staged approaches to generate and optimize superstructures proposed by Linninger and Chakraborty (1999, 2002, 2003) and by Cavin (2003) also included degrees of freedom related to both sub-problems, like the selection of the process or equipment structure, the processing conditions, and the task-unit assignment, among others. Additionally, the MINLP superstructure studied by Iribarren et al. (2004) settled the optimization of integrated problems. However, the process performance in batch process stages was simplified in this case through the use of time and size factors that depended on the synthesis decisions considered.

Regarding the adjustment of processing conditions, even though it was considered in several contributions as part of the process synthesis, few of them allow tackled the definition of dynamic trajectories. In fact, those works which did so had to assume other decisions. For instance, Charalambides et al. (1995, 1996) employed DO to optimize simultaneously dynamic profiles and equipment sizing through the assumption of predefined process structures or their solution in an outside loop. Sharif et al. (1999) solved a similar problem with predefined task sequence and structural decisions, but considering discrete values for the equipment sizing, thus resulting into a MIDO problem. In the case of Allgor (1997), Allgor et al. (1999) and Allgor & Barton (1999a), structural decisions were included into MIDO formulations, which were simplified into MINLP by representing the process performance with algebraic approximations, namely the *screening models*. Afterwards, this strategy was incorporated into an iterative procedure where complementary upper bounds were provided through DO solution (Allgor & Barton, 1999b), hence solving the complete MIDO. Simon et al. (2008) proposed a hierarchical approach to evaluate batch plant modifications in three levels –*i.e.* plant, process, and unit operation. Dynamic indicators were included in the unit operation level, as well as the definition of dynamic control profiles.

Finally, various works have proposed strategies to develop new processes in order to introduce the production of new chemicals in existing plants (Cavin, 2003, Cavin et al., 2004, 2005, Mosat et al., 2007, 2008) and to improve batch processes through the incorporation of sustainable targets in retrofit scenarios (Halim & Srinivasan, 2006, 2008, Simon et al., 2008, Carvalho et al., 2009, Halim et al., 2011, Bumann et al., 2011, Banimostafa et al., 2011, 2012). These strategies can be also applied in grassroots scenarios, by improving a base case which should be initially defined.

2.4.2 Recipe modifications in allocation of batch plants

The most widespread problems of batch plant allocation in academy have been: (i) the optimization of individual batch units where one or various process stages are carried out and (ii) the design of single-product, multiproduct, and multipurpose plants. However, the solution of these subsystems in isolation only provides a partial assessment of process allocation in a manufacturing facility because the performance of each task affects the state properties of the material transferred to subsequent process stages. Consequently, tasks' interactions in the sequence of allocated equipment items is rarely accounted for, neither in the optimization of individual units, nor in the design of batch plants. In the former problem, process performance is evaluated in isolated units. In the latter problem, the use of fixed or approximated recipes hinders the adaptation of recipe parameters according to global targets. In this section, the efforts devoted to integrate recipe modifications during the solution of batch plant allocation are reviewed, with the outstanding contributions summarized in Table 2.2.

One of the pioneer works analyzing the interactions of process performance among

Reference	Solution approach	Process performance representation	Recipe modifications	Allocation decisions	Application
Robinson & Loonkar (1972), Biegler et al. (1997)	Calculus and optimization-based solutions	Constant time and size factor model	Fixed processing times	Equipment sizing	Single-product and multiproduct batch plant design
Knopf et al. (1982)	MINLP optimization: generalized reduced gradient solution method	Size factor model, fixed time in batch units, residence time as a function of unit size and processing rate in semi-continuous units	Processing time in semi-continuous units, equipment selection from an inventory	Use of parallel units	Plant design involving batch and semi-continuous operations
Espuña & Puigjaner (1989)	Heuristic approach: gradient computations	Time and size factor model	Processing times as a function of batch size	Unit sizing, operating mode (*i.e.* parallel in-phase, out-of-phase)	Single-product batch/semicontinuous plant design
Modi & Karimi (1989)	Heuristic approach	Time and size factor model	Processing times as a function of batch size	Unit sizing, intermediate storage allocation	Single-product batch/semicontinuous plant design
Wilson (1987)	Ad hoc search of key variables, DAE simulation (Runge-Kutta)	DAE system	Processing variables	Distillation column sizing	Reactive batch distillation process design
Barrera & Evans (1989)	Hierarchical strategy: NLP optimization for specific structural alternatives (SQP solution method)	DAE system	Dynamic profiles of control variables, processing times, product purity and temperature restrictions	Unit sizing, No. parallel units, storage policy	Multiproduct batch plant design and operation

Table 2.2: Integrated recipe modifications in the allocation of manufacturing facilities.

Reference	Solution approach	Process performance representation	Recipe modifications	Allocation decisions	Application
Tricoire (1992)	Optimization-based (SA solution method)	Correlation between key processing variables and size factor and cycle time	Time-invariant control variables	Size and cycle time factors, structural decisions (*e.g.* plant allocation, unit sizing)	Multiproduct batch polymer plant planning and design
Salomone & Iribarren (1992)	NLP optimization	Posynomial model	Time-invariant control variables	Size and cycle time factors as a function of processing conditions	Single-product batch plant design
Montagna et al. (1994)	NLP optimization	Posynomial model	Time-invariant control variables	Size and cycle time factors as a function of processing conditions, unit sizing	Single-product and multiproduct batch plant design
Salomone et al. (1994, 1997)	Iterative approach: NLP optimization with approximated models and detailed dynamic simulation	Posynomial model and DAE system	Time-invariant control variables	Size and cycle time factors as a function of processing conditions, unit sizing	Single-product and multiproduct batch plant design
Bhatia & Biegler (1996)	DO including relaxed integer variables	Multistage dynamic model, a DAE system for each stage	Dynamic profiles of control variables	Equipment sizing, batch phase processing times, continuous design parameters, production capacity and schedules, predefined task sequence	Multiproduct batch plant design, scheduling, and production planning

Table 2.2 (cont.): Integrated recipe modifications in the allocation of manufacturing facilities.

Reference	Solution approach	Process performance representation	Recipe modifications	Allocation decisions	Application
Asenjo et al. (2000), Pinto et al. (2001)	MINLP optimization; iterative MINLP-NLP optimization with fixed time and size factors in the MINLP iteration	Posynomial model	Time-invariant control variables	Size and cycle time factors as a function of processing conditions, processing times for semi-continuous units, unit sizing, operating mode (*i.e.* parallel in-phase or out-of-phase), intermediate storage allocation	Design of multiproduct batch plants for protein production
Corsano et al. (2004, 2006)	NLP optimization	discretized DAE system (trapezoidal method)	Dynamic profiles of control variables	Task sequence, No. processing units, operating mode (*i.e.* series, parallel out-of-phase, or both), unit sizing	Fermentation single-product batch plant design
Corsano et al. (2007)	Combined approach, sequential decision-making: heuristic procedure, NLP optimization-based steps	DAE system	Dynamic profiles of control variables, processing times	Task sequence, No. processing units, operating mode (*i.e.* series, parallel out-of-phase, or both), unit sizing, recycle and blend allocation, material and energy resources allocation, production rates, heat and cooling areas, power consumption, No. distillation trays, cycle time for each product, unit cycle and idle times, No. batches, mixed campaign configuration	Fermentation multiproduct batch plant design

Table 2.2 (cont.): Integrated recipe modifications in the allocation of manufacturing facilities.

consecutive tasks was the publication by Barrera & Evans (1989). Three types of trade-offs were specified therein, namely:

1. Cycle time of the complete process versus processing intensity at individual tasks;
2. Effect of upstream task performance over downstream stages; and
3. Total rental costs or investments versus operational costs corresponding to the processing rate of the entire system.

These authors demonstrated that recipe modification was critical to the success of the design, since the consideration of these interactions allowed to improve process performance and guaranteed feasibility of the process tasks.

Regarding the various types of decisions to be included in the problem, Barrera & Evans (1989) elucidated the differentiation within the set of decisions addressed in the integrated problem according to their nature, which were classified into *performance* and *structure sub-problems*. On the one hand, the performance sub-problem involved the determination of optimal operating policies and processing conditions for a pre-specified sequence of process tasks. The works by Wilson (1987) and Charalambides et al. (1995, 1996) served as an example. On the other, the structure sub-problem focused on the optimization of the equipment configuration during the allocation of equipment items, excluding decisions on stage procedures and processing conditions. This problem has been usually addressed in scheduling and plant design problems (Reklaitis, 1990, Rippin, 1993, Méndez et al., 2006, Barbosa-Póvoa, 2007, Maravelias, 2012). Overall, to deal with the simultaneous solution of performance and structure sub-problems and to evaluate processing trade-offs in the allocation problem, most contributions have concentrated on the development of mathematical models to represent the process behavior within the problem formulation. Different degrees of detail have been proposed, like time and size factor models and algebraic and dynamic performance models, which are following presented.

Up to date, the most popular representation of tasks' completion in the design and scheduling of batch plants since the early contributions in this area is the so-called *constant time and size factor model* (Robinson & Loonkar, 1972, Biegler et al., 1997, Ravemark & Rippin, 1998) due to its reduced mathematical complexity. Therein, task processing times are predefined with a fixed value, while the required equipment volume to shelter the task is calculated using a size factor S_j, which defines the volume of vessel j required to produce a particular amount of final product. One of the first works to go a step further was presented by Knopf et al. (1982), who introduced the calculation of residence times in semi-continuous units to define their processing duration as a function of unit size and production rate in batch plant design. Later, the task processing time was also defined as a function of the batch size by several authors, like Espuña & Puigjaner (1989) and Modi & Karimi (1989), among others.

Additionally, algebraic performance models were introduced to represent the process behavior in batch facility allocation. Tricoire (1992) evaluated the effect of modifying key processing conditions together within design, synthesis, and scheduling problems. He argued that detailed models could not be used for complex processes, like polymerization ones. Hence, he defined correlations to evaluate the effect of the selected processing variables over size factors and cycle times of the batch tasks. Improvement was obtained with regard to designs with fixed processing conditions. Contemporary, Salomone & Iribarren (1992) approximated batch processing operations into algebraic models that were following rearranged symbolically. This way, size factors and processing times were represented as explicit *posynomial functions* of certain operating parameters. Several works followed in the application of posynomial functions for batch plant design. Montagna et al.

(1994) extended the work by Salomone & Iribarren (1992) to cover equipment sizing as well. They proved that optimal operating conditions differed whether a given product was produced in a dedicated single-plant facility or in a multiproduct plant. The solution of discrete decisions regarding plant design was not solved simultaneously therein; thus, the determination of the number of parallel units, storage tanks allocation, or task-unit assignments should be undertaken either before the plant and recipe design or in an outer optimization loop.

The use of posynomial models was also considered by Asenjo et al. (2000) and Pinto et al. (2001) to solve the design of multiproduct batch plants for the production of recombinant proteins using batch and semi-continuous operation. The problem was formulated as a MINLP which included structural, plant design, and recipe decision variables, as shown in Table 2.2. Moreover, solution strategies for the simultaneous optimization of the structure and the process variables were also explored (Asenjo et al., 2000). In particular, the following approaches were compared: (i) MINLP solution with fixed size and times, (ii) simultaneous MINLP solution including posynomial models, and (iii) iterative approach decomposing the problem into the solution of the processing variables with fixed structure and the solution of the structure with fixed time and size factors. It was found that the iterative approach was faster and still provided near-optimal solutions in comparison to the simultaneous optimization.

However, algebraic process performance models had some drawbacks, like the mistrust on obtained solutions, due to the simplification of complex dynamic behavior of process stages into algebraic approximations, and the need to rearrange equations symbolically, which was not always possible. Non-convexities in the mathematical model would difficult the further introduction of integer decisions. As a result, detailed dynamic models were also pursued to describe the behavior of individual batch operations and to address recipe modifications in the allocation of manufacturing facilities. The use of simulation of detailed DAE systems to represent the behavior of batch tasks was first addressed by Wilson (1987). In this study, the design of a reactive batch distillation process was determined, including the optimization of the process performance by using an ad hoc manual search over the key variables and assuming a given structure. The process was composed of a reaction and a separation stage which could be conducted in the same unit. Both the processing conditions and column size were optimized according to the capital cost of the reactive distillation unit, the processing cost, and the raw material expenses.

Later, Barrera & Evans (1989) proposed a hierarchical solution strategy where the performance and the structural sub-problems were solved iteratively. Each iteration comprised the following steps: (1) definition of the unit size, the number of parallel units, and the storage policy, (2) the distribution of horizon time among products, (3) the definition of processing conditions and times, and (4) the system simulation, cost calculation, and constraints evaluation. To determine the processing conditions and times, the process performance sub-problem was formulated as a NLP for particular structural alternatives and equipment allocation. Each optimization included the determination of optimal profiles for the selected control variables and the fulfillment of operating constraints related to product purity and temperature.

Salomone et al. (1994, 1997) proposed an iterative algorithm where posynomial functions (Salomone & Iribarren, 1992) and DAE models were combined in optimization and dynamic simulation steps respectively. The complete process was first optimized using the algebraic expressions and was following simulated for evaluation purposes. The size factors and posynomial expressions were updated at each iteration. This strategy was proved to be a robust and reliable methodology for the design of single-product (Salomone et al.,

1994) and multiproduct plants (Salomone et al., 1997) which included equipment sizing decisions.

The use of DO formulations was also used in batch plant design to capture the dynamic aspects of the batch processes and to optimize the profiles of processing conditions along the time. In addition to the abovementioned contributions by Charalambides et al. (1995, 1996), Sharif et al. (1999), and Allgor & Barton (1999b) addressing batch process synthesis, other works were published in the area of scheduling and plant design. For instance, Bhatia & Biegler (1996) considered the simultaneous optimization of dynamic control profiles and equipment sizing in multiproduct batch plant design, scheduling, and production planning, assuming a predefined sequence of batch process stages. This problem was formulated as a DO, where integer decisions had been relaxed into continuous variables. Additionally, Corsano et al. (2004, 2006) proposed to formulate the simultaneous optimization of synthesis, design, and operation of batch plants as a NLP. Specifically, dynamic models to represent the batch process behavior in process stages were defined through DAE systems and these were discretized in finite-difference equations using a trapezoidal method. Besides, structural, plant design, and process decision variables were included in the formulation. To avoid the use of integers, particular variables were enforced to zero when the corresponding alternative was not selected Corsano et al. (2007) extended this work to optimize several lines in multi-product campaigns. To do so, a combined approach was used, which consisted of a heuristic procedure and an optimization-based step in a sequential decision-making.

To conclude, improved solutions were provided in the abovementioned research works with regard to the use of fixed recipes. The modification of processing conditions and recipe parameters during equipment allocation favors the holistic consideration of processing trade-offs, enunciated by (Barrera & Evans, 1989). The possible variation of task performance is presented not only as an important problem, but also as a difficult one. However, a constant progress and increase of complexity is registered in the reviewed publications, despite the cautious concerns to verify that potential benefits will justify and outweigh the effort and time required to generate and optimize complex models.

2.5 Related work in batch process management

Similar problems to the *synthesis of conceptual processing schemes* and the *allocation of manufacturing facilities* in batch process design arouse for batch process management. First, the problem of allocating manufacturing facilities was necessary both in a process development stage, as well as in a manufacturing stage (Stephanopoulos et al., 1999). Particularly, *short-term scheduling* to optimize the operation of batch plants is a well-established area of research, where significant progress has been done in the last thirty years to improve production performance in single-product, multiproduct, and multipurpose batch plants (Méndez et al., 2006, Maravelias, 2012). A parallelism is also presented between scheduling problems that include process dynamics and plant design with recipe modifications. Second, a further area of research to improve the batch plant operation is the automation of the synthesis of operating procedures or *process coordination*. Operating procedures are defined as the detailed sequence of operations and phases to be executed safely and optimally (Viswanathan et al., 1998a) and correspond to the strategy for carrying out a process (ANSI/ISA-88). Particularly, master recipes should be transformed into control recipes to be executed at a specific time. This activity requires the derivation of plant- and time-based information according to a scheduling solution. Both problems are here compared to batch process development problems.

2.5.1 Short-term scheduling with process dynamics

The scheduling problem is a the process of deciding how to commit resources between a variety of possible tasks. The general chemical production scheduling problem can be posed as follows (Maravelias, 2012):

> *Given: (a) the production facility data, (b) the production recipes, (c) the equipment unit-task compatibilities, (d) the production costs, (e) the material availability, (f) the resource availability, and (g) the production targets or orders with due dates, determine: (a) the selection and sizing of tasks and batches to be carried out –i.e. batching–, (b) the assignment of tasks to processing or storage units or general resources, (c) the sequence of tasks on processing or storage units, and (d) the timing of tasks, such that: production targets and resource constraints are satisfied, and the performance metrics are optimized –e.g. cost minimization, tardiness or lateness minimization, earliness minimization, or profit or throughput maximization.*

Historically, scheduling formulations rely on the use of approximated recipes represented by fixed times and size factor models, like in batch plant design. Some works proposed the use of flexible recipes in reactive scheduling approaches to deal with uncertainty through small modifications of processing conditions around nominal processing conditions (Ferrer-Nadal et al., 2007, 2008b). This way, most of the works searching optimal schedules are based on trade-offs strictly related to cycle time and equipment allocation. The solution of this problem implies that equipment utilization is maximized with the purpose of reducing the campaign length and the costs associated to resource allocation.

However, production costs related to material use –*i.e.* raw material, energy and waste costs– can be only reduced through the manipulation of the operating policies according to process performance considerations. Additionally, the consideration of dynamics in this problem is further incentivized by the need to re-accommodate the production assignments in case that an abnormal events takes place (Muñoz et al., 2011). The modification of recipe parameters could provide an opportunity to fulfill demands at strict due dates in those situations, even thought extreme processing conditions and higher costs can be necessary. Overall, the consideration of process dynamics and recipe modifications in short-term scheduling allows the evaluation of these trade-offs according to in-time needs. As a matter of fact, the integration of scheduling problems with other planning and operational activities has been posed as an issue of paramount importance to tackle Enterprise-Wide Optimization, as exposed by several authors (Harjunkoski et al., 2009, Maravelias, 2012, Engell & Harjunkoski, 2012). Specifically, the vertical integration of scheduling with process optimization and control has been underlined.

Several works have been devoted to the integration of operational scheduling and control decision-levels to solve both the scheduling of batch processes (Bhatia & Biegler, 1996, Mishra et al., 2005, Capón-García et al., 2011b, 2013, Nie et al., 2012, Frankl et al., 2012b) and in the scheduling of transition grades for continuously-operated processes (Gallestey et al., 2003, Nyström et al., 2005, 2006, Flores-Tlacuahuac & Grossmann, 2006, Busch et al., 2007, Terrazas-Moreno et al., 2007, 2008, Prata et al., 2008, Flores-Tlacuahuac & Grossmann, 2010). These problems have been mostly addressed through the introduction of models that represent the transient process behavior into MILP or MINLP short-term scheduling formulations. Like in the case of batch plant design, algebraic process performance models and detailed DAE systems –which lead to DO and MIDO problems– have been considered.

To conclude, a parallelism between the allocation problem during batch process development and the short-term scheduling during process manufacturing is found. However, both problems have essentially the following differences:

1. **The nature of the problem.** On the one hand, the integrated process development is focused on planning decisions in an annual basis in the early stages of the process lifecycle. On the other, the scheduling problem with recipe flexibility during product manufacturing deals with operational decisions in a weekly basis in the final stages of the process lifecycle.
2. **The decision variables.** Batch process development goes in hand with additional degrees of freedom with respect to scheduling problems, namely the selection of process stages or tasks, their sequence, splitting or merging, the chemical components involved –*e.g.* reagent, solvents, catalysts–, which are always assumed in scheduling problems.
3. **The model complexity.** The level of detail in the operational problem have to be limited in order to keep the problem manageable and solvable in shorter computational times, since it should be solved on-line within a temporal horizon of days or weeks. Thus, multistage models to represent operations and phases within each process stage are unlikely to be compatible with short-term scheduling.

2.5.2 Automating the synthesis of operating procedures

In addition to the assignment of equipment items to execute the process and the optimization of individual units operation, a further area of study related to process allocation is the synthesis of operating procedures. This problem was referred to as the *recipe to manufacture* by Venkatasubramanian et al. (2001). Viswanathan et al. (1998a) defined the synthesis of operating procedures problem as follows:

> *Given: (a) the general recipe coarse-grained information and (b) the plant specific details; determine: (a) the refined control recipe form, according to the allocation of equipment and resources to the various operations in the process (arbitrated by the production planning and scheduling control activity).*

Moreover, this problem should be solved through the combined effects of the recipe management and the production planning and scheduling activities. Particularly, the recipe management problem should create, modify, and maintain the various types of recipes, classified as general, site, master, and control recipes in the Standard S88 (ANSI/ISA-88, 2010).

The automation of this problem received a special attention in the literature. A special emphasis was placed on the improvement of efficiency, reliability, and risk reduction, by avoiding operating procedures generated by plant engineers, which required considerable amount of time and efforts (Lakshmanan, 1990). Various frameworks and methodologies have been proposed. Their major challenge has been the development of systematic mechanisms to automatically and structurally build the procedural knowledge and link it to the corresponding plant structure (Gabbar et al., 2005). The systematic representation of operating procedures is also provided in most cases.

For instance, Lakshmanan (1990) proposed a framework based on a model-based operation planning mechanism to synthesize operating procedures for chemical plants. Later, Viswanathan et al. (1998a) developed a hierarchical planning strategy that used declarative and procedural knowledge to generate inferred knowledge incrementally, leading to operating procedures. It was based on the discrete event modeling tool Grafcet. This framework was implemented by Viswanathan et al. (1998b) in the automated system *i*TOPS, an Intelligent Tool for operating procedure synthesis. Besides, Aylett et al. (2001) applied Artificial Intelligence (AI) planning tools to the synthesis of operating procedures of a chemical plant. Moreover, the intelligent system *i*TOPS was merged with the expert system Batch HAZOPExpert for automated HAZOP analysis of batch processes (Zhao et al., 2000b,a, Venkatasubramanian et al., 2001, Zhang et al., 2004). At the same time, Hoshi et al. (2002, 2003) proposed a recursive algorithm based on directed graph representations in a sub-graph isomorphism framework. The approach was extended later to deal with the operation of heat exchange and separation for the synthesis of operating procedures (Kaneko et al., 2003) and to handle energy-conversion systems along with material conversion processes (Yamashita et al., 2004). Additionally, Gabbar et al. (2005) presented and automated solution called AOPS to synthesize master recipe and generate the corresponding control recipe, using Recipe Formal Definition Language (RFDL) to represent the operating procedures in batch plants. Recently, Muñoz et al. (2011, 2012) proposed the use of ontological systems to coordinate the definition of control recipes from scheduling solutions as well as to integrate the two decision levels. The proposed framework allowed the information exchange among the different modeling paradigms and conventions for Enterprise-Wide Optimization based on Standards S88 (ANSI/ISA-88, 2010) and S95 (ANSI/ISA-95, 2000) for modeling enterprise and control systems.

2.6 Concluding remarks

The problem of batch process development is presented once a new product is identified –together with the general guidelines for its production in the laboratory– and has the objective of providing the master recipe for its commercial-scale manufacturing, which details the processing scheme that should be implemented in a particular production facility. Basically, such problem entails several decisions compromising process and plant elements. This chapter has surveyed the different areas of research of PSE which handle part of decision-making from both perspectives, that is using the process and plant reference.

However, these elements are strongly interrelated. One example of the unavoidable connection between process and plant is noted in the solution of batch reactors' operation. There, the optimization of feed-forward trajectories of control variables and the definition of phase transition policies can be understood as: (1) the determination of a process stage during the solution of process synthesis problem or (2) the adjustment of unit procedures during the solution of plant allocation problem. Other example of this interrelation is that of plant design problems allowing the modification of processing conditions or the merger of distinct tasks in a unique processing unit.

Overall, this close connection has made difficult the development of an accurate terminology that denotes unambiguously each degree of freedom or decision variable. Certainly, huge steps have been taken toward standardization of batch process management in last twenty years, providing unified guidelines to define several elements and functionalities of batch processing systems (*e.g.* ANSI/ISA-95, ANSI/ISA-88). Additionally, established terminologies and classification of problems have been provided for batch plant design (Rippin, 1983a, Reklaitis, 1990, Barbosa-Póvoa, 2007) and for batch process scheduling (Méndez et al., 2006, Maravelias, 2012). Nonetheless, the use of these terminologies has not fully penetrated the field of batch process development, where concepts related to process and plant elements are sometimes used interchangeably in spite of their theoretical distinction.

Various examples in the literature evidence the vast complexity of the problem and the lack of an unified and structured notation which clearly distinguishes each element in the decision-making of process development. For instance, different authors have used heterogeneous terms to denote each sub-problem. Essentially, all of them refer to similar schemes of decision, but using different concepts:

(i) Synthesis of processing schemes –including waste treatment options– and allocation of manufacturing facilities (Rippin, 1983b, Stephanopoulos et al., 1999, Stephanopoulos & Reklaitis, 2011) –this is the notation adopted in this thesis;
(ii) Process synthesis, process design, and allocation of manufacturing facilities (Allgor, 1997);
(iii) Laboratory-scale synthesis, process scale-up, and process design (Cavin, 2003);
(iv) Process synthesis, operational design, process control, and plant design (Papaeconomou, 2005).

In this context, this thesis aims to incorporate the common terms and definitions used by the PSE community dedicated to batch processing as well as the guidelines of Standard S88 (ANSI/ISA-88).

Chapter 3

Optimization model for integrated batch process development

> *"In 1980, optimization on engineering problems beyond linear programming was often viewed as a curious novelty without benefit. Now, optimization applications are essential in all areas of process systems engineering including design, identification, control, estimation, scheduling, and planning."*
>
> Stephanopoulos & Reklaitis (2011, p. 4282)

This thesis proposes and optimization-based approach to solve the problem of integrated batch process development. For that, all structural alternatives are combined in a unique superstructure, following formulated into an optimization model which is later solved to minimize a cost function. In this process, the modeling step is a key issue, where the optimization model should be defined integrating decisions from the *synthesis of batch processing schemes* and the *allocation of manufacturing facilities* sub-problems and taking into account the *plant design*. Specifically, the mathematical formulation is subject to: (i) the construction of a superstructure that involves all synthesis and allocation alternatives, (ii) the representation of dynamic process performance and dynamic control variable profiles, (iii) the consideration of discrete events to represent batch phase and operation transitions, (iv) the combination of quantitative and qualitative information in the optimization model, (v) the need of synchronizing material transference between unit procedures to ensure batch integrity, and (vi) the combination of batch and semi-continuous processing elements.

In this chapter, the degrees of freedom related to each sub-problem are first stated, subject to the problem definitions provided in Chapter 2. Additionally, previous works addressing the modeling issues for integrated batch process development are reviewed. Next, a novel modeling strategy is proposed according to such requirements and the available solution tools. Finally, each of the process synthesis and plant allocation decisions subject to be included in the optimization model is represented in a mathematical formulation. The problem statement and the proposed modeling approach are illustrated through two motivating examples along the chapter.

3.1 Degrees of freedom and problem statement

The problem tackled in this work corresponds to the optimization of master recipes in grassroots and retrofit scenarios, to introduce a new or modified product to be produced in single-product campaign. For that, the simultaneous solution of *batch process synthesis* and *allocation* decisions is addressed. In order to embrace a comprehensive description of the particular degrees of freedom, two motivating examples are provided. The first one consists of a unique process stage of reduced dimension. The second example presents a system extension that incorporates additional degrees of freedom. The plant and process flowsheet presented in both examples serves to identify the problem, clarify the terminology used in this thesis, and understand the problem statement. The specific tasks, equipment pieces, interconnections, allowed technologies, chemicals, recirculation flows, buffer tank locations, and allowed alternatives for equipment configuration have to be defined for each particular case. Additionally, existing and potentially installed equipment and piping should be represented in the superstructure.

3.1.1 Motivating example 1: process synthesis and allocation of a single process stage

The first example covers a process cell, defined as the set of equipment items required for the production of one or more batches (ANSI/ISA-88), where a process stage should be executed. The diagram of the process cell is shown in Figure 3.1, composed by two batch units U_1 and U_2 which can be connected through different flow distributions. Additional equipment pieces are necessary for that purpose, namely mixers Mx_1 and Mx_2, splitters Sp_1 and Sp_2, and connecting pipelines 1 to 9, as well as storage tanks for raw material T_{raw} and final products T_{prod}.

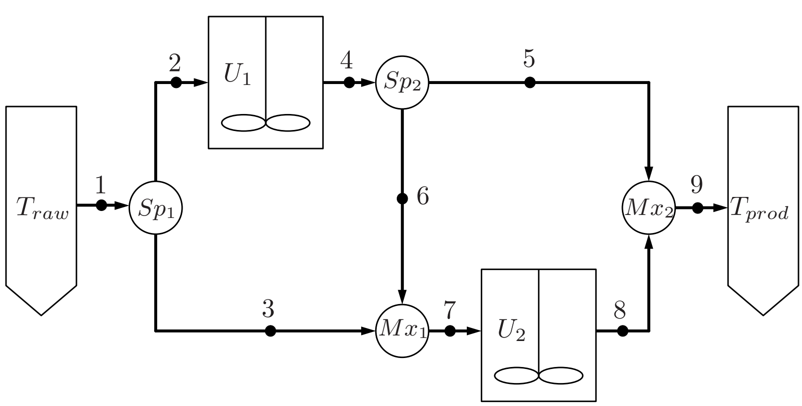


Figure 3.1: Process cell diagram and SEN superstructure of example 1.

The equipment diagram corresponds to the SEN superstructure of the problem, proposed by Smith & Pantelides (1995), where equipment and material states are interconnected. Particularly, the states are indicated by bullets in the Figure and correspond to flow rates and properties, which change along time through dynamic profiles. Equipment items are represented by empty shapes. The **operating mode** –or equipment configuration– alternatives to be evaluated should be comprised in the superstructure. In the example, the following cases are considered: operation of U_1 and U_2 in parallel in-phase and with equal phase durations, operation in series with U_1 followed by U_2, or operation in one single unit, either U_1 or U_2. Each configuration determines the set of **equipment items** from the SEN that are required to drive the process. In addition, the configuration selection is precisely related to the decision on **task splitting**, by determining whether a process stage is divided in several unit procedures.

The superstructure of task alternatives can also be described using the STN representation proposed by Kondili et al. (1993), as illustrated in Figure 3.2. The circles indicate the states –*i.e.* flow rates and properties– and the rectangles indicate the tasks and their division into subtasks. The STN superstructure is related to the SEN one, since the final target is the combination of process and plant within a master recipe to be executed, rather than their modeling and design in isolation. Consequently, it is necessary to pre-assign tasks and subtasks to batch units and are referred to as **unit procedures**, which are characterized by the pre-specified unit U_1 or U_2 and their occupation order 1 or 2, as shown in the STN. Moreover, each unit can only execute one unit procedure for each solution: merging tasks in the same unit and recirculation of intermediate flow during the processing of the same batch is not considered. Finally, it should be noted that physical limitations in batch unit connections can exclude tasks alternatives, as reflected in the STN. For instance, the unit procedure U_1 *subtask* 2 cannot be performed in the process cell structure from Figure 3.1 unless a new piping connection from U_2 to U_1 were contemplated.

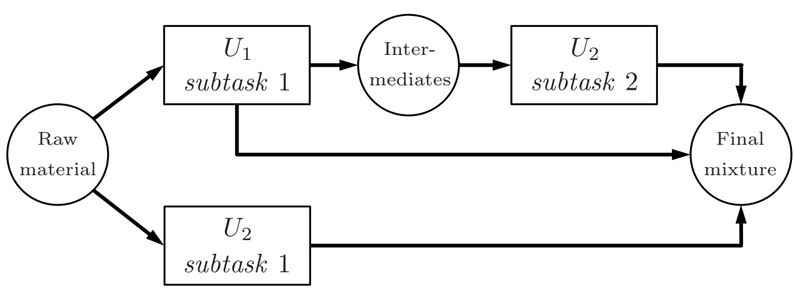


Figure 3.2: STN superstructure of example 1.

In each equipment unit, a specific **unitary operation** takes place with its associated physicochemical phenomena and properties. Either a batch or a semi-continuous procedure can be predefined therein. The former is composed by a fixed number of **operations and phases**, whereas the latter is referred to the intermittent use of continuously operated plant elements. In the example, both units U_1 and U_2 are assumed to work in batch mode following three typical phases –*i.e.* filling, holding, and emptying the reactor–, and all other plant elements are assumed to follow semi-continuous procedures. Several decisions at control level can be considered in the process design of unit procedures, namely the **batch phase duration** and the feed-forward trajectories of **flow rates** in input and output pipelines and of **internal variables**. Internal variables should be defined as a function of the degrees of freedom of each unit procedure model –*e.g.* temperature or reactant dosage profiles in procedures of reactors U_1 and U_2, or valve aperture in splitters Sp_1 and Sp_2.

Additionally to process synthesis and allocation sub-problems, plant design decisions are included, namely the **sizing** of processing and storage units to be installed or occupied. These decisions usually adopt discrete values to facilitate the equipment acquisition. In retrofit scenarios, equipment size of existing units are transformed into constraints.

In order to solve the simultaneous batch process synthesis and allocation problem, the above decisions have to be included as degrees of freedom in the optimization model, together with the use of a **global objective function** which embraces all the design phases. A commonly used decision criteria is the economic cost function, which can include entries like equipment investment, occupation costs, labor, processing costs, raw material costs, waste treatment costs, and economic impact of product quality. Non-economic objectives are also used to account for ecological concerns, environmental impact, safety issues, or social driving factors.

3.1.2 Motivating example 2: extension of process synthesis and allocation decisions

In addition to degrees of freedom presented in previous example to optimize a process stage, other decisions should be considered to face more general problems. Let us bear in mind that the final target is to optimize complete productions systems in batch plants, rather than an isolated process stage. This second example serves to illustrate the incorporation of further elements in the superstructure, which is represented in Figure 3.3.

In this example, the first decision is the selection or not of the entire **process stage**. This decision relies on splitter Sp_3, which determines whether processing or bypassing the input flow. Second, the possibility to **recirculate** intermediate flow 11 to be used in subsequent batches is also considered. It is a very common situation that waste and side products have the appropriated physicochemical properties to be reused and thus reduce environmental impact and raw material costs. In the proposed superstructure, the recirculation of flow 9 is determined by splitter Sp_4. Moreover, buffer tank T^r_{11} is potentially required to store the intermediate material in order that it can be later loaded in following batches. Buffer tanks for intermediate products are also necessary to allow different **cycle times** or **batch sizes** between successive process stages.

Additionally, in this second example, there are two options A and B regarding the **technological specification** of unit procedures in U_1. Technologies represent processing alternatives that can be used for a particular unitary operation. Each technology is characterized by specific set of physicochemical equations and properties governing the process and is attained by a specific arrangement of the equipment design. For instance, an evaporator and a distillation column represent two different technological specifications, even though they are used for the same unitary operation, the Liquid-Vapor separation. Technological specifications A and B are differentiated in the superstructure by $U_{1,A}$ and $U_{1,B}$. Finally, the selection between two different **chemicals** c^s_1 and c^s_2 in the second reactor is also considered in this example. Unlike the case of the technological specification, the selection of chemicals –*i.e.* reactants, solvents, or catalysts– does not necessarily affect balance equations in unit procedure models and only requires the adaptation of process parameters.

3.1.3 Problem statement

The decisions detailed in the two motivating examples are following formalized in the problem statement for *integrated batch process development* problem to tackle the simultaneous *synthesis of batch processing schemes* and *allocation of manufacturing facilities* sub-problems, taking into account the *plant design*. The goal is to optimize master recipes that should be later used in a particular plant to produce a batch of a specific product.

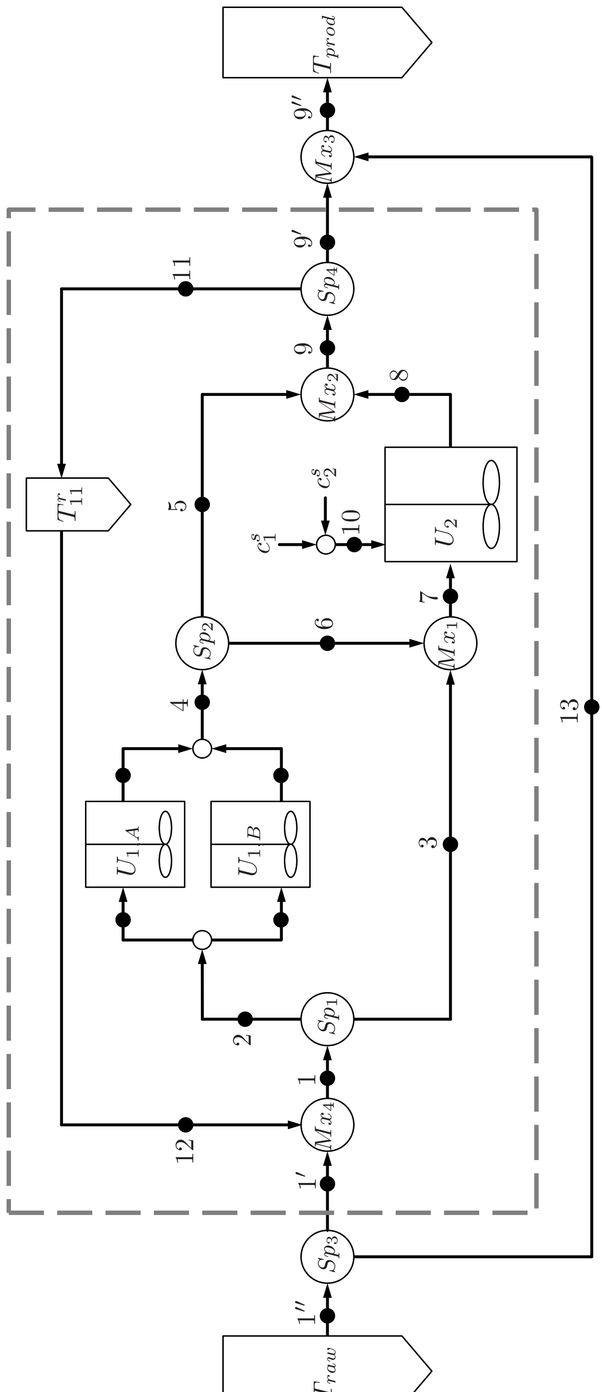


Figure 3.3: SEN superstructure of example 2.

According to the need of each case study, a part or the complete set of the following decisions should be taken as degrees of freedom to be optimized. For instance, the main difference between grassroots and retrofit problems is that equipment volumes are considered as a degree of freedom in the former case, whereas they are fixed in the latter case, thus becoming model constraints. Overall, the problem statement when all the decision variables are integrated is defined as follows:

Given:

- **Planning data:** set of final products, intermediates, and raw materials, expected demand of final products, and maximum time horizon;
- **Plant diagram:** the SEN superstructure of available and potentially installed equipment units for each process stage, pipelines and connection nodes like mixers and splitters;
- **Task network:** potential and mandatory process stages, alternative chemicals involved in each process stage –*i.e.* reactants, solvents, or catalysts–, allowed technologies, and possible reuse of intermediates;
- **Batch process operation:** allowed task-unit assignments, batch operations and phases within each unit procedure, phase to phase switching conditions, and set of limiting processing conditions for each unit;
- **Process dynamics:** DAE systems to represent the process behavior in each unit procedure, initial conditions, and set of process variables and dynamic or time-invariant controls;
- **Data related to performance evaluation:** decision criteria and specific data to evaluate the objective function –*e.g.* selling price of final product, direct cost of raw materials, investment, amortization, operating costs in processing units, environmental impact indicators;

the goal is to determine:

- **Synthesis of processing schemes decisions:** selection of process stages and splitting into subtasks, technological specification, selection of chemicals involved –*i.e.* reactants, solvents, or catalysts–, reference trajectories of the feed-forward control variables, duration of batch phases composing each task, recirculation of intermediate flows, and material transfer synchronization between tasks –*i.e.* synchronization of flow rates, compositions, and starting and final times;
- **Allocation of manufacturing facilities decisions:** task-unit assignment –*i.e.* unit procedure selection–, selection of processing and storage units, operating mode –*i.e.* single, series, or parallel operation–, and batch sizes;
- **Plant design decisions:** equipment sizing;

such that the adopted performance metrics are optimized. For the sake of completeness, it is worth to emphasize that there are other potential synthesis and allocation decisions which are out of the scope of this study, as is the case of decisions associated to multiproduct and multipurpose campaigns, *e.g.* batch order.

3.2 Proposed modeling strategy

An optimization-based approach is proposed to solve the problem of *integrated batch process development* defined above and to provide optimal master recipes with the necessary information to produce a particular product in a specific plant. Essentially, optimization-based approaches that include synthesis decisions consist of three steps, namely the representation of a superstructure with all processing alternatives, the formulation of such superstructure to construct an optimization model, and its solution (Grossmann & Guillén-Gosálbez, 2010). This methodology is adopted in this thesis, combining in an integrated model the degrees of freedom for the process synthesis and plant allocation sub-problems and taking into account the plant design.

3.2.1 Modeling requirements

In optimization-based approaches, the strategy to represent the problem superstructure and to develop the corresponding mathematical models is a key issue in the solution of the optimization problem, which is by far no trivial task (Oldenburg et al., 2003). The modeling issues that should be considered in the superstructure representation and model construction for solving integrated batch process synthesis and plant allocation are following capitulated:

(i) **Synthesis and allocation alternatives.** First, the superstructure representation in optimization-based approaches has the purpose of representing all challenging alternatives in a unique diagram, in order that the alternative paths can be later formulated in a unique model. In the case of batch processes, the complexity of the superstructure generation increases because process and plant elements are differentiated, thus requiring a combinatorial assessment to match equipment and task networks (Allgor, 1997, Gani & Papaeconomou, 2006).

(ii) **Dynamic process performance and dynamic control variable profiles.** Second, to represent accurately the physicochemical behavior of batch processes, the use of dynamic models that reflect the evolution of processing conditions along time in each task is mandatory to provide actual feasible solutions (Barton et al., 1998, Srinivasan et al., 2003). Moreover, the optimization of dynamic reference trajectories of control variables allows to enlarge the attainable region of the process performance, thus permitting the further improvement of the process efficiency and driving holistic optimizations of the master recipe.

(iii) **Discrete events for phase and operation transitions.** In addition, in batch processing schemes, each task is composed of a chain of operations and phases. This way, the optimization problem has to include discrete event modeling to represent the batch phase and operation sequence and transitions (Barton et al., 1998). The corresponding set of equations complement the above dynamic process performance balances to define each process task, by accounting for the external actions applied to the system.

(iv) **Quantitative and qualitative information.** Moreover, not only quantitative information but also qualitative one should be represented in the optimization model. Particularly, the latter involves synthesis and allocation decisions, like the task selection, sequence, and splitting, or the task-unit assignment.

(v) **Synchronization of material transference.** Batch integrity along the process stages is a fundamental issue in the synthesis and allocation problem. Each batch is subject to a series of material transformations from raw material until the final product is obtained, and batch integrity is understood as the coherent transfer of the material composing each batch along the chain of tasks. Batch integrity should be ensured in each processing alternative, independently to the equipment units to whom the process is assigned and to the order in which each equipment operates. To that end, synchronization of unit procedures is necessary, having into account that their order is not known beforehand and that each process stage has an effect on downstream tasks through their connection via outflows and inflows.

(vi) **Batch and semi-continuous processing elements.** Finally, in addition to batch processing units, semi-continuous elements should be also contemplated in the superstructure, like connecting items and storage tanks. Unlike the case of batch unit procedures, which are composed by a number of operations and phases, semi-continuous elements are continuously operated plant items characterized by an intermittent use.

To sum up, the batch nature of the process involves not only the need of matching equipment and task networks through a combinatorial assessment (Allgor, 1997, Gani & Papaeconomou, 2006), but also an evolution of processing conditions along time in each process stage, requiring dynamic models to represent process performance instead of steady-state ones and dynamic profiles of control variables instead of continuous set-points (Barton et al., 1998, Srinivasan et al., 2003). Moreover, process operation is featured by discrete events that determine the batch operation and phase transitions (Barton et al., 1998). Qualitative information should be also covered in the optimization model, involving decisions like task selection, sequence, and splitting, equipment assignments, or chemicals selections, among others. Finally, batch integrity should be ensured in all processing path alternatives by synchronizing material transference between batch and semi-continuous plant elements, as a function of the selected processing scheme and the task performance achieved.

3.2.2 Related work

Following, most relevant contributions that give a partial response to the abovementioned modeling issues are reviewed. Specifically, SEN representation of superstructures, DO tools for optimization problems with transient states and dynamic control profiles, multistage modeling for systems with and discrete events, GDP for mixed-logic modeling and optimization, and their combination in MLDO problems are surveyed. Most of these tools and strategies have been developed to solve other problems in PSE and have been adopted in this thesis to solve the problem of integrated batch process development, due to the similitude of the modeling issues addressed.

Superstructure representation

The representation of the problem superstructure should be defined in consonance to the mathematical modeling strategy used to formulate the problem. Researchers solving batch process synthesis, plant design, and scheduling problems developed various representations of the task network, where plant, process, and material states are combined in different ways. The most widespread proposals are the State-Task Network (STN) by Kondili et al. (1993), the maximal State-Task Network (mSTN) by Barbosa-Póvoa & Macchietto (1994a), the Resource-Task Network (RTN) by Pantelides (1994), and the State-Equipment Network (SEN) by Smith & Pantelides (1995). The use of RNT, STN, m-STN representations was compared by Pinto et al. (2008) for the design of multipurpose batch plants. These are the most widespread representations used for batch plant design and scheduling problems. Moreover, SEN representation has been proposed by other authors to deal with batch processes. For instance, recently Nie et al. (2012) based their proposal in the SEN representation to solve the scheduling problem including process dynamics, formulated as a MLDO problem.

The SEN superstructure entails equipment items and states of transferred material, facilitating the formulation of equations associated to equipment items required in the representation of unit procedures. In contrast, process stages are not explicitly included in the superstructure, and they have to be defined through allocation constraints or pre-specified task-unit assignments. A relevant feature in SEN representation is that the state definition is not unique; the properties of the material transferred from each equipment unit depend on the particular task that the equipment performs (Yeomans & Grossmann, 1999). Specifically, the performance of each unit procedure is subject to: (i) the input material provided by previous unit procedures and (ii) the decision-making on each unit procedure, *i.e.* task-unit assignment, processing conditions, batch operations and phases, and processing order. The relation between these decision variables and the states of material transferred from one equipment piece to the next one in the SEN is represented in the optimization model. Overall, the SEN representation embraces a great flexibility required by the proposed problem.

Hybrid discrete/continuous models

A survey of dynamic models that represent batch process performance and batch events is presented by Cruse et al. (2006). These kinds of models are termed discrete/continuous or hybrid models, due to the combination of continuous and discrete variables employed. According to the type of model discontinuities represented, discrete/continuous models render different degrees of complexity that categorizes the models in three classes: single-stage, multistage, and general discrete/continuous hybrid models. First, *single-stage models* are composed solely by DAE systems with corresponding initial boundary conditions, and path and end-point constraints, excluding discrete events. It is the simplest case and a single batch phase or operation with a specific duration can be represented therein. Second, *multistage models* incorporate explicit discontinuities , understood as the representation of operation or phase transitions at explicit events that do not depend on the process state –*i.e.* transitions at particular times. Each modeling stage, referred to the period between discrete events, can represent a batch phase, operation, or process stage. Finally, *general discrete-continuous hybrid models* additionally incorporate implicit discontinuities, by defining stage transitions as a function of process variables –*e.g.* shift to next batch phase when a specific conversion is achieved. This case was generalized by Barton & Pantelides in 1994 and includes DAE systems, initial conditions for the first modeling stage, path and end-point constraints for each stage, stage-to-stage matching conditions, and transition conditions. The formulation of a general discrete/continuous hybrid model involving a set of $K \in \{1, ..., n_K\}$ stages reads as:

$$
\begin{gathered}
f_k\left(\dot{z}_k(t), z_k(t), y_k(t), u_k^{dyn}(t), p\right) = 0,\ t \in [t_{k-1}, t_k], \forall k \in K, \\
l\left(\dot{z}_1(t_0), z_1(t_0)\right) = 0, \\
g_k\left(z_k(t), y_k(t), u_k^{dyn}(t), p\right) \leq 0,\ t \in [t_{k-1}, t_k], \forall k \in K, \\
g_k^e\left(z_k(t_k), y_k(t_k), u_k^{dyn}(t_k), p\right) \leq 0,\ \forall k \in K, \\
z_{k+1}(t_k) - m_k\left(z_k(t_k)\right) = 0,\ \forall k \in \{1, ..., n_K - 1\}, \\
\gamma = h(z_{n_K}(t_{n_K}), y_{n_K}(t_{n_K}), u_{n_K}^{dyn}(t_{n_K}), p),
\end{gathered}
\tag{3.1}
$$

where t_k is the final time of stage $k \in K$, $z_k(t)$, $y_k(t)$, and $u_k^{dyn}(t)$ are the differential, algebraic, and control variables along time in stage k, γ are the time-invariant algebraic variables, and p are the model parameters. Moreover, l are the relations that define initial conditions, f_k, g_k, g_k^e, and m_k are the DAE system, path constraints (PC), end-point constraints (EPC), and stage-to-stage continuity in stage k, and h are the algebraic equations evaluated at the final time. For the sake of practicality, in this thesis the term *multistage model* is used for those systems with both explicit and implicit discontinuities.

The optimization of the process performance using the above discrete-continuous models and considering the dynamic profiles of the control variables constitutes the OC or DO problem. In broad terms, the goal is to minimize a cost criterion associated to a unit procedure or an entire process by adjusting the process variables within some pre-specified bounds under consideration of operational constraints, and considering the variation of control variables along time as degrees of freedom (Schlegel, 2004). The general formulation of DO problems, involving a single-stage model, where the stage subindex k has been eliminated, reads as:

$$\begin{aligned} \underset{u^{dyn}(t),t^{end}}{\text{minimize}} \quad & \Phi(z(t), y(t), u^{dyn}(t), \gamma, p), \\ s.t. \quad & f(\dot{z}(t), z(t), y(t), u^{dyn}(t), p) = 0,\ t \in [t^s, t^{end}], \\ & l(\dot{z}(t^s), z(t^s)) = 0, \\ & g(z(t), y(t), u^{dyn}(t), p) \leq 0,\ t \in [t^s, t^{end}], \\ & g^e(z(t^{end}), y(t^{end}), u^{dyn}(t^{end}), p) \leq 0, \\ & \gamma = h(z(t^{end}), y(t^{end}), u^{dyn}(t^{end}), p), \end{aligned} \tag{3.2}$$

where t^s and t^{end} are initial and final times, $z(t)$, $y(t)$, and $u^{dyn}(t)$ are differential, algebraic, and control variables along time, γ are the time-invariant algebraic variables, and p are the model parameters. Moreover, Φ, f, l, g, g^e, and h are the objective function, DAE system, initial conditions, path constraints, end-point constraints, and algebraic equations evaluated at the final time. To consider several mathematical stages, variables $z(t)$, $y(t)$, and $u^{dyn}(t)$ and equations f, g, and g^e would be defined for each stage $k \in K$, and stage-to-stage continuity m is incorporated for each stage $k \in \{1, ..., n_K - 1\}$, as defined previously in the hybrid discrete/continuous model (Eq. 3.1).

This formulation was originally applied to aerospace engineering, and extended later to solve the design and operation of individual batch units (Pollard & Sargent, 1970, Sargent & Sullivan, 1979). After important advances in the 1980s and 1990s regarding analytical and numerical methods to solve DO problems (see the reviews by Binder et al., 2001, Srinivasan et al., 2003, Schlegel, 2004), these tools acquired a great popularity in the last decades, being applied to a variety of unitary operations, as reviewed in Chapter 2 (p. 33). Dynamic trajectories of control variables within a sequence of unit procedures has been applied in a more reduced number of contributions to different problems of PSE:

- Batch process synthesis: Charalambides et al. (1995, 1996), Allgor & Barton (1999b), and Sharif et al. (1999);
- Batch plant design: Barrera & Evans (1989), Bhatia & Biegler (1996), and Corsano et al. (2004, 2006, 2007); and
- Short-term scheduling: Mishra et al. (2005), Capón-García et al. (2013), Nie et al. (2012), and Frankl et al. (2012a), among others.

It should be noted that some of these works address the problem through hierarchical strategies, as reviewed in Chapter 2 (p. 38-39, 42-48).

Logic-based modeling

To include quantitative and qualitative information in the optimization problem, modeling strategies based on the use of integer or logical variables may be applied. MILP formulations were first proposed by Papoulias and Grossmann (1983c, 1985) to solve the synthesis of continuous processes, which were later extended to capture the nonlinear behavior of connecting items and processing elements in MINLP formulations (Duran & Grossmann, 1986a).

Contemporary, Balas (1985) proposed the use of Disjunctive Programming, the first methodology to introduce logics in mathematical modeling, which was later generalized into the GDP (Raman & Grossmann, 1991, 1993, Floudas & Grossmann, 1994, Grossmann & Daichendt, 1996, Grossmann et al., 1999). Logic-based modeling strategies allowed a direct incorporation of available process knowledge and heuristic rules in the mathematical model. These modeling strategies were one of the most important advances in continuous process synthesis using optimization-based approaches, limiting the combinatorial explosion and making the solution of optimization models manageable. Qualitative decisions could be introduced in the formulation through Boolean variables, and logical relations could be formulated using logical propositions like disjunctive equations or using algebraic equations. The general formulation of GDP problems reads as:

$$
\begin{aligned}
\underset{u_i^{Bool}}{\text{minimize}} \quad & \Phi(\gamma, p), \\
s.t. \quad & h(\gamma, p) \leq 0, \\
& \underset{i \in ID}{\underline{\vee}} \begin{bmatrix} u_i^{Bool} \\ h_i^d(\gamma, p) \leq 0 \end{bmatrix}, \\
& \Omega(u_i^{Bool}) = true,
\end{aligned}
\tag{3.3}
$$

where γ are time-invariant algebraic variables, p are model parameters, $u_i^{Bool} \in \{true, false\}$ are Boolean variables that control the disjunctive term $i \in ID$ in disjunctive equations, Φ is the objective function, h and h_i^d are algebraic equations that are hold either globally or in the particular disjunctive term $i \in ID$ in disjunctive equations, and Ω is the set of logical propositions.

In the case of batch processes, dynamic behavior should be also represented. Formulations that combine dynamic equations with mixed-logic formulations have been applied to other problems of PSE. One of the first steps was the MLD optimization by Bemporad & Morari (1999) to solve model predictive control problems with lineal or linearized equations. Later, mixed-logic modeling with process dynamics were applied to simultaneous design and control (Bansal et al., 2002a,b), design of individual batch units (Oldenburg et al., 2002, 2003, 2005, 2008), and scheduling of continuous processes with grade transitions (Nyström et al., 2005, 2006, Prata et al., 2008).

Overall, in the development of batch processes problem, strategies for mixed-logic dynamic formulations have been only partially exploited. On the one hand, Linninger and Chakraborty (1999, 2002, 2003) addressed batch process synthesis and allocation problem including logical rules in the superstructure formulation, but omitting dynamic performance models to represent the tasks behavior and approximating models instead. On the other hand, Oldenburg and Marquardt (2003, 2008) used mixed-logic formulations with dynamic process performance models to address the optimal configuration, sequencing and operation of batch equipment units, including structural decisions. Precisely, the importance of their work is related to the combination of hybrid discrete/continuous models with GDP formulations, permitting the simultaneous representation of quantitative information regarding the process behavior in individual units –including discrete events and dynamic profiles of the control variables–, as well as qualitative information regarding the structural alternatives in the equipment design.

Particularly, the proposed modeling approach by Oldenburg and Marquardt, (2003, 2008) is a MLDO problem, which is based on the nesting of hybrid discrete/continuous models in disjunctive equations, defining the process performance as a function of qualitative variables and associating each mathematical stage to a batch phase or operation. The general form of MLDO problems, involving a single-stage model and disjunctive equations with two terms u^{Bool} and $\neg u^{Bool}$, reads as:

$$
\begin{aligned}
\underset{u^{dyn}(t),t^{end},u^{Bool}}{\text{minimize}} \quad & \Phi(z^d(t), y(t), u^{dyn}(t), \gamma, p), \\
s.t. \quad & f(\dot{z}(t), z(t), y(t), u^{dyn}(t), p) = 0,\ t \in [t^s, t^{end}], \\
& l(\dot{z}(t^s), z(t^s)) = 0, \\
& g(z(t), y(t), u^{dyn}(t), p) \leq 0,\ t \in [t^s, t^{end}], \\
& g^e(z(t^{end}), y(t^{end}), u^{dyn}(t^{end}), p) \leq 0, \\
& \gamma = h(z(t^{end}), y(t^{end}), u^{dyn}(t^{end}), p), \\
& \begin{bmatrix} u^{Bool} \\ f^d(\dot{z}(t), z(t), y(t), u^{dyn}(t), p) = 0,\ t \in [t^s, t^{end}], \\ l^d(\dot{z}^d(t^s), z^d(t^s)) = 0, \\ g^d(z(t), y(t), u^{dyn}(t), p) \leq 0,\ t \in [t^s, t^{end}], \\ g^{d,e}(z(t^{end}), y(t^{end}), u^{dyn}(t^{end}), p) \leq 0 \\ \gamma = h^d(z(t^{end}), y(t^{end}), u^{dyn}(t^{end}), p), \end{bmatrix} \underline{\vee} \\
& \begin{bmatrix} \neg u^{Bool} \\ B^d(\dot{z}(t), z(t), y(t), u^{dyn}(t), \gamma, p) = 0,\ t \in [t^s, t^{end}] \end{bmatrix}, \\
& \Omega(u^{Bool}) = true,
\end{aligned}
\tag{3.4}
$$

where t^s and t^{end} are initial and final times, $z(t)$, $y(t)$, and $u^{dyn}(t)$ are differential, algebraic, and control variables along time, γ are time-invariant algebraic variables, p are the model parameters, and $u^{Bool} \in \{true, false\}$ are Boolean variables that control disjunctive equations. Φ is the objective function, f, l, g, g^e, and h are the objective function, DAE system, initial conditions, path constraints, end-point constraints, and algebraic equations evaluated at the final time that are hold independently to the Boolean decisions, f^d, l^d, g^d, $g^{d,e}$, and h^d are the analogous functions that are hold in case that variable u^{Bool} is $true$, B^d defines the system in case that u^{Bool} is $false$, and Ω is the set of logical propositions.

However, the MLDO formulation proposed by these authors only accounted for individual units design, rather than the synthesis of complete processes, with several alternatives for processing routes. Therefore, the synchronization of unit procedures as a function of task allocation and ordering is not necessary and was not covered. Thus, the modeling strategy has to be extended to cover multiple unit procedures and their free ordering and synchronization. To the author's knowledge, there are no available references yet in the context of batch process development or batch plant design that address this problem.

Concurrent single-stage and multistage models for synchronization purposes

To represent batch and semi-continuous procedures in the superstructure, single-stage and multistage models can be used respectively, which should be combined in the optimization model. Moreover, to account for batch integrity it is necessary that material transference is synchronized between subsequent unit procedures according to each processing path alternative. For that, the single-stage and multistage models should be overlapped in transfer operations or phases, according to the selected synthesis alternative and unit procedure sequence. However, from practical point of view, up to now neither a modeling framework nor a respective software tool is available to handle concurrent multistage and single-stage models.

The use of both types of models and their synchronization was not required in previous works of process synthesis with dynamic profiles of control variables (Charalambides et al., 1995, Charalambides, 1996, Allgor & Barton, 1999b, Sharif et al., 1999) for three principal reasons. First, a free ordering of batch unit usage was not required in most of these works because task sequence and allocation were predefined or solved in later steps. However, these assumptions may limit potential improvement in the solution, especially in the case of retrofit scenarios where the consideration of all potential equipment items for each task is crucial to define the best equipment assignment. Second, material transfer operations and phases in source and sink units were approximated to one unique state and the models included neither material transfer phases nor process variable dynamics therein. This way, synchronization of flow rates and properties profiles was not required and constraints to ensure batch integrity were defined through the fulfillment of material and energy balances with a unique transition state in a specific time point. The drawback with this approximation is that dynamic profiles for loading and unloading operations cannot be studied. For instance, dynamic profiles in reactant loads can render solution improvement in competitive reaction systems. Third, tasks were not divided into a sequence of operations and phases. As a result, a unique multistage model was sufficient to represent a complete process, by designating one modeling stage to each of the tasks. In this case, process behavior in unit procedures is approximated, thus overestimating or underestimating the attainable feasible area.

3.2.3 Overview of the proposed approach

This section presents a novel modeling strategy to solve integrated batch process development. The fundamental guidelines for understanding the superstructure representation and the mathematical formulation are provided. The strategy relies on the combination of several of the reviewed modeling and optimization contributions, giving a response to the modeling requirements to address simultaneously the synthesis and the allocation sub-problems. Particularly, SEN superstructure representation, DO with hybrid discrete/continuous models, GDP, and synchronization of single-stage and multistage models are combined into a MLDO model as following detailed.

The superstructure of processing alternatives is based on the SEN representation (Smith & Pantelides, 1995) in order that the plant restrictions and equations associated to unit procedures can be explicitly represented. Additionally, the SEN superstructure provides great flexibility in the representation of material transfer states, which are not fixed to a pre-defined value but are subject to the selected unit procedures and their performance for each particular solution. Moreover, process stages that are potentially needed should be assigned to specific equipment pieces in the SEN, which come in hand to a set of physical restrictions like the maximum volume or the maximum allowed temperature. For instance, in motivating example 2 with the SEN superstructure from Figure 3.3, reaction technology A could be assigned to processing unit $U_{1,A}$ according to its equipment specifications, whereas reaction technology B could be allocated in processing units $U_{1,B}$ or U_2. The composition and internal conditions of the output flow $9''$ are not fixed, but depend on the technologies and units selected.

To mathematically formulate the superstructure and all the associated decisions, a modeling strategy based on MLDO with hybrid discrete/continuous models –referred to as multistage models in this thesis– is used. Particularly, the proposed MLDO form by Oldenburg & Marquardt (2008) is extended to combine and organize single-stage and multistage models according to each processing path alternative. Each model represents the procedure, which may involve a dynamic process performance, associated to each of the elements in the SEN superstructure. Particularly, single-stage models are used to represent semi-continuous procedures, whereas multistage models represent batch procedures, each of them being composed by a set of batch operations or phases. Going back to the motivating example 1, loading, reaction, and unloading operations are defined for unit procedures in U_1 and U_2.

The coexisting use of single-stage and multistage models allows the modular representation of each processing element in order that the time coordinates of batch units can be moved with respect to the time horizon of the entire recipe. Moreover, the order of each unit procedure in each alternative solution is defined as a function of the task-unit assignments. For instance, according to the SEN representation in Figure 3.1, the unit procedure in U_2 of example 1 could operate at first place, after U_1, or at the same time than U_1 in parallel, thus requiring a different ordering 1 or 2, a different value for the starting time $t^{U_2,s}$, and a different material input, from flow 3 or flow 6.

To facilitate their coordination, unit procedures and decision variables are distributed in two modeling levels, dividing the superstructure in Levels 0 and 1 as shown in Figure 3.4 for the example 1. Every batch unit procedure, like those in U_1 and U_2, is located at the first modeling level (Level 1) and is represented by its own multistage model. In contrast, mass balances in connection nodes like splitters Sp_1 and Sp_2, mixers Mx_1 and Mx_2, storage tanks like T_{raw} and T_{prod}, and possible semi-continuous processing units, are represented by single-stage models and are associated to the basic level (Level 0). Coexistence of single-stage and multistage models is illustrated in Figure 3.5a. The synchronization in terms of time of the models at both levels will be defined through disjunctive equations and logical propositions in the formulation. This way, time coordinates of batch units can be moved with respect to the time horizon of the entire recipe.

In addition to the model distribution at Levels 0 and 1, a specific treatment of the equations –including both internal model equations and synchronization constraints– should be done, in order that the problem can be handled by ordinary optimization tools. Particularly, it is necessary to relate the mathematical stages of multistage models associated to each batch procedure as follows: First, stages that represent material input operation in destination units should be related to the corresponding material output operation in source units. Second, all stages in multistage models require a connection to the time horizon in the entire recipe and the single-stage models of semi-continuous procedures. Moreover, stage times should be defined as an explicit variable in order that they can be considered as a degree of freedom. For that, it is necessary to address:

1. **Transformation of single-stage models at Level 0 to multistage ones.** First, a correspondence across Levels 0 and 1 is established. For that purpose, single-stage

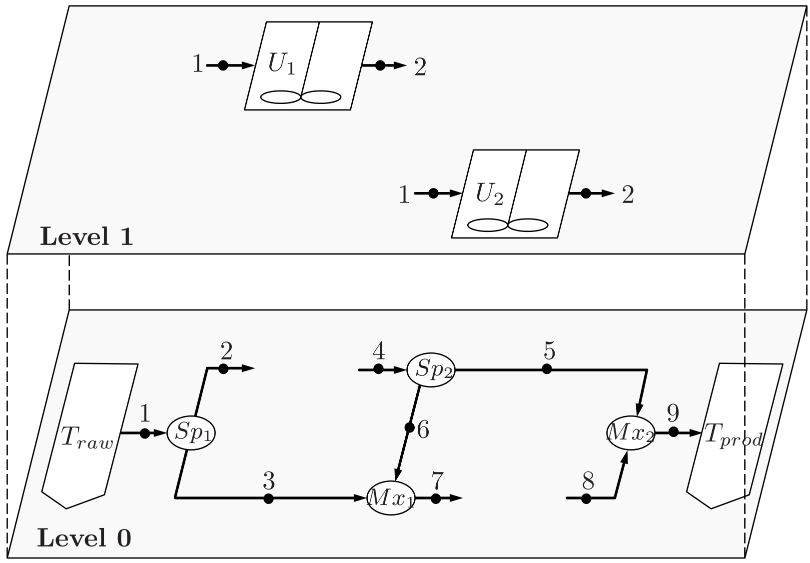


Figure 3.4: Two-level superstructure distribution of example 1.

models at Level 0 are transformed into multistage models that contain all potential stages from Level 1, as shown in Figure 3.5b. Then, equations of the original model at Level 0 are replicated for the total number of stages required, and continuity of process variables from stage-to-stage is provided by adding the corresponding equations. Moreover, starting and final times of batch unit phases should fit particular stage transitions at Level 0. Therefore, starting and final times in parallel unit procedures are assumed to be identical, in order to avoid an exponential growth in the number of allowed stage transitions at Level 0.

2. **Transformation of multistage models at Levels 0 and 1 to single-stage ones.** Secondly, models at Levels 0 and 1 may have a different number of stages. For instance, Level 0 now contains stages associated to all feasible combinations of batch units. To unify this number and to combine all equations in a unique normalized model, all sequenced stages are timed in parallel in a same time axis. This way, an equivalent single-stage model is constructed as shown in Figure 3.5c, where all the time intervals have been normalized and initial conditions are treated as control variables which should ensure continuity from previous stage at every stage except for the actual first stage, which has fixed initial conditions. For the normalization of time intervals, differential equations are multiplied by their stage duration and their integration interval is redefined to be from 0 to 1.
3. **Explicit treatment of stage durations.** Finally, in order to establish the time equivalence between synchronized stages across the different models, stage durations have to be expressed as explicit variables, what is accomplished with the normalization of time intervals realized in the previous step.

All these transformations have been applied to the equations presented in the formulation in next section (§ 3.3). However, the individuality of each stage is kept in the definition of the models at both Levels 0 and 1 because it is needed and represents a key issue in the synchronization of unit procedures, despite solution of all stages is done in parallel as a single stage.

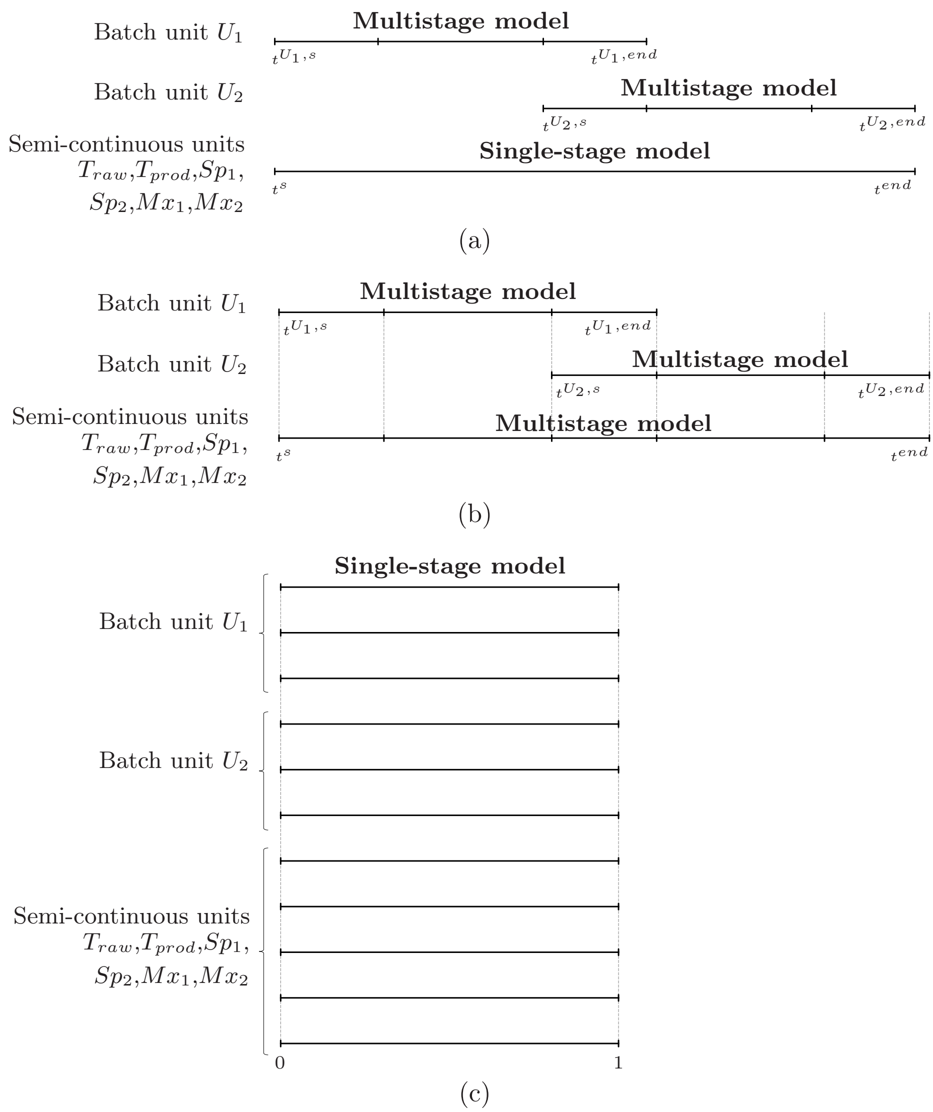


Figure 3.5: Multistage and single-stage models of example 1 to represent batch and semi-continuous plant elements respectively: (a) coexistence of models, (b) transformation of single-stage models at Level 0 to multistage ones, and (c) transformation of multistage models at Levels 0 and 1 to single-stage normalized ones.

3.3 Problem formulation

According to the problem statement, several elements are meant to be combined in the formulation of the simultaneous synthesis of processing schemes and plant allocation problem as shown in Figure 3.6. Specifically, the optimization model should contain information regarding: the models of batch and semi-continuous procedures, the technological specification alternatives for each unitary operation, the candidate chemicals to be selected, the synchronization of tasks and connecting flows, the alternative configurations of unit procedures, the selection of process stages, and the possible recirculation of intermediate materials. In this section, the construction of the optimization model that integrates all these elements is detailed.

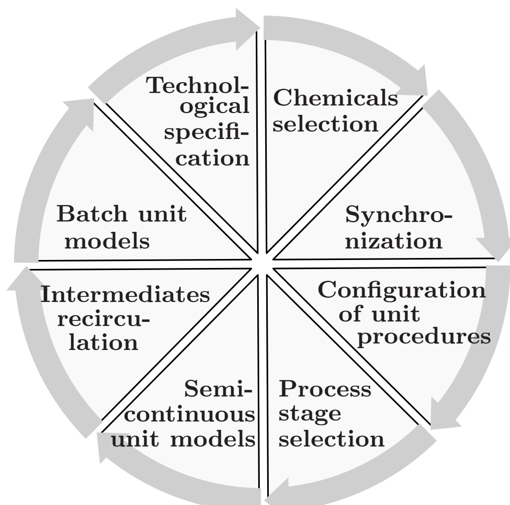


Figure 3.6: Elements of the integrated batch process development problem combined in the formulation.

3.3.1 Notation

The notation and control variables description is first presented, being the support to connect and interrelate prior information elements that compose the optimization model. Table 3.1 summarizes the sets of elements required in the formulation, which are illustrated by means of specific elements of the motivating example 1. The cardinality of any of these sets S is denoted by $|S|$. Tables 3.2 and 3.3 gather the modeling parameters and general variables, including the particular values of example 1 as well. In order to shed light on the defined sets, parameters, and variables, it is necessary to consider the following particularities of the modeling strategy.

The correspondence across both modeling levels is established by relating the mathematical stages at Level 1 to particular stages at Level 0. Thus, the sets of stages at both levels, $K_j, j \in U$ and L respectively, are defined separately and maintain their individuality, in order that the synchronization of batch unit procedures can be carried out according to their processing order. In addition, the set of necessary stages at Level 0 is subject to the process stages selected $i \in PS$ and their configuration $\psi \in \Psi_i$. For instance, configuration α of example 1, defined as the single operation of U_1 (see Ψ_i in Table 3.1),

Set	Definition	Elements in example 1
U	Set of existing and potential batch units	U=$\{U_1, U_2\}$
T	Set of existing and potential storage tanks	T=$\{T_{raw}, T_{prod}\}$
Sp	Set of existing and potential splitters	Sp=$\{Sp_1, Sp_2\}$
Mx	Set of existing and potential mixers	Mx=$\{Mx_1, Mx_2\}$
J	Set of all existing and potential equipment pieces, J=$U \cup T \cup Sp \cup Mx$	J=$\{U_1$,U_2,T_{raw}, T_{prod},Sp_1,Sp_2, Mx_1,$Mx_2\}$
PS	Set of potential process stages or tasks	PS=$\{1\}$
J_i⊆J	Set of equipment pieces within potential task i∈PS,	J_1=J
Ψ_i	Set of configurations in task i∈PS	Ψ_1=$\{\alpha, \beta, \pi, \sigma\}$, α: single U_1, β: single U_2, π: parallel, σ: series U_1-U_2
Λ_i	Set of technological specifications in task i∈PS	Λ_1= {Denbigh}
Λ_j⊆Λ_i	Set of technological specification of unit j∈U in task i∈PS, $\|\Lambda_j\|$=1, ∀j∈U	Λ_{U_1}=Λ_{U_2}= {Denbigh}
L	Set of potential stages at Level 0, L=$\{1,...,L^{\max}\}$	L=$\{1, ..., 5\}$
L^a⊆L	Set of active stages at Level 0	L_α=L_β=L_π= $\{1,...,3\}$, L_σ=$\{1,...,5\}$
K_j	Set of stages for unit j∈U at Level 1	K_{U_1}=K_{U_2}= $\{1,...,3\}$
I_j⊆K_j	Set of input stages for unit j∈U at Level 1	I_{U_1}=I_{U_2}=$\{1\}$
O_j⊆K_j	Set of output stages for unit j∈U at Level 1	O_{U_1}=O_{U_2}=$\{3\}$
N	Set of pipelines at Level 0	N=$\{1, ..., 9\}$
$N_i \subseteq N$	Set of pipelines at Level 0 for task $i \in PS$	N_1=N
$N_i^{in} \subseteq N_i$	Subset of input pipelines to process stage $i \in PS$	N_1^{in}=$\{1\}$
$N_i^b \subseteq N_i$	Bypass pipeline for process stage $i \in PS$, $\|N_i^b\|$=1	N_1^b=$\{\emptyset\}$
N_j^{in}⊂N	Set of input pipelines to equipment j∈J at Level 0	$e.g.$ $N_{U_1}^{in}$=$\{2\}$, $N_{U_2}^{in}$=$\{7\}$
N_j^{out}⊂N	Set of output pipelines from equipment j∈J at Level 0	$e.g.$ $N_{U_1}^{out}$=$\{4\}$, $N_{U_2}^{out}$=$\{8\}$
$N_{i,\psi}^0$⊆N	Set of pipelines at Level 0 whose flow rate is restricted to zero in configuration ψ∈Ψ_i of task i∈PS	$N_{1,\alpha}^0$=$N_{1,\beta}^0$=$N_{1,\pi}^0$= $\{6\}$, $N_{1,\sigma}^0$=$\{3, 5\}$
N_i^f⊆N	Set of pipelines at Level 0 for task i∈PS whose flow rate is fixed by the preceding task, $\|N_i^f\|$=1 except for process stages preceded by a buffer j∈T	N_1^f=$\{\emptyset\}$
N^r⊆N	Set of pipelines at Level 0 for recirculation	N^r=$\{\emptyset\}$
T_n^r⊆T	Buffer tank for potential recirculation of flow n∈N^r, $\|T_n^r\|$=1,∀n∈N^r	T_n^r=$\{\emptyset\}$
M_j	Set of pipelines for unit j∈U at Level 1	M_{U_1}=M_{U_2}=$\{1, 2\}$
M_j^{in}⊆M_j	Set of input pipelines to unit j∈U at Level 1	$M_{U_1}^{in}$=$M_{U_2}^{in}$=$\{1\}$
M_j^{out}⊆M_j	Set of output pipelines from unit j∈U at Level 1	$M_{U_1}^{out}$=$M_{U_2}^{out}$=$\{2\}$

Table 3.1: Sets in the proposed formulation to solve integrated batch process development and elements in example 1.

Set	Definition	Elements in example 1
Q	Set of ordered positions that can be assumed by unit procedures of $j \in U$, $Q=\{1, ..., \lvert U \rvert\}$	$Q=\{1,2\}$
$L_j^0 \subseteq L$	Set of stages at Level 0 where unit $j \in U$ can start its operation,$L_j^0=\{1, \lvert K_{j'} \rvert$-$\lvert O_{j'} \rvert+1 \mid j' \neq j,\ j' \in U\}$	$L_{U_1}^0=L_{U_2}^0=\{1,3\}$
$D_{i,\psi} \subseteq U_i$	Subset of batch units U_i in task $i \in PS$ whose input flow rate is a control variable in configuration $\psi \in \Psi_i$. It is defined such that $\lvert D_{i,\psi} \rvert = DOF_{i,\psi} - \lvert U_i \rvert$, where $\lvert U_i \rvert$ represents DOF removed by output flow rates	$D_{1,\alpha}=D_{1,\beta}=D_{1,\pi}$ $=\{U_1, U_2\}$, $D_{1,\sigma}=\{U_1\}$
C	Set of chemical compounds involved in the process	$C=\{\emptyset\}$
$C_j^s \subseteq C$	Subset of potential reactants, solvents, or catalysts in unit $j \in U$ subject to be selected	$C_j^s=\{\emptyset\}$
$P \subset C$	Subset of desired products	$P=\{\emptyset\}$

Table 3.1 (cont.): Sets in the proposed formulation to solve integrated batch process development and elements in example 1.

Parameter	Definition	Values in example 1
$L^{\max}$	Maximum number of stages at Level 0,	$L^{\max}=5$
$l_{j,q}^0$	Starting stage of unit $j \in U$ when the task-unit Boolean $W_{j,q}$ is $true$, $l_{j,q}^0$=q-th element of the ascending sort of L_j^0 of unit $j \in U$	$l_{U_1,1}^0=l_{U_2,2}^0=1$, $l_{U_1,2}^0=l_{U_2,2}^0=3$
$DOF_{i,\psi}$	Degrees of freedom with regard to the flow rates at Level 0 at process stage $i \in PS$, according to each configuration $\psi \in \Psi_i$, $DOF_{i,\psi}$=$No.variables$ - $No.equations$ - $No.fixed\ variables$ $=\lvert N_i \rvert$-$\lvert Sp_i \cup Mx_i \rvert$-$\lvert N_{i,\psi}^0 \rvert$-$\lvert N_i^f \rvert$, where $\lvert N_i \rvert$: number of flow rates in the set of pipelines N_i, $\lvert Sp_i \cup Mx_i \rvert$: number of total material balances in connection nodes, $\lvert N_{i,\psi}^0 \rvert$: number of flow restrictions, $\lvert N_i^f \rvert$: number of predefined flow rates	$DOF_{1,\alpha}=4$, $DOF_{1,\beta}=4$, $DOF_{1,\pi}=4$, $DOF_{1,\sigma}=3$
$p_{j,c}$	Values for the set of process parameters p_j in unit $j \in U$ when potential chemical alternative $c \in C_j^s$ is selected	$p_{j,c}=\{\emptyset\}$
$Demand_p$	Demand of product $p \in P$	$Demand_p=\{\emptyset\}$

Table 3.2: Parameters in the proposed formulation to solve integrated batch process development and values in example 1.

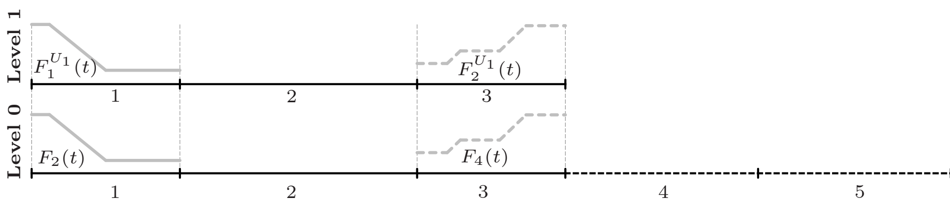
Variable	Definition
Z_i (*)	Process stage Boolean to indicate whether process stage $i \in PS$ is selected (Z_i=$true$) or not (Z_i=$false$)
Y_j (*)	Equipment Boolean to indicate whether processing or storage unit $j \in U \cup T$ is selected (Y_j=$true$) or not (Y_j=$false$)
X^i_ψ (*)	Configuration Boolean to indicate whether alternative $\psi \in \Psi_i$ of process stage $i \in PS$ is selected (X^i_ψ=$true$) or not (X^i_ψ=$false$)
$W_{j,q}$ (*)	Task-unit assignment Boolean to indicate whether unit procedure order $q \in Q$ is assigned to unit $j \in U$ ($W_{j,q}$=$true$) or not ($W_{j,q}$=$false$)
V^j_λ (*)	Technology Boolean to indicate whether technological specification $\lambda \in \Lambda_j$ of processing unit $j \in U$ is selected (V^j_λ=$true$) or not (V^j_λ=$false$)
S^j_c (*)	Chemical compound Boolean to indicate whether reactant, solvent, or catalyst $c \in C^s_j$ is selected in unit $j \in U$ (S^j_c=$true$) or not (S^j_c=$false$)
R_n (*)	Recirculation Boolean to indicate whether intermediate flow in pipeline $n \in N^r$ is recirculated (R_n=$true$) or not (R_n=$false$)
T^f	Total time at Level 0
t_l (*)	Duration of stage $l \in L$ at Level 0
t^s	Starting time in at Level 0
t^{end}	Final time at Level 0
$T^{j,f}$	Total time of unit $j \in U$ model at Level 1
t^j_k	Duration of stage $k \in K_j$ of unit $j \in U$ at Level 1
$t^{j,s}$	Starting time of unit $j \in U$ at Level 1
$t^{j,end}$	Final time of unit $j \in U$ at Level 1
$F_{n,l}(t)$	Flow rate for every pipeline $n \in N$ and stage $l \in L$ at Level 0
$x_{c,n,l}(t)$	Flow composition of compound $c \in C$ for every pipeline $n \in N$ and stage $l \in L$ at Level 0
$F^j_{m,k}(t)$(*)	Flow rate for every input or output pipeline $m \in M^{in}_j \cup M^{out}_j$ and stage $k \in K_j$ of unit $j \in U$ at Level 1
$x^j_{c,m,k}(t)$	Flow composition of compound $c \in C$ for every input or output pipeline $m \in M^{in}_j \cup M^{out}_j$ and stage $k \in K_j$ of unit $j \in U$ at Level 1
int^j_k(t) (*)	Internal control variable for every stage $k \in K_j$ of unit $j \in U$ at Level 1 and $k \in L$ of unit $j \in J \backslash U$ at Level 0
NB_p (*)	Number of batches of product $p \in P$
$Batch_p$	Production size associated to each batch of product $p \in P$
$Shortfall_p$	Unaccomplished demand of product $p \in P$
$Size^j$ (*)	Capacity of unit $j \in U \cup T$ with a discrete value
$v^j_k(t)$	Volume of material in batch unit $j \in U$ at stage $k \in K_j$ or in storage tank $j \in T$ at stage $k \in L$

(*) Control variables in the modeling framework

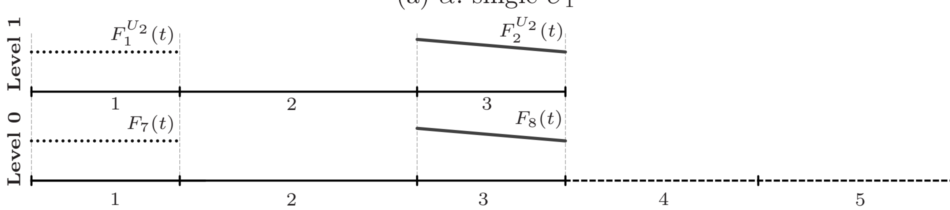
Table 3.3: Variables in the proposed formulation to solve integrated batch process development.

involves the three stages load, hold, and unload unit U_1 as is represented in Figure 3.7a. In contrast, two additional stages are required in configuration σ, defined as the series operation of U_1 followed by U_2 (see Ψ_i in Table 3.1), to complete the hold and unload phases in unit U_2 as is represented in Figure 3.7d. The **maximum number of stages** $L^{\max}$ concerning all structural solutions may be defined as the over-specified solution with all batch procedures in series. Figure 3.7 shows the division of the total time T^f at Level 0 into such maximum number of stages $L^{\max}$ in all structural alternatives. Out of the resulting set of $L = \{1, ..., L^{\max}\}$, only the subset L^a composed by the so-called **active stages** is effective in each option.

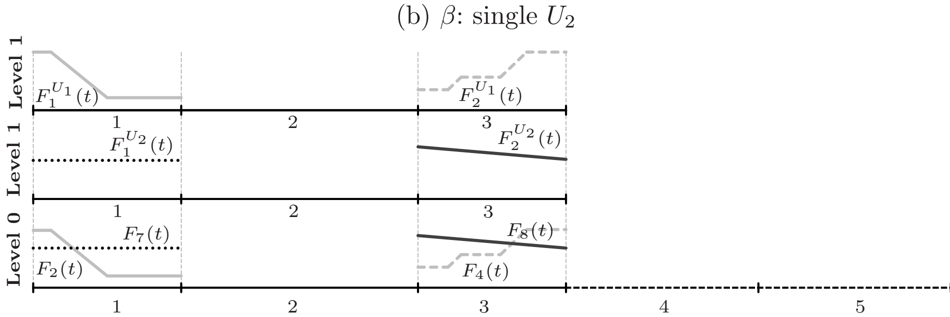
Additionally, models at Levels 0 and 1 are linked by relating stages that represent material transfer operations to/from units $j \in U$ with batch procedures. A stage $k \in K_j$



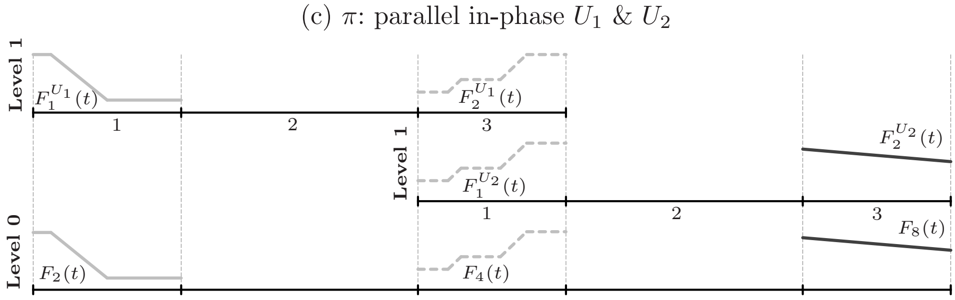
(a) α: single U_1



(b) β: single U_2



(c) π: parallel in-phase U_1 & U_2



(d) σ: series U_1 followed by U_2

Figure 3.7: Synchronization of batch stages and flow rates at Levels 0 and 1 for configurations α, β, π, and σ of example 1, where $|K_j|$=3, $\forall j \in \{U_1, U_2\}$.

that represents an input or output material transfer operation is termed an **input** or **output stage** in the multistage model of unit $j \in U$. The subsets of input and output stages are denoted by $I_j \subseteq K_j$ and $O_j \subseteq K_j$ respectively. Furthermore, ingoing and outgoing pipelines in batch units are represented at both modeling levels, entailing that a relation between both representations have to be set. The variables that characterize these pipelines are flow rates $F^j_{m,k}(t)$ and compositions $x^j_{c,m,k}(t)$ in input and output pipelines $m \in M^{in}_j \cup M^{out}_j$ and are termed **input** and **output variables** in the model of unit $j \in U$. As is illustrated in Figure 3.8, the flow rates in those stages that are not input $K_j \backslash I_j$ or output $K_j \backslash O_j$ stages should be restricted to zero to represent the absence of material transfer. The system state inside a unit is defined uniquely by its input and output variables and by its internal dynamic or approximated model.

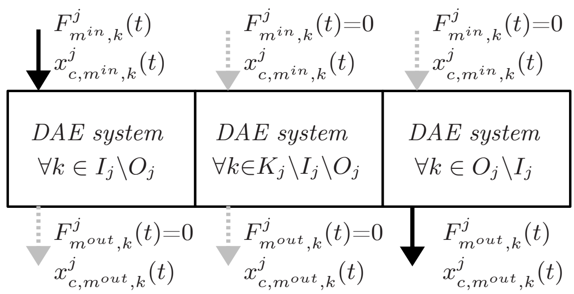


Figure 3.8: Input and output variables and stages of batch unit $j \in U$ model, where $c \in C$, $m^{in} \in M^{in}_j$ and $m^{out} \in M^{out}_j$.

Control variables

The decision variables for the optimization problem are identified by an asterisk (*) in parenthesis in Table 3.3. They are also distributed in the two modeling levels, as is illustrated in Figure 3.9. Deciding on dynamic flow rate profiles in connecting pipelines is associated to input and output flow $m \in M^{in}_j \cup M^{out}_j$ of batch units $j \in U$ (variables $F^j_{m,k}(t)$), and thus corresponds to Level 1. Each equipment piece $j \in U$ at Level 1 or $j \in J \backslash U$ at Level 0 may have additional internal control variables associated (variables int^j_k(t)) –*e.g.* temperature in reactors or valve aperture in splitters.

Batch phase durations (variable t_l) are decided at Level 0, since all potential stages in the system are contained therein, once single-stage models at Level 0 are transformed to multistage ones (see Figure 3.5b). Regarding qualitative the decisions, selection of batch unit $j \in U$ to be used is located at Level 1 (Boolean Y_j), as well as its corresponding technological specification $\lambda \in \Lambda_j$ (Boolean V^j_λ), the selection of chemicals involved $c \in C^s_j$ (Boolean S^j_c), and the assignment of processing order $q \in Q$ (Boolean $W_{j,q}$). On the contrary, the selection of process stage $i \in PS$ (Boolean Z_i), the operating mode $\psi \in \Psi_i$ of process stage $i \in PS$ (Boolean X^i_ψ), the selection of semi-continuous unit or storage tank $j \in J \backslash U$ (Boolean Y_j), and the recirculation of intermediate flow $n \in N^r$ (Boolean R_n), are associated to Level 0.

For the sake of effectiveness, decision variables are classified in three categories depending on their mathematical nature. Namely, dynamic control variables consist of flow rates and internal control variables $u^{dyn}_k(t) = \{F^j_{m,k}(t),\, int^j_k(t)\}$, static or time-invariant decision variables consist of stage durations, $u^{stat} = \{t_l\}$, integer decision variables consist

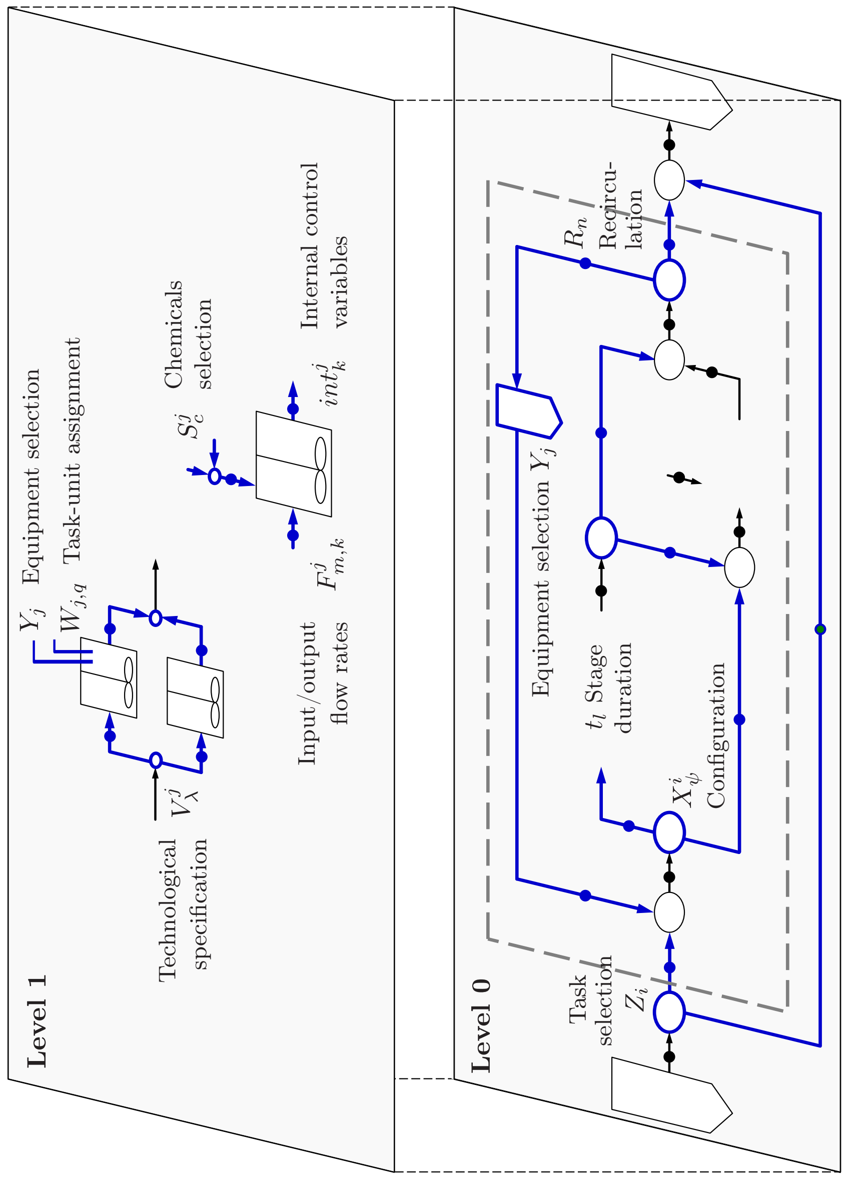


Figure 3.9: Representation of control variables in the two-level superstructure of example 2.

of the number of batches and discrete equipment sizing $u^{int} = \{NB_p,\, Size^j\}$, and logical decision variables or Booleans consist of the task, unit, operating mode, processing order, technological specification, chemical compounds, and recirculation flow selection $u^{Bool} = \{Z_i,\, Y_j,\, X^i_\psi,\, W_{j,q},\, V^j_\lambda,\, S^j_c, R_n\}$.

As a matter of fact, practical degrees of freedom (DOF) are smaller than the sum of all the control variables here comprehended. The DOF are reduced by decisions pre-specified in advance and by equations that relate control variables with each other. To solve the optimization model, it is advisable to analyze the DOF and reduce the allowed control variables accordingly, in order to avoid over-specified systems and minimize the number of decision variables to be optimized. Relevant examples are integer decisions and dynamic profiles in stages representing transfer operations of consecutive unit procedures. Particularly, the latter decisions require the definition of the subset of batch units $D_{i,\psi} \subseteq U_i \subseteq U$ and of the parameter $DOF_{i,\psi}$ to reduce the number of control variables in each allowed configuration $\psi \in \Psi_i$ of process stage $i \in PS$. The reduction of the number of control variables is analyzed in the end of this chapter on the basis of the optimization model developed.

3.3.2 Batch procedures at Level 1

Models of batch units

Let us consider units $j \in U$ with batch procedures, here referred to as batch units, located at Level 1 of the superstructure in Figures 3.4 and 3.9.

Their process performance and operation behavior are represented by a $|K_j|$-stage model. For each unit, a two-term disjunction driven by the Boolean Y_j is introduced. If Y_j is $true$, this unit is selected to allocate one task and its corresponding $|K_j|$-stage model is activated inside the disjunctive term associated to Y_j. On the contrary, if Y_j is $false$, the unit is not selected and the so-called bypass strategy (Oldenburg & Marquardt, 2008) is applied by setting $|K_j|$ equivalent stages where any process takes place. They are termed bypass stages, and their mathematical purpose is represented in the Petri net of Figure 3.10, where circles typify stages and bars represent stage-to-stage transitions. For every bypass stage $k \in K_j$, dynamic equations and constraints are removed and stage durations t^j_k are set to zero. Specifically, the equations should be active either for every stage in the set K_j or for none of them. Hence, it is not necessary to control each batch stage by a different logical variable, as it could be $Y_{j,k}$, but Y_j controls the complete multistage model of unit $j \in U$. Moreover, such multistage model is a function of time-invariant control variables u^{stat}, namely the stage durations t^j_k, and integer variables u^{int}, like the equipment size $Size^j$. Overall, a disjunction with respect to unit $j \in U$ is defined by the following form, bearing in mind that the time interval has been normalized as is shown in Figure 3.5c:

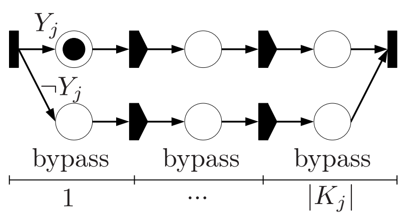


Figure 3.10: Petri net representing active and bypass stages $k \in K_j$ in the model of batch unit $j \in U$ at Level 1.

$$
\left[\begin{array}{c}
Y_j \\
f^d_{j,k}(\dot{z}_{j,k}(t), z_{j,k}(t), y_{j,k}(t), u^{dyn}_{j,k}(t), u^{stat}, u^{int}, p_j),\ t \in [0,1], \forall k \in K_j, \\
l^d_j(\dot{z}_{j,1}(0), z_{j,1}(0)), \\
g^d_{j,k}(z_{j,k}(t), y_{j,k}(t), u^{dyn}_{j,k}(t), u^{stat}, u^{int}, p_j) \leq 0,\ \ t \in [0,1], \forall k \in K_j, \\
g^{d,e}_{j,k}(z_{j,k}(1), y_{j,k}(1), u^{dyn}_{j,k}(1), u^{stat}, u^{int}, p_j) \leq 0,\ \ \forall k \in K_j, \\
z_{j,k+1}(0) - m^d_{j,k}(z_{j,k}(1)) = 0,\ \ \forall k \in \{1, ..., |K_j| - 1\}, \\
\gamma_j = h^d_j(z_{j,|K_j|}(1), y_{j,|K_j|}(1), u^{dyn}_{j,|K_j|}(1), u^{stat}, u^{int}, p_j), \\
T^{j,f} = \sum_{k \in K_j} t^j_k,\ \ t^{j,end} = t^{j,s} + T^{j,f}
\end{array}\right] \underline{\vee}
$$

$$
\left[\begin{array}{c}
\neg Y_j \\
B^d_j(\dot{z}_{j,k}(t), z_{j,k}(t), y_{j,k}(t), u^{dyn}_{j,k}(t), u^{stat}, u^{int}, \gamma_j, p_j) = 0,\ t \in [0,1], \\
t^j_k = 0,\ \ \forall k \in K_j, \\
T^{j,f} = 0,\ \ t^{j,end} = 0,\ \ t^{j,s}_j = 0
\end{array}\right], \quad \forall j \in U, \tag{3.5}
$$

where $f^d_{j,k}$, $g^d_{j,k}$, $g^{d,e}_{j,k}$, and $m^d_{j,k}$ are the DAE system, path constraints (PC), end-point constraints (EPC), and stage-to-stage continuity in stage $k \in K_j$ of unit $j \in U$. l^d_j are the relations that define initial conditions, h^d_j is the set of equations to calculate time-invariant variables γ_j evaluated at the final time ($t = 1$) of last stage $|K_j|$, and B^d_j are the equations that define the system in bypass stages. Moreover, time relations contribute to define the model. Each stage $k \in K_j$ contains time dependent differential $z_{j,k}(t)$, algebraic $y_{j,k}(t)$, and control $u^{dyn}_{j,k}(t)$ variables. Therein, input and output variables regarding flow rates $F^j_{m,k}(t)$ and compositions $x^j_{c,m,k}(t)$, and internal control variables $int^j_k(t)$ are included. The multistage model is also characterized by process parameters p_j and time-invariant variables γ_j, which may contribute to the evaluation of the objective function or other key performance indicators (KPIs), like the product selectivity or final conversion in a processing item $j \in U$.

To complete batch unit models at Level 1, input and output variables should be dismissed according to Figure 3.8 in those stages which are not input or output stages respectively by restricting their value to zero. To do so, the following equation should be added to complement the first disjunctive term:

$$
\left[\begin{array}{c}
Y_j \\
F^j_{m^{in},k}(t) = 0,\ \ \forall m^{in} \in M^{in}_j, \forall k \in K_j \backslash I_j, \\
F^j_{m^{out},k}(t) = 0,\ \ \forall m^{out} \in M^{out}_j, \forall k \in K_j \backslash O_j
\end{array}\right], \forall j \in U. \tag{3.6}
$$

Additionally, the volume $\upsilon^j_k(t)$ of material processed at unit $j \in U$ can not surpass the equipment size $Size^j$ in any stage $k \in K_j$, either $Size^j$ is a free decision variable associated to a newly installed unit or it is a constraint associated to an existing item. This restriction is formulated as:

$$
\upsilon^j_k(t) \leq Size^j,\ \ t \in [0,1], \forall k \in K_j, \forall j \in U. \tag{3.7}
$$

Technological specification

The technological specification is used to distinguish between processing alternatives from the set Λ_i that can be used for the same unitary operation in process stage $i \in PS$. The equipment arrangement required for each technology has particular features that imply different physicochemical equations and parameters to describe the unit procedure, as well as different types of processing costs, investment weights, required chemicals or resources, and even different sequence of batch phases or operations. Hence, each equipment piece is associated to a unique and particular technology $\Lambda_j \subseteq \Lambda_i$, $|\Lambda_j| = 1$, $\forall j \in U_i$ in the formulation. In order to consider several technologies in the same process stage, at least one equipment piece should be defined for each alternative, so that the corresponding DAE systems can be differentiated.

The technology $\lambda \in \Lambda_j$ associated to each equipment unit $j \in U$ is represented by Boolean V_λ^j. This variable is related to the equipment Boolean Y_j as follows:

$$Y_j \Leftrightarrow V_\lambda^j, \quad \forall \lambda \in \Lambda_j, j \in U. \tag{3.8}$$

If technological specification λ is selected ($V_\lambda^j = true$), equipment unit j is active ($Y_j = true$).

Selection of chemicals

The selection of chemicals, such as reactants, solvents, or catalysts, involved in a unit procedure in unit $j \in U$ is a synthesis decision represented by Boolean S_c^j. It indicates whether potential chemical $c \in C_j^s$ is selected ($S_c^j = true$) or not ($S_c^j = false$). Unlike the case of technological specification, the use of alternative chemicals does not necessarily affect the balance equations in the entire unit procedure model controlled by Y_j. In this case, the selection of a particular compound affects exclusively the set of parameters p_j in unit $j \in U$. Thus, parameters are specified for each chemical alternative S_c^j as follows:

$$\underset{c \in C_j^s}{\veebar} \begin{bmatrix} S_c^j \\ p_j = p_{j,c} \end{bmatrix}, \forall j \in U, \tag{3.9}$$

where $p_{j,c}$ are the values for parameters in unit j when chemical alternative $c \in C_j^s$ is used.

3.3.3 Synchronization

The time axis for the models of batch units $j \in U$ that are active (Eqs. 3.5 and 3.6, being $Y_j = true$) should be moved along the total time at Level 0 according to the selected configuration, as was illustrated in Figure 3.7. This means that each of these models should be synchronized with the other elements of the process cell, by relating its set of stages K_j at Level 1 to specific stages from the set L at Level 0.

In particular, task-unit assignment Booleans $W_{j,q}$ are used to lead the synchronization, by indicating the processing order $q \in Q$ of unit $j \in U$, which determines the task-unit assignment and the location of the corresponding unit procedure within the total time of Level 0. If unit $j \in U$ is active, then one and only one processing order is assigned to that unit:

$$Y_j \Leftrightarrow \underset{q \in Q}{\veebar} W_{j,q}, \quad \forall j \in U, \tag{3.10}$$

and such task is started in stage $l_{j,q}^0 \in L_j^0 \mid W_{j,q}{=}true$. In example 1, where unit U_1 can never operate at order 2, variable $W_{U_1,2}$ is always $false$ and unit U_1 can never allocate reaction *sub-task* 2.

Specifically, the synchronization is driven in two steps. First, for each stage at Level 1 $k \in K_j$, its corresponding stage $l \in L$ at Level 0 is defined as a function of the processing order $q \in Q$ by $l = k + l^0_{j,q} - 1 \in L$. Secondly, several variables in the model of unit $j \in U$ at Level 1 are related to the analogous variables in the general flow sheet model at Level 0:

- Starting time $t^{j,s}$ of the unit procedure at Level 1 is calculated from the starting time t^s at Level 0 and the duration t_l of stages that precede $l^0_{j,q}$ at Level 0, by:

$$\underset{q\in Q}{\veebar} \begin{bmatrix} W_{j,q} \\ t^{j,s} = t^s + \sum_{l=1}^{l^0_{j,q}-1} t_l \end{bmatrix}, \ \forall j \in U; \tag{3.11}$$

- Stage durations t^j_k at Level 1 are set to be equal to the duration of corresponding stages t_l at Level 0, by:

$$\underset{q\in Q}{\veebar} \begin{bmatrix} W_{j,q} \\ t_l = t^j_{l-l^0_{j,q}+1}, \\ \forall l \in \left\{l^0_{j,q}, ..., |K_j| + l^0_{j,q} - 1\right\} \end{bmatrix}, \ \forall j \in U; \tag{3.12}$$

- Input variables ($F^j_{m^{in},k}(t)$ and $x^j_{c,m^{in},k}(t)$, $\forall c \in C$) in input pipeline at Level 1 $m^{in} \in M^{in}_j$ are set to be equal to their analogous variables ($F_{n^{in},l}(t)$ and $x_{c,n^{in},l}(t), \forall c \in C$) in the corresponding pipeline at Level 0 $n^{in} \in N^{in}_j$. In non-synchronized stages at Level 0, these variables are fixed to zero, as well as in the case that no task is assigned to unit $j \in U$ ($Y_j = false$). The resulting equation reads as:

$$\underset{q\in Q}{\veebar} \begin{bmatrix} W_{j,q} \\ F_{n^{in},l}(t) = F^j_{m^{in},l-l^0_{j,q}+1}(t), \\ x_{c,n^{in},l}(t) = x^j_{c,m^{in},l-l^0_{j,q}+1}(t), \\ t \in [0,1], \forall l \in \left\{l^0_{j,q}, ..., |K_j| + l^0_{j,q} - 1\right\}, \\ F_{n^{in},l}(t) = 0, \ x_{c,n^{in},l}(t) = 0, \\ t \in [0,1], \forall l \in L \backslash \left\{l^0_{j,q}, ..., |K_j| + l^0_{j,q} - 1\right\} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ F_{n^{in},l}(t) = 0, \\ x_{c,n^{in},l}(t) = 0, \\ t \in [0,1], \\ \forall l \in L \end{bmatrix}, \quad \forall j \in U; \tag{3.13}$$

- Output variables ($F^j_{m^{out},k}(t)$ and $x^j_{c,m^{out},k}(t), \forall c \in C$) in output pipeline at Level 1 $m^{out} \in M^{out}_j$ are set to be equal to their analogous variables ($F_{n^{out},l}(t)$ and $x_{c,n^{out},l}(t), \forall c \in C$) in the corresponding pipeline at Level 0 $n^{out} \in N^{out}_j$. The definition of output variables follows the same pattern than input variables above:

$$\underset{q\in Q}{\veebar} \begin{bmatrix} W_{j,q} \\ F_{n^{out},l}(t) = F^j_{m^{out},l-l^0_{j,q}+1}(t), \\ x_{c,n^{out},l}(t) = x^j_{c,m^{out},l-l^0_{j,q}+1}(t), \\ t \in [0,1], \forall l \in \left\{l^0_{j,q}, ..., |K_j| + l^0_{j,q} - 1\right\}, \\ F_{n^{out},l}(t) = 0, \ x_{c,n^{out},l}(t) = 0, \\ t \in [0,1], \forall l \in L \backslash \left\{l^0_{j,q}, ..., |K_j| + l^0_{j,q} - 1\right\} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ F_{n^{out},l}(t) = 0, \\ x_{c,n^{out},l}(t) = 0, \\ t \in [0,1], \\ \forall l \in L \end{bmatrix}, \quad \forall j \in U. \tag{3.14}$$

3.3.4 Process stages

Process stage selection

Selection of process stage $i \in PS$ is represented by logical variable Z_i. In case that a process stage is mandatory, Z_i is fixed to be *true* and does not require any additional element in the superstructure. On the contrary, if the selection of such task is optional, a splitter controlled by Z_i is required in the process superstructure, as is shown in Figure 3.9. Such splitter determines whether the output flow of preceding task is directed to the process stage i or bypassed to the following task. It is worth to note that both alternatives have to be exclusive, what is defined as follows:

$$\begin{bmatrix} Z_i \\ F_{b,l}(t) = 0,\ t \in [0,1], \forall l \in L \end{bmatrix} \veebar \begin{bmatrix} \neg Z_i \\ F_{b,l}(t) = F_{n,l}(t),\ t \in [0,1], \forall l \in L \end{bmatrix}, \quad \forall n \in N_i^{in}, \forall b \in N_i^b, \forall i \in PS. \tag{3.15}$$

Operating mode or configuration

Out of the set of allowed configurations Ψ^i in each process stage $i \in PS$, only one can be selected. For that, the following proposition is defined:

$$Z_i \Leftrightarrow \underset{\psi \in \Psi_i}{\veebar} X_\psi^i, \tag{3.16}$$

where $X_\psi^i, \psi \in \Psi_i$ is the configuration Boolean that represents the operating mode $\psi \in \Psi_i$ in process stage $i \in PS$. The principal purpose of configuration Booleans is to control the selected equipment items through $Y_j, j \in U$ and their task-unit assignment through $W_{j,q}, j \in U, q \in Q$ by relating such variables to each other. A logical proposition is defined for each configuration, complemented with Eq. 3.10. For the set $\Psi_i = \{\alpha, \beta, \pi, \sigma\}$, $i \in \{1\}$ in example 1, the following propositions are defined:

$$X_\alpha^i \Leftrightarrow W_{U_1,1} \wedge \neg Y_{U_2}, \tag{3.17}$$

$$X_\beta^i \Leftrightarrow W_{U_2,1} \wedge \neg Y_{U_1}, \tag{3.18}$$

$$X_\pi^i \Leftrightarrow W_{U_1,1} \wedge W_{U_2,1}, \tag{3.19}$$

$$X_\sigma^i \Leftrightarrow W_{U_1,1} \wedge W_{U_2,2}. \tag{3.20}$$

Additionally, configuration Booleans X_ψ^i enforce a specific flow distribution for each configuration $\psi \in \Psi_i$ in the process cell of task $i \in PS$. This is accomplished by restricting to zero the flow rates of a specific set of pipelines $N_{i,\psi}^0$ for each operating mode:

$$\underset{\psi \in \Psi_i}{\veebar} \begin{bmatrix} X_\psi^i \\ F_{n,l}(t) = 0,\quad t \in [0,1], \forall n \in N_{i,\psi}^0, \forall l \in L \end{bmatrix}, \quad \forall i \in PS. \tag{3.21}$$

3.3.5 Plant elements at Level 0

Active stages at Level 0

The bypass strategy (Oldenburg & Marquardt, 2008) is also applied at Level 0 to dismiss the set of stages $L \backslash L^a$ that are not necessary for each structural option, out of the $L^{\max}$ stages specified at this level. The set of active stages L^a depend on task Booleans Z_i and configuration Booleans X_ψ^i. When a plant item $j \in J \backslash U$ with semi-continuous procedure is used, the bypass strategy is not applied to the corresponding model in its entirety, but only to the set of extra stages for each structural solution as represented in Figure 3.11. Bypass stages are set by removing dynamic equations and constraints associated to j and enforcing stage durations t_l to zero in every extra stage $l \in L \backslash L^a$ as detailed next.

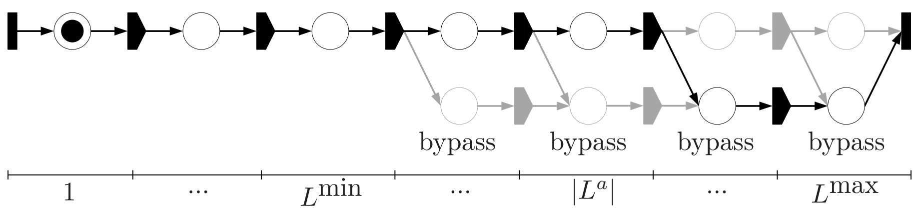


Figure 3.11: Petri net representing active stages $l \in L^a = \{1, ..., |L^a|\}$ and bypass stages $l \in L \backslash L^a = \{|L^a| + 1, ..., L^{\max}\}$ for semi-continuous elements at Level 0, where the set L^a is a function of the selected process stages $i \in PS$ and their corresponding configuration $\psi \in \Psi_i$. Grey elements represent feasible paths corresponding to other locations of stage $|L^a|$.

Models of plant elements with semi-continuous procedures

Time relations at Level 0 have the form:

$$\begin{aligned} T^f &= \textstyle\sum_{l \in L} t_l, \\ t^{end} &= t^s + T^f, \end{aligned} \tag{3.22}$$

where the total time T^f starts at initial time t^s, ends at final time t^{end} of the process control model, and is divided in $|L| = L^{\max}$ intervals with duration t_l. Stage duration should be set to zero in every extra stage $l \in L \backslash L^a$ in order to implement the bypass strategy represented in Figure 3.11. In contrast, this variable should be comprised between its lower $t^{\mathcal{L}}$ and upper $t^{\mathcal{U}}$ bounds in active stages $l \in L^a$:

$$\begin{gathered} t^{\mathcal{L}} \leq t_l \leq t^{\mathcal{U}}, \quad \forall l \in \{1, ..., |L^a|\}, \\ \text{bypass stages: } t_l = 0, \quad \forall l \in \{|L^a| + 1, ..., L^{\max}\}. \end{gathered} \tag{3.23}$$

The flow sheet model is also constructed at this level through mass balances in connecting nodes, by relating flow rates $F_{n,l}(t)$ and compositions $x_{c,n,l}(t)$, $c \in C$ of pipeline $n \in N$ and stage $l \in L$. Every mixer $j \in Mx$ has several input flows $|N_j^{in}| > 1$ and a single output flow $|N_j^{out}| = 1$ represented by n^{out} and is described by:

$$\sum_{n \in N_j^{in}} F_{n,l}(t) = F_{n^{out},l}(t), \quad t \in [0,1], \forall l \in L, \forall j \in Mx, \tag{3.24}$$

$$\sum_{n \in N_j^{in}} F_{n,l}(t) x_{c,n,l}(t) = F_{n^{out},l}(t) x_{c,n^{out},l}(t), \ t \in [0,1], \forall c \in C, \forall l \in L, \forall j \in Mx, \tag{3.25}$$

whereas every splitter $j \in Sp$ has a single input flow $|N_j^{in}| = 1$ represented by n^{in} and several output ones $|N_j^{out}| > 1$ and is described by:

$$F_{n^{in},l}(t) = \sum_{n \in N_j^{out}} F_{n,l}(t), \ t \in [0,1], \forall l \in L, \forall j \in Sp, \tag{3.26}$$

$$x_{c,n^{in},l}(t) = x_{c,n,l}(t), \ t \in [0,1], \forall c \in C, \forall n \in N_j^{out}, \forall l \in L, \forall j \in Sp. \tag{3.27}$$

According to Figure 3.4 of example 1: $N^{in}_{Mx_1}$={3, 6}, $N^{out}_{Mx_1}$={7}, $N^{in}_{Mx_2}$={5, 8}, $N^{out}_{Mx_2}$={9}, $N^{in}_{Sp_1}$={1}, $N^{out}_{Sp_1}$={2, 3}, $N^{in}_{Sp_2}$={4}, and $N^{out}_{Sp_2}$={5, 6}. It is not necessary to apply any special treatment to these equations in bypass stages. Flow rates of input and output pipelines to batch units $j \in U$ are enforced to zero in model stages where those units are not operating (Eq. 3.13 and 3.14), being this the case of bypass stages precisely. Through the relations in Eqs. 3.24 and 3.26 above, these variables oblige all other flow rates and compositions at Level 0 to take a zero value.

Additionally, models for storage units $j \in T$ are set up at Level 0, being their equations equally replicated in a $|L|$-stage model. Thus, such models can be also defined by functions $f^d_{j,l}$, l^d_j, $g^d_{j,l}$, $g^{d,e}_{j,l}$, h^d_j, and $m^d_{j,l}$ from Eq. 3.5 where $j \in T$ and $l \in L$. Since these units operate continuously, $f^d_{j,l}=f^d_{j,l+1}$, $g^d_{j,l}=g^d_{j,l+1}$ and $g^{d,e}_{j,l}=g^{d,e}_{j,l+1}$, $\forall l \in \{1, ..., L^{\max}-1\}$. Moreover, the bypass strategy is applied in two situations in their case. First, if storage $j \in T$ is not selected, the equations of the corresponding model are deactivated like in the case of batch units $j \in U$. Secondly, the bypass method is also applied to differentiate active L^a and bypass $L \backslash L^a$ stages according to Figure 3.11, provided that such storage unit is selected. Summarizing, the model of each storage tank $j \in T$ is defined by:

$$\begin{bmatrix} Y_j \\ f^d_{j,l}(\dot{z}_{j,l}(t), z_{j,l}(t), y_{j,l}(t), u^{dyn}_{j,l}(t), u^{stat}, u^{int}, p_j),\ t \in [0,1], \forall l \in \{1, ..., |L^a|\}, \\ l^d_j(\dot{z}_{j,1}(0), z_{j,1}(0)), \\ g^d_{j,l}(z_{j,l}(t), y_{j,l}(t), u^{dyn}_{j,l}(t), u^{stat}, u^{int}, p_j) \le 0,\ \ t \in [0,1], \forall l \in \{1, ..., |L^a|\}, \\ g^{d,e}_{j,l}(z_{j,l}(1), y_{j,l}(1), u^{dyn}_{j,l}(1), u^{stat}, u^{int}, p_j) \le 0,\ \ \forall l \in \{1, ..., |L^a|\}, \\ z_{j,l+1}(0) - m^d_{j,l}(z_{j,l}(1)) = 0,\ \ \forall l \in \{1, ..., |L^a|-1\}, \\ \gamma_j = h^d_j(z_{j,|L^a|}(1), y_{j,|L^a|}(1), u^{dyn}_{j,|L^a|}(1), u^{stat}, u^{int}, p_j), \\ \text{bypass stages: } B^d_j(\dot{z}_{j,l}(t), z_{j,l}(t), y_{j,l}(t), u^{dyn}_{j,l}(t), u^{stat}, u^{int}, \gamma_j, p_j) = 0, \\ t \in [0,1], \forall l \in \{|L^a|+1, ..., L^{\max}\} \end{bmatrix} \veebar \tag{3.28}$$
$$\begin{bmatrix} \neg Y_j \\ B^d_j(\dot{z}_{j,l}(t), z_{j,l}(t), y_{j,l}(t), u^{dyn}_{j,l}(t), u^{stat}, u^{int}, \gamma_j, p_j) = 0, t \in [0,1], \forall l \in L \end{bmatrix}, \quad \forall j \in T,$$

where $z^d_{j,l}(t)$, $z_{j,l}(t)$, and $u^{dyn}_{j,l}(t)$ are the time dependent differential, algebraic, and control variables in each stage $l \in L$, u^{stat} are time-invariant control variables, namely the stage durations t_l, u^{int} are the integer decisions such as the storage tank size, p_j are process parameters, and γ_j are the time-invariant variables which may contribute to the evaluation of the objective function or KPIs in unit $j \in T$. According to the superstructure of example 1 in Figure 3.4, storage input and output pipelines are $N^{out}_{T_{raw}}$={1} and $N^{in}_{T_{prod}}$={9}. Finally, the maximum volume restriction should be also formulated in the case of storage tanks, which reads as:

$$v^j_l(t) \le Size^j,\ \ t \in [0,1], \forall l \in L, \forall j \in T, \tag{3.29}$$

where $v^j_l(t)$ is the volume of material stored in unit $j \in T$ in stage $l \in L$, which can not surpass the size $Size^j$ of the storage tank.

Recirculation of intermediate material

The recirculation of an intermediate material flow to be used in the processing of a subsequent batch is associated to piping $n \in N^r$. In particular, this decision is controlled by Boolean variable R_n, which determines whether recirculation is allowed with a flow rate between the lower $F_n^{\mathcal{L}}$ and upper $F_n^{\mathcal{U}}$ bounds or not:

$$\left[\begin{matrix} R_n \\ F_n^{\mathcal{L}} \leq F_{n,l}(t) \leq F_n^{\mathcal{U}},\ t \in [0,1], \forall l \in L \end{matrix}\right] \veebar \left[\begin{matrix} \neg R_n \\ F_{n,l}(t) = 0,\ t \in [0,1], \forall l \in L \end{matrix}\right], \quad \forall n \in N^r. \tag{3.30}$$

In the superstructure, flow recirculation requires buffer tanks $j \in T_n^r$ that first store the intermediate material that is later supplied in a subsequent batch. The logical proposition reads as:

$$R_n \Leftrightarrow Y_j, \quad \forall j \in T_n^r, \forall n \in N^r. \tag{3.31}$$

Mathematically, the temporary sequence of model stages in input and output flows are related to the stages of interconnected sink and source units, instead of stages $l \in L$ in recirculation tanks T_n^r.

3.3.6 Batching

The batching problem consists of the division of the total product demand into a number of batches with a specific production size. Typical approaches to solve scheduling problem address the batching activity in a first stage, followed by a second one that includes allocation, timing, and task sequencing sub-problems. In the integrated batch process development problem here tackled, the batching is incorporated to the optimization model and solved simultaneously through the following equation:

$$NB_p\ Batch_p + Shortfall_p \geq Demand_p, \quad \forall p \in P, \tag{3.32}$$

where $Demand_p$ is the total demand, NB_p is the number of batches, $Batch_p$ is the production size associated to each batch, and $Shortfall_p$ is the unaccomplished demand of product $p \in P$.

3.3.7 Objective function

The decision criteria is to minimize an objective function Φ that reads as:

$$\underset{\substack{u_k^{dyn}(t), u^{stat}, \\ u^{int}, u^{Bool}}}{\text{minimize}} \quad \Phi\left(z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, u^{Bool}, \gamma_j, p\right) \tag{3.33}$$

according to the control variables $u_k^{dyn}(t) = \{F_{m,k}^j(t), int_k^j(t)\}$, $u^{stat} = \{t_l\}$, $u^{int} = \{NB_p, Size^j\}$, and $u^{Bool} = \{Z_i, Y_j, X_\psi^i, W_{j,q}, V_\lambda^j, S_c^j, R_n\}$ summarized in Table 3.3 and to the degrees of freedom following analyzed.

Degrees of freedom in the optimization model

The degrees of freedom (DOF) in the system is defined as the number of decision variables subtracting the number of equations and predefined decisions. This parameter determines the number of practical control variables. For instance, the number of **Boolean decisions** $u^{Bool} = \{Z_i, Y_j, X_\psi^i, W_{j,q}, V_\lambda^j, S_c^j, R_n\}$ is reduced by logical propositions (Eqs. 3.8, 3.10, 3.16, 3.17-3.20, 3.31). **Dynamic profiles of input and output stages** $F_{m,k}^j(t) \subseteq u_k^{dyn}(t)$

are also related to each other through global balances in mixers and splitters (Eqs. 3.24 and 3.26).

The evaluation of DOF is especially relevant in the case of input and output flow rates $F^j_{m,k}(t)$ to/from consecutive unit procedures. In fact, when the system is over-specified, the simultaneous consideration of all these flow rates as control variables deteriorates the performance of the solution procedure. Hence, the number of flow rates $F^j_{m,k}(t)$ of batch units $j \in U$ that should be considered as control variables in process stage $i \in PS$ corresponds to the degrees of freedom $DOF_{i,\psi}$ regarding flow rates at Level 0, which depends on the number of flow rates, the number of equations in splitters and mixers, and the number of fixed flow rates, as is defined in Table 3.2. Thus, $DOF_{i,\psi}$ varies with the number of restricted flow rates in pipelines $N^0_{i,\psi}$ in each configuration $\psi \in \Psi_i$ and with the number of flow rates defined in preceding process stage $ii \in PS\ |ii = i-1$, which corresponds to the cardinality of the set of pipelines N^f_i. This way, both inter- and intra-process stages relations are taken into account.

At this point, it is established that the outflow of every batch unit is always a control variable:

$$F^j_{m^{out},k}(t) \in u^{dyn}_k(t),\ t \in [0,1], \forall m^{out} \in M^{out}_j, \forall k \in O_j, \forall j \in U_i, \forall i \in PS, \tag{3.34}$$

and the number of free decision variables is limited through the inflows. Thus, only the input flows of the subset of batch units $D_{i,\psi} \subseteq U_i$ are established as control variables in configuration $\psi \in \Psi_i$ of process stage $i \in PS$. This subset is defined such that $|D_{i,\psi}| = DOF_{i,\psi} - |U_i|$, where $|U_i|$ represents the DOF removed by output flows in Eq. 3.34. The resulting equation reads as:

$$\underset{\psi \in \Psi_i}{\veebar} \left[\begin{array}{c} X^i_\psi \\ F^j_{m^{in},k}(t) \in u^{dyn}_k(t), t \in [0,1], \forall m^{in} \in M^{in}_j, \forall k \in I_j, \forall j \in D_{i,\psi} \end{array} \right], \forall i \in PS. \tag{3.35}$$

3.4 Summary and concluding remarks

In this chapter, the problem of integrated batch process development has been formulated as a MLDO problem which combines the decisions associated to different sub-problems, namely the synthesis of conceptual schemes, the plant allocation, and the plant design. As previously presented (§§ 1.1, 1.2, and 2.1), the simultaneous computation of their degrees of freedom is crucial to avoid suboptimal solutions in grassroots scenarios and to guarantee an improved plant utilization in retrofit situations.

The proposed modeling strategy relies on a SEN representation (Smith & Pantelides, 1995) of processing alternatives and on the combination of multistage models, GDP, and DO. Specifically, the SEN superstructure is comprised of the potential equipment items to allocate particular process stages and operations as well as the states in transfer operations. The mathematical formulation of the superstructure and the associated decisions is carried out by considering: (i) the coexistence of single-stage and multistage models to represent equipment items with semi-continuous and batch procedures respectively, (ii) the distribution of these models in two modeling levels in the SEN representation, (iii) the use of logical propositions to control qualitative decisions, and (iv) the synchronization of material transfer operations as a function of the selected processing route. The general form of the resulting MLDO model reads as:

$$
\begin{aligned}
\underset{\substack{u_k^{dyn}(t), u^{stat},\\ u^{int}, u^{Bool}}}{\text{minimize}} \quad & \Phi(z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, u^{Bool}, \gamma, p),\\
s.t. \quad & f_k(\dot{z}_k(t), z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, p) = 0,\ t \in [0,1], \forall k \in K,\\
& l(\dot{z}_1(0), z_1(0)) = 0,\\
& g_k(z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, p) \leq 0,\ \ t \in [0,1], \forall k \in K,\\
& g_k^e(z_k(1), y_k(1), u_k^{dyn}(1), u^{stat}, u^{int}, p) \leq 0,\ \ \forall k \in K,\\
& z_{k+1}(0) - m_k(z_k(1)) = 0,\ \ \forall k \in \{1, ..., |K|-1\},\\
& \gamma = h(z_{j,|K|}(1), y_{|K|}(1), u_{|K|}^{dyn}(1), u^{stat}, u^{int}, p),\\
& \begin{bmatrix} u^{Bool} \\ f_k^d(\dot{z}_k(t), z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, p) = 0, t \in [0,1], \forall k \in K, \\ l^d(\dot{z}_1(0), z_1(0)) = 0, \\ g_k^d(z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, p) \leq 0,\ \ t \in [0,1], \forall k \in K, \\ g_k^{d,e}(z_k(1), y_k(1), u_k^{dyn}(1), u^{stat}, u^{int}, p) \leq 0,\ \ \forall k \in K, \\ z_{k+1}(0) - m_k^d(z_k(1)) = 0,\ \ \forall k \in \{1, ..., |K|-1\}, \\ \gamma = h^d(z_{|K|}(1), y_{|K|}(1), u_{|K|}^{dyn}(1), u^{stat}, u^{int}, p) \end{bmatrix}\\
& \underline{\vee} \begin{bmatrix} \neg u^{Bool} \\ B^d(\dot{z}_k(t), z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, \gamma, p) = 0,\ t \in [0,1] \end{bmatrix},\\
& \Omega(u^{Bool}) = true,
\end{aligned}
\tag{3.36}
$$

where $z_k(t)$, $y_k(t)$, and $u_k^{dyn}(t)$ are the differential, algebraic, and control variables along time for each stage $k \in K$, where K is the set of mathematical stages defined for each element in the model, *e.g.* $K_j, \forall j \in U$ at Level 1 or L at Level 0. Let us note that the time has been normalized in each stage. u^{stat}, u^{int}, and u^{Bool} are the static, integer, and Boolean decision variables, all them detailed in Table 3.4. γ are the static algebraic variables evaluated at the final time of last stage $|K_j|$ and p are the model parameters. Φ is the objective function, l defines the initial conditions, h is the set of equations to calculate time-invariant variables, and f_k, g_k, g_k^e, and m_k are the DAE system, path constraints, end-point constraints, and stage-to-stage continuity in stage $k \in K$, which are hold independently to the Boolean decisions u^{Bool}. Accordingly, l^d, h^d, f_k^d, g_k^d, $g_k^{d,e}$, and m_k^d are the analogous functions that are hold in the case that variable u^{Bool} is $true$ in disjunctive equations and B^d defines the system in case that u_d^{Bool} is $false$. Finally, Ω is the set of logical propositions that infer qualitative knowledge by relating logical variables u^{Bool} to each other.

Overall, the proposed integrative approach based on optimization clearly contrasts with decomposition strategies which are more typically applied to address batch process development. Generally, cautious steps have been taken by the scientific community toward the use of optimization-based approaches that address a big number of decisions simultaneously in a single formulation. The principal reason is that of the sever complexity of the resulting problem and the risk of obtaining mathematically intractable systems. However, the proposed modeling strategy presents outstanding advantages, like: the great flexibility of the SEN superstructure, the modularity in the definition of each processing element through specific single-stage or multistage models, the possibility of evaluating the interactions between different unit procedures, the consideration of dynamic profiles optimization, the possibility of incorporating qualitative information and decisions into the model, and the introduction of synchronization constraints to ensure batch integrity in all processing alternatives. The matter on how to solve the MLDO problem is addressed in the next chapter.

Dynamic control variables $u_k^{dyn}(t)=\{F_{m,k}^j(t), int_k^j(t)\}$	
$F_{m,k}^j(t)$	Flow rate for every input and output pipeline $m \in M_j^{in} \cup M_j^{out}$ and batch phase $k \in K_j$ of unit $j \in U$
$int_k^j(t)$	Internal control variable in batch phase $k \in K_j$ of unit $j \in U$, *e.g.* reaction temperature
Time-invariant or static decision variables $u^{stat}=\{t_l\}$	
t_l	Duration of mathematical stage $l \in L$, which includes all batch operations $k \in K_j$ in all batch units $j \in U$
Integer decision variables $u^{int}=\{NB_p, Size^j\}$	
NB_p	Number of batches of product $p \in P$
$Size^j$	Capacity of unit $j \in U \cup T$
Boolean or logical decision variables $u^{Bool}=\{Z_i, Y_j, X_\psi^i, W_{j,q}, V_\lambda^j, S_c^j, R_n\}$	
Z_i	Process stage Boolean to indicate whether task $i \in PS$ is selected
Y_j	Equipment Boolean to indicate whether processing or storage unit $j \in U \cup T$ is selected
X_ψ^i	Configuration Boolean to indicate whether alternative $\psi \in \Psi_i$ of process stage $i \in PS$ is selected
$W_{j,q}$	Task-unit assignment Boolean to indicate whether unit procedure order $q \in Q$ is assigned to unit $j \in U$
V_λ^j	Technology Boolean to indicate whether technological specification $\lambda \in \Lambda_j$ of processing unit $j \in U$ is selected
S_c^j	Chemical compound Boolean to indicate whether reactant, solvent, or catalyst $c \in C_j^s$ in unit $j \in U$ is selected
R_n	Recirculation Boolean to indicate whether intermediate flow in pipeline $n \in N^r$ is recirculated

Table 3.4: Decision variables in integrated batch process development.

Chapter 4

Solution methods for integrated batch process development based on MLDO

"The effectiveness of the existing computer-aided solution methodologies varies for different classes of problems and is a strong function of the problem size, since most of the problems are NP-hard."
Stephanopoulos & Reklaitis (2011, p. 4297)

Different kinds of solution strategies can be used to tackle integrated batch process development formulated as a Mixed-Logic Dynamic Optimization (MLDO) problem. In this chapter, deterministic, stochastic, and hybrid solution methods are reviewed and specific procedures and methodologies are proposed. First, a classical deterministic method is detailed, namely a direct-simultaneous approach, which consists of the reformulation of the MLDO model into a Mixed-Integer Dynamic Optimization (MIDO) one to be following transformed into a Mixed-Integer Non-Linear Programming (MINLP) problem that is solved using conventional solution strategies. Next, a stochastic and a hybrid approach are proposed, representing solution alternatives to the deterministic method. Their goal is to keep solution goodness while seeking for the improvement of computational requirements. Specifically, a Differential Genetic Algorithm (DGA) and its combination with a deterministic direct-simultaneous approach that converts the problem into a Non-Linear Programming (NLP) are proposed and tested. The potential of the three strategies is compared and their suitability for the solution of small and large sized problems is evaluated.

4.1 State-of-the-art: MLDO solution methods

The solution of MLDO problems can be addressed using deterministic, stochastic, and hybrid solution methods. The majority of deterministic methods guarantee that a local optimum is found and most advanced algorithms are also able to provide global solutions under fairly general assumptions, *e.g.* Sahinidis (1996). Generally, deterministic methods are based on gradient analysis; thus, the solution of the MLDO model for simultaneous process synthesis and plant allocation becomes quite demanding due to its mathematical features, namely the presence of non-linearities and non-convexities, Boolean variables, discrete events, and dynamic profiles to define control variables. Consequently, stochastic solution methods are posed as a potential alternative to solve the integrated model, despite having the disadvantage that only near optimum solutions can be guaranteed, provided that suitable tuning parameters are found. Finally, hybrid methods combine both deterministic and stochastic approaches and can represent be a very attractive option to overcome their corresponding limitations.

4.1.1 Deterministic solution methods to solve MLDO

Several deterministic approaches to solve MLDO problems are available in the literature and current state-of-the-art –as it is reviewed by Stein et al. (2004) and Oldenburg & Marquardt (2008)– in order to address the problem of batch process development. These methodologies have been applied to solve similar problems in the context of continuous process synthesis (*e.g.* Raman & Grossmann, 1993, Türkay & Grossmann, 1996b, 1998), batch process design with structural decisions (*e.g.* Oldenburg, 2005), or jobshop scheduling (*e.g.* Lee & Grossmann, 2000). Basically, deterministic approaches are classified into three categories, which are illustrated in Figure 4.1. In the first place, classical solution strategies are based on the reformulation of the MLDO model into a MIDO to following apply mixed-integer solution strategies. A second alternative is continuous reformulation of Booleans to obtain DO problems that avoid the use of either logical or integer variables. Finally, logic-based search methods have been also developed, which directly attack the problem represented by its original logic formulation.

Classical solution strategies. The core idea of classical solution strategies is that every disjunctive optimization problem can be reformulated into a mixed-integer one (Balas, 1985, Grossmann & Hooker, 2000, Oldenburg & Marquardt, 2008), transforming the MLDO model into a MIDO. For that, Boolean variables $u^{Bool} \in \{true, false\}$ are replaced by binaries $u^{bin} \in \{0, 1\}$, disjunctive constraints are relaxed to mixed-integer equations, and logical propositions are expressed as linear constraints. The two main relaxation methods are big-M (Raman & Grossmann, 1991) and Convex-Hull Relaxation (CHR) (Balas, 1985, Türkay & Grossmann, 1998), among others like the binary multiplication which is detailed in next section (§ 4.2.1). Besides, logical propositions may lead systematically to linear constraints through their Conjunctive (CNF) (Clocksin & Mellish, 1981) or Disjunctive Normal Form (DNF) (Quine, 1952).

Next, the obtained MIDO problem can be solved using three different methods, namely: (i) Dynamic Programming (DP) based on Hamilton-Jacobi-Bellman formulation to transform the original problem into a system of partial differential equations (Bellman, 1957, Luus, 1990), (ii) indirect methods through necessary conditions of optimality (NCO) derived from Pontryagin's formulation (Bryson & Ho, 1975), or (iii) direct methods which convert the time-continuous optimization problem into a finite-dimensional nonlinear programming problem by discretization. These methods have specific advantages and disadvantages. The interested reader in this topic is addressed to the comparative overviews by Binder et al. (2001) and Srinivasan et al. (2003). Briefly, Dynamic Programming is very attractive because it is one of the few methods that provide global solutions. However, its application is restricted to problems with small dimension. As for indirect methods, they have the drawback of requiring suitable initial guesses for the trajectories of process variables and the switching structure of the optimal solution. Moreover, they

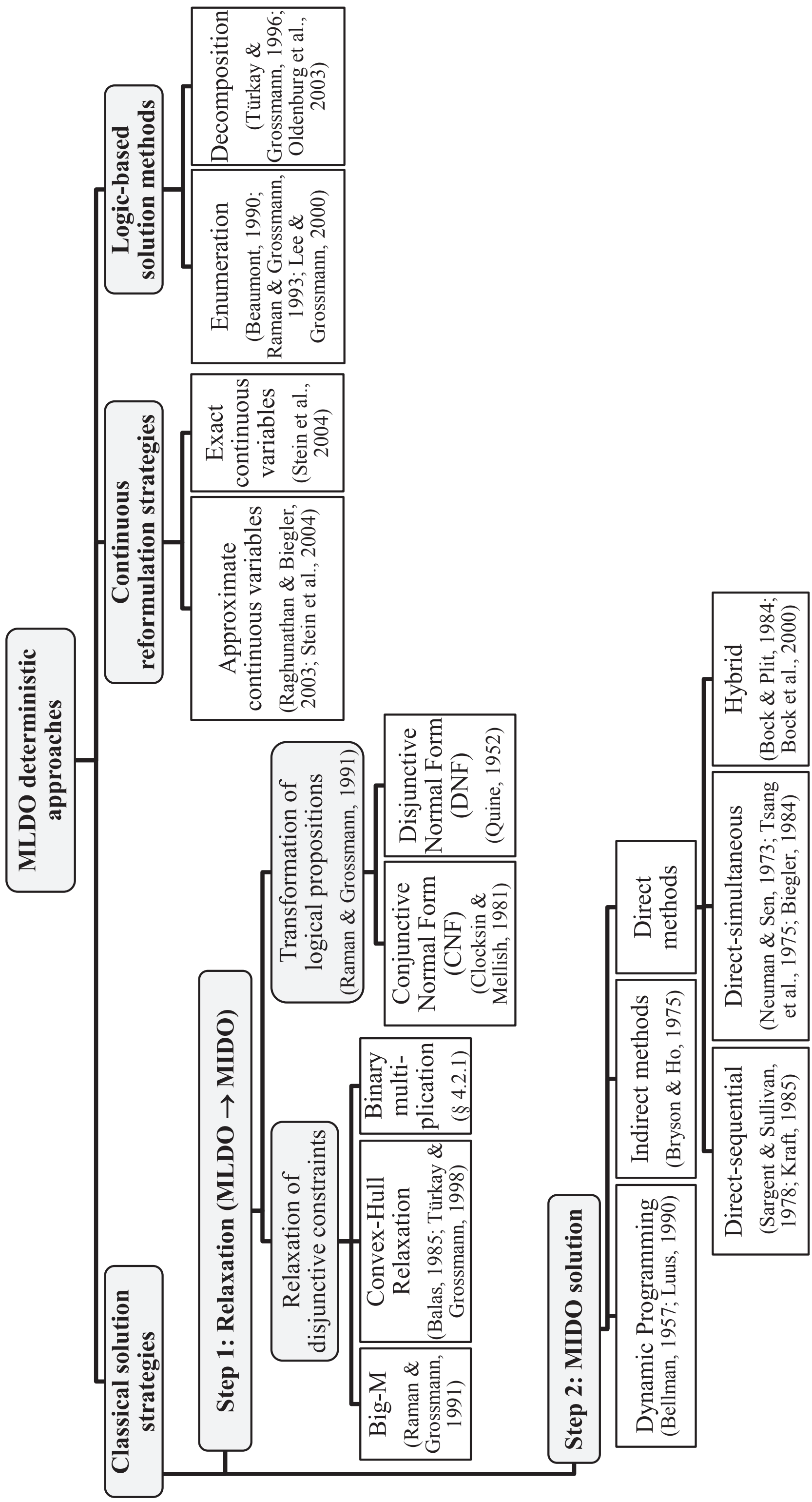


Figure 4.1: Deterministic solution methods for MLDO problems.

are subject to the existence of necessary conditions of optimality. In contrast, direct methods do not require an explicit derivation of the necessary conditions of optimality and the adjoin equations. These techniques rely on the discretization of time-dependent variables of the original problem to obtain some form of Mathematical Programming (MP) problems such as Non-Linear Programming (NLP) or Mixed-Integer Non-Linear Programming (MINLP). The possibility to exploit widespread NLP and MINLP solution strategies and well established solvers is the principal advantage of classic approaches.

In fact, depending on the way how the variables are discretized, direct methods can be divided into sequential (originally introduced by Sargent & Sullivan, 1978, Kraft, 1985) and simultaneous ones (originally introduced by Neuman & Sen, 1973, Tsang et al., 1975, Biegler, 1984). The former are based on discretizing control variables and solving the dynamic model numerically with a suitable integration method at each iteration step (Schlegel, 2004). The latter methods consist of fully discretizing the dynamic model to approximate both state and control variable profiles at the same time (Biegler, 2007), as it is later detailed in § 4.2.1. Sequential methods are well-suited for large-scale because the problem dimension does not increase excessively. In contrast, simultaneous methods do not require sensitivities, second order derivatives computation, and obligatory variable continuity to be solved. In order to exploit the advantages of both approaches, sequential and simultaneous methods are combined in hybrid methodologies, such as direct multiple shooting (originally introduced by Bock & Plitt, 1984, Bock et al., 2000), where the dynamic model is numerically integrated independently in subintervals of the time horizon.

Continuous reformulation of Booleans. Later, a strategy that allowed to transform Booleans into continuous variables to obtain a purely continuous optimization problem was posed (Raghunathan & Biegler, 2003, Stein et al., 2004), which is referred to as continuous reformulation of Booleans. For that, additional complementarity or equilibrium constraints are necessary to enforce the continuous variables representing discrete events to take discrete values, although inevitably imply new nonlinear terms into the model. Originally, Raghunathan & Biegler (2003) used approximated continuous variables to replace discrete variables, leading to non-linear degenerate constraints. This is the case of reformulation by complementarity condition (Raghunathan & Biegler, 2003) and reformulation by circle condition (Stein et al., 2004). Later, Stein et al. (2004) found out that using exact continuous variables would lead to non-degenerate constraints with better theoretical features. For instance, these authors proposed to reformulate the problem through binary multiplication or tailored big-M constraints. Overall, the principal advantage of relaxing the MLDO problem by means of continuous variables is that of obtaining purely continuous NLP problems. Due to the elusion of the combinatorial part of the problem, NLP solution algorithms are more efficient than mixed-integer ones.

Logic-based solution techniques. Finally, logic-based solution techniques have been also developed by adapting original mixed-integer solution algorithms to mixed-logic ones, either based on enumeration (*e.g.* Beaumont, 1990, Raman & Grossmann, 1993, Lee & Grossmann, 2000) or on decomposition (*e.g.* Türkay & Grossmann, 1996b, Oldenburg et al., 2003). The leverage of logic-based methods is not only to avoid the reformulation of the original MLDO model, but also to be able to exploit the logical structure of the problem. For instance, in the case of Branch-and-Bound (B&B), the problem size may be reduced at each node by using logical knowledge to remove the slack equations of *false* disjunctive terms (Beaumont, 1990). Moreover, the number of nodes to be enumerated may be reduced by using logical and symbolic inference to decide on the branching of variables and whether additional variables can be fixed at each node (Raman & Grossmann, 1993). This way, Lee & Grossmann (2000) reported a logic-based B&B algorithm for non-linear problems. In turn, Türkay & Grossmann (1996b) developed logic-based decomposition algorithms, namely logic-based methods based on Outer Approximation (OA) and Generalized Benders Decomposition (GBD). Such algorithms lead to disjunctive linear (LP) master problems and non-linear (NLP) primal problems, characterized by: a smaller number of equations, the elimination of zero flows, and the reduction of non-convexities in those constraints associated to non-selected disjunctions. Next, the logic-based OA method was extended to include dynamic equations by Oldenburg et al. (2003), who proposed a tailored, logic-based solution algorithm.

4.1.2 Stochastic and hybrid solution methods to solve MLDO: Genetic Algorithms

Stochastic and hybrid approaches are another challenging option to address optimization problems due to their simple concept, plain structure, and independence of gradient information. In fact, these strategies are considered as a practical alternative to deterministic algorithms in the area of Operations Research (Reeves & Rowe, 2003). Particularly, stochastic approaches consist of heuristic procedures that use random searching algorithms to reach near optimum solutions. One of the most extended stochastic optimization methods would be the so-called **Genetic Algorithm** (GA) proposed by Holland (1975) and Hollstien (1971), an evolutionary algorithm that evokes natural evolution. Such methods improve the solution through an adaptive search procedure that selects and combines the better solutions found at each iteration. Regarding hybrid methods, these consist of stochastic procedures complemented by deterministic methods in order to provide optimal solutions.

In the context of PSE, stochastic and hybrid approaches have been successfully applied to different types of optimization problems. Specifically, there are several reported applications of GAs in optimization problems like scheduling (*e.g.* Murata et al., 1996, Gonçalves et al., 2005, Capón-García, 2011, Bai et al., 2012, among others) and supply chain management (*e.g.* Altiparmak et al., 2009, Kannan et al., 2010, among others). Process synthesis problems are also an important area of application of GAs and other evolutionary algorithms, such as Tabu Search (TS), Simulated Annealing (SA), or Harmony Search (HS). For example, the synthesis of different process systems have been considered in the literature, such as heat exchanger networks (HENs) (*e.g.* Wang et al., 1998, Ravagnani et al., 2005, Ponce-Ortega et al., 2007, Gorji-Bandpy et al., 2011, among others) or the design of distillation sequences (*e.g.* Fraga & Senos Matias, 1996, Leboreiro & Acevedo, 2004, García-Herreros et al., 2011, among others).

Most of the aforementioned problems were formulated as Mixed-Integer Linear Programming (MILP) and Mixed-Integer Non-Linear Programming (MINLP) problems, where the discrete and continuous variables were treated either together –*i.e.* using the so-called mixed-coded stochastic and hybrid methods– or separately –*i.e.* using the so-called two-level optimization strategies where the integer and the non-linear parts of the problem are solved iteratively by using stochastic-deterministic or stochastic-stochastic strategies. Moreover, all these contributions were focused on static problems, where the dynamic behavior of batch operations along time is not represented, thus avoiding the use of DAE systems and the definition of dynamic trajectories for the control variables.

Regarding stochastic solution procedures for DO problems, the particular extension of GAs termed **Differential Genetic Algorithms (DGAs)** (Michalewicz et al., 1992) constituted a suitable approach because it allowed that some decision variables were expressed as vectors of discretized dynamic control trajectories. In fact, DGAs represent purely stochastic approaches to solve optimal control problems. Many contributions can be found in this direction (*e.g.* Lee et al., 1999, Li et al., 2008, Lopez Cruz et al., 2003, Michalewicz et al., 1992, Upreti, 2004, and many others).

Going a step further, Wongrat et al. (2011) proposed a two-level optimization strategy combining stochastic-deterministic algorithms. Specifically, the hybrid method was based on a MIDO formulation and conventional GAs to solve simultaneously the synthesis and operational design of individual units with transient regimes. This approach attacked the integrated problem by combining GAs with deterministic direct-sequential methodologies. Due to the use of conventional GAs, the dynamic profiles were optimized in the deterministic step of the procedure while the stochastic part focused only on equipment synthesis decisions.

To the author's knowledge, there is no contribution that carries out the explicit solution of mixed-logic problems by means of evolutionary algorithms that incorporate logical variables and equations.

4.2 Application of deterministic methods

Classical deterministic methods are the most extended to solve MLDO problems because they allow to exploit the advantages of mixed-logic modeling –*e.g.* the incorporation of previous knowledge and rules to optimization-based approaches– and, through the reformulation of the optimization model, they still permit to use well established MIDO solution strategies. As seen in previous section (§ 4.1), classical methods comprise two steps: (1) the reformulation of the mixed-logic (MLDO) model into a mixed-integer (MIDO) one and (2) the MIDO solution, which in turn can be addressed through different strategies.

Among the different classical methods, direct-simultaneous strategies deal with the MIDO solution by means of a full discretization of the dynamic model, thus approximating process and control variable profiles to finite points along the time horizon. As a result, a MINLP is obtained. The possibility to exploit widespread mixed-integer programming strategies and established MINLP solvers to solve the problem has motivated the selection of a direct-simultaneous approach to attack the MLDO problem for integrated batch process development. Specifically, the proposed strategy includes several tools, namely binary multiplication, CNF reformulation, orthogonal collocation on finite elements, and the use of initial feasible solutions (IFS) to initialize the search procedure, as is following detailed.

4.2.1 Direct-simultaneous method

The proposed direct-simultaneous method is divided in two steps: (1) the reformulation of the MLDO into a MIDO and (2) the MIDO solution.

Step 1: Relaxation of the MLDO into a MIDO

Classical methods are based on the relaxation of the original MLDO problem into a MIDO one. For that, three transformations are required. First, Boolean variables $u^{Bool} \in$

$\{true, false\}$ are replaced by binaries $u^{bin} \in \{0,1\}$. Thus, the vector of Boolean decision variables $u^{Bool} = \{Z_i, Y_j, X_\psi^i, W_{j,q}, V_\lambda^j, S_c^j, R_n\}$, presented in Table 3.4 is transformed into a vector of binary variables $u^{bin} = \{z_i, y_j, x_\psi^i, w_{j,q}, v_\lambda^j, s_c^j, r_n\}$, whose 0 and 1 values correspond to prior $false$ and $true$ values respectively.

Following, disjunctive equations are transformed into mixed-integer ones. This transformation is done through **binary multiplication**, which is a further alternative to big-M (Raman & Grossmann, 1991) and CHR (Türkay & Grossmann, 1998), as summarized in Figure 4.1. Specifically, differential and algebraic variables $\dot{z}_k(t)$, $z_k(t)$, and $y_k(t)$, and time-invariant variables γ are decomposed into contributions $\dot{z}_{k,i}(t)$, $z_{k,i}(t)$, $y_{k,i}(t)$, and γ_i for each disjunctive term $i \in ID$ of disjunctive equations, which are multiplied by their corresponding binary variable u_i^{bin}. Thus, the following example function $f_{k,i}^d$:

$$\underset{i \in ID}{\veebar} \begin{bmatrix} u_i^{Bool} \\ f_{k,i}^d(\dot{z}_k(t), z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, \gamma, p) = 0, \\ t \in [0,1], \forall k \in K \end{bmatrix} \tag{4.1}$$

is reformulated into the form:

$$\begin{gathered} f_{k,i}^d(\dot{z}_{k,i}(t), z_{k,i}(t), y_{k,i}(t), u_k^{dyn}(t), u^{stat}, u^{int}, \gamma_i, p) = 0,\ t \in [0,1], \forall k \in K, i \in ID, \\ \dot{z}_k(t) = \sum_{i \in ID} \dot{z}_{k,i}(t)\, u_i^{bin},\ \ z_k(t) = \sum_{i \in ID} z_{k,i}(t)\, u_i^{bin},\ \ y_k(t) = \sum_{i \in ID} y_{k,i}(t)\, u_i^{bin},\ \ \forall k \in K, \\ \gamma_i = \sum_{i \in ID} \gamma_i\, u_i^{bin}, \qquad \sum_{i \in ID} u_i^{bin} = 1. \end{gathered} \tag{4.2}$$

Disjunctive equations of the MLDO model of Eq. 3.36 include only two terms which can be represented by one single binary u^{bin}: term u^{Bool} ($i = 1$ where $u_1^{bin} = u^{bin}$) and term $\neg u^{Bool}$ ($i = 0$ where u_0^{bin}=1-u^{bin}). Therefore, disjunctions are transformed into the following set of equations:

$$\begin{gathered} f_k^d(\dot{z}_{k,1}(t), z_{k,1}(t), y_{k,1}(t), u_k^{dyn}(t), u^{stat}, u^{int}, p) = 0,\ t \in [0,1], \forall k \in K, \\ l^d(\dot{z}_{1,1}(0), z_{1,1}(0)) = 0, \\ g_k^d(z_{k,1}(t), y_{k,1}(t), u_k^{dyn}(t), u^{stat}, u^{int}, p) \leq 0,\ \ t \in [0,1], \forall k \in K, \\ g_k^{d,e}(z_{k,1}(1), y_{k,1}(1), u_k^{dyn}(1), u^{stat}, u^{int}, p) \leq 0,\ \ \forall k \in K, \\ z_{k+1,1}(0) - m_k^d(z_{k,1}(1)) = 0,\ \ \forall k \in \{1, ..., |K|-1\}, \\ \gamma_1 = h^d(z_{|K|,1}(1), y_{|K|,1}(1), u_{|K|}^{dyn}(1), u^{stat}, u^{int}, p) \\ B^d(\dot{z}_{k,0}(t), z_{k,0}(t), y_{k,0}(t), u_k^{dyn}(t), u^{stat}, u^{int}, \gamma_0, p) = 0,\ t \in [0,1] \\ \dot{z}_k(t) = \dot{z}_{k,1}(t)\ u^{bin} + \dot{z}_{k,0}(t)\ (1 - u^{bin}),\ \ t \in [0,1], \forall k \in K, \\ z_k(t) = z_{k,1}(t)\ u^{bin} + z_{k,0}(t)\ (1 - u^{bin}),\ \ t \in [0,1], \forall k \in K, \\ y_k(t) = y_{k,1}(t)\ u^{bin} + y_{k,0}(t)\ (1 - u^{bin}),\ \ t \in [0,1], \forall k \in K, \\ \gamma = \gamma_1\ u^{bin} + \gamma_0\ (1 - u^{bin}). \end{gathered} \tag{4.3}$$

Finally, logical propositions are expressed as linear constraints. This transformation can be done systematically by formulating the CNF of the original logical equations to obtain an expression like $C_1 \wedge C_2 \wedge ... \wedge C_N$ where C_n are the clauses that must be $true$ in the problem, which are related by "and" operators ($\wedge$). This procedure involves the application of a series of pure logical operations, which were first formalized by Clocksin & Mellish (1981) as is reported by Raman & Grossmann (1991). The operations are:

1. To replace the implication by its equivalent disjunction:

$$u_1^{Bool} \Rightarrow u_2^{Bool} \quad \Leftrightarrow \quad \neg u_1^{Bool} \vee u_2^{Bool}; \tag{4.4}$$

2. To move the negation inward by applying DeMorgan's Theorem:
$$\neg(u_1^{Bool} \wedge u_2^{Bool}) \;\Leftrightarrow\; \neg u_1^{Bool} \vee \neg u_2^{Bool}, \tag{4.5}$$
$$\neg(u_1^{Bool} \vee u_2^{Bool}) \;\Leftrightarrow\; \neg u_1^{Bool} \wedge \neg u_2^{Bool}, \tag{4.6}$$
3. To recursively distribute the "or" operator ($\vee$) over the "and" operator ($\wedge$) by using the following equivalence:
$$(u_1^{Bool} \wedge u_2^{Bool}) \vee u_3^{Bool} \;\Leftrightarrow\; (u_1^{Bool} \vee u_3^{Bool}) \wedge (u_2^{Bool} \vee u_3^{Bool}). \tag{4.7}$$

Once obtained the CNF $C_1 \wedge C_2 \wedge ... \wedge C_N$, each clause C_n is transformed into an algebraic equality or inequality using the relation between logical and algebraic expressions summarized in Table 4.1. All these transformation should be applied to the set of logical propositions Ω of Eq. 3.36, which is reformulated into an algebraic equations system:
$$\Omega(u^{bin}) \leq 0. \tag{4.8}$$

Logical operator	Logical expression	Algebraic equation
Conjunction "and" ($\wedge$)	$u_1^{Bool} \wedge u_2^{Bool} \wedge ... \wedge u_N^{Bool}$	$u_1^{bin} \geq 1, u_2^{bin} \geq 1, ...u_N^{bin} \geq 1$
Disjunction "or" ($\vee$)	$u_1^{Bool} \vee u_2^{Bool} \vee ... \vee u_N^{Bool}$	$u_1^{bin} + u_2^{bin} + ... + u_N^{bin} \geq 1$
"exclusive or" ($\veebar$)	$u_1^{Bool} \veebar u_2^{Bool} \veebar ... \veebar u_N^{Bool}$	$u_1^{bin} + u_2^{bin} + ... + u_N^{bin} = 1$
Implication ($\Rightarrow$)	$u_1^{Bool} \Rightarrow u_2^{Bool}$	$1 - u_1^{bin} + u_2^{bin} \geq 1$
	or $\neg u_1^{Bool} \vee u_2^{Bool}$	or $u_1^{bin} - u_2^{bin} \leq 0$
Equivalence ($\Leftrightarrow$)	$(u_1^{Bool} \Rightarrow u_2^{Bool}) \wedge (u_2^{Bool} \Rightarrow u_1^{Bool})$	$u_1^{bin} - u_2^{bin} \leq 0,\; u_2^{bin} - u_1^{bin} \leq 0$
	or$(\neg u_1^{Bool} \vee u_2^{Bool}) \wedge (\neg u_2^{Bool} \vee u_1^{Bool})$	or $u_1^{bin} = u_2^{bin}$

Table 4.1: Basic logical operators expressed using logical and algebraic equations (Raman & Grossmann, 1991).

Step 2: MIDO solution

The resulting MIDO problem is solved using a direct-simultaneous approach, based on the full discretization of the dynamic model by approximating state and control variable profiles through a set of polynomials on finite times (Neuman & Sen, 1973, Tsang et al., 1975, Biegler, 1984). In particular, this thesis uses the orthogonal collocation method originally introduced by Cuthrell & Biegler (1989) to solve optimal control problems which have discontinuous control profiles, as it is the case of the batch processes with phase transitions handled herein. Details of the stability, symmetry, and accuracy properties rendered by this strategy can be found in the paper by Cuthrell & Biegler (1989, §3.1).

The orthogonal collocation method consists of dividing the time axis into a number of intervals –termed finite elements– and specific time points –termed collocation points– and approximating the state and control variable profiles, as it is represented in Figure 4.2. The location of the collocation points can be carried out by computing the roots of orthogonal polynomials, *e.g.* roots of Hermite polynomials, Laguerre polynomials, Jacobi polynomials, Chebyshev polynomials, or Legendre polynomials, among others. As for the approximation of the state and control variables, monomial basis representations can be used, which are defined through different forms, such as power series, Lagrange form representation, or Runge-Kutta equations.

In this thesis, the collocation points are calculated using a shifted Legendre polynomial, say $P(\tau)$, of order $M = 3$, which is defined as:
$$P(\tau) = 20\,\tau^3 - 30\,\tau^2 + 12\,\tau - 1. \tag{4.9}$$

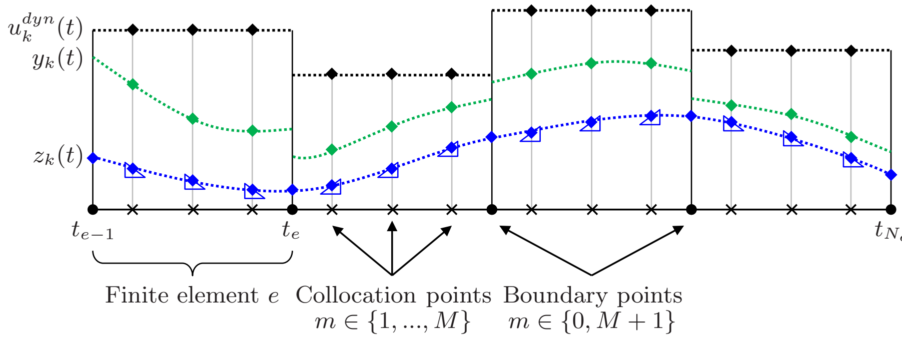


Figure 4.2: Finite elements discretization for differential $z_k(t)$, algebraic $y_k(t)$, and control $u_k^{dyn}(t)$ variable profiles, where continuity is only enforced for the fist ones. Diamonds represent $z_{k,e,m}$, $y_{k,e,m}$, and $u_{k,e,m}^{dyn}$ and triangles represent $\dot{z}_{k,e,m}$ approximations in finite elements $e \in \{1, ..., N_e\}$ and points $m \in \{0, 1, ..., M, M+1\}$.

The roots of the above polynomial provide the normalized locations $\tau_m = \{0.1127, 0.5000, 0.8873\}$ of collocation points $m \in \{1, ..., M\}$, in addition to the boundary points located at $\tau_0 = 0$ and $\tau_{M+1} = 1$, as is illustrated in Figure 4.2. Moreover, Lagrange polynomials are implemented to approximate the state and control variables. In particular, the polynomials for the differential $z_k(t)$, algebraic $y_k(t)$, and control $u_k^{dyn}(t)$ variables and the derivative $\dot{z}_k(t)$ in finite element $e \in \{1, ..., N_e\}$ have the following form:

$$\begin{aligned} z_k(t) &= \sum_{m=0}^{M} z_{k,e,m}\, \phi_m(t), & \dot{z}_k(t) &= \sum_{m=0}^{M} z_{k,e,m}\, \dot{\phi}_m(t), \\ y_k(t) &= \sum_{m=1}^{M} y_{k,e,m}\, \theta_m(t), & u_k^{dyn}(t) &= \sum_{m=1}^{M} u_{k,e,m}^{dyn}\, \theta_m(t), \end{aligned} \tag{4.10}$$

where $z_{k,e,m}$, $y_{k,e,m}$, and $u_{k,e,m}^{dyn}$ represent the approximations of the differential, algebraic, and control variables in finite element $e \in \{1, ..., N_e\}$ in collocation or boundary points $m \in \{0, 1, ..., M, M+1\}$, $M = 3$, with normalized locations $\tau_m = \{0,\ 0.1127,\ 0.5000,\ 0.8873,\ 1\}$. $\phi_m(t)$ and $\theta_m(t)$ are the basis functions defined by:

$$\phi_m(t) = \prod_{\substack{m'=0,\\ m' \neq m}}^{M} \frac{(t - t_{e,m'})}{(t_{e,m} - t_{e,m'})}, \qquad \theta_m(t) = \prod_{\substack{m'=1,\\ m' \neq m}}^{M} \frac{(t - t_{e,m'})}{(t_{e,m} - t_{e,m'})}. \tag{4.11}$$

According to Eqs. 4.10 and 4.11, the polynomials of differential variables $z_k(t)$ have been defined to be one order higher M^{th} than the polynomials of algebraic $y_k(t)$ and control variables $u_k^{dyn}(t)$, with order $(M-1)^{th}$. The reason is that polynomials with order M^{th} allow to define the boundary conditions of differential variables $z_{k,e,0}$ in each finite element e thanks to the symmetry properties of the method, what is necessary to enforce their continuity from previous element $e-1$ in time t_e. Thus, accurate initial conditions $z_{k,e,0} = z_k(t_e) = z_{k,e-1,M+1}$ can be calculated through the evaluation of the first polynomial in Eq. 4.10 at the final point $\tau_{M+1} = 1$ of each finite element:

$$z_{k,e,0} = \sum_{m=0}^{M} z_{k,e-1,m}\, \phi_m(\tau_{M+1} = 1), \quad \forall e \in \{2, ..., N_e\}. \tag{4.12}$$

In contrast, continuity across neighboring elements is not necessary for algebraic and control variables, thus they are defined with a lower order $(M-1)^{th}$. Specifically, Figure 4.2

shows that control variables are approximated to a piecewise constant (PWC) function, by establishing $u^{dyn}_{k,e,m} = u^{dyn}_{k,e}$.

The resulting MINLP problem can be solved through a variety of search algorithms available in literature. For a thoughtful overview of MINLP solution approaches, the reader is addressed to the paper by Grossmann (2002). Essentially, the diverse strategies are either based on enumeration, such as Branch-and-Bound (B&B) methods with NLP subproblems (Nemhauser & Wolsey, 1988, Floudas, 1995, Leyffer, 2001), or on decomposition, such as Outer Approximation (OA) (Duran & Grossmann, 1986a, Kocis & Grossmann, 1987, Viswanathan & Grossmann, 1990, Fletcher & Leyffer, 1994) or Generalized Benders Decomposition(GBD) (Geoffrion, 1972).

On the one hand, the advantage of **decomposition approaches** compared to enumeration ones is their higher efficiency, since the problem is iteratively solved through MILP master problems with linearized equations and NLP primal problems with fixed integer variables. It should be noted that generally MILP models are handled efficiently while NLP models can be expensive and difficult to solve. However, this strategy can experience difficulties if many or all the NLP sub-models are infeasible or if the linearizations used for the MILP model create ill-conditioned models. Besides, only local optima can be guaranteed unless the nonlinear objective function and constraints are convex.

On the other hand, **enumeration strategies** like the B&B non-linear global optimization solver BARON (Sahinidis, 1996) may guarantee global solutions under fairly general assumptions, *e.g.* the availability of finite lower and upper bounds on the variables and their expressions in the NLP or MINLP to be solved. Nevertheless, these kinds of search strategies have the disadvantage of rendering costlier computational loads, since they operate through the systematic enumeration of integer combinations and have to solve a NLP problem for each integer solution.

Many of the MINLP solution algorithms have been implemented in commercial software. For example, the modeling systems GAMS (Brooke et al., 1988) or AIMMS (Bisschop & Entriken, 1993) provide an interface with solvers like: BARON, just mentioned, SBB, which combines the standard B&B method used for solving MILP problems with standard NLP solvers, or DICOPT, which is based on the OA algorithm (Duran & Grossmann, 1986a), among others.

In this thesis, DICOPT (Duran & Grossmann, 1986a) is used in most examples, using CONOPT 3.15D and CPLEX 12.4 to handle the NLP and MILP sup-problems in GAMS (Brooke et al., 1988) version 23.8.2. Being a decomposition-based strategy, global optimality can not be guaranteed due to the existence of non-convex terms in the model, *e.g.* the bilinear functions associated to the mixers. As a result, it is convenient to repeat the optimization procedure for several initial feasible solutions (IFS), in order to improve the chances to find a global optimum. Therefore, the problem is first solved with constant control profiles and fixed configurations chosen randomly to provide several IFS to the MINLP solver. This small heuristic contributes to the identification of local optima and to the success of the integrated solution of process development sub-problems.

4.3 Application of stochastic & hybrid methods

Stochastic and hybrid solution approaches are posed as an alternative to deterministic ones. Particularly, their purpose is to keep solution goodness while improving the solution performance and facilitating the assessment of larger dimension systems. The final objective is to find a suitable strategy which allows to handle industrial sized problems, which could include complex structural decisions and a large number of process stages to complete full production systems. In this thesis, due to the characteristics of the integrated batch process development problems to be solved, a Differential Genetic Algorithm (DGA) is selected because it considers the optimization of dynamic trajectories of control variables that may change along time. Overall, this method serves as a basis for the stochastic and the hybrid approaches proposed. The core idea is to combine in the DGA chromosomes the several decision variables that characterize the problem solution, in order to reduce the combinatorial complexity to be handled by the standard deterministic solvers. For that, the MIDO model is taken as an starting point, obtained from the original MLDO model in Eq. 3.36 with disjunctive equations and logic proposition reformulated into Eqs. 4.3 and 4.8 as explained in step 1 of the direct-simultaneous method (§ 4.2).

4.3.1 Vector of control variables

Genetic Algorithms (GAs) in general require that the several kinds of decision variables are combined in the so-called *vector of control variables*. Dynamic $u_k^{dyn}(t)$, time-invariant u^{stat}, integer u^{int}, and binary u^{bin} variables that replace Booleans u^{Bool} from Table 3.4 should be contained therein as degrees of freedom. Thus, the vector of control variables is here defined in three parts $C = \{c_I,\ c_{II},\ c_{III}\}$ as follows:

- **Dynamic control variables.** The profiles of dynamic control variables $u_k^{dyn}(t)$, including flow rates $F_{m,k}^j(t)$ and internal variables $int_k^j(t)$ like the reaction temperature, are discretized along the time horizon into a number of finite elements N_e by assuming a specific discretization profile. Particularly, a PWC behavior is selected, following the same discretization pattern for dynamic control variables than in the orthogonal collocation on finite elements strategy of the direct-simultaneous method (Figure 4.2). The PWC profile is represented in Figure 4.3, where the value of $u_k^{dyn}(t)$ in each finite element $e \in \{1, ..., N_e\}$ is approximated to $u_{k,e}^{dyn}$. Then, the first part of the vector is composed by the concatenated parameters $u_{k,e}^{dyn}$ characterizing the discrete function at each time interval e:

$$c_I = \{u_{k,e}^{dyn}\},\ \ u_{k,e}^{dyn} = \{F_{m,k,e}^j, int_{k,e}^j\},\ \ e \in \{1, ...N_e\}. \tag{4.13}$$

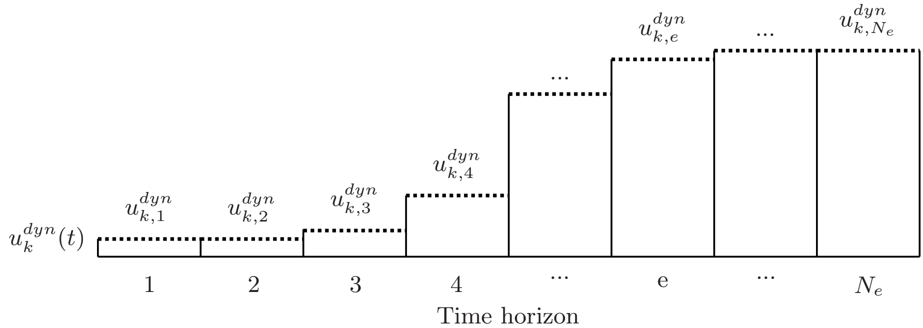


Figure 4.3: Discretization of dynamic control variables $u_k^{dyn}(t)$ into finite intervals $e \in \{1, ..., N_e\}$ using a PWC approximation.

- **Time-invariant decision variables.** Time-invariant or static decisions u^{stat} correspond to the duration of batch operations t_l and constitute the second part of the vector:

$$c_{II} = \{u^{stat}\}, \quad u^{stat} = \{t_l\}. \tag{4.14}$$

- **Integer and binary decisions.** The final part of the vector of control variables corresponds to integer decisions u^{int}, namely the number of batches NB_p and the equipment size $Size^j$, including binaries u^{bin}, like the task binary z_i, the equipment binary y_j, or the configuration binary x^i_ψ, among others:

$$\begin{gathered} c_{III} = \{u^{int}, u^{bin}\}, \\ u^{int} = \{NB_p, Size^j\}, \quad u^{bin} = \{z_i, y_j, x^i_\psi, w_{j,q}, v^j_\lambda, s^j_c, r_n\}. \end{gathered} \tag{4.15}$$

The sets of dynamic $u^{dyn}_k(t)$ and binary u^{bin} control variables, and hence the lengths of c_I and c_{III} respectively, can be reduced by analyzing the DOF according to the model equations and predefined variables, as was explained in Chapter 3 (§ 3.3.7). Specifically, global material balances in mixers Mx and splitters Sp and restricted flow rates in pipelines $N^0_{i,\psi}$ and N^f_i defined in functions f_k, f^d_k, and B^d from Eqs. 3.36 and 4.3 determine the reduction of DOF regarding $u^{dyn}_k(t)$. Additionally, relations Ω established in Eq. 4.8 affect the DOF regarding u^{bin}. The analysis of DOF of the problem to reduce the vector of control variables is useful to avoid over specified systems and thus limit the complexity of the optimization process.

4.3.2 Stochastic method: DGA

As justified above, the stochastic method used in this thesis is a DGA (Michalewicz et al., 1992) where the vector of control variables C (Eqs. 4.13 to 4.15) generates a chromosome of continuous and integer genes. According to the composition of C, the chromosome comprises three parts, illustrated in Figure 4.4. Particularly, each gene in the first part of the chromosome (I) represents the set of continuous variables $u^{dyn}_{k,e}$ from the discretization of each dynamic control variable $u^{dyn}_k(t)$. The second part of the chromosome (II) also contains genes of continuous variables, corresponding to the time-invariant controls u^{stat}. The last part of the chromosome (III) involves genes of integer variables u^{int} and of binary variables associated to the reduced vector of qualitative decisions u^{bin}.

The final goal is to drive an evolutionary search procedure that finds the better values for the vector of control variables C such that the objective function Φ is minimized. In this process, Φ has to be evaluated several times for each definition of the vector C along the search. To this end, the DAE system in the MIDO model (Eq. 3.36 with disjunctive equations and logic proposition reformulated into Eqs. 4.3 and 4.8, as explained in § 4.2.1) should be integrated. Moreover, inequality restrictions should be satisfied. However, since the method does not consider this type of constraints, they are eliminated from the MIDO equations system and are transformed into penalizations in the fitness function that evaluates the challenge of each individual inside a population. Thus, the fitness function $\Phi_{Fitness}$ is defined to include the original minimization objective function Φ and the penalization of model unsupported restrictions $f_p \cdot P$ as follows:

$$\Phi_{Fitness} = \Phi + f_p \cdot P. \tag{4.16}$$

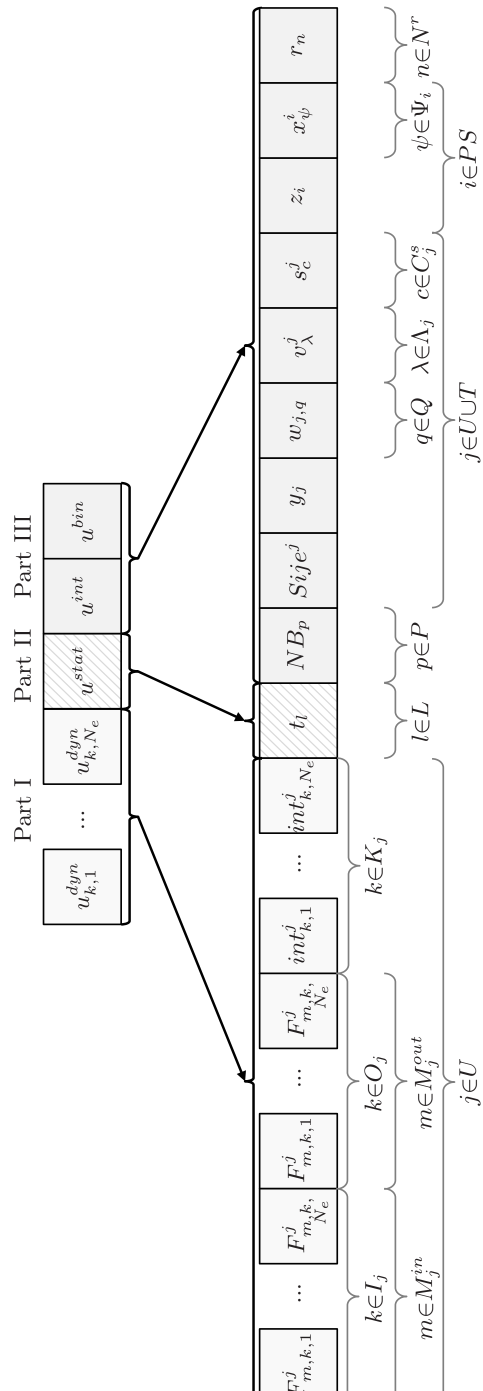


Figure 4.4: Representation of the chromosome of the DGA method to solve integrated batch process development.

Penalization weights f_p should be sufficiently small to avoid converting any non-penalized solution in a super-individual, but large enough to avoid convergence toward penalized individuals with an underrated objective function.

The solution algorithm includes the following general steps in GA methods (Haupt & Haupt, 2004) and the particular features to face the problem here proposed:

- **Initial population generation.** Random normalized values are assigned to each variable in the chromosome.

- **Fitness function evaluation and ranking selection.** $\Phi_{Fitness}$ is evaluated according to Eq. 4.16 for each individual of the population. Then, individuals are ranked from lower (best) to upper (worst) fitness function values.

- **Evolution of individuals by crossover and mutation operators.** Matchmaking is done using rank weighted random pairing. Besides, crossover is carried out through cyclic chromosomes with an even number of crossover points. In continuous genes, the value of the two new offsprings is calculated from parents' genes by using heuristic crossover with a random repartition parameter. As for mutation, random normalized values are assigned, except for the case of genes for input and output flow rates $F^j_{m,k,e}$, $\forall m \in M^{in}_j \cup M^{out_j}$, which are provided by a random normally distributed mutation around the original value. This type of mutation introduces preservative variations in the flow profiles, thus driving their evolution at a slower pace, avoiding to fall into sharp search paths.

- **Termination.** The algorithm is defined to stop when the both following conditions are meet: (1) the penalization of the best individual satisfies a predefined tolerance boundary, and (2) there is no more improvement in indicators of the evolution in two consecutive populations, namely $\Phi_{Fitness}$ minimum and mean values.

4.3.3 Hybrid method: DGA-NLP

The hybrid approach aims at exploiting the strengths of both stochastic and deterministic solution tools. Figure 4.5 shows the detailed solution procedure. In step 1, a number of N_{IFS} initial feasible solutions are calculated through DGAs with fixed structural solutions –*i.e.* predefined u^{int} and u^{bin} in part III of the chromosome– and constant profiles for dynamic variables instead of PWC ones –*i.e.* $u^{dyn}_{k,e} = u^{dyn}_{k,e+1}$, $\forall e \in \{1, ..., N_e - 1\}$. In step 2, the resulting approximated solutions are included in a following DGA, now incorporating dynamic PWC profiles and free integer decisions in part III of the chromosome. In final step 3, the integer part of the problem is fixed according to the best solution obtained in step 2 and the problem becomes a DO one. Then, such solution is improved by using a deterministic solution approach. Particularly, the obtained DO problem is solved through a direct-simultaneous approach, by discretizing state $z_k(t)$ and $y_k(t)$ and control variables $u^{dyn}_k(t)$ using orthogonal collocation on finite elements (Cuthrell & Biegler, 1989) as was explained previously in step 2 of the proposed deterministic approach (§ 4.2.1). This way, a NLP problem is obtained and the solver performance is improved with respect to the MINLP solvers because the combinatorial part of the problem associated to integer control variables u^{int} and u^{bin} has been dismissed from the optimization problem, solved in previous steps of the hybrid strategy.

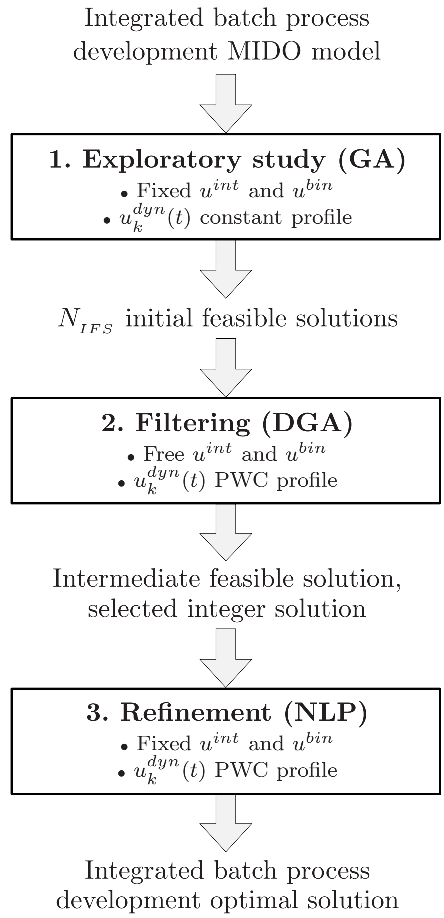


Figure 4.5: Proposed hybrid DGA-NLP approach to solve integrated batch process development.

4.4 Concluding remarks

In this chapter, three different solution approaches have been proposed, namely a deterministic direct-simultaneous approach, a stochastic DGA, and their combination in a hybrid solution method. For comparative purposes, the three methods have been used to solve a preliminary example of batch process development in a retrofit scenario. This example is presented in Appendix D, where promising results are shown.

The general features of the propsed MLDO solution methods are summarized in Table 4.2. On the one hand, despite the direct-simultaneous approach can lead to suboptimal solutions due to the non-linear non-convex characteristics of the MLDO model, the deterministic solution obtained is not beat by the DGA or the DGA-NLP ones. On the other, the proposed stochastic and hybrid approaches provide near-optimal solutions compared to the direct-simultaneous one and, thus, can be considered as a plausible solution alternative. The tested DGA and DGA-NLP methods present a crucial advantage in front

	Advantages	Disadvantages
Deterministic direct-simultaneous approach	• Local optimality • Tuning of search algorithm parameters not required	• IFS required • Numerical error due to the discretization of process variables
Stochastic DGA	• Physically feasible solutions • IFS not required	• Near-optimal solutions • Tuning of DGA parameters required
Hybrid DGA-NLP	• Local optimality • IFS not required	• Numerical error due to the discretization of process variables • Tuning of DGA parameters required

Table 4.2: General features of the proposed MLDO solution methods.

of the deterministic method, that is the possibility to find solutions that are physically feasible without requiring IFS. Moreover, the DGA search procedure does not require the discretization of the process variables and the DAE system –only the control variables have to be discretized–, which eliminates a significant portion of the numerical error. However, these methods present a drawback, that is the need of carrying out a good tuning of the DGA parameters in order to ensure their success.

Taking into account these considerations and the results of the example presented in Appendix D, it is considered that the direct-sequential method with the proposed IFS strategy leads to solutions that are more reliable than the ones obtained with the DGA and DGA-NLP with a blind misguided algorithm tuning, even though global optimality can not be guaranteed in any case. For that reason, the examples solved in Chapters 5 and 6 of this thesis are attacked with the proposed direct-simultaneous approach. With a previous study of the tuning strategy to be used, the DGA and NLP-DGA methods could be used as well.

Chapter 5

Integrated batch process development in retrofit scenarios

"In 2012, the European Medicines Agency (EMA) issued 59 positive opinions recommending marketing authorization for new human medicines."

Annual Report 2012, EMA

Batch manufacturing facilities are characterized by a clear differentiation between the physical plant and the process that is performed therein, since they are meant to assimilate and execute many different processes along their lifecycle. Specialty chemical industries, like the pharmaceutical, the crop science, or the high-tech materials ones, require the fast introduction of new products into the market system to keep competitive. The investment of time and resources to design, construct, and validate a new plant each time that a new product is approved for commercialization is not a viable strategy in most cases. Therefore, batch plants are frequently adapted and reconfigured to embrace the production of new products, involving none or partial plant modifications. Additionally, many processes should be later improved, giving a response to further economic or non-economic incentives.

In this chapter, the integrated development of batch processes in retrofit scenarios is addressed. Concretely, the process synthesis and plant allocation sub-problems are solved simultaneously, while tacking into account the physical restrictions of the existing manufacturing facilities that allocate the process. Two case studies are presented to illustrate the solution of this problem by means of the modeling strategy and solution methods described in Chapters 3 and 4. The first one consists of a competitive reaction system, the Denbigh reaction mechanism (Denbigh, 1958), to produce a specialty chemical in an existing reactor network. The equipment configuration is a decision variable that permits to adapt the operating mode according to different objective functions and economic scenarios, dismissing any modification of the physical plant and considering the capacity expansion of batch processing units. The second case study is the optimization of a photo-Fenton process to eliminate an emergent wastewater pollutant in a given pilot plant. The modification of the physical system by installing new piping or processing equipment is not considered in this case.

5.1 Batch process development in retrofit scenarios

The organization of plant, product, and process lifecycles in an enterprise presented in Figure 5.1 is the common situation in most batch industries, where the adaptation of manufacturing facilities to incorporate newly defined or improved processes is a mandatory activity. On the one hand, each time that a new chemical is introduced into the production system, its corresponding process has to be defined. On the other, some processes should be later improved to embrace: (i) changes in the economic scenario and (ii) changes in production policies and decision criteria, all of them reflected in the optimization function. That being so, the objective of batch process development in retrofit scenarios is to develop new or improved master recipes to be implemented in existing plants.

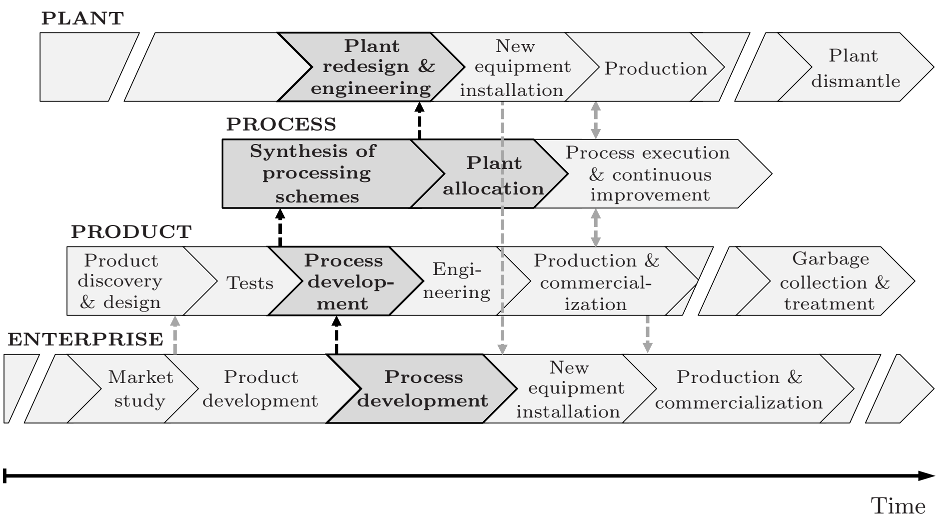


Figure 5.1: Lifecycles in an enterprise: retrofit scenario (adapted from Marquardt et al., 2000).

5.1.1 Introduction to retrofit problems

According to Barbosa-Póvoa (2007), retrofit design may be defined as the redesign of an existing facility to improve process economics. Specifically, this can be done by: expanding the capacity of the existing plant, reducing operating costs, or accommodating a revised product portfolio (Reklaitis, 1990). In last decades, plant modernization has been also motivated by driving factors beyond the economic improvement, pursuing the development of sustainable process that were also ecological, environmentally friendly and safe (Grossmann et al., 1987, Simon et al., 2008, Grossmann & Guillén-Gosálbez, 2010). The most widespread retrofit incentives are summarized in Table 5.1. In broad terms, retrofit design is a response to several factors, like the uncertainty in prices and in feedstock and energy availability, patent expiration, new emission regulations, or changes in market demands (Grossmann et al., 1987, Simon et al., 2008). Additionally, retrofit problems in batch plants are also related to the opportunities of introducing new specialty products in the market-place (Cavin, 2003, Reklaitis, 1990).

Several actions can be taken in retrofit problems: (i) the modification of processing conditions, (ii) the adaptation of equipment diagram by changing the piping connections,

Economic incentives:	
• Production increase • Reduction of processing costs and energy requirements • Improvement of flexibility and controllability • Increase of the feedstock conversion	• New chemical production • Introduction of a newly developed process or technology • Process debottlenecking • Change of feedstock
Non-economic incentives:	
• Waste volume reduction • Improvement of product quality • Improvement of process safety	• Reduction of environmental impact of existing processes

Table 5.1: Usual retrofit incentives (Grossmann et al., 1987, Barbosa-Póvoa, 2007, Simon et al., 2008, Banimostafa et al., 2011).

(iii) the re-sizing of equipment pieces, or (iv) the installation of additional processing and storage units (Grossmann et al., 1987). The resulting investment costs increase from actions i to iv. This way, the plant design problem deals with different situations in retrofit scenarios, which vary between two extreme cases. In the first one, no plant modifications are allowed and thus the plant design problem is not addressed at all. In the other extreme case, the consideration of installing additional pipelines, processing units, and storage tanks involves a general plant design problem where the number, size, and location of new plant elements should be defined. In addition, Reklaitis (1990) cite further decisions that should be considered when facing a retrofit problem in the batch industry, as is the case of campaign lengths, sizing levels, operating modes, and changes in processing times like cycle times.

Overall, the imperative objective of retrofit problems is to take into account the available physical elements of the plant to make the best use of them according to the new production targets. However, this goal has important mathematical implications. First, it is necessary to take into account the features of the existing equipment items to ensure that the new or modified process can be executed therein. Thus, each equipment piece should be associated to a set of constraints that determine their connectivity with other units and the permitted processing conditions. In addition, there is a combinatorial explosion due to the consideration of several equipment options and constraints (Reklaitis, 1990) in addition to the combinatorial problem of tasks and subtasks selection and sequencing associated to batch processes development. Finally, the constraints associated to the existing equipment items are complemented by the degrees of freedom related to new plant elements, in case that plant modifications are allowed.

Comparing the process development problem in retrofit scenarios with grassroots ones, where manufacturing facilities are newly designed in their entirety, several differences are found regarding the modeling and solution requirements, as outlined in Table 5.2. Particularly, it should be emphasized that the interaction between the batch process development sub-problems –*i.e.* process synthesis, plant allocation, and plant design– is stronger in retrofit scenarios because the equipment specifications, which are typically defined at the end, should be fixed in the beginning of the solution procedure according to the existing plant and thus constrain the whole decision-making. For instance, the sequential solution in this case does not ensure that feasible solutions are found within the available equipment. Therefore, iterative or simultaneous solution approaches should be considered.

	Retrofit scenario	Grassroots scenario
Typical solution approach	Simultaneous modification of processing schemes, plant allocation, and plant design	Sequential: (1) process synthesis, (2) plant allocation, (3) plant design
Processing conditions	Performance of existing units working beyond the nominal conditions	Nominal behavior in processing units
Restrictions	Constraints associated to the process and to the existing plant restrictions, *e.g.* diagram, available space, piping, and processing units	Constraints associated to the process
Combinatorial problem	Tasks selection and sequencing, allocation of tasks to specific equipment pieces from the set of available ones	Tasks selection and sequencing

Table 5.2: Comparison of modeling features for process development problem in retrofit and grassroots scenarios.

5.1.2 Related work

Various reviews are available in the literature analyzing academic solutions to improve chemical batch processes and plants, *e.g.* Grossmann et al. (1987), Reklaitis (1990), and Barbosa-Póvoa (2007). To present a general scope of the batch retrofit panorama, these contributions are here classified according to the problem tackled at each case, namely: (i) the introduction of new processes in existing batch plants, (ii) the introduction of sustainable incentives for batch process improvement, and (iii) the retrofit of batch plants.

Regarding the solution approaches, there are several proposals for evaluating the retrofit potential of a chemical plant according to the abovementioned objectives. Following the classification of solution approaches presented in Chapter 2, the literature for retrofit problems plays tribute to knowledge-based, optimization-based, or combined methodologies. Many of the them have been developed to particular applications (Grossmann et al., 1987), like the retrofit of HEN or reaction sequences. Moreover, a great emphasis is placed on developing methods that are systematic, due to the large complexity of the retrofit problems. Note also that many of the proposals for retrofit problems can be applied to process development in grassroots scenarios as well.

Introduction of new processes in existing batch plants

One of the problems that should be considered most frequently in the batch industry is the modification of the product portfolio to include the manufacturing of new chemicals. In these cases, the retrofit problem is related to the adaptation of batch plants to allocate the new productions lines by re-organizing their available equipment items, introducing modifications like the expansion of vessel sizes, or installing additional processing and storage units.

Several contributions addressed this problem in the literature, like the works by Cavin (2003), Cavin et al. (2004, 2005), and Mosat et al. (2007, 2008) presented in Chapter 2 (p. 37). Particularly, Cavin (2003) solved sequentially the synthesis of waste treatment paths and the plant allocation sub-problems. The former was addressed through an iterative approach. The latter, using a two-step hybrid method consisting of: (1) a knowledge-based step for the generation of the problem superstructure, which included the selected waste treatment schemes, and (2) a MO optimization step for solving the allocation subproblem using TS as search method. The second step (Cavin et al., 2004, 2005, Mosat et al., 2007, 2008) covered issues like the combination of economic and environmental decision criteria, uncertainty in the process parameters, and robustness optimization.

Overall, the great contribution of these works was to address the allocation problem in retrofit scenarios, providing the most efficient path for producing a new product to be implemented in already exiting multi-purpose facilities. The resulting optimization models often included decisions like new equipment investment. Restrictions to ensure that the predefined conditions in each task fitted the physically feasible temperature and pressure ranges of the assigned existing units were also considered. However, processing conditions in each process stage were not considered as degrees of freedom in the optimization problem, what could lead to a misuse of the existing units.

Sustainable incentives for batch process improvement

Despite the improvement of the economic performance is the most widespread motivation to enlarge the firm's value, an increasing concern for sustainable processes can be noticed in recent publications. This way, several authors have posed a special stress over the need of retrofitting processes to incorporate energy consumption and environmental impact reduction –which in many cases was not considered in the initial process design– complementing the economic optimization (Halim & Srinivasan, 2006, 2008, Halim et al., 2011, Simon et al., 2008, Carvalho et al., 2009, Bumann et al., 2011, Banimostafa et al., 2011, 2012). Most of the proposed approaches have been developed by extending well established knowledge-based and combined methodologies for the retrofit of continuous processes. Moreover, these methodologies are generally applicable to different stages of the process design lifecycle, including the improvement of processes already implemented in a production facility as well as the development of new ones.

For instance, Halim & Srinivasan (2006, 2008) proposed a systematic methodology for waste minimization in batch processes, implemented in the AI system Batch-ENVOPExpert. The approach was based on the use of heuristic procedures and guidewords –*e.g.* larger pressure or smaller temperature– to diagnose waste sources and generate waste minimization alternatives (Halim & Srinivasan, 2006). It was complemented by quantitative material and energy balances to evaluate energy utilization and economic contributions (Halim & Srinivasan, 2008). Eventually, a MO optimization problem was addressed, which combined environmental and economic targets and was solved through the stochastic SA search method. Later, Halim et al. (2011) combined the capabilities of the Batch-ENVOPExpert system with the computer tool SustainPro (Carvalho et al., 2008), which was based on the evaluation of alternatives through indicators like profit and resource usage, *e.g.* energy, water, or raw material. The DOF in these works are defined terms of structural alternatives and process variable modifications. However, both types of decisions are addressed sequentially, losing an important part of their interaction. This way, structural variables are decided through a heuristic procedure, whereas processing conditions are optimized in a later step, assuming constant profiles for the feed-forward control trajectories.

Recently, other studies have addressed the retrofit of batch processes for sustainable designs through a general framework based on path flow decomposition of the process flow sheet and indicator-based identification of retrofit potential (Simon et al., 2008, Carvalho et al., 2009, Bumann et al., 2011, Banimostafa et al., 2011, 2012), originally developed for continuous processes (Uerdingen et al., 2003, 2005, Carvalho et al., 2008). This way, Simon et al. (2008) sought the improvement of process performance through production capacity expansion, based on a heuristic method covering three decision levels: plant, process, and unit operations. An extensive set of indicators was used to evaluate the processing alternatives, which were associated to the different levels and ranged from global economic indicators like productivity to path flow indicators like energy and waste costs. At the same time, Carvalho et al. (2009) combined the indicator-based methodology with sensitivity analysis using sustainable metrics, safety indices, and waste reduction parameters to evaluate the improvement alternatives. Later, Bumann et al. (2011) incorporated a MO process assessment to find retrofitting actions pursuing economic and ecological objectives. Finally, Banimostafa et al. (2011, 2012) enhanced both monetary and non-monetary objectives through the definition of path flow indicators belonging to green chemistry, namely the EHS and the LCIA indicators. It should be noted that all these approaches rely on a problem decomposition and heuristic rules, losing part of the interaction between process synthesis, plant allocation, and plant re-design decisions. Besides, processing conditions were considered as time-invariant decision variables in most cases, also losing the improvement potential that is associated to the optimization of dynamic feed-forward profiles for the control variables.

Additionally, the retrofit of batch HEN is reviewed by Fernández et al. (2012). Early studies applied methods previously developed for continuous processes. However, due to the transient behavior of batch processes, later research has focused on heat by defining time-dependent heat recovery constraints. There has been also a significant amount of work devoted to the study of thermal storage to improve heat integration in batch systems. But again, each phase is approximated using time-invariant information.

Retrofit of batch plants

Despite the abovementioned contributions, most of the work regarding retrofit problems in batch plants has dealt with the modernization of existing multiproduct and multipurpose plants, assuming fixed recipes for a given product slot, as was reviewed by Reklaitis (1990) and Barbosa-Póvoa (2007). The typical incentives to address the retrofit problem were the enhancement of economic performance, for example involving the modification of product demands, the incorporation of new products, capacity expansions, the optimization of the production levels, plant debottlenecking, and increasing the plant flexibility, reliability, or maintainability.

Regarding the solution procedures, several approaches have been applied in this case: (i) optimization-based approaches where the problem was represented by MILP and MINLP models (Vaselenak et al., 1987, Wellons, 1989, Fletcher et al., 1991, Papageorgaki et al., 1992, Papageorgaki & Reklaitis, 1993, Barbosa-Póvoa & Macchietto, 1994b, Subrahmanyam et al., 1994, Georgiadis et al., 1997, Yoo et al., 1999, Lee et al., 2000, Carvalho & Soletti, 2000, Montagna, 2003, Goel et al., 2004, Pinto et al., 2005, Moreno et al., 2007), by stochastic optimization models (Petkov & Maranas, 1998, Dedieu et al., 2003, Dietz et al., 2008), or by disjunctive optimization models (van den Heever & Grossmann, 1999, García-Ayala et al., 2012), (ii) heuristic strategies (Espuña & Puigjaner, 1989), and (iii) combined approaches that included heuristic rules and optimization techniques (Lee et al., 1993, 1996). The typical decisions considered in these works are the following:

- Addition of extra equipment to existing facilities;
- Sizing of new equipment;
- Elimination of old inefficient units;
- Operating mode, *i.e.* parallel in-phase or out-of-phase;

- Location of intermediate storage units
- Processing time as a function of the batch size; and
- Cleaning policies.

These decisions involve structural alternatives and continuous design variables. However, the modification of processing conditions is not considered within the pre-established recipes. All in all, the problem solved in most cases is the plant allocation and design, instead of the complete process development.

Remarks on the solution approaches

As presented above, knowledge-based approaches have been the most commonly used approaches to generate and evaluate the development of new processes or the improvement of existing ones in retrofit scenarios. Particularly, empirical process knowledge helps to untangle the large complexity of the retrofit problem by stating a series of rules, defined by the user, to guide the search of design variations, which are evaluated by simulation. This way, the problem is decomposed and solved sequentially in most cases, using the existing system as the natural starting point for the search.

For instance, Cavin (2003), Cavin et al. (2004, 2005), and Mosat et al. (2007, 2008) separated the synthesis of processing and waste treatment schemes from the plant allocation sub-problem. Besides, the heuristic and guideworkds procedure proposed by Halim & Srinivasan (2006, 2008) and Halim et al. (2011) –implemented in the computer tools Batch-ENVOPExpert and SustainPro– addressed first the structural decisions and following the performance ones. The same philosophy was behind the general framework based on path flow decomposition and indicator-based evaluation employed by Simon et al. (2008), Carvalho et al. (2009), Bumann et al. (2011) and Banimostafa et al. (2011, 2012).

The heuristic procedures of several of these works have been also combined with the optimization of particular solutions. To do so, the problem was also addressed sequentially: heuristic approaches were first used to generate and propose retrofit actions in batch plants, which were followed by simulation and optimization of the best solutions or specific subsystems of the flow sheet –*e.g.* energy use, distillation columns, or reaction units. Overall, while decomposition and the sequential procedures are efficient and relatively simple to implement, they require a great deal of trial and error and suboptimal designs could be met for not evaluating the interaction among sub-problems in the decision-making process.

In contrast, the retrofit of batch plants has been mostly addressed through optimization-based approaches. In this case, the complexity of the process synthesis problem is eliminated by assuming fixed recipes where the process behavior is approximated in each process stage. One of the most important advantages of optimization-based approaches is that all the structural alternatives can be evaluated simultaneously in a the optimization model and equipment constraints can be included therein as linear constraints. The difficulty in retrofit scenarios is that the combinatorial problem grows exponentially because the assignment of all the batch tasks should be evaluated for each of the existing plant elements, in addition to the potential units.

Most of these references represented the retrofit problem through MINLP formulations. Regarding the search procedure, several methods have been used, like deterministic solvers, stochastic optimization algorithms, metaheuristics, or logic-based searching procedures. For instance, evolutionary algorithms were proposed by Dedieu et al. (2003) and

Dietz et al. (2008) to reduce the solution complexity in their MO problem for the design and retrofit of multi-purpose batch plants. Another alternative is the mathematical formulation of heuristics to be incorporated into the optimization model. However, very few works, like van den Heever & Grossmann (1999) and García-Ayala et al. (2012), bet for this alternative, all of them dealing with the retrofit design of batch plants.

Regarding the processing conditions, the physical restrictions of the existing units were generally taken into account to ensure that the predefined processing conditions at each task fitted the physically feasible range of the assigned existing units. However, only some contributions for batch process development and improvement considered processing conditions as DOF, which were usually optimized in a final step. Moreover, despite batch processes are characterized by a transient behavior, few of these works defined dynamic trajectories of the control variables. Finally, the use of fixed recipes in the retrofit design of batch plants dismiss any potential improvement by modifying processing conditions.

Beyond the solution approach, the following engineering tools listed by Grossmann et al. (1987) have become important components in many approaches for retrofit of continuous and batch processes:

- Targets and bounds to provide a measure of potential improvement, *e.g.* Fisher et al. (1987), Allgor (1997);
- Physical insights to support the identification of bottlenecks and to suggest favorable modifications, *e.g.* Jaksland et al. (1995), Carvalho et al. (2009);
- Performance indicators to assess economics, flexibility, controllability, and safety targets of the existing design and the potential modifications, *e.g.* Uerdingen et al. (2003, 2005), Simon et al. (2008), Carvalho et al. (2009), Bumann et al. (2011), Banimostafa et al. (2011, 2012);
- Sensitivity analysis to identify dominant variables and the potential improvement of proposed modifications, *e.g.* Carvalho et al. (2008, 2009), Halim et al. (2011);
- Short-cut models to propose quickly sizing modifications, *e.g.* Fisher et al. (1987);
- Rigorous simulation models to verify the feasibility of the proposed retrofits, *e.g.* Vidal et al. (2002), Halim & Srinivasan (2005, 2008);
- Optimization techniques to handle discrete and continuous decisions, *e.g.* Lee et al. (1993, 1996); and
- Interactive computer environments with graphic displays.

5.2 Application of the MLDO-based strategy

In this context, the modeling strategy and the solution approach proposed in this thesis contribute to the integrated solution of process synthesis and allocation sub-problems, in order to tackle the development of new batch processes or the improvement of existing ones. Particularly, the DOF associated to each sub-problem (see problem statement, § 3.1.3, p. 56) are optimized simultaneously, while taking into account the existing plant as problem constraints. To reduce the computational requirements associated to the combinatorial problem, mixed-logic modeling is used to incorporate available process knowledge into the optimization model. Moreover, dynamic profiles are considered for the optimization of the feed-forward trajectories of control variables, enlarging the attainable area of the objective function.

To sum up, the modeling strategy based on MLDO and the direct-simultaneous solution method proposed in Chapters 3 and 4 are applied to address this problem. Despite the proposed approach does not guarantee that the global optimum of the optimization problem is met –due to the mathematical features of the MLDO model and the available optimization tools–, improved solutions are expected with regard to: the sequential solution of decomposed problems, the use of fixed recipes, and the definition of time-invariant processing conditions in previous publications.

5.2.1 Optimization model

The optimization model is constructed following the formulation presented in § 3.3 (p. 69), which is generalized in Eq. 3.36 (§ 3.4, p. 84). In the case of batch process development in retrofit problems, the following issues should be also taken into account to formulate the optimization model.

Plant constraints

In retrofit scenarios, plant features like the capacity of installed equipment items or the boundaries of processing conditions constitute physical restrictions to be considered in the optimization problem. Additionally, new plant elements may be also installed, which relax the physical constraints associated to such particular element and involve an investment cost. In broad terms, the retrofit problem may solved considering the following problem specifications with an increasing number of DOF associated to the physical plant:

(i) No allowed installation of new processing or storage units or pipelines;
(ii) Allowed installation of new connecting pipelines;
(iii) Re-sizing of processing or storage units;
(iv) Allowed installation of new processing or storage units.

Aside from the decision criteria evaluation, the first is the ideal situation in practice because it does not require additional time for installing and validating the new system. Let us bear in mind that procedures like Good Manufacturing Practices (GMP) and HAZOP analysis are necessary to face any plant modification, in order to verify that the safety and operational measures are correct. The drawback of not considering the installation of new plant elements is that the attainable area for the objective function, and thus the improvement potential, is limited with respect to the other three options.

Single-objective problems

The most widespread decision criteria in chemical industry are economic targets because they determine the viability of producing a particular chemical. Therefore, several economic contributions to the objective function are defined in this chapter to compare processing alternatives, which are combined in single-objective (SO) optimization problems defined by:

$$\underset{\substack{u^{dyn}(t),u^{stat},\\ u^{int},u^{Bool}}}{\text{minimize}} \quad \Phi(z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, u^{Bool}, \gamma, p), \tag{5.1}$$

subject to the set of equations for simultaneous batch process synthesis and plant allocation. Generally this minimization problem may represent the profit maximization or cost minimization problems with the following contributions to the objective function Φ:

- **Product revenue:** The total revenue of product p is determined by the amount of product obtained in each batch. It can be calculated as a function of the level variation in the storage tank as follows:

$$Revenue_p = \hat{p}_p \left(\eta_p^{T_{prod}}(t^{end}) - \eta_p^{T_{prod}}(t^s) \right), \tag{5.2}$$

in monetary units per batch, where $\hat{p}_p$ is the selling price and $\eta_p^{T_{prod}}(t^s)$ and $\eta_p^{T_{prod}}(t^{end})$ are the initial and final amounts of product p in the storage tank T_{prod}.

- **Raw material cost:** Accordingly, the cost of raw material c is determined by the amount of raw material consumed in each batch and can be calculated as a function of the level variation in the raw material tank as follows:

$$Cost_c = \hat{p}_c \left(\eta_c^{T_{raw}}(t^s) - \eta_c^{T_{raw}}(t^{end}) \right), \tag{5.3}$$

in monetary units per batch, where $\hat{p}_c$ is the unitary cost and $\eta_c^{T_{raw}}(t^s)$ and $\eta_c^{T_{raw}}(t^{end})$ are the initial and final amounts of raw material c in the storage tank T^{raw}.

- **Processing cost:** The processing cost is associated to the resource consumption in unit procedures of $j \in U$ in each batch, in case that this unit is selected. Typical processing costs are water, energy, or reactant dosage, among others. The general form to define the processing cost is:

$$\begin{bmatrix} Y_j \\ Cost_{j,p} = \hat{c}_j \; Resource_j \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ Cost_{j,p} = 0 \end{bmatrix}, j \in U, \tag{5.4}$$

in monetary units per batch, where $\hat{c}_j$ is the economic weight of the unitary resource consumption and $Resource_j$ is the total amount required in unit $j \in U$ to produce each batch.

- **Occupation cost:** The occupation cost of batch unit $j \in U$ corresponds to the economic load of sharing equipment items among different processes. It is represented mathematically as a rental cost that prices the occupation time of each unit that is selected. Moreover, other factors like cleaning operations and labor are also associated to the equipment usage. Overall, the occupation cost is defined as follows:

$$\begin{bmatrix} Y_j \\ Cost_{j,o} = \bar{c}_{j,A} + \bar{c}_{j,B} \, Size^j + \bar{c}_{j,C} \sum_{k \in K_j} t_k^j \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ Cost_{j,o} = 0 \end{bmatrix}, j \in U, \tag{5.5}$$

in monetary units per batch, where $Size^j$ is the equipment capacity and t_k^j is the duration of batch operations associated to mathematical stages $k \in K_j$. The cleaning cost and labor are related to a fixed and to a size-dependent cost contribution defined by parameters $\bar{c}_{j,A}$ and $\bar{c}_{j,B}$ respectively. Besides, the rental cost is related to a time-dependent cost contribution defined by parameter $\bar{c}_{j,C}$.

- **Amortization cost:** The investment expenses associated to the installation of new pieces of equipment are defined assuming an amortization period, *e.g.* two years. This parameter depends on planning level decisions. The amortization cost of a new unit $j \in U \cup T$, either it is selected in a particular master recipe (Y_j) or not ($\neg Y_j$), is defined as follows:

$$Cost_{j,a} = \frac{\check{c}_j \left(Size^j / Size^0 \right)^n Horizon}{NB_p}, \quad j \in U \cup T, \tag{5.6}$$

in monetary units per batch, where $Size^j$ and $Size^0$ are the equipment capacity and the base equipment capacity and n is the power in the amortization function. Particularly, $Size^j$ is usually defined as a discrete variable to facilitate the equipment purchase. $Horizon$ is the maximum processing time to fulfill the total product demand. Besides, $\check{c}_j$ is the base amortization cost, calculated as the base equipment cost for installing a unit j with capacity $Size^0$ divided by the number of working-hours considered in the total amortization period. For instance, if a period of 2 years with 52 weeks and 168 working-hours per week is considered, $17,472$ working-hours are obtained. This parameter $\check{c}_j$ should have a zero value in those units that are already installed and are not subject to any modification. Finally, the amortization cost is divided by the number of batches NB_p to express this cost in a batch basis and be consistent with previous economic contributions.

- **Shortfall penalty:** The unaccomplished demand of product p is penalized with an additional cost, besides the revenue reduction due to unsold product. This cost is defined as:

$$Penalty_p = \hat{p}_{penalty}\ Shortfall_p\ /NB_p, \tag{5.7}$$

in monetary units per batch, where $\hat{p}_{penalty}$ is the economic loss associated to the unaccomplished part of the demand $Shortfall_p$, which is usually related to the selling price $\hat{p}_p$ of product p. The penalty is divided by the number of batches NB_p to express this cost in a batch basis and be consistent with previous economic contributions.

Given these definitions in a batch basis, the total profit maximization is formulated by the equivalent minimization problem:

$$\Phi = -\sum_p (Revenue_p - Cost_c - \sum_j (Cost_{j,p} + Cost_{j,o} + Cost_{j,a}) - Penalty_p)\ NB_p, \tag{5.8}$$

where the economic load is evaluated for the production of all batches NB_p.

Multi-objective problems

Decision-making in chemical plants usually involve multiple objectives. When several KPI have a predominant role in the decision-making, it may be necessary to pose an optimization problem with multiple objectives, where the effect of each target is evaluated. Beyond economical objectives, the product quality, production time, safety, or risk measures are also common decision criteria in batch process development. Specially, the concern for sustainable processes that also consider the ecological and social impact of production systems has gained importance in last decades. In multi-objective optimization problems, the single-objective function represented in Eq. 5.1 is substituted by:

$$\underset{\substack{u^{dyn}(t), u^{stat},\\ u^{int}, u^{Bool}}}{\text{minimize}}\ \Phi_n(z_k(t), y_k(t), u_k^{dyn}(t), u^{stat}, u^{int}, u^{Bool}, \gamma, p), \qquad n \geq 2, \tag{5.9}$$

subject to the set of equations for simultaneous batch process synthesis and plant allocation. Generally, these objectives are conflicting. So, achieving the optimal value according to one objective involves the compromise on other ones. The solutions where none of the objective functions can be improved without degrading other objective values is termed non-dominated or Pareto optimal solution. The set of non-dominated solutions is the so-called Pareto frontier, whose representation provides a graphical support to elucidate the trade-off between multiple objectives. For example, Figure 5.2 illustrates a set of dominated (light) and non-dominated (dark) solution and the Pareto frontier for a bi-objective minimization problem. The extreme points of the Pareto frontier are termed anchor points, and are obtained through the optimization considering each decision criteria individually. All the solutions of the Pareto frontier are equally good and require subjective information in the decision-making process to differentiate among each other.

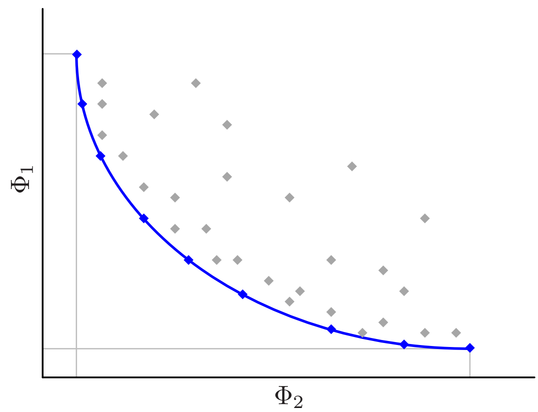


Figure 5.2: Pareto frontier and dominated solutions for a bi-objective minimization problem: non-dominated or Pareto optimal solutions (dark) and dominated solutions (light).

5.2.2 Methodology

Figure 5.3 summarizes the principal steps to implement the modeling strategy, formulation, and solution methods proposed Chapters 3 and 4 of this thesis to solve integrated batch process development. These steps rely on the typical problem solution through model-based optimization approaches that include synthesis decisions. In particular, once the problem statement and required information have been defined, all processing alternatives are first represented in a superstructure, which is later formulated into a MP model to be finally optimized (Grossmann & Guillén-Gosálbez, 2010).

(a) Gathering information

The objective of the integrated batch process development problem to be solved should be first defined according to the general problem statement in § 3.1.3 and the general knowledge about the process to be solved. Thus, a **process description** and particular **problem statement** should provided. On this basis, the required data for each process stage should be also identified and gathered together. For instance, it is necessary information like the appropriated technologies, the practical control variables, economic data, the definition of the mandatory and optional process stages, dynamic or approximated models and the process parameters to represent the process performance in each stage, the potential reuse of material by recirculating intermediate flows, or the tasks where the process can be partitioned to operate using different cycle times, among other information.

(b) SEN superstructure representation

Second, the SEN superstructure is constructed, integrating all the potential synthesis alternatives. Moreover, equipment items should be distributed in Level 0 and 1 according to their semi-continuous or batch nature, as it is detailed in § 3.2.3.

(c) Superstructure formulation

Next, the problem is formulated into a mathematical model according to the MLDO-based formulation presented in § 3.3. To that end, logical variables and disjunctive equations are used to represent mathematically the qualitative alternatives in the decision-making. Logical propositions can be also formulated to incorporate the available logical knowledge of the process into the model, limiting the dimension of the combinatorial problem. Moreover, multistage models are used to represent each potential process stage. Material input and output stages should be identified therein to allow the synchronization with other tasks. Dynamic, steady state, or linearly approximated models can be used according to the impact of each process stage on the decision criterion and the processing trade-offs.

(d) MLDO solution

The resulting MLDO model should be optimized. In particular, the deterministic direct-simultaneous method explained in § 4.2.1 (p. 92) is applied in the examples of this thesis.

Recalling, the MLDO model is first normalized and transformed into a MIDO one. To do so, Booleans are substituted by binaries and the set of logical equations is reformulated into algebraic ones using the binary multiplication strategy and the CNF of logical propositions.

Next, the MIDO is solved through full discretization of process and control variables via orthogonal collocation in finite elements with 3 collocation points in shifted Legendre

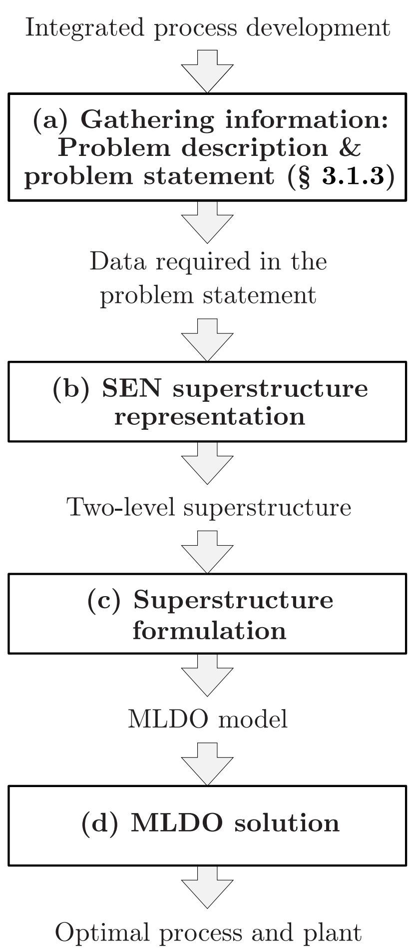


Figure 5.3: Main steps of the optimization-based approach to solve integrated batch process development.

roots and using Lagrange polynomials to approximate the state and control variable profiles. The number of finite elements should be carefully selected. On the one hand, a high number of discretization intervals should be chosen to ensure the best possible approximation of the original DAE system within the resulting finite-dimensional problem. On the other, fewer intervals reduce the size of the discretized model and provide a more cost-effective problem from a computational point of view, losing accuracy in the solution in return.

The discretized problem becomes a MINLP which is implemented in GAMS version 23.8.2 and solved through the decomposition-based OA solver DICOPT (Duran & Grossmann, 1986a), using CONOPT 3.15D and CPLEX 12.4 to handle the NLP and MILP subproblems respectively. Constant control profiles and fixed configurations chosen randomly are used to calculate the IFS provided to the MINLP solver.

Specific methods for multi-objective problem management. A large number of solution methods are suitable to address multi-objective problems, which are basically classified as: no-preference, a priori, interactive, and a posteriori methods, depending on the decision-maker intervention in the optimization process. Non-preference methods identify a neutral compromise solution without preference information. A priori methods require the initial definition of a priority order for the sequential optimization of objective functions. In interactive approaches the search is directed on the basis of the information obtained along the optimization process. A posteriori ones involve the generation of a set of solutions in the trade-off region with the best compromise solutions. The last approaches provide the Pareto frontier for the studied range.

In this thesis, an a posteriori method is used in those problems that require the evaluation of another decision criterion apart from the economical one. For that, the graphical representation of the Pareto optimal solutions –like the one in Figure 5.2– is used to support the decision-making process. There are several alternatives to generate the non-dominated solutions that compose the Pareto frontier for multiple objectives, such as the Normal Boundary Intersection, the Normal Constraint, or the Successive Pareto Optimization method, among others, where the several Pareto optimal solutions are obtained by defining different scalarizations of the objective functions. Evolutionary algorithms have been also applied, like the multi-objective Genetic Algorithm (Capón-García et al., 2011a), which define the population evolutions using Pareto-based ranking schemes. Once the Pareto frontier has been generated, subjective preferences of the decision-maker are required to choose the final solution.

5.3 Denbigh case study: process development in a retrofit scenario

This section presents an example tackling the integrated batch process synthesis and allocation problem of a competitive reaction system in a retrofit scenario. Particularly, a competitive reaction mechanism, the Denbigh reaction system (Denbigh, 1958), is considered to introduce the production of a specialty chemical into an existing plant through a single-product campaign.

Dealing with a retrofit problem, the process is subject to the restrictions of the existing equipment. Specifically, the plant structure in this example corresponds to the reactor network of the motivating example 1 presented in § 3.1.1 (Figure 3.1) which comprises two batch reactors U_1 and U_2. The construction of new piping and processing and storage equipment is not allowed in this example. Moreover, batch unit procedures in each reactor comprise three batch operations, namely load, hold, and unload, which are defined by the input and output flow rates and reaction temperature as control variables.

The methodology presented above (§ 5.2.2, Figure 5.3) is applied in the next sections as follows: (a) gathering information, in §§ 5.3.1, 5.3.2, A.1, and A.2, (b) SEN superstructure representation, in § 5.3.3, (c) formulation of the MLDO model, in §§ 5.3.4 and A.3, and (d) MLDO solution, in § 5.3.5.

5.3.1 Process description

The Denbigh case study consists of a competitive reaction system first proposed by Denbigh (1958) to study temperature control profiles. The reaction mechanism is defined by:

$$\begin{tikzcd} A \arrow[r, "1"] \arrow[d, "2"'] & R \arrow[r, "3"] \arrow[d, "4"'] & S \\ T & U. & \end{tikzcd} \tag{5.10}$$

Later, this example was adopted as a benchmark case study and used by several authors to study process synthesis in continuous, semi-batch, and batch systems. In this thesis, the problem parameters defined by Schweiger & Floudas (1999a) have been used to calculate activation energies $E_{a,r}$ and standard kinetic constants $k_{0,r}$, assuming that those authors worked at a nominal temperature T_{nom} of 80°C. In addition, reaction enthalpy $\triangle h_r$ data have been defined in order to incorporate energy balances into the problem. To do so, all reactions are considered endothermic and reference heats of formation and combustion (Perry & Gree, 1999, Tables 2-220 and 2-221) have been taken into account to provide consistent orders of magnitude. To sum up, the kinetic data used in the Denbigh case study are presented in Table 5.3. Like in the work by Schweiger & Floudas (1999a), a molar density ρ of 6 $kmol/m^3$ is assumed for all the chemical compounds A, R, S, T, and U, as well as a molecular weight MW of 130 $kg/kmol$.

Reaction r	$E_{a,r}$ $[kcal/kmol]$	$k_{0,r}$ $[h^{-1}]$ or $[m^3/(kmol\ h)]$	$k_{nom,r}$ $[h^{-1}]$ or $[m^3/(kmol\ h)]$	c_r	n_r	$\triangle h_r$ $[kcal/kmol]$
1	1000	4.16	1	A	2	$42{\cdot}10^3$
2	2580	23.75	0.6	A	1	$38{\cdot}10^3$
3	1800	7.81	0.6	R	1	$40{\cdot}10^3$
4	1210	0.56	0.1	R	2	$44{\cdot}10^3$

Table 5.3: Kinetic constants in Denbigh case study, adapted from Schweiger & Floudas (1999a) assuming T_{nom}=80°C as nominal temperature: activation energy $E_{a,r}$, standard and nominal kinetic constants $k_{0,r}$ and $k_{nom,r}$, reactant c_r, reaction order n_r, and reaction enthalpy $\triangle h_r$.

5.3.2 Problem statement

The objective is to optimize the master recipe to produce 21 tn of product S through Denbigh reaction system in the given process cell by minimizing the raw material expenses within a maximum time horizon of 144 hours. Additionally, a penalty is applied to the unfulfilled demand. Overall, the problem statement for this example is defined as follows:

Given:

- **Planning data:** final product, byproducts, intermediates, and raw material, expected demand of final product, and maximum time horizon;
- **Plant diagram:** the SEN superstructure of available equipment units for each process stage, pipelines, and connection nodes like mixers and splitters;
- **Task network alternatives:** mandatory reaction stage;
- **Batch process operation:** allowed task-unit assignments, batch operations and phases within unit procedures of batch units, phase to phase switching conditions, and set of limiting processing conditions for each unit;
- **Process dynamics:** DAE systems to represent the process behavior in each unit procedure, initial conditions, and set of process variables and dynamic controls;
- **Data related to performance evaluation:** specific data to evaluate the raw material cost, the shortfall penalty minimization function, and other KPIs *i.e.* direct cost of raw materials and of product shortfall, price of the final product, unitary processing costs, occupation costs, and amortization costs;

the goal is to determine:

- **Process synthesis decisions:** splitting of reaction stage into subtasks, reference trajectories of the feed-forward control variables, which include input and output flow rates and processing temperature at each operation in batch units, duration of batch operations, and material transfer synchronization between tasks –*i.e.* synchronization of flow rates, compositions, and starting and final times;
- **Allocation of manufacturing facilities decisions:** selection of processing units and task-unit assignment, operating mode in single unit, series, or parallel equipment configuration, and number of batches;

such that the expenses for raw material and unaccomplished demand are minimized. In this retrofit scenario, the installation of new equipment units is not considered and thus equipment sizes are not a DOF. Besides, the capacities of existing units are introduced into the optimization model as restrictions.

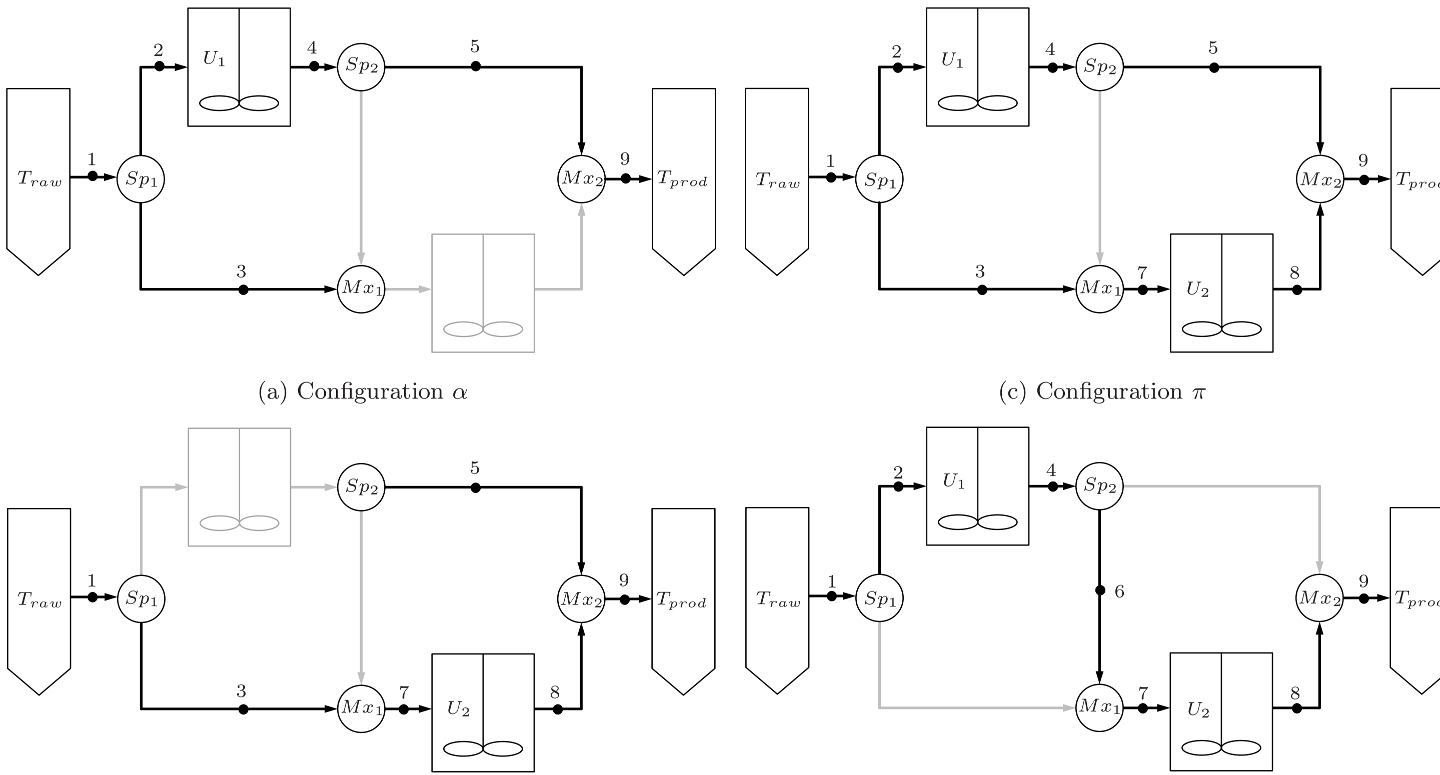
5.3.3 SEN superstructure

The SEN superstructure correspond to the process cell where the process should be implemented (Figure 3.1, § 3.1.1). Considering that the installation of new units and pipelines is not evaluated, the four operating modes of Figure 5.4 can be selected: (a) operation in one single unit U_1, *i.e.* configuration α, (b) or in one single unit U_2, *i.e.* configuration β, (c) operation of U_1 and U_2 in parallel in-phase and with equal phase durations, *i.e.* configuration π, and (d) operation in series with U_1 followed by U_2, *i.e.* configuration σ.

5.3.4 Optimization model

The objective function in this example is to minimize the raw material cost and shortfall penalty, formulated by:

$$\underset{\substack{u_k^{dyn}(t),u^{stat},\\ u^{int},u^{Bool}}}{\text{minimize}} \quad \Phi = Cost_{\mathrm{A},total} + Penalty_{\mathrm{S},total}, \tag{5.11}$$



(a) Configuration α

(c) Configuration π

(b) Configuration β

(d) Configuration σ

Figure 5.4: Allowed operating modes in the Denbigh case study: (a) one single unit U_1 –configuration α, (b) one single unit U_2 –configuration β, (c) both reaction units U_1 and U_2 in parallel in-phase –configuration π, and (d) unit U_1 followed by U_2 in series –configuratoin σ. Grey lines and equipment represent flow rates restricted to zero and processing units disregarded in the formulation.

where $u_k^{dyn}(t)$ are the dynamic control variables, namely the input $F_{1,k}^j(t)$ and output $F_{2,k}^j(t)$ flow rates and the reaction temperature $\theta_k^j(t)$ in stages $k \in \{1, 2, 3\}$ which correspond to load, hold, and unload operations of batch units $j \in \{U_1, U_2\}$ in this example, u^{stat} are the time-invariant continuous decision variables, namely the duration t_l of mathematical stages l which correspond to batch operations in the selected unit procedures, u^{int} are the integer decision variables, involving the number of batches NB_{S} of product S, and u^{Bool} comprise equipment Booleans Y_j, task-unit assignment Booleans $W_{j,q}$, and configuration Booleans X_ψ^1 in reaction stage 1. The first term of the objective function Φ refers to raw material expenses of the complete production campaign:

$$Cost_{\mathrm{A},total} = NB_{\mathrm{S}}\; Cost_{\mathrm{A}}, \tag{5.12}$$

where $Cost_{\mathrm{A}}$ denotes the raw material cost of each batch and is calculated according to Eq. 5.3 with a price of raw material $\hat{p}_{\mathrm{A}}$ of $4.8\, c€/kg$. As for the second term of Φ, it represents the economic impact of the unaccomplished demand, where $\hat{p}_{penal}$ is a function of twice the selling price $\hat{p}_{\mathrm{S}}$ of final product S, which has a value of $43.1\, c€/kg$, according to Eq. 5.7. Then, the penalty function for the entire production reads as:

$$Penalty_{\mathrm{S},total} = 2\; \hat{p}_{\mathrm{S}}\; Shortfall_{\mathrm{S}}. \tag{5.13}$$

Besides the objective function, the set of equations that define optimization model is formulated according to the modeling strategy and formulation proposed in Chapter 3. The exhaustive MLDO of this problem is provided in Appendix A, accompanied by the specification of the sets and parameters to solve the integrated batch process development problem. For instance, it is there detailed how logical propositions from Eqs. 3.10 and 3.17-3.20 remove six degrees of freedom associated to Booleans and therefore permit to reduce the ten logical decisions u^{Bool}=$\{Y_j,\, W_{j,q},\, X_\psi^1\}$ of the model to four, namely the selection of the processing mode X_ψ^1. Moreover, the four input and output flow rates of batch units that behave as control variables at Level 1 are reduced to three in series configuration σ, since its flow distribution involves that two flow rates –*i.e.* $N_{1,\sigma}^0$=$\{3, 5\}$– are constrained to zero instead of one –*i.e.* $N_{1,\psi}^0$=$\{6\}$, ψ=$\{\alpha,\beta,\pi\}$– and thus removes one extra DOF.

The evaluation of additional KPIs of the solution performance is also defined in Appendix A. For instance, the product selectivity is a measure of the process efficiency. Another crucial indicator is the profitability, which not only ensures the economic viability of the solution, but also takes into account the production time to promote fast deliveries.

Finally, the existing plant of this example is characterized by a reactor capacity of $1\, m^3$ in U_1 and U_2, by a maximum input and output flow rates of $7.7\, m^3/h$, and by a maximum permitted temperature of 80°C in reactor U_1 and of 110°C in reactor U_2. Raw material enters the reaction system with a temperature of 25°C and a molar composition of 100% of reactant A.

5.3.5 Problem solution

The MLDO is reformulated into a MINLP using 32 finite elements in this example. Table 5.4 summarizes the features of the resulting MINLP models implemented in GAMS. Four IFS are first generated using constant profiles for the control variables $F_{1,k}^j(t)$, $F_{2,k}^j(t)$, and $\theta_k^j(t)$ in each mathematical stage $k \in \{1, 2, 3\}$ and unit $j \in \{U_1, U_2\}$ and fixing the configuration Booleans X_ψ=$true$ alternatively for each possible configuration $\psi \in \{\alpha, \beta, \pi, \sigma\}$.

Next, the complete MINLP problem is solved without any IFS and with the four IFS previously obtained.

Overall, this simple heuristic to carry out the optimization using several IFS solutions in the search procedure aims at identifying local optima and increase the probability to find the best solution. However, it is necessary to bear in mind that the global optimum can not be guaranteed. For instance, four different feasible solutions have been obtained solving this example. From them, only the solution obtained through the MINLP optimization with IFS 4 provides the best solution. In this case, 5 major and 1,085,864 minor iterations are required in the search procedure of DICOPT solver. The optimal solution is obtained at the major iteration 2.

	No. equations	No. continuous variables	No. discrete variables	Non-zero elements	Non-linear terms	Solution time
IFS 1 (fixed α)	103,209	98,339	6	346,759	159,578	490 s.
IFS 2 (fixed β)						648 s.
IFS 3 (fixed π)						663 s.
IFS 4 (fixed σ)						747 s.
MINLP with IFS 4	102,633	98,321	10	345,643	159,586	10,856 s.

Table 5.4: Features of the MINLP models implemented in GAMS in retrofit Denbigh example, obtained using 32 finite elements and 3 collocation points in the discretization step: IFS solutions for each fixed configuration with X_ψ=*true*, $\psi \in \{\alpha, \beta, \pi, \sigma\}$ and complete MINLP problem initialized with IFS 4.

5.3.6 Results and discussion

For comparative purposes, the optimal solution of problem stated above is contrasted with a fixed recipe with a predefined production size of 300 $kg/batch$ of product S, requiring a production of 70 batches and a batch processing time of 2.06 $h/batch$ to fulfill the demand of 21 tn in its entirety within the time horizon of 144 hours. The operating mode is also fixed to configuration β, setting Boolean decisions to X_β^1, Y_{U_2}, and $W_{U_2,1}$ with a *true* value. Additionally, unit U_2 is defined to operate with maximum input and output flow rates (7.7 m^3/h) in input and output operations and with maximum reaction temperature (110°C) to guarantee a feasible production.

Additionally, the optimization problem is solved for three cases with different DOF to track the effect of the structural and performance decisions:

- **Dynamically optimal recipe:** optimization of dynamic profiles with fixed configuration β;
- **Structurally optimal recipe:** optimization of structural decisions with constant profiles for control variables $F_{1,1}^j(t)$, $F_{2,3}^j(t)$, and $\theta_k^j(t), k \in \{1,2,3\}$, $j \in \{U_1, U_2\}$; and
- **Optimal recipe:** optimization of dynamic profiles and structural decisions according to the problem statement previously defined.

In all cases, the number of batches and the duration of batch operations are free decision variables. The optimal operating mode for both optimizations that include structural decisions corresponds is series configuration σ, as is illustrated in Figure 5.5. This configuration activates the multistage models associated to units U_1 and U_2, which should be synchronized such that the unload operation of the former unit becomes the input operation of the latter one.

For the case of the optimal recipe with all the DOF of the problem statement, the synchronization of batch operations is detailed in Figure 5.6 which illustrates the mathematical stages at Levels 1 and 0 for the production of one batch. The time connection across the three time axes is accomplished through synchronization equations of the formulation proposed in Chapter 3 (p. 79). Additionally, the trajectories of dynamic control variables $F^j_{1,1}(t)$, $F^j_{2,3}(t)$, and $\theta^j_k(t), k \in \{1,2,3\}$, $j \in \{U_1, U_2\}$ are illustrated in Figure 5.7(b1-c1,b2-c2), where all the profiles range between lower and upper bounds in this recipe. There, the correspondence between output flow rate from unit U_1 $F^{U_1}_{3,2}$ and input flow rate to unit U_2 $F^{U_2}_{1,1}$ can be observed since they are also synchronized in transfer operations, unlike the case of temperature which is an internal variable of each unit procedure. Additionally, Figure 5.7(b3-c3,b4-c4) presents the most relevant process variables, which are the reaction volume and molar composition, and all of them are compared to the trajectories of the fixed recipe in batch unit U_2 in Figure 5.7(a1-a4).

The incentives to improve the process performance through the proposed modeling strategy are estimated by comparing the raw material expenses obtained for each recipe with regard to the fixed one, since the all of them are successful in the fulfillment of the entire demand –therefore reducing to zero the shortfall penalty in the objective function Φ. Compared to the fixed recipe, a decrease of the 12% in the total raw material consumption is achieved by optimizing the dynamic profiles with a predefined configuration β, whereas

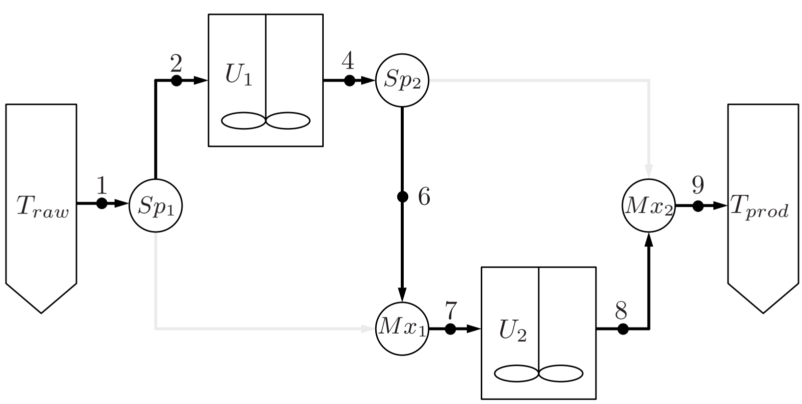


Figure 5.5: Optimal operating mode in all optimizations that include structural decisions in retrofit Denbigh example: equipment configuration σ.

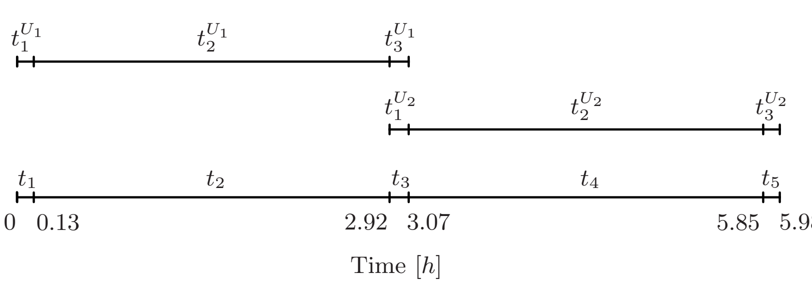


Figure 5.6: Synchronization of global and unit stages and optimal transition times in retrofit Denbigh example.

it is reduced as far as a 24% when qualitative decisions are considered as degrees of freedom with constant profiles. This improvement becomes a 25% when all decisions are considered in the optimal recipe. Thus, the total cost of raw material descends from 2,250 € to 1,989 €, 1,715 €, and 1,687 € respectively, as is shown in Table 5.5. In this table, further KPIs and economic weights, like the product selectivity, the total energy consumption, the profit, or the processing costs, are summarized to provide a comprehensive assessment of each recipe.

The reduction of raw material expenses is related to the increase of the product selectivity from 0.448 in the fixed recipe to 0.507 in the dynamically optimal recipe in unit U_2, 0.588 in the structurally optimal recipe with constant control profiles, and 0.597 in the optimal recipe. The selectivity improvement is related to the molar fractions profiles presented in Figure 5.7(a4-c4), which show how the final amount of product S achieves a higher value in the final time of the optimal recipe –in the second unit procedure– compared to the final time of the fixed recipe. At the same time, consumption of intermediate R rises dramatically in the optimal recipe; the fraction of R becomes almost zero in the final time in front to the near 0.1 value in the fixed one. Moreover, the generation of byproducts like T is considerably lower in the optimal recipe.

Essentially, the improvement of product selectivity is due to the optimization of the dynamic temperature profile and, most important, to the arrangement of the two reaction units in series –configuration σ. First, the temperature starts at the lower bound 50°C in the first unit procedure in U_1 of the optimal recipe, as is shown in Figure

KPI	Fixed recipe	Dynamically optimal	Structurally optimal	Optimal recipe
Equipment configuration	β	β	σ	σ
No. Batches	70	54	48	47
Batch size [$kg/batch$]	300	389	438	447
Total processing time [h]	144.03	144.03	144.03	144.03
Batch processing time [$h/batch$]	2.06	2.67	5.88	5.98
Batch cycle time [$h/batch$]	2.06	2.67	3.00	3.06
Shortfall of product S [kg]	0	0	0	0
Total Profit [€]	4,764	5,332	5,037	5,097
Total revenue	9,046	9,046	9,046	9,046
Raw material cost	**2,250**	**1,989**	**1,715**	**1,687**
Processing cost in U_1	0	0	733	727
Processing cost in U_2	967	899	92	95
Occupation cost in U_1	0	0	735	720
Occupation cost in U_2	1,065	825	735	720
Amortization in U_1	0	0	0	0
Amortization in U_2	0	0	0	0
Penalty	**0**	**0**	**0**	**0**
Profit per batch [€/$batch$]	68	113	107	108
Profitability [€/h]	33	37	35	35
Selectivity of S [$kmol$ S/$kmol$ $total$]	0.448	0.507	0.588	0.597
Total energy consumption [kWh]	38,692	35,973	32,974	32,879

Table 5.5: KPIs and individual economic weights in retrofit Denbigh example: fixed recipe, dynamically optimal recipe in U_2, structurally optimal recipe with constant profiles of the control variables, and integrated optimal recipe for all DOF in the problem statement. Items in bold correspond to the objective function.

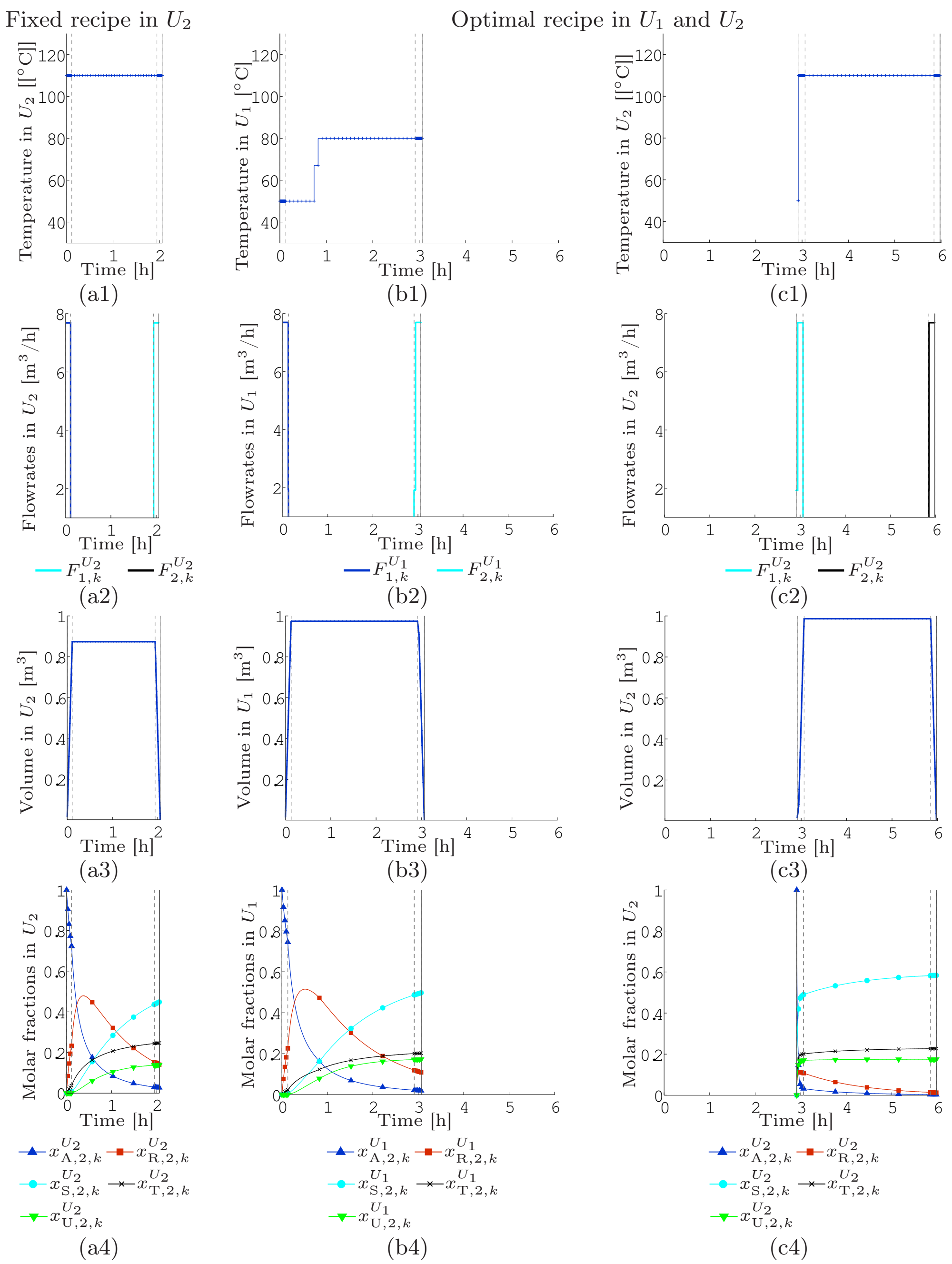


Figure 5.7: Control and process variable profiles in the fixed and the optimal recipes in retrofit Denbigh example: (a) unit procedure in U_2 in the fixed recipe, (b) unit procedure in U_1 in the optimal recipe, and (c) unit procedure in U_2 in the optimal recipe.

5.7b1, thus encouraging the selectivity of R with respect to T by favoring reaction 1 ($E_{a,1}$=1000 $kcal/kmol$) with respect to reaction 2 ($E_{a,2}$=2580 $kcal/kmol$) of the reaction mechanism. The profile gradually increases to the upper bound 80°C, favoring reaction 3 ($E_{a,3}$=1800 $kcal/kmol$) with respect to reaction 4 ($E_{a,4}$=1210 $kcal/kmol$), thus promoting the production of the desired product S instead of U. In the second unit procedure in U_2, presented in Figure 5.7c1, the temperature profile rises even more, up to the upper bound of 110°C in this unit.

Second, production is restricted in all recipes by the maximum time horizon of 144 h, as is seen in Table 5.5, and by the available equipment capacities of 1 m^3 in U_1 and U_2 which restrict the reaction volume, as is illustrated in Figure 5.7(a3-c3). This way, series operating mode σ favors the process performance by enlarging the reaction volume. For the same reason, parallel configuration π, which duplicates the reaction volume in the same way, also provides a reduction of the raw material costs that is only slightly smaller than for the optimal σ configuration. The predominance of the last operating mode is probably due to an upper bound in unit U_1 being much lower than the upper bound in unit U_2. This temperature restriction would have certainly a major impact if applied to the complete unit procedure assigned to this unit than if applied uniquely to a first reaction stage –favored by lower temperatures as previously discussed– which is followed by a second reaction stage with a higher temperature range. In contrast, configuration α characterized by the single operation of unit U_1 provides the worst case, with a cost increase of the 1% with respect to the fixed recipe in U_2. This increase is due to the limitation of the reaction temperature at 80° in the complete operation frame, partially mitigated by the optimization of the batch size, which is increased to almost 340 $kg/batch$ with respect to the 300 $kg/batch$ in the fixed recipe. Thus, the number of batches is reduced from NB_S=70 to 62, and the batch processing time can be longer, raising from 2.06 to 2.32 $h/batch$. In summary, the time and space restrictions could be also overcome by the replacement of existing units U_1 and U_2 by equipment of larger size. This possibility will be studied in a forthcoming example.

In contrast, the use of dynamic control variables in transfer operations barely affects the solution. The feed-forward trajectories of flow rates in the optimal recipe are lead to their upper bound in most of the trajectory, as is shown in Figure 5.7(b2-c2), obtaining profiles similar to the ones in the fixed recipe in Figure 5.7a2. Thus, load and unload operations tend to be as short as the pumping capacity and the charge requirement permit. Moreover, the dynamic feed-forward profile of reaction temperature is neither exploited in input and output stages, and is kept constant as it can be observed in Figure 5.7(b1-c1). On the face of it, the optimization of a unique set-point in these stages provides similar results, as is prove with the structural optimization with constant control profiles.

Further conclusions can be made by taking a look to other KPIs of Table 5.5. The trade-off between selectivity of product S and heating cost does not affect the definition of the temperature profile in this example, given that this cost is not included into the objective function. Nevertheless, processing costs associated to heat consumption also diminish, principally due to the reduction of the energy consumption associated to side reactions 2 and 4, which are endothermic, thanks to the limiting of their conversion. In addition, the increase of product S selectivity goes hand in hand to a reduction of the reactant A required in each batch and to a reduction in the total reaction mixture in the system. As a result, the heat to reach the processing temperature is smaller and the optimal recipe benefits from a collateral 15% reduction of processing costs. Besides, null amortization costs are obtained in all recipes, since new investments are not considered in this example. Nevertheless, the improvement in the total profit is only a 6.5% in the optimal recipe with configuration σ, smaller than the 11.9% achieved in optimal recipe with configuration β –*i.e.* the dynamically optimal recipe–, despite the diminution in both raw material and energy costs. This results from the fact that occupation costs increase dramatically due to the use of two reactors, what involves the duplication of the associated labor costs, like cleaning and rental costs, as is further discussed in next example.

5.4 Denbigh case study: process improvement in retrofit scenarios

The Denbigh example presented in previous section (§ 5.3) is extended. The objective is to evaluate the potential of the proposed approach for process improvement according to different decision criteria and economic situations. The process should be implemented in the same reactor network (Figure 3.1, p. 54) where the installation of new plant elements is not considered. To that end, the master recipe is optimized in consonance with the objective function defined in each retrofit scenario, allowing the four equipment configurations α, β, π, and σ previously presented (Figure 5.4, p. 119). The prior methodology of section § 5.2.2 is applied, following the steps of Figure 5.3 (p. 115).

5.4.1 Retrofit scenarios

The batch process improvement here addressed corresponds to the problem statement of previous example (p. 117) with different objective functions. Particularly, the problem is solved for these cases:

- **(i)** **Profit maximization:** base case, which pursues the total profit maximization in the production of 21 tn of product S through Denbigh reaction system in the given process cell with a maximum time horizon of 144 hours and the economic scenario 1 from Table 5.6;
- **(ii)** **Higher raw material price:** equivalent problem to case i with a duplication in the price of raw material $\hat{p}_{\mathrm{A}}$, what corresponds to the economic scenario 2 from Table 5.6;
- **(iii)** **Higher processing costs:** equivalent problem to case i with an increase of three times in the energy cost $\hat{c}_j$, what corresponds to the economic scenario 3 from Table 5.6;
- **(iv)** **Profitability maximization:** equivalent problem to case i now maximizing the profitability instead of the total profit in the economic scenario 1 from Table 5.6;
- **(v)** **Production of R:** equivalent problem to case i now satisfying a demand of 21 tn of product R instead of product S, what corresponds to the economic scenario 4 from Table 5.6.

The optimal solutions are compared to the fixed recipe. Like in the previous example, this is defined to produce batches with a production size of 300 $kg/batch$, a batch processing time of 2.06 $h/batch$, and configuration β. Therein, unit U_2 is defined to operate with maximum load and unload flow rates (7.7 m^3/h) and maximum reaction temperature (110°C) for the production of product S, in order to enable the total demand production within the given time horizon. The fixed recipe for product R is the same, except for the reaction temperature, which is defined with the minimum value (50°C) to favor the conversion of reaction 1 rather than reaction 3.

5.4.2 Results and discussion

The results for the retrofit cases i-v are summarized in Table 5.7. Figures 5.8 to 5.12 illustrate the profiles of control and state variables in the fixed and the optimal recipes of each case.

Case i: Profit maximization

In previous example, where raw material expenses and shortfall penalty were minimized, the optimal configuration obtained was σ, with units U_1 and U_2 operating in series. This configuration provided the higher selectivity of product S with a value of 0.597, which has a tight relation with the reduction of the feedstock consumption. Now, the objective function is the profit maximization, which is defined through the equivalent minimization problem:

$$\begin{aligned} \underset{\substack{u_k^{dyn}(t),u^{stat},\\ u^{int},u^{Bool}}}{\text{minimize}} \quad \Phi =& -Profit_{total} \\ =& -Revenues_{\mathrm{S},total} - Penalty_{\mathrm{S}} - Cost_{\mathrm{A},total} \\ & -\textstyle\sum_{j\in\{U_1,U_2\}} \left(Cost_{j,p,total} + Cost_{j,o,total} + Cost_{j,a,total}\right). \end{aligned} \tag{5.14}$$

As a result, the incorporation of occupation costs into the objective function dampers structural solution σ. Configuration π, with units U_1 and U_2 operating in parallel, becomes the optimal one. The reason is that operating mode σ involves nearly the double equipment utilization compared to π, understood as the number of times that a unit is started. In particular, both configuration use two units per batch but σ requires 47 batches in front of the 23 needed by π. As a result, operation π provides a total occupation cost of $360\,€/batch$ in each unit (Table 5.7) in contrast to the $720\,€/batch$ in each unit (Table 5.5) provided by σ.

Examining the profiles of control and process variables, presented in Figure 5.8, it is noted that configuration π maintains similar reaction volume and time than σ (Figure 5.7). Previous unit procedures in units U_1 and U_2 are now merged in a unique procedure either in unit U_1 or in unit U_2 with a higher time span –*i.e.* $6.26\,h$ in configuration π compared to $3.06\,h$ in σ. Therefore, each processing unit is occupied a less number of times with a double duration. Overall, how the occupation costs are defined affects considerably to the optimal configuration obtained.

Regarding the temperature profiles in Figure 5.8(b1-c1), the unit procedure in U_1 reaches the maximum temperature (80°C). However, a compromise is met in the case of U_2, which operates at 94°C and not at the upper bound (110°C). Additionally, both units are charged with a same amount of raw material A since they reach a same volume at

Scenario	$\hat{c}_j$ [$c€/kWh$]	$\bar{c}_{j,A}$ [$€/batch$]	$\bar{c}_{j,B}$ [$€/m^3 batch$]	$\bar{c}_{j,C}$ [$€/h\,batch$]	$\check{c}_j$ [$€/h$]	$\hat{p}_{\mathrm{A}}$ [$c€/kg$]	$\hat{p}_{\mathrm{S}}$ [$c€/kg$]	$\hat{p}_{\mathrm{R}}$ [$c€/kg$]	$\hat{p}_{penalty}$ [$c€/kg$]
1	2.5	5	10	0.21	0	4.8	43.1	-	$2\,\hat{p}_p$
2	2.5	5	10	0.21	0	9.6	43.1	-	$2\,\hat{p}_p$
3	10	5	10	0.21	0	4.8	43.1	-	$2\,\hat{p}_p$
4	2.5	5	10	0.21	0	4.8	-	35.8	$2\,\hat{p}_p$

Table 5.6: Parameters of economic scenarios 1-4 in retrofit Denbigh example: unitary processing costs $\hat{c}_j$, unitary occupation costs $\bar{c}_{j,A}$, $\bar{c}_{j,B}$, and $\bar{c}_{j,C}$, and base amortization cost $\check{c}_j$ of reactors $j \in U$, price of raw material A $\hat{p}_{\mathrm{A}}$, price of final products $\hat{p}_p$, $p \in \{\mathrm{S},\mathrm{R}\}$, and shortfall penalty $\hat{p}_{penal}$.

KPI	Case i		Case ii		Case iii		Case iv		Case v	
Equipment configuration	(β)	π	(β)	π	(β)	π	(β)	π	(β)	α/β
No. Batches	(70)	23	(70)	23	(70)	24	(70)	31	(70)	53
Batch size [$kg/batch$]	(300)	913	(300)	913	(300)	875	(300)	677	(300)	396
Total processing time [h]	(144.03)	144.03	(144.03)	144.03	(144.03)	144.03	(144.03)	66.49	(33.90)	27.66
Batch processing time [$h/batch$]	(2.06)	6.26	(2.06)	6.26	(2.06)	6.00	(2.06)	2.14	(0.48)	0.52
Batch cycle time [$h/batch$]	(2.06)	6.26	(2.06)	6.26	(2.06)	6.00	(2.06)	2.14	(0.48)	0.52
Shortfall of product S [kg]	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0
Total Profit [€]	**(4,764)**	**5,841**	**(2,515)**	**4,147**	**(1,862)**	**3,501**	(4,764)	4,861	**(4,147)**	**4,389**
Revenue	(9,046)	9,046	(9,046)	9,046	(9,046)	9,046	(9,046)	9,046	(7,538)	7,538
Raw material cost	(2,250)	1,696	(4,499)	3,380	(2,250)	1,767	(2,250)	2,286	(1,937)	1,949
Processing cost in U_1	(0)	389	(0)	387	(0)	1,514	(0)	458	(0)	402
Processing cost in U_2	(967)	400	(967)	411	(3,869)	1,514	(967)	497	(401)	0
Occupation cost in U_1	(0)	360	(0)	360	(0)	375	(0)	472	(0)	798
Occupation cost in U_2	(1,065)	360	(1,065)	360	(1,065)	375	(1,065)	472	(1,054)	0
Amortization in U_1	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0
Amortization in U_2	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0
Penalty	(0)	0	(0)	0	(0)	0	(0)	0	(0)	0
Profit per batch [€/$batch$]	(68)	254	(36)	180	(27)	146	(68)	157	(59)	83
Profitability [€/h]	(33)	41	(17)	29	(13)	24	**(33)**	**73**	(122)	159
Selectivity of S [$kmol$ S/$kmol\ total$]	(0.448)	0.595	(0.448)	0.597	(0.448)	0.571	(0.448)	0.441	(0.520[a])	0.517[a]
Total energy consumption [kWh]	(38,692)	31,558	(38,692)	31,957	(38,692)	30,286	(38,692)	38,211	(16,026)	16,078

[a] Selectivity of R [$kmol$ R/$kmol\ total$]

Table 5.7: KPIs and individual economic weights in retrofit Denbigh example for the fixed and the optimal recipes in the following cases: (i) profit maximization in the base case, (ii) case i with duplication of raw material cost $\hat{p}_A$, (iii) case i with an increase of three times in processing cost $\hat{c}_j$, (iv) case i maximizing profitability, and (v) case i with demand of product R instead of S. Each of the cases is compared to its corresponding fixed recipe in brackets. Items in bold indicate the objective function.

the end of the first stage in Figure 5.8(b3-c3). However, due to the different temperature profiles, the final molar fraction of product S is 0.586 in U_1 and slightly higher 0.591 in U_2.

Finally, the obtained KPIs are shown in Table 5.7 (case i). There, an improvement of the 23% in the total profit is recorded with regard to the use of the fixed recipe, scaling from $4,764$ € to $5,841$ € for the total production of $21\,tn$ of product S. This increase is related to a reduction of 24.6% in total raw material costs (from $2,250$ to $1,696$ €), 32.4% in occupation costs (from $1,065$ to 720 €), and 18.4% in total processing costs (from 967 to 789 €). In turn, these gains are caused by a higher selectivity, a lower energy consumption, and a reduction in the number of unit start-ups.

Case ii: Higher raw material price

To evaluate the adaptability potential, the profit maximization problem is solved now considering a duplication in raw material price $\hat{p}_{\mathrm{A}}$. The optimal solution in this retrofit case is very similar to the previous one, with the same configuration π, the same number of batches 23, and very similar profiles in the input and output flow rates. The major difference is that now the temperature profile in unit U_2 tends toward the upper bound, as is illustrated in Figure 5.9(b1-c1). This way, the molar fraction in U_2 is slightly higher than in case i, with a value of 0.594, while it achieves the same value of 0.586 in U_1, as is shown in in Figure 5.9(b4-c4). Since the raw material cost has a more important role in the objective function, the selectivity improves as much as possible –*i.e.* up to a value of 0.597– by means of the temperature modification. Nevertheless, configuration σ, which is characterized by a high selectivity, is prevented due to the high occupation costs associated, as was previously discussed.

Other KPIs are summarized in Table 5.7 (case ii). In this case, the improvement in the total profit with regard to the fixed recipe is even more convincing, with a percentage of the 65% involving a rise from $2,515$ to $4,147$ €. The higher improvement percentage indicates the higher effect of selectivity rise and raw material savings in the objective function. In this case, the diminution of raw material expenses, occupation costs, and processing costs represents a 24.9% (from $4,499$ to $3,380$ €), 32.4% (from $1,065$ to 720 €), and 17.4% (from 967 to 798€) respectively.

Case iii: Higher processing costs

An increase in the unitary heating cost $\hat{c}_j$ in units U_1 and U_2 is now considered, changing from $2.5\,c€/kWh$ to an hypothetic case where energy cost rises to $10\,c€/kWh$. This solution involves again parallel equipment configuration π, but with 24 batches instead of 23. However, principal difference with the optimal solution in case i is referred to the feed-forward temperature profiles. In this case, the temperature in both reactors U_1 and U_2 decreases down to nearly the lower bound, as is shown in Figure 5.10(b1-c1), since the processing costs depend on the required energy consumed for heating the mixture and for driving the endothermic reaction system. Then, the goal is to reduce the energy requirements as much as possible, since the heating cost now has a predominant role in the objective function.

The KPIs are shown in Table 5.7 (case iii), where it can be observed that the increase in parameter $\hat{c}_j$ implies a dramatic increment of processing costs compared to the retrofit scenario i, despite working almost at the minimum temperature. Raw material expenses are also higher. The reason is that the selectivity of product S suffers a slight diminution down to 0.571. This is reflected in lower molar compositions of product S at final time, with a value of 0.565 in the both units U_1 and U_2 that have an identical behavior (Figure 5.10(b4-c4)). Overall, the lower selectivity derives in a raise of raw material consumption.

Finally, the largest improvement in the objective function with regard to the fixed recipe is obtained in this retrofit case, with a 88% improvement in the total profit with regard to the fixed recipe, scaling from $1,862$ to $3,501$ €. The associated improvement in raw material, occupation, and processing costs are the 21.5% (from $2,250$ to $1,767$ €), 29.6% (from $1,065$ to 750 €), and 21.7% (from $3,869$ to 3028€) respectively.

Case iv: Profitability maximization

An alternative situation is screened by considering a different objective function that take into account the processing time, the profitability. The optimization problem in this case is defined by:

$$\begin{aligned} \underset{\substack{u_k^{dyn}(t), u^{stat}, \\ u^{int}, u^{Bool}}}{\text{minimize}} \quad \Phi &= -Profitability \\ &= -Profit_{total}/T^{total}, \end{aligned} \tag{5.15}$$

where $Profit_{total}$ and T^{total} are the profit and processing time with regard to the total production of $21\,tn$ of S. This way, processing time is contemplated indirectly in the objective function and the optimal solution will take into account the compromise between the economic gain and the possible reduction of the processing time.

The optimal configuration obtained is the use of parallel equipment configuration π. The KPIs of this retrofit scenario are summarized in Table 5.7 (case iv), whereas Figure 5.11 illustrates the profiles of control and process variables. The process is accelerated by reducing the batch size to $677\,kg/batch$ in front of the 875-913 $kg/batch$ defined in previous retrofit scenarios i-iii and increasing the reaction temperature to the upper bound in each reactor (80°C in U_1 and 110°C in U_2) in most of the operation. As a result, the optimal solution now exhibits higher processing costs than the previous identified solutions, as shown in Table 5.7 (case iii). Additionally, a worse selectivity and raw material expenses are also reported, as well occupation costs. In contrast, the total processing time is extremely reduced to less than a half (*i.e.* 66.5 hours), providing a huge time margin in the 144 hours of time horizon.

To sum up, the objective function improves a 121% with respect to its corresponding fixed recipe, with a profitability value rising from 33 to 73 €$/h$. This is mostly obtained through the reduction of the total processing time while the total profit is maintained with a similar value $4,764$ in the fixed recipe and $4,861$€ in the optimal one.

It is interesting to note that the feed-forward trajectory of the temperature control in both reactors follows a dynamic profile, despite the objective of this recipe is to produce each batch as fast as possible regardless the achieved selectivity of product S. In contrast, input and output flow rates are set in their upper bounds during the whole time interval. This proves that dynamic profiles can have a beneficial influence for specific control variables, at least in competitive reaction systems where it is necessary to favor some particular reactions and hinder others. Nevertheless, it is necessary to select carefully which control variables are worth to be dynamic, in order to find an equilibrium between challenging solutions and computational load in the optimization process.

Case v: Production of R

Additionally, the proposed strategy for process synthesis and allocation in retrofit scenarios may also applied to give a response to a new demanded product. In this case, the

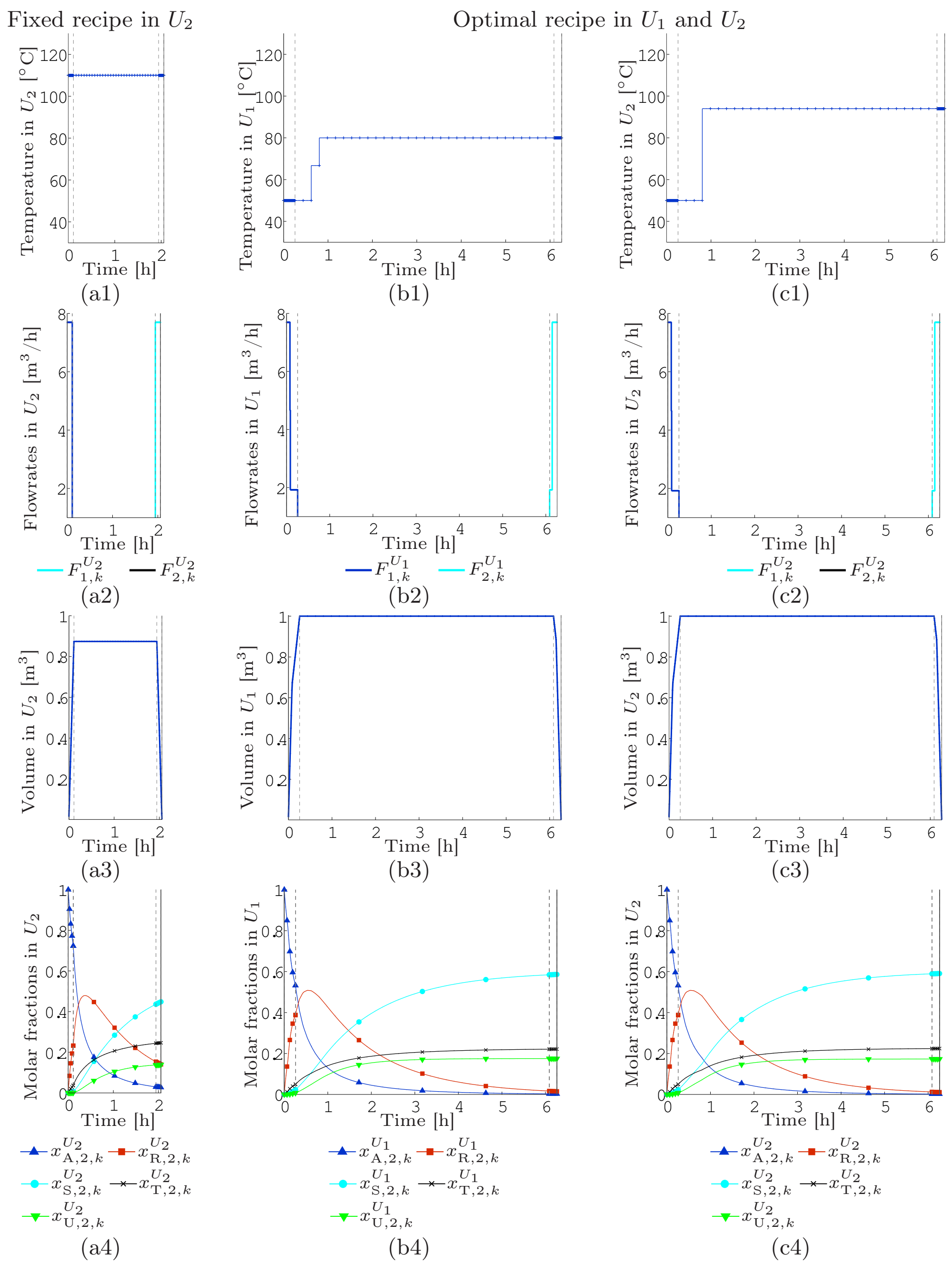


Figure 5.8: Control and process variable profiles in the fixed and the optimal recipes in retrofit Denbigh example (case i): (a) unit procedure in U_2 in the fixed recipe, (b) unit procedure in U_1 in the optimal recipe, and (c) unit procedure in U_2 in the optimal recipe.

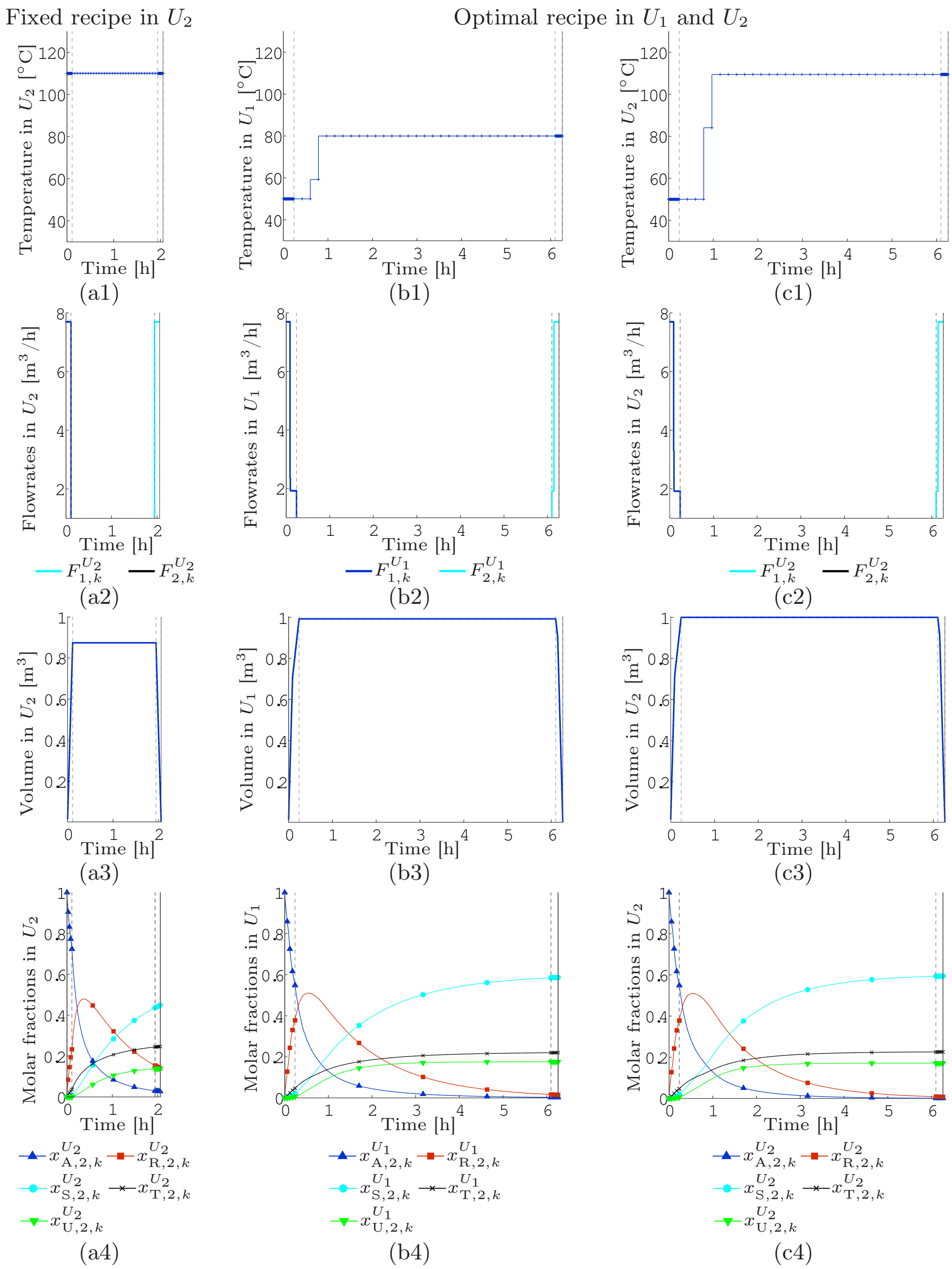


Figure 5.9: Control and process variable profiles in the fixed and the optimal recipes in retrofit Denbigh example (case ii): (a) unit procedure in U_2 in the fixed recipe, (b) unit procedure in U_1 in the optimal recipe, and (c) unit procedure in U_2 in the optimal recipe.

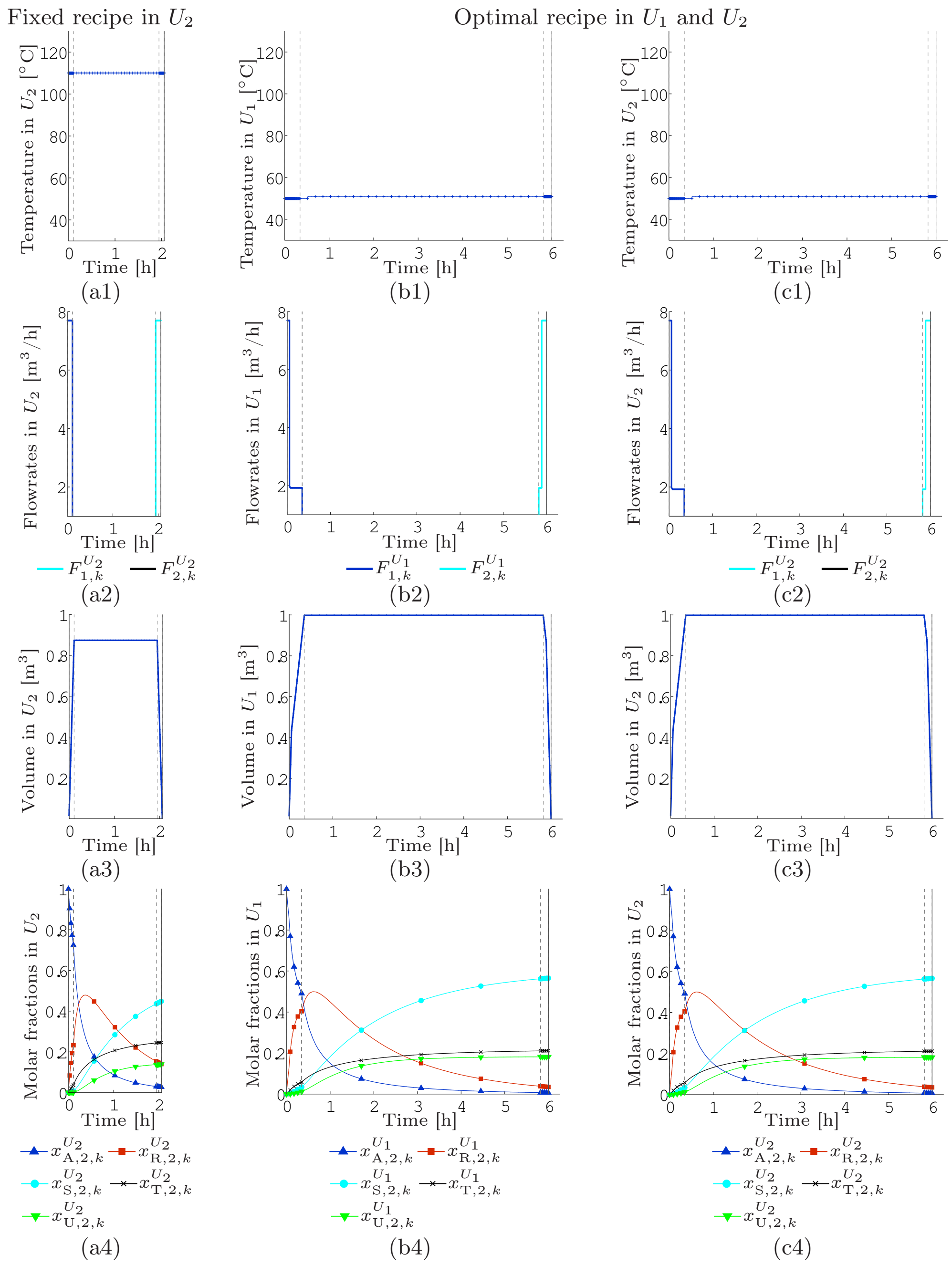


Figure 5.10: Control and process variable profiles in the fixed and the optimal recipes in retrofit Denbigh example (case iii): (a) unit procedure in U_2 in the fixed recipe, (b) unit procedure in U_1 in the optimal recipe, and (c) unit procedure in U_2 in the optimal recipe.

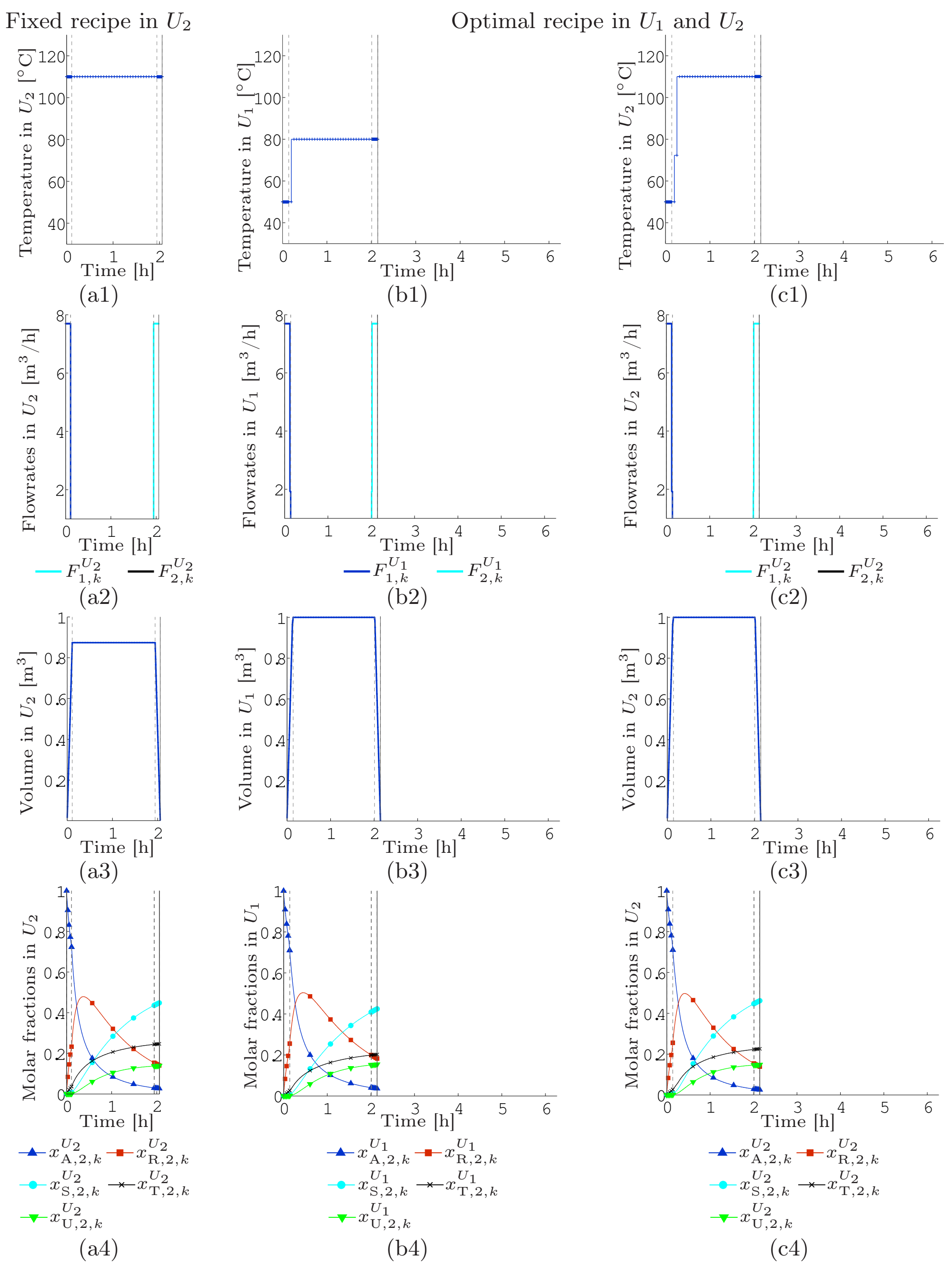


Figure 5.11: Control and process variable profiles in the fixed and the optimal recipes in retrofit Denbigh example (case iv): (a) unit procedure in U_2 in the fixed recipe, (b) unit procedure in U_1 in the optimal recipe, and (c) unit procedure in U_2 in the optimal recipe.

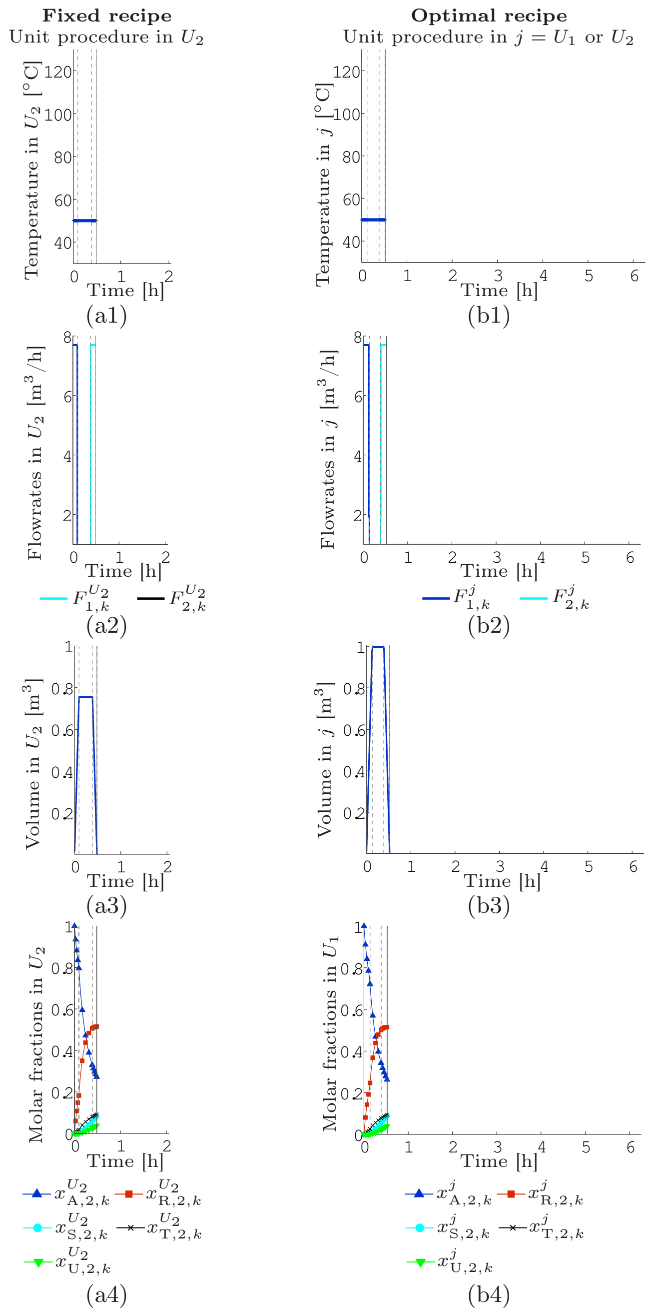


Figure 5.12: Control and process variable profiles in the fixed and the optimal recipes in retrofit Denbigh example (case v): (a) unit procedure in U_2 in the fixed recipe, (b) unit procedure in U_1 or U_2 in the optimal recipe.

desired product considered is R instead of S, which is produced through reaction 1 (faster) and consumed through reactions 3 and 4 (slower) from Eq. 5.10. The objective function reads as:

$$\begin{aligned}\underset{\substack{u_k^{dyn}(t),u^{stat},\\ u^{int},u^{Bool}}}{\text{minimize}} \quad \Phi =& -Profit_{total}\\ =& -Revenue_{\mathrm{R},total} - Penalty_{\mathrm{R}} - Cost_{\mathrm{A},total}\\ & -\textstyle\sum_{j\in\{U_1,U_2\}} \left(Cost_{j,p,total}+Cost_{j,o,total} + Cost_{j,a,total}\right).\end{aligned} \tag{5.16}$$

The optimal configuration obtained in this retrofit scenario is the operation of one single unit, either U_1 with configuration α or U_2 with configuration β, with minimum temperature (50°C). The profiles of control and process variables are illustrated in Figure 5.12. Compared to the equivalent solution using a fixed recipe model– which was also defined to operate at the minimum temperature in U_2–, the objective function does not improve more than a 5.8%, with the profit slightly rising from 4, 147 to 4, 389 €. The KPIs associated to this solution are shown in Table 5.7 (case v).

Analyzing these results, it is evident that the optimization of dynamic profiles does not provide any real advantage, beyond to find the extreme conditions where the reaction of interest is promoted and the side reactions are mitigated. This is probably related to the fact that producing R relies on one single reaction of the kinetic scheme and, therefore, a constant value for the control variables is the optimal along the complete time span. In any case, it can be concluded that it is necessary to discern in which situations it is worth to define the feed-forward control variables with dynamic profiles or with constant variables. Moreover, this process is extremely fast in comparison to the production of S. Therefore, there are no capacity limitations and the operation in a single unit is equally advantageous to the production in series or parallel.

Final remarks

To sum up, the proposed methodology to address the problem of integrated batch process development provides a great flexibility and adaptability to face the different situations and objectives. Overall, improvements between the 5.8% in the worst case (*i.e.* case v) and the 121% in the best case (*i.e.* case iv) have been obtained by optimizing the four basic configurations and the dynamic profiles of the control variables. It should be beard in mind that the five cases solved, as well as the one in previous example (§ 5.3, p. 116), have to be implemented in a process cell with limited capacity for the production requirements.

In the studied retrofit scenarios, the crucial decision variables that allow such improvements are: (a) the configuration, because it permits to duplicate the reaction volume and make the best use of each processing unit, and (b) the temperature, because it allows to untangle the trade-off among the different reaction yields and it determines the compromise in the consumption of the different resources, like energy or feedstock. Regarding the synchronization of the control variable profiles between unit procedures, it does not have a crucial role in this case and it is presumable that an equivalent optimization problem without synchronization Eqs. 3.13 and 3.14 (§ 3.3, p. 79) could provide similar results. In contrast, the synchronization of transfer operation durations between consecutive procedures has a great influence on the achieved selectivity in each unit procedure, since the time is a limiting variable in the entire recipe.

To conclude, while it can be observed how the influence of some of the control variables is minimal –*e.g.* input and output flow rates–, other DOF are fundamental to adapt the process to each objective –*e.g.* temperature profiles, equipment configuration, duration of batch operations–, obtaining improvements as convincing as a 88% (*i.e.* case iii) and 121%

(*i.e.* case iv) with regard to the fixed recipe. Moreover, once the optimization model has been constructed, the proposed methodology to solve the integrated problem becomes an excellent strategy for identifying the critical variables in the process performance, evaluating the optimal recipe in a variety of scenarios, and comparing processing schemes easily.

5.5 Denbigh case study: process improvement with unit capacity expansion

In this example the re-sizing of batch processing units is considered. The Denbigh example is now solved allowing the expansion of unit capacities. The purpose is to evaluate the potential of process improvement associated to plant modifications. To do so, the base case i of previous example (§ 5.4) is now optimized with additional DOF, namely the capacity $Size^j$ of reactors U_1 and U_2. Accordingly, the objective is to maximize the total profit to produce $21\,tn$ of product S through Denbigh reaction system (Denbigh, 1958) with a maximum time horizon of 144 hours taking into account the economic scenario 1 from Table 5.6. The reactor network with equipment expansions also allows the four equipment configurations α, β, π, and σ presented in Figure 5.4 (p. 119).

5.5.1 Capacity expansion

The capacity expansion is introduced into the optimization model by considering the variable $Size^j$ as a degree of freedom. In this example, batch units originally have a default vessel volume of $1\,m^3$ which can be modified with the associated investment costs as was defined in Eq. 5.6. To facilitate the purchase of the reaction vessel, this variable is defined to be discrete with increments of $0.25\,m^3$ between $1\,m^3$ –*i.e.* the original reactor capacity– and $10\,m^3$ –*i.e.* a pre-established upper bound. The base amortization cost $\check{c}_j$ is defined to be zero when the reactor capacity is not modified and $1.03\,€/h$ when it is extended. This parameter is calculated considering a base equipment cost of $71,833\,€$ and an amortization period of 8 year with 52 weeks and 168 working-hours per week. The base equipment capacity $Size^0$ and the power in the amortization function n are set to $3.8\,m^3$ and 0.5 respectively. These values have been extracted from Perry & Gree (1999, p. 9-67 to 9-68) incorporating an economic upgrade.

5.5.2 Results and discussion

The obtained results are provided in Table 5.8. There, it may be observed that the consideration of expanding the capacity of processing units hardly improves the total profit, rising from a value of $5,841\,€$ without equipment expansion to $5,948\,€$ if the size of reaction unit U_1 is increased to $3.5\,m^3$. In this case, the single operation in this unit –configuration α– is posed as the optimal one, saving the occupation costs in the smaller unit U_2. At first glance, these results may not appear very promising, since a long amortization period is established in order to consider an small impact of the investment related to the capacity re-sizing. But this is not reflected in a large improvement in the objective function. Presumably, the reason is that the original two-reactor plant was provided already with the necessary capacity to fulfill the requested demand of product S. This hypothesis is corroborated in an example of next chapter, where the optimal plant for this demand is characterized by a total processing volume of $2\,m^3$, although distributed in one single reactor instead of two.

KPI	No plant modifications	Capacity expansion in $j \in U$
Modified units U	-	U_1
Size of units U $[m^3]$	{1, 1}	{3.5 1}
Equipment configuration	π	α
No. Batches	23	13
Batch size $[kg/batch]$	913	1,615
Total processing time $[h]$	144	144
Batch processing time $[h/batch]$	6.26	11.08
Batch cycle time $[h/batch]$	6.26	11.08
Shortfall of product S $[kg]$	0	0
Total Profit [€]	**5,841**	**5,948**
Revenue	9,046	9,046
Raw material cost	1,696	1,692
Processing cost in U_1	389	729
Processing cost in U_2	400	0
Occupation cost in U_1	360	535
Occupation cost in U_2	360	0
Amortization in U_1	0	142
Amortization in U_2	0	0
Penalty	0	0
Profit per batch [€$/batch$]	254	458
Profitability [€$/h$]	41	41
Selectivity of S $[kmol\ \mathrm{S}/kmol\ total]$	0.595	0.596
Total energy consumption $[kWh]$	31,558	29,159
Temperature range in U_1 [°C]	[50, 80]	50
Temperature range in U_2 [°C]	[50, 94.0]	-

Table 5.8: KPIs and individual economic weights in retrofit Denbigh example with equipment capacity expansion, compared to the retrofit problem without plant modifications. Items in bold correspond to the objective function.

The modification of the plant affects to the distribution of the costs in the optimal recipe. In broad terms, all the costs are reduced except for the amortization load. Raw material cost reduction can be dismissed, going from $1,696$ € to $1,692$ €. However, total occupation cost decreases from 720 € to 535 € and processing cost is reduced from 789 € to 729 €. This improvement is achieved through the increase of the batch processing time, from 6.26 $h/batch$ in the optimal recipe with no plant modifications to 11.03 $h/batch$ in the optimal recipe expanding U_1 capacity, and through the descent of the temperature profiles, which are now set in 50°C, the lower bound.

5.6 Photo-Fenton case study

This example studies an Advanced Oxidation Process (AOP) to reduce paracetamol (PCT) and Total Organic Carbon (TOC) concentrations from a given effluent in a retrofit scenario. The objective is to apply the proposed optimization-based approach to optimize the master recipe that should be executed in an existing AOPs plant. This is composed of a single photo-reactor with a UV lamp of a fixed intensity. Thus, structural decisions associated to equipment configuration are not considered and thus the MLDO problem is simplified in a great deal, becoming a more common DO problem. In contrast, the effect of the dosage of hydrogen peroxide (H_2O_2) is studied by means of a PWC profile, which is compared with other dosage protocols. Additionally, two objectives are taken into account in the optimization, namely the batch processing time and the cost minimization. The results show that cost reductions can be obtained when applying the model-based optimization techniques proposed, and hint new opportunities for AOPs enhancement.

5.6.1 Process description

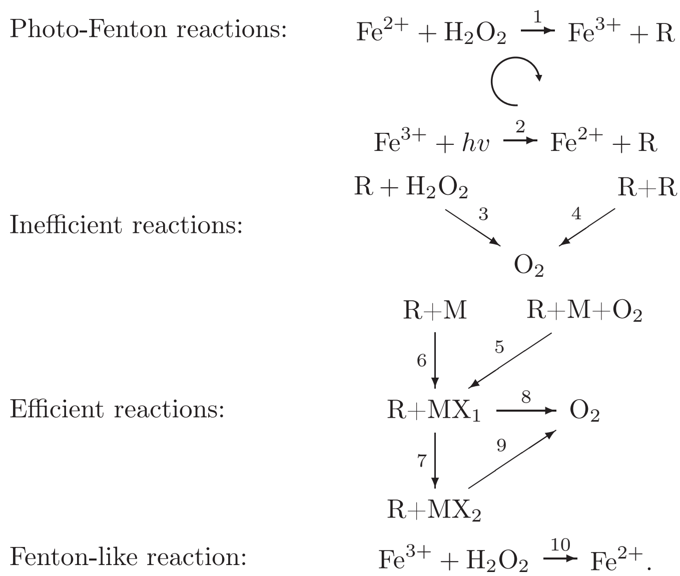
Advanced Oxidation Processes (AOPs) are treatment technologies aimed at degrading and mineralizing recalcitrant organic matter from wastewater through reaction with hydroxyl radical ($^\bullet$OH). Recently, these technologies have been proposed as a solution to treat emerging contaminants, especially pharmaceuticals and personal care products (Pignatello et al., 2007). AOPs' reactions can be further promoted by iron catalysts (Fe^{2+}) and UV irradiation, giving rise to photo-Fenton systems.

The optimal design, operation, and control of these processes can be driven by challenging process systems engineering tools that combine AOPs science, photo-Fenton chemistry, and leading technologies with model-based optimization strategies. However, the use of optimization tools requires the availability of reliable models. A significant amount of work has been devoted to identify intermediate products, model kinetic mechanisms, and identify key variables in AOPs systems, where interaction of complex reactions occurs (Andreozzi et al., 2000). For instance, operational variables such as reagent dosage, pollutant load, pH, and UV source, have been investigated as variables affecting the accomplishment of degradation targets.

Most preliminary AOPs studies were based on design of experiments (DOE) techniques (Pérez-Moya et al., 2008, Arslan-Alaton et al., 2010, Dopar et al., 2011), and they provide limited information regarding intermediate products and side reactions. That entails the risk of making wrong design or operational decisions. In contrast, rigorous models have been reported, describing in detail the degradation mechanism of simple molecules, like formic acid (Rossetti et al., 2004, Farias et al., 2009). The very recent work by Cabrera Reina et al. (2012) addresses the degradation of PCT by introducing a kinetic model aimed at describing the evolution of the system in terms of lumped observable variables such as TOC. In all these studies hydrogen peroxide (H_2O_2) dosage arises as a critical issue to be managed due to the presence of secondary reactions scavenging this reactant. However, few studies seeking for the optimal design of AOPs are found in the literature, like the work by Coenen et al. (2013) where the optimization of single and multi-lamp photo-reactors for continuous operation is addressed.

Kinetic mechanism

In this example, the model proposed by Cabrera Reina et al. (2012) is adapted to predict the kinetic behavior of the process variables, namely the concentrations of PCT, H_2O_2, Fe^{2+}, Fe^{3+}, dissolved oxygen, $^\bullet$OH radical (R), and TOC, including dummy intermediates. Hence, the Fenton-like reaction is added to the model (Kusic et al., 2006). In addition, the TOC consumption is represented by phantom degradation rate that is calculated using an approximated degradation constant and a first reaction order with regard to the TOC and $^\bullet$OH radical concentrations. The reaction scheme reads as:



(5.17)

The kinetic constants and expressions are summarized in Table 5.9. Reaction rates are calculated assuming that the order of reaction with respect to each reactive corresponds to the stoichiometric coefficients.

Reaction r	Reaction rate r_r	k_r $[mM^{-1}h^{-1}]$
1	$r_1{=}k_1\, C_{\mathrm{Fe}^{2+}}\, C_{\mathrm{H_2O_2}}$	8.81^a
2	$r_2{=}k_2\, C_{\mathrm{Fe}^{3+}}\, C_I$	5.63^a
3	$r_3{=}k_3\, C_{\mathrm{R}}\, C_{\mathrm{H_2O_2}}$	75.8^a
4	$r_4{=}k_4\, C_{\mathrm{R}}^2$	42.8^a
5	$r_5{=}k_5\, C_{\mathrm{M}}\, C_{\mathrm{R}}\, C_{\mathrm{O_2}}$	9643^a
6	$r_6{=}k_6\, C_{\mathrm{M}}\, C_{\mathrm{R}}$	257^a
7	$r_7{=}k_7\, C_{\mathrm{MX_1}}\, C_{\mathrm{R}}$	2865^a
8	$r_8{=}k_8\, C_{\mathrm{MX_1}}\, C_{\mathrm{R}}$	271^a
9	$r_9{=}k_9\, C_{\mathrm{MX_2}}\, C_{\mathrm{R}}$	107^a
10	$r_{10}{=}k_{10}\, C_{\mathrm{Fe}^{3+}}\, C_{\mathrm{H_2O_2}}$	0.02^b
11	$r_{11}{=}k_{11}\, C_{\mathrm{TOC}}\, C_{\mathrm{R}}$	0.7375

Table 5.9: Kinetic constants k_r and expressions to calculate the reaction rates r_r in the photo-Fenton case study. Sources: [a]Cabrera Reina et al. (2012), [b]Pignatello (1992).

5.6.2 Problem statement

In this context, this example considers the optimization of the master recipe to be implemented in an existing AOPs plant to remediate a PCT effluent with a volume of 15 L and concentration of 0.52 mM of PCT, eliminating the 99.9% of substrate and 90% of TOC within a maximum time horizon of 10 hours. The objective is to study of the effect of the H_2O_2 dosage profile to drive the process at minimum batch processing time and minimum treatment expenses. Overall, the problem statement for this example is defined as follows:

Given:

- **Planning data:** contaminant, reactants, representation of the lumped intermediates, expected degradation, and maximum time horizon;
- **Plant diagram:** features of the installed photo-reactor and UV lamp;
- **Task network:** photo-Fenton reaction stage, chemicals and resources involved;
- **Batch process operation:** batch operation and limiting processing conditions of the photo-reactor;
- **Process dynamics:** DAE system to represent the process behavior, initial conditions, and set of process variables and dynamic controls;
- **Data related to performance evaluation:** definition of the optimization objectives, namely batch processing time and processing costs, definition of the environmental constraints, namely the minimum degradation of PCD and TOC, and data to evaluate them –*i.e.* prices of reactants ($\hat{p}_{\mathrm{Fe}^{2+}}$=12.62 €/$mol$ and $\hat{p}_{\mathrm{H_2O_2}}$=3.17 €/$mol$) and electricity ($\hat{p}_{\epsilon}$=0.1456 €/$kWh$);

the goal is to determine:

- **Synthesis of processing schemes decisions:** initial concentration of reactants H_2O_2 and Fe^{2+} for the photo-Fenton degradation ($C^0_{\mathrm{Fe}^{2+}}$ and $C^0_{\mathrm{H_2O_2}}$), feed-forward trajectories of the H_2O_2 dosage along the time horizon ($q(t)$), and duration of the batch operation (t^{end});

such that the processing time and the treatment cost are minimized, while fulfilling a set of environmental constraints, operational restrictions, and plant physical restrictions. Particularly, the reactor capacity ($Size$) is 15 L and the available lamp intensity (I) is 36 W/m^2. The installation or expansion of the existing equipment is not considered. As for the boundaries of the decision variables, the initial concentration of Fe^{2+} is set between 0 and 0.179 mM –which satisfies the legal iron concentration allowed in effluents (DOGC, 2003)– and the concentration of H_2O_2 is constrained to a typical concentrations range between 0 and 45 mM during all the process. Besides, since there is one single process stage and one single reactor, the task-unit assignment is fixed beforehand.

5.6.3 Optimization model

In this example, a bi-objective optimization problem is addressed to minimize the treatment expenses and the processing time. According to Eq. 5.9, this problem reads as:

$$\begin{aligned} \underset{u^{dyn}(t),u^{stat}}{\text{minimize}} \quad & \Phi_1 = Cost_{\mathrm{Fe}^{2+}} + Cost_{\mathrm{H_2O_2}} + Cost_{\epsilon}, \\ & \Phi_2 = t^{end}, \end{aligned} \tag{5.18}$$

where $u^{dyn}(t)$ are the dynamic control variables, namely the input flow of H_2O_2 along time $q(t)$, and u^{stat} are the time-invariant control variables, namely the initial concentrations of reactants Fe^{2+} and H_2O_2 in the reactor $C^0_{\mathrm{Fe}^{2+}}$ and $C^0_{\mathrm{H_2O_2}}$ and the duration of the process t^{end}. The treatment cost comprises the cost of reagents Fe^{2+} and H_2O_2 and the cost of electricity consumption in the lamp, which are defined as follows:

$$Cost_{\mathrm{Fe}^{2+}} = \hat{p}_{\mathrm{Fe}^{2+}} C^0_{\mathrm{Fe}^{2+}}\ \upsilon, \tag{5.19}$$

$$Cost_{\mathrm{H_2O_2}} = \hat{p}_{\mathrm{H_2O_2}}(C^0_{\mathrm{H_2O_2}}\ \upsilon + \int_{t^s}^{t^{end}} q(t)\, dt), \tag{5.20}$$

$$Cost_{\epsilon} = \hat{p}_{\epsilon}\, I\, A_w\, t^{end}, \tag{5.21}$$

where $\hat{p}_{\mathrm{Fe}^{2+}}$, $\hat{p}_{\mathrm{H_2O_2}}$, $\hat{p}_{\epsilon}$ are the prices of raw materials and electricity, υ is the reaction volume, which correspond to the $15\,L$ treated in each batch, t^s is the initial processing time, I is the lamp intensity, and A_w is the irradiation surface. Since the installation of new equipment elements is not considered, investment cost contributions are not accounted for in Φ_1.

The optimization model also includes constraints to guarantee the accomplishment of minimum yields χ_{PCT} and χ_{TOC} in the final PCT and TOC reduction:

$$\frac{C^0_{\mathrm{PCT}} - C_{\mathrm{PCT}}(t^{end})}{C^0_{\mathrm{PCT}}}\,100 \geq \chi_{\mathrm{PCT}}, \tag{5.22}$$

$$\frac{C^0_{\mathrm{TOC}} - C_{\mathrm{TOC}}(t^{end})}{C^0_{\mathrm{TOC}}}\,100 \geq \chi_{\mathrm{TOC}}. \tag{5.23}$$

Finally, the optimization problem is subject to the DAE system that defines the material balances for each component along the batch reaction. This is defined according to the reaction mechanism and kinetics previously detailed in Eq. 5.17 and Table 5.9. Eventually the problem becomes a DO problem because qualitative decisions are not considered and thus the mixed-logic part of the modeling strategy can be omitted. The complete multi-objective model is provided in Appendix B.

5.6.4 Problem solution

The bi-objective optimization problem of this example is solved using an a posteriori method that consists of the following steps:

1. Generation and graphic representation of the Pareto frontier of the treatment cost and processing time minimization problem, assuming that the all the H_2O_2 is charged at the initial processing time t^s and there is no dosage profile, *i.e.* $C_{\mathrm{O_2H_2}}$ is optimized and $q(t)$ is fixed to 0 for the whole interval;
2. Intervention of the decision-maker to select the processing time t^{end} from the Pareto frontier;
3. Dynamic optimization given the processing time t^{end} selected in previous step, using a direct-simultaneous solution approach and a PWC profile for the feed-forward trajectory of the input H_2O_2 $q(t)$; the solution is compared to the use of a stepwise dosage protocol (Yamal-Turbay et al., 2012) whose parameters are also optimized.

Pareto frontier: treatment cost versus processing time

The importance of the processing time t^{end} becomes apparent in the objective functions defined in Eq. 5.18 and the resource expenses in Eqs. 5.19-5.21. This variable appears in the cost function Φ_1 related to the electricity contribution $Cost_{\epsilon}$. Moreover, t^{end} is a decision variable that implicitly affects the process performance: an increase of t^{end} leads to a dramatic reduction of reagents consumption and, consequently, a decrease in $Cost_{\mathrm{Fe}^{2+}}$ and $Cost_{\mathrm{H_2O_2}}$, whose effect is more evident in function Φ_1. As a result, if a single-objective optimization problem with decision criteria Φ_1, the value of the processing time would tend to the upper bound in the optimal solution. The incorporation of t^{end} as a second objective Φ_2 serves to elucidate the trade-off between the cost and the allowed time.

Thus, the Pareto frontier is generated and graphically represented to show the compromise between the two functions. For that, function Φ_1 is minimized with different upper bounds for the processing time: $t^{end,\mathrm{U}} \in \{0.7\,h, ..., 10\,h\}$. In this step, only the time-invariant decision variables are optimized, namely the initial concentrations of reactants $C^0_{\mathrm{Fe}^{2+}}$ and $C^0_{\mathrm{H_2O_2}}$, while the dosage profile $q(t)$ is fixed to zero in the whole time interval. Since this problem does not require the discretization of dynamic control variables, it can be solved using a direct-sequential approach, where the decision variables are defined at each search iteration, and the DAE system is solved using numerical integrators. In particular, the *fmincon* function of the Matlab Optimization Toolbox is used in this example.

Dosage profile optimization for a given processing time

Once the processing time t^{end} has been selected based on the Pareto frontier and the subjective information of the decision-maker, the dynamic profile of H_2O_2 addition rate $q(t)$ is optimized, together with $C^0_{\mathrm{Fe}^{2+}}$ and $C^0_{\mathrm{H_2O_2}}$ decisions. In this step, two different dosage profiles are used to define feed-forward trajectory of variable $q(t)$:

(i) Dosage protocol. The optimization of a dosage protocol proposed by Yamal-Turbay et al. (2012) is used as a reference solution. The protocol consists of an initial load of reagent, and a constant addition of the remaining during a specific time interval, as is illustrated in Figure 5.13. The addition profile is characterized by the total amount of H_2O_2 that is charged in the reaction system ($N_{\mathrm{H_2O_2}}$), the initial dosage time (t^i), the fraction of total reagent that is completed at time t^i (F^i), and the continuous dosage span ($\triangle t^{add}$). It is a particularization of a PWC profile with two single step functions to start and to stop the reagent addition. It was previously introduced for practical experimentation procedures. From an mathematical perspective, it allows to characterize a dynamic dosage profile by means of continuous time-independent control variables (*i.e.* $N_{\mathrm{H_2O_2}}$, F^i, t^i, and $\triangle t^{add}$), then simplifying the optimization problem.

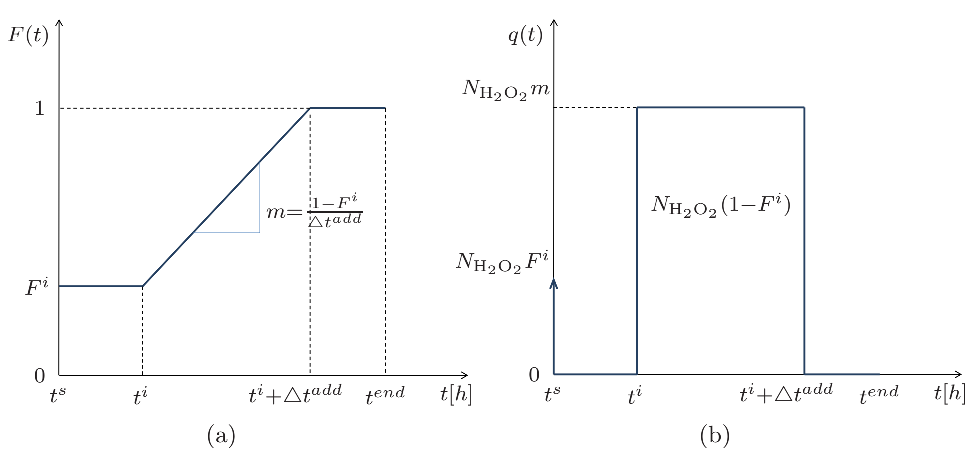


Figure 5.13: Pre-established dosage protocol (Yamal-Turbay et al., 2012) in the photo-Fenton case study: (a) fraction of the total H_2O_2 added along time $F(t)$ (b) input H_2O_d flow $q(t)$.

(ii) PWC profile. The feed-forward trajectory of variable $q(t)$ is defined through a PWC profile, as is illustrated in Figure 5.14. In that case, the optimization problem is solved through the direct-simultaneous approach as explained in § 4.2.1 (p. 92). Overall, the DO problem is reformulated into a NLP using 16 finite elements in the discretization step. Next, the NLP model is implemented in GAMS and is solved using a NLP solver, namely CONOPT.

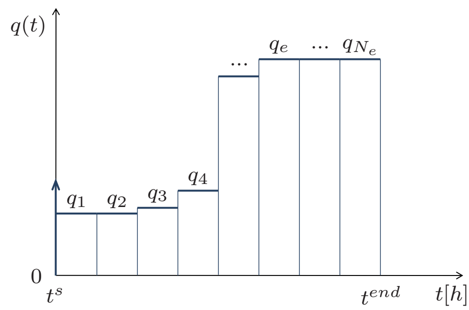


Figure 5.14: PWC dosage profile in the photo-Fenton case study: discretization of the input H_2O_d flow $q(t)$ in N_e=16 finite elements.

Handling inequalities in the optimization model

Inequalities with process variables, such as the constraints for the final PCT and TOC concentrations (Eqs. 5.22 and 5.23), can be transformed into penalization terms in the objective functions (Eq. 5.18). This strategy is used in the implementations in Matlab, which otherwise require special tool-packages. For instance, Eq. 5.23 is transformed into the following quadratic penalty function:

$$Penalization_{\mathrm{TOC}} = 1000 \left(\frac{C_{\mathrm{TOC}}(t^{end})}{C_{\mathrm{TOC}}(t^s)} - 0.1 \right)^2 . \tag{5.24}$$

Other penalty-like terms could be used, such as logarithmic or inverse barrier functions.

5.6.5 Results and discussion

The Pareto optimal solutions obtained through the optimization problem with no dosage are presented in Figure 5.15. The critical trade-off between the cost function (Φ_1) and the processing time (Φ_2) is located between 0.7 and 3 hours. On the one hand, the TOC elimination of 90% is not achieved at lower final times. On the other, upper final times do not affect to the reactant consumption and the processing cost tends to $6.98\,10^{-2}$ € per batch. At this point, the advantage of including the processing time as a second objective in this example is clear. Otherwise, the final time would be driven up to upper bound defined in the optimization model, regardless the cost reduction obtained could not be worth the increase in the processing time. This is a subjective criterion that undoubtedly requires a MO optimization and the intervention of the decision-maker.

A processing time of 2 hours is selected, with a treatment cost of 9.62 c€ per batch. Although the PCT and TOC elimination can be achieved at lower processing times, the interest was set on reducing the cost at the expense of extending the reactor occupation.

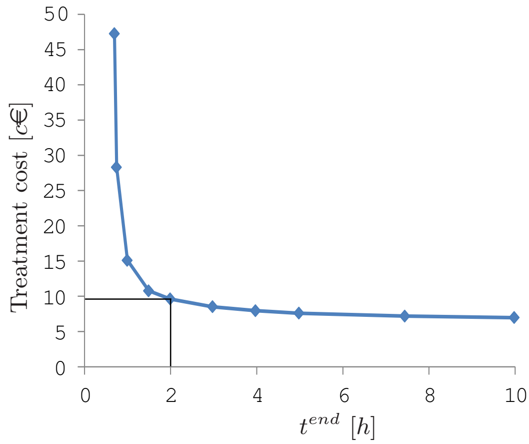


Figure 5.15: Pareto frontier for cost function (Φ_1) versus processing time (Φ_2) in the photo-Fenton case study: optimization with no dosage profile.

Next, the process recipe is further improved using the dosage protocol and the PWC profile optimization with a maximum processing time of 2 hours. These solutions are also compared to a base case where typical values of $0.14\,mM$ and $132.3\,mM$ for the initial concentration of Fe^{2+} and H_2O_2 are used, with no dosage. The obtained KPIs in each case are summarized in Table 5.10, whereas Figure 5.16 shows the profiles of most relevant process variables, namely the consumed H_2O_2 and the normalized concentrations of TOC, H_2O_2, and PCT along time.

Overall, the results improve hugely by optimizing the process instead of implementing a predefined recipe according to typical values. An improvement of the 78.4% is obtained in the optimal solution with no dosage, with respect to the base case. The solution is further improved up to the 79.1% and 79.5% of cost reduction by optimizing the dosage protocol and the PWC profile of the H_2O_2 addition rate. Particularly, the processing cost descends from 9.62 c€ to 9.30 c€ and 9.13 c€ per batch, respectively. The dosage profile along the processing time is shown in Figure 5.16c-d: the black line represents the total H_2O_2 added and the red line represents the normalized concentration of H_2O_2.

As a result, the total improvement with respect to the base case is almost the 80%

KPI	Base case	No dosage	Dosage protocol	PWC dosage profile
Treatment cost [c€]	44.57	9.62	9.30	9.13
Treatment cost reduction [%]	-	78.4[a]	79.1[a] (3.3[b])	79.5[a] (5.1[b])
Fe^{2+} consumption [mmol]	2.100	2.459	2.425	0.268
H_2O_2 consumption [mmol]	132.3	20.5	19.6	18.1
Time 99.9% PCT reduction [h]	0.13	0.49	0.64	0.69
Time 90% TOC reduction [h]	0.89	1.99	1.99	2.00
Final PCT elimination [%]	100	100	100	100
Final TOC elimination [%]	99.42	90.1	90.1	90.0

[a] Reduction regarding the base case
[b] Reduction regarding the optimal solution without dosage

Table 5.10: KPIs for the base case and for the optimal solutions in the photo-Fenton case study.

when the PWC profile is used. However, the determinant factor for the cost reduction is the dramatic reduction in H_2O_2 consumption, which is achieved solely through the optimization of the initial concentrations of raw materials. In fact, the Fe^{2+} consumption is also reduced, which determines the total Fe present in the effluent. This way, the environmental impact is also mitigated, being a collateral gain obtained through an economic objective function. The improvement by using the dosage profile is lower than expected, representing a 5.1%. It is likely that the solution would further improve by considering more dosage intervals beyond the 16 used in this example. However, other degrees of freedom should be considered to fully exploit the optimization approach.

Future studies for process improvement could contemplate further decision variables for the development of AOPs processes subject to be installed in wastewater treatment plants. For instance, the potential installation of other lamp intensities could be evaluated, as well as the potential combination of the photo-Fenton process with other primary or secondary wastewater treatment operations, the installation of additional equipment, the use of other operating modes –*i.e.* in parallel or series–, the potential recirculation of intermediate flows, or the treatment of several effluents in multiproduct campaigns. Most of the listed decisions can be formulated using the proposed MLDO-based approach.

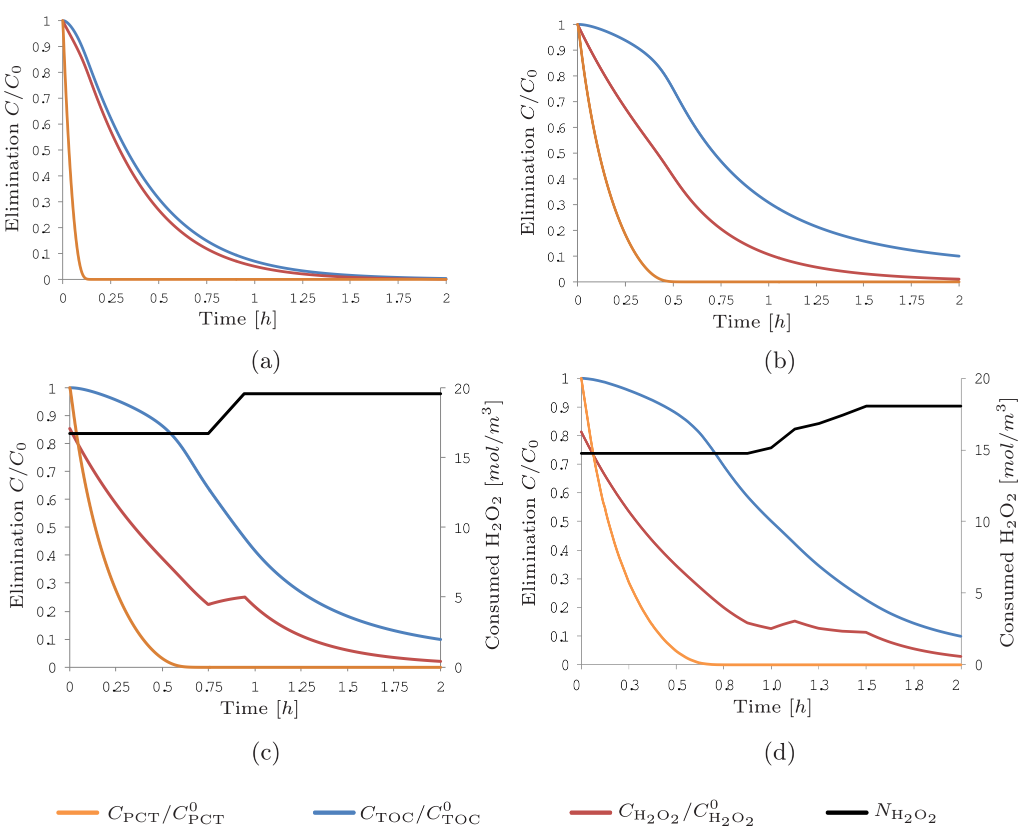


Figure 5.16: Process variable profiles in the photo-Fenton case study, including consumed H_2O_2 ($N_{H_2O_2}$) and normalized concentrations of TOC (C_{TOC}/C^0_{TOC}), H_2O_2 ($C_{H_2O_2}/C^0_{H_2O_2}$), and PCT (C_{PCT}/C^0_{PCT}): (a) base case, (b) selected Pareto optimal solution with no dosage, (c) with dosage protocol, and (d) with PWC profile.

5.7 Concluding remarks

The proposed optimization-based approach to solve integrated batch process development in retrofit scenarios permits to identify and quantify the significant interactions between batch process synthesis and plant allocation sub-problems. This way, the arduous activity of evaluating compromising solutions is facilitated. For instance, a greater influence on structural decisions has been identified in the first case of retrofit Denbigh example, compared to the effect of optimizing dynamic profiles (Table 5.5). The latter provided an improvement of 12% by optimizing the dynamic profiles with a predefined configuration, whereas it went as far as a 24% when qualitative decisions were considered as degrees of freedom with constant variable profiles.

The promising results obtained in the examples also corroborate the advantages of carrying out an holistic evaluation of the decision criteria, as opposed to the use of predefined recipes. Particularly, improvements between the 21% and 121% in the objective function have been obtained in all the retrofit scenarios of Denbigh case study to produce specialty chemical S compared to the use of fixed recipes. This is accomplished thanks to a better utilization of plant capabilities, even though the installation of new equipment is not evaluated in most cases. In the particular example where equipment re-sizing is considered –with the associated investment–, the objective function shows only a slight improvement of the 0.85% with regard to the problem solution without plant modifications. Likewise, the optimization of dynamic profiles in the recipe design for emergent pollutants through Advanced Oxidation Processes leads to reductions of nearly the 80% in the treatment cost again compared to typical predefined recipes.

Finally, the resulting optimization model has the capability to easily incorporate changes affecting the economic scenarios, the decision criteria, or the production policy. This competence also enables the prompt evaluation of combined synthesis alternatives and the study of multiple objectives, since a unique optimization model that includes all the potential alternatives has been defined.

Chapter 6

Integrated batch process development and flexible plant design

"The big advantage of a multipurpose batch plant, its flexibility, also poses the problem of making the best use of it."
Mauderli & Rippin (1979)

Batch manufacturing is mostly devoted to specialty chemicals industry and requires the frequent adaptation of production facilities to market fluctuations, in order to face internal and external uncertainties. Products manufactured in batch plants near the end of their lifetime are most probably unknown at the time of their design. As a result, batch industry encounters the need of general-purpose and flexible plants that are able to produce an initial product portfolio as well as to be reconfigured to embrace the incorporation of future product demands.

In this chapter, the proposed modeling strategy is applied to integrated synthesis, allocation, and plant design in grassroots scenarios. Seeking for plant flexibility, a two-stage stochastic formulation of the optimization problem is used, with the purpose of maximizing the expected profit considering several demand scenarios. In addition, a heuristic solution algorithm is proposed, which allows the evaluation of plant design under uncertainty, while accounting for process synthesis and allocation decisions. The Denbigh case study presented in Chapter 5 is now solved in a grassroots scenario. In this example, an important role is played by process development decisions in the flexibility of the resulting plant design. Decisions like the reference trajectories for the feed-forward control or the selection of the operating mode permit the adaptation of master recipes, in order that the entire range of uncertain demands can be fulfilled in most of the plant solutions. Additionally, an industrial-size case study for acrylic fiber production is presented, illustrating other synthesis and allocation decisions, namely the selection of process stages, technological alternatives, and chemicals, as well as the potential solvent recovery and reuse. For the sake of simplicity, a deterministic demand is assumed in this second example.

6.1 Batch process development in grassroots scenarios

Grassroots scenarios are characterized by the sequential settlement of product, process, and plant lifecycles in an enterprise, as is presented in Figure 6.1. The use of divide and conquer strategies where batch process development sub-problems are solved subsequently makes more sense in grassroots problem, compared to retrofit ones. This is because the process synthesis and plant allocation are not restricted by physical plant constraints in this case. Then, equipment features, such as size or operating restrictions, become degrees of freedom which can be determined as a function of the process requirements, rather than the other way around. Nevertheless, the simultaneous solution of process synthesis, plant allocation, and plant design sub-problems permits to account for the interactions between the DOF associated to each sub-problem and represents a challenge to avoid suboptimal systems. The resulting problem is defined as the integrated solution of batch process development and plant design.

Additionally, in the design of batch manufacturing facilities, plant flexibility should be posed as one of the crucial objectives in the decision-making procedure. That is to say, the design of batch plants should be governed by the maximization of future performance at minimum investment cost, by incorporating into the optimization problem the forecasting of external and internal factors that are susceptible to vary. These factors should be reflected in uncertain parameters included in the optimization model during the plant design activity.

The integrated solution of batch process development and plant design is here tackled. Moreover, uncertainty in the demand of a particular product is considered to reflect changing market conditions and variations of the plausible customer orders. Uncertainty in model parameters could be also included in future studies, to reflect process variability and model inaccuracy. The resulting problem is defined as the optimization of a chemical plant and the set of master recipes to be used in the probability space of uncertain parameters to manufacture a particular product. The objective is to find flexible plant solutions which maximize an expected profit criteria, perform well under all scenarios, and ensure optimal demand order satisfaction for the demand probability space.

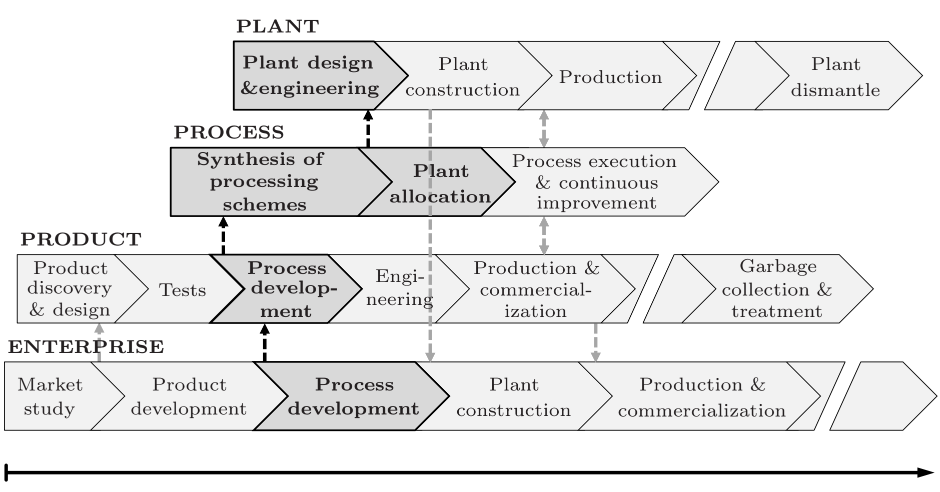


Figure 6.1: Lifecycles in an enterprise: grassroots scenario (adapted from Marquardt et al., 2000).

6.1.1 Integrated batch process development and plant design

The simultaneous process and plant optimization problem corresponds to the highest degree of integration. This problem was referred to as *total process optimization* by Ali (1999, p. 55), where process synthesis and plant allocation are accompanied by plant design decisions. In particular, batch plant design consists of the development of a processing facility for the production of a desired product portfolio. Essentially, this problem tackles the definition of the equipment –*i.e.* number, type, capacity, and connectivity of equipment items–, the assignment of process stages to appropriated equipment items, and the definition of operational decisions (Rippin, 1983b). Therefore, solving the optimal plant design requires the incorporation of scheduling decisions, which determines the use of the selected resources to achieve the production targets –*i.e.* timing, storage policies, batch sizes, amounts transferred and task-equipment allocation. Regarding the operational decisions, the major concerns considered to optimize the batch plant design are: the operating mode, the batch size, the storage tank location, and the duplication of units.

Ideally, the best allocation solutions should be also specified according to physical and chemical calculations in process stages (Rippin, 1993) to match the process model to the final recipe to be implemented in a particular plant and to take into account the trade-offs between structural and performance decisions (Barrera & Evans, 1989). However, it is frequent in batch plant design that the use of fixed or approximated recipes hinders the adaptation of recipe parameters –*e.g.* set-points and reference trajectories for control variables– according to the global targets.

In the literature, the integrated batch process development and plant design problem is related to different research topics. On the one hand, several efforts have been devoted to the definition of recipe modifications in allocation of multiproduct and multipurpose plants instead of using fixed recipes. Most of the reported contributions have focused on the definition of models that represent the process performance in each task. These are characterized by different detail level –most of them being algebraic approximations– and should be related to the plant design problem either using simultaneous or iterative decision-making strategies.

On the other hand, some contributions are found in the literature, which introduce equipment sizing in batch process development. In this case, process synthesis decisions are further detailed. For instance, the recipe definition may involve chemicals selection and the use of dynamic models to represent the process performance is more extended. In this regard, Charalambides et al. (1995, 1996) and Sharif et al. (1999) integrated equipment sizing decisions with process synthesis and allocation optimization by means of DO and MIDO problems. However, task sequence and allocation decisions had to be defined in advance. Later, Iribarren et al. (2004) introduced equipment sizing decisions in a MINLP model where process synthesis –*i.e.* the selection of microorganism involved and the selection of separation and purification alternatives– and allocation decisions –*i.e.* definition of the operating mode and processing order for each product– were also optimized simultaneously. However, the process performance in batch process stages was simplified in this case through the use of time and size factors that depended on the synthesis decisions considered.

6.1.2 Flexibility in batch plant design

To address the problem of batch plant design at the early stages of the plant lifecycle, it is necessary to assume given product slates and processing schemes. However, some parameters may not be fully defined or may involve uncertainty, due to internal and external conditions (Acevedo & Pistikopoulos, 1998, Puigjaner & Laínez, 2008). First, chemical plants are often characterized by internal plant parameters quite different from those considered at the design stage –*e.g.* kinetic constants, heat transfer coefficients, or machine efficiency and reliability. Second, rapidly changing market environments will have an effect on the variability of demands, cancellations, and returns of products, of raw material availability, of prices of chemicals, and of environmental parameters.

Simplifying hypotheses are often used in the solution of plant design to mitigate partly the effect of possible future variations in internal and external parameters. For instance, the consideration of extreme or mean values or the application of safety factors, based on past experience and engineering judgment, are typically employed (Schuëller & Jensen, 2008). However, these simplifications do not ensure the reliability of the designed system –understood as its capacity to feasibly operate in an uncertain environment– within the actual uncertainty margin. Pursing the objective of versatile plants which are able to be adapted in plausible future scenarios and to provide an efficient operation, it is paramount to account for parameter variability during the design problem. The ability of a specific design or operational plan to deal with a set of uncertain parameters is defined as plant flexibility (Sahinidis, 2004). Overall, flexible plant design ensures a manageable response to changes in the business environment, increases the accuracy of decisions, allows the adaptation of master recipes, and improves process performance.

Solution approaches: design with uncertainty

Consequently, the incorporation of uncertainty in the batch plant design problem is an important area of research and several approaches have been proposed in the literature. The goal is to find a solution that optimizes the expected value of the objective function, taking into account parameter uncertainty, and that is feasible for all –or almost all– the uncertain data range.

The three outstanding methodologies to deal with optimization under uncertainty, according to Sahinidis (2004), are: stochastic programming, fuzzy programming, and stochastic dynamic programming. **Stochastic programming** methods address optimization problems incorporating uncertain parameters governed through known or estimated probability functions. These methods are basically the two-stage programming, the robust stochastic programming, and the probabilistic programming. In the case of **fuzzy programming**, the uncertainty is modeled by considering random parameters as fuzzy numbers and constraints as fuzzy sets. There are two types of fuzzy programming, namely the flexible programming and the possibilistic programming. Finally, **stochastic dynamic programming** is the extension of the dynamic programming (DP) approach by Luus (1990) to solve dynamic systems, now including uncertainty in parameters, which is represented through probability distribution functions. Besides, a variety of approaches for robustness assessment have been followed, including minimization of expectation, minimization of deviations from goals, minimization of maximum costs, and optimization over soft constraints. The interested reader is referred to Sahinidis (2004) for an overview of these methodologies, as well as their typical areas of application.

This work centers on stochastic programming approaches, since they are the most extended to address the design of chemical processing systems with uncertainty. For instance, they are preferred to stochastic programming. The reason is that these last ones are an extension of DP methods (Bellman, 1957, Luus, 1990), which are used to solve optimal control problems based on the Hamilton-Jacobi-Bellman formulation to transform the original problem into a system of partial differential equations. As a result, they are not recommended for the solution of large-scale dynamic optimization problems (Schlegel, 2004). In stochastic programming, the probability distribution functions that represent uncertain parameters may be defined by means of continuous functions or a finite number of scenarios where the probability distribution has been discretized. According to the mathematical model used to describe each source of uncertainty, Ierapetritou & Pistikopoulos (1996) and Acevedo & Pistikopoulos (1998) proposed to split the vector of uncertain parameters in two subsets: (i) *deterministic* uncertain parameters ($\xi_\delta^s \,|\, \xi^{\mathrm{L}} \leq \xi_\delta^s \leq \xi^{\mathrm{U}},\ s \in \{1, ..., N_S\}$), modeled through a series of periods or scenarios $s \in \{1, ..., N_S\}$ with particular values and associated to a probability or weight w^s, and (ii) *stochastic* uncertain parameters ($\xi_\sigma \,|\, \xi_\sigma \in J(\xi_\sigma)$), described by a probabilistic distribution function $J(\xi_\sigma)$.

Two-stage programming. In particular, programming with recourse (Pai & Hughes, 1987, Pistikopoulos & Ierapetritou, 1995) is one of the most widespread stochastic methodologies, which is considered to be very effective in the solution of process engineering problems (Acevedo & Pistikopoulos, 1998). It is also referred to as **two-stage programming strategy** due to the differentiation between *first-stage* variables, which remain fixed once selected and correspond to plant design decisions, and *second-stage* variables, which correspond to process decisions. The latter were originally interpreted as corrective actions or recourses against infeasibilities that could arise due to a particular realization of the uncertainty. However, the role of second-stage variables may be not only the way to achieve feasibility but also the chance to improve process performance.

Robust stochastic programming. It is basically an extension of the two-stage programming strategy which additionally captures risk assessment in the objective function. Specifically, risk is represented through a variability measure of the second-stage costs –*e.g.* variance– and a risk tolerance. As a result, the search for robust design appears often as a multiple criteria decision problem, where trade-offs between expected performance and dispersion measures are found, rendering a compromise in the resulting robust optimal solutions (Schuëller & Jensen, 2008).

Probabilistic programming. Finally, probabilistic programming is focused on the reliability of the system. With this purpose, probabilistic programming strategies incorporate a reliability constraint expressed as a minimum requirement on the probability of satisfying the problem constraints.

Several authors have applied two-stage programming strategies to solve batch plant design under uncertainty. For instance, Reinhart & Rippin (1986) addressed the design of flexible batch plants with uncertain demands. Shah & Pantelides (1992) tackled the design of multipurpose batch plants with uncertain production requirements using a stochastic formulation that considered different scenarios. Ierapetritou & Pistikopoulos (1996) solved multipurpose plant design with uncertainty, formulated as a MILP model. Cao & Yuan (2002) optimized the design of batch plants with uncertain demands allowing different operating modes in parallel units for different products. Alonso-Ayuso et al. (2005) solved the problem of product selection and plant dimensioning under uncertainty in product price, demand, and production cost, and using a scenario-based representation. Aguilar-Lasserre et al. (2009) addressed the problem of flexible plant design with uncertain product demands through multi-objective optimization, including three objectives: investment cost, operation cost, and total production time. Pinto-Varela et al. (2009) addressed the design and scheduling of multipurpose batch plants under production demand uncertainty, considering a scenario-based representation and discrete probability functions and formulating the problem as a MILP. Wang et al. (2010) solved multi-product batch plant design under uncertainty, formulated as a multi-objective stochastic programming problem where profit and environmental impacts were included in the objective function. Moreno & Montagna (2012) tackled multi-period production planning and design of batch plants with uncertainty in product demands, addressed through a scenario approach with the possibility of plant capacity expansion in particular production periods.

6.2 Application of the MLDO-based strategy

In this chapter, the integrated process development and flexible plant design under uncertainty is formulated as a two-stage stochastic programming problem (Pai & Hughes, 1987, Pistikopoulos & Ierapetritou, 1995). The following modeling features are considered therein:

(i) The expected profit maximization is defined as objective function, composed of revenues, raw material expenses, amortization, occupation costs, and processing costs, defined in previous chapter (§ 5.2.1, p. 111); it is evaluated in the feasible operating region of the batch plant to obtain a compromise between economic performance and plant flexibility;

(ii) Demand accomplishment constraints are relaxed through the introduction of the shortfall penalty associated to the unfulfilled part of demand in the objective function; this contribution ensures the best utilization of plant resources for the optimal demand satisfaction, understood as the optimal demand that can be satisfied in each scenario pursuing the common good in the selection of equipment investments;

(iii) Uncertainty in the product demand is represented through multi-scenario deterministic probabilities, where each plausible demand case is associated to a normalized probability weight;

(iv) First-stage plant design decisions –whose assigned value is the same in all uncertain scenarios– correspond to new equipment capacities, whereas second-stage decisions –whose value can vary among different scenarios– are related to process synthesis and allocation degrees of freedom, permitting different optimal processing schemes –*e.g.* equipment occupation, operating modes– in each demand scenario.

6.2.1 Optimization model

In broad terms, the formulation of the integrated problem in grassroots scenarios according to the modeling strategy proposed in Chapter 3 (§ 3.3, p. 69) provides and equivalent model to that in retrofit situations (§ 5.2.1, p. 111), except for two elements. First, the problem starts from an nonexistent plant. Therefore, equipment restrictions are excluded and equipment characteristics are only considered as additional DOF. Second, uncertainty is incorporated through a two-stage model formulation. This form allows to optimize plant decisions according to the given multi-scenario deterministic probability and to the process synthesis and plant allocation decisions in each finite demand scenario.

Problem with uncertainty

In the presence of uncertainty, the two-stage stochastic programming problem can be reformulated by defining an expectancy of the objective function, which is divided in two terms: Φ_1 and Φ_2. Φ_1 is the contribution to the objective function that depends uniquely on first-stage decisions $u_1 \in U_1$, whose values are not affected by uncertain parameters. Φ_2 is the contribution to the objective function that depends additionally on second-stage decisions $u_2 \in U_2$ and uncertain parameters $\xi \in \Xi$. $Q(u_1, \xi)$ is the optimal value of the second-stage problem for a given value of first-stage decisions $u_1 \in U_1$ and uncertain parameters $\xi \in \Xi$, and E is the expectancy of Φ_2, taking into account the complete probability space $\Xi = \{\xi \,|\, \xi \in P(\xi),\ \xi^{\mathrm{L}} \leq \xi \leq \xi^{\mathrm{U}}\}$. The general form of these kinds of optimization problems is given by Sahinidis (2004):

$$
\begin{aligned}
&\underset{u_1 \in U_1}{\text{minimize}} \;\; \Phi_1(u_1) + E_{\xi \in \Xi}[Q(u_1, \xi)], \quad s.t.\ f_1(u_1) \leq 0, \\
&\text{with} \\
&Q(u_1, \xi) = \underset{u_2 \in U_2}{\text{minimize}} \;\; \Phi_2(u_1, u_2, \xi), \quad s.t.\ f_2(u_1, u_2, \xi) \leq 0,
\end{aligned}
\tag{6.1}
$$

where f_1 and f_2 are the problem constraints.

For the integrated batch process development and plant design, the above general form for two-stage stochastic problems corresponds to a MLDO problem, where plant design decisions –*e.g.* size of processing units– involve the first-stage optimization variables while process synthesis and allocation decisions –*e.g.* dynamic control variables, batch operation durations, active equipment selection, task-unit assignments, among others– involve the second-stage optimization variables. According to the proposed MLDO problem recapitulated in Eq. 3.36 (§ 3.4, p. 85), the general form in Eq. 6.1 becomes:

$$
\begin{aligned}
&\underset{u_1 \in \{Size^j\}}{\text{minimize}} \; \Phi_1(u_1, p) + E_{\xi \in \Xi}[Q(u_1, \xi)], \\
&\text{with } Q(u_1, \xi) = \\
&\underset{\substack{u_2 \in \{u_k^{dyn}(t), u^{stat}, \\ u^{int}, u^{Bool}\} \setminus u_1}}{\text{minimize}} \quad \Phi_2(z_k(t), y_k(t), u_1, u_2, \gamma, p, \xi), \\
&\qquad s.t. \;\; f_k(\dot{z}_k(t), z_k(t), y_k(t), u_1, u_2, p, \xi) = 0,\ t \in [0,1], \forall k \in K, \\
&\qquad\qquad l(\dot{z}_1(0), z_1(0)) = 0, \\
&\qquad\qquad g_k(z_k(t), y_k(t), u_1, u_2, p, \xi) \leq 0, \;\; t \in [0,1], \forall k \in K, \\
&\qquad\qquad g_k^e(z_k(1), y_k(1), u_1, u_2, p, \xi) \leq 0, \;\; \forall k \in K, \\
&\qquad\qquad z_{k+1}(0) - m_k(z_k(1)) = 0, \;\; \forall k \in \{1, ..., |K| - 1\}, \\
&\qquad\qquad \gamma = h(z_{j,|K|}(1), y_{|K|}(1), u_1, u_2, p, \xi), \\
&\qquad\qquad \begin{bmatrix} u^{Bool} \\ f_k^d(\dot{z}_k(t), z_k(t), y_k(t), u_1, u_2, p, \xi) = 0, t \in [0,1], \forall k \in K, \\ l^d(\dot{z}_1(0), z_1(0)) = 0, \\ g_k^d(z_k(t), y_k(t), u_1, u_2, p, \xi) \leq 0, \;\; t \in [0,1], \forall k \in K, \\ g_k^{d,e}(z_k(1), y_k(1), u_1, u_2, p, \xi) \leq 0, \;\; \forall k \in K, \\ z_{k+1}(0) - m_k^d(z_k(1)) = 0, \;\; \forall k \in \{1, ..., |K| - 1\}, \\ \gamma = h^d(z_{|K|}(1), y_{|K|}(1), u_1, u_2, p, \xi) \end{bmatrix} \\
&\qquad\qquad \underline{\vee} \begin{bmatrix} \neg u^{Bool} \\ B^d(\dot{z}_k(t), z_k(t), y_k(t), u_1, u_2, \gamma, p, \xi) = 0,\ t \in [0,1] \end{bmatrix}, \\
&\qquad\qquad \Omega(u^{Bool}) = true,
\end{aligned}
\tag{6.2}
$$

where $Size^j$ is the capacity of new equipment unit $j \in J$ and corresponds to first-stage decisions $u_1 \in U_1$, whereas second-stage decisions $u_2 \in U_2$ comprise the remaining dynamic $u^{dyn}(t)$, time-invariant u^{stat}, integer u^{int}, and Boolean u^{Bool} decision variables. $z(t)$ and $y(t)$ are the differential and algebraic process variables, and p and ξ are the deterministic and the stochastic parameters respectively. In particular, the latter are represented through scenario-based uncertain parameters $\xi_\delta^s \,|\, \xi^{\mathrm{L}} \leq \xi_\delta^s \leq \xi^{\mathrm{U}}$, $s = \{1, ..., N_S\}$ and through a weigh or probability w^s of each scenario $s \in \{1, ..., N_S\}$ that is likely to occur.

The contribution to the objective function in the first stage of the problem Φ_1 involves the calculation of amortization costs associated to the installation of new units in a total production basis, as defined in Chapter 5 (Eq. 5.6, p. 112). Regarding the contribution to the objective function in the second stage of the problem Φ_2, it is associated to the product revenue, to raw material cost, to occupation and processing costs associated to selected units, and to shortfall penalty in a total production basis, as defined in Chapter 5 (Eqs. 5.2 - 5.5, 5.7, p. 111). The latter depend not only on equipment capacity but also on process synthesis and allocation decisions. Additionally, they are affected by the final realization of the uncertain demand.

6.2.2 Methodology

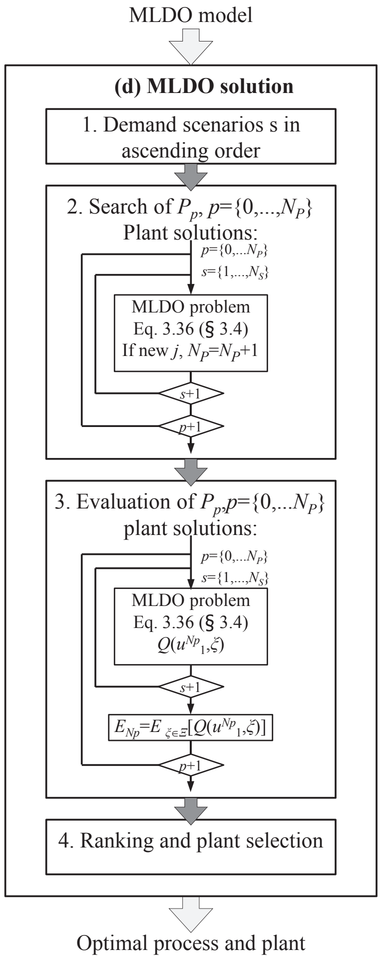
As discussed in previous chapters, the integrated problem proposed in this thesis is characterized by a great complexity due to the simultaneous optimization of decisions which are typically addressed in independent sub-problems, namely batch process synthesis, allocation, and design of manufacturing facilities. The resulting MLDO model is non-linear, non-convex, and subject to a great combinatory. Nevertheless, it has been proved in previous chapter that MLDO solution methods provide optimal solutions when deterministic values of the model parameters are used.

To solve the integrated process development and flexible plant design, the complete solution procedure is carried out taking into account the methodology previously explained in § 5.2.2 (Figure 5.3, p. 114), consisting of the steps: (a) gathering information, (b) SEN superstructure representation, (c) MLDO formulation with a two-stage objective function (Eq. 6.2), and (d) MLDO solution. Since the problem has been reformulated as a two-stage stochastic programming problem with scenario-based uncertainty representation, the complexity of the optimization problem is further increased. For this reason, a heuristic procedure is here proposed to solve the MLDO problem in last step (d). Particularly, the proposed heuristic allows the partitioning of the decision-making procedure for the flexible plant design and the master recipe optimization through an iterative rule-based procedure. At each iteration, the deterministic MLDO problem of Eq. 3.36 (p. 85) is solved through the direct-simultaneous approach explained in § 4.2.1 (p. 92) using the deterministic parameter values associated to each uncertain scenario. This strategy is further detailed in next section.

Heuristic for flexible plant design

The proposed heuristic is used to solve the MLDO two-stage stochastic programming problem for integrated process development and flexible plant design with demand uncertainty as it is presented in Eq. 6.2. Figure 6.2 summarizes the heuristic procedure and provides the pseudo-code of the algorithm, which comprises four main steps:

1. Definition of the N_S demand scenarios $s \in \{1, ..., N_S\}$, characterized by the forecasted production target $\xi^s_{Demand_p}$ ordered from lowest to highest demand value $\xi^s_{Demand_p}$ and by the normalized weight w^s, *i.e.* $\sum_{s \in S} w^s{=}1$;
2. First-stage optimization of the two-stage formulation in Eq. 6.2 (§ 6.2.1, p. 155), in order to determine the plant design variables –*i.e.* equipment capacities. With that purpose, an iterative loop is posed, where each plant P_p, $p \in \{0, ..., N_P\}$ is used as a base solution to be improved for each of the N_S demand scenarios. Each iteration involves the creation and solution of a deterministic MLDO problem minimizing the function $\Phi = \Phi_1(U_1, p) + \Phi_2(z_k(t), y_k(t), u_1, u_2, \gamma, p, \xi^s_{Demand_p})$, what corresponds to the general MLDO of Eq. 3.36 (§ 3.4, p. 85). The set of plants P_p, $p \in \{0, ..., N_p\}$ is upgraded if solutions with additional processing units j are found. The optimization of process synthesis and allocation with plant design is also integrated in this step, in order to take into account the best plant utilization –through the optimization



Algorithm 6.2.1: FLEXIBLE PLANT$(\xi^s_{Demand_p}, w^s)$

$P_p, p = \{0, ..., N_P\},\ N_P = 0,$
$s^0_0 = 0,$
$p = 0,$
repeat
  for $s \leftarrow s^0_p + 1$ **to** N_S,
    do $\begin{cases} \text{Extend } P_p, \\ \textbf{if } \text{New equipment:} \\ \quad \textbf{then } \begin{cases} N_P = N_P + 1, \\ s^0_{N_P} = s, \end{cases} \end{cases}$
  $p = p + 1$
until $p > N_p$
for $p \leftarrow 0$ **to** N_P,
  do $\{E_{N_P} = E_{\xi\in\Xi}[Q(u_1^{N_P}, \xi)],$
Best flexible plant $= fp \mid$
$E_{fp} = \max\limits_{p\in\{0,\ldots,N_P\}} (E_{\xi\in\Xi}[Q(u^p_1, \xi)])$
return (Best flexible plant)

Figure 6.2: Heuristic procedure to solve integrated process development and flexible plant design formulated in Eq. 6.2. The set of decision variables for each plant solution P_p, $p \in \{1, ..., N_P\}$ is represented by u^p_1.

of the master recipe for the demand scenario at each iteration– before posing a new plant solution, with the computational load involved. A pre-specified termination criteria should be defined, *e.g.* no new solutions are found;

3. Evaluation of the expected profit at each plant solution P_p, $p \in \{0, ..., N_P\}$ taking into account the demand $\xi^s_{Demand_p}$ and probability w^s associated to each scenario $s \in \{1, ..., N_S\}$. In this step, the same deterministic MLDO problem is solved, but equipment sizing is not a degree of freedom. Herein, the second-stage decisions –*i.e.* process synthesis and allocation sub-problems– are optimized for a fixed plant P_p, $p \in \{1, ..., N_P\}$ and for each demand scenario $s \in \{1, ..., N_S\}$, in order to calculate the expected profit for a given plant solution.
4. Selection of the best plant out of the final N_P solutions obtained. With that purpose, the plant solutions are ranked according to the expected profits computed and the forefront solution is selected.

Let us note that some rules have been established to simplify the solution algorithm. For instance, the iterative loop in step 2 only allows finding plants with larger capacity with respect to the initial plant provided. Thus, it may be assumed that such plant P_p will have capacity to feasibly and optimally produce lower demands to the demand $\xi^s_{Demand_p}$ with which it had been calculated. Such demand scenario is represented by variable s^0_p for each plant. To sum up, an important feature of this approach is that it avoids screening all plant alternatives, and only founds the improvements over plant solutions calculated in previous steps. This way, the combinatorial load is reduced and so does the computational time. Nevertheless, it is clear that the optimal solution having into account all demand scenarios may not correspond to the optimal solution of any of the particular demand scenarios found, so global optimality can not be guaranteed in a general case.

6.3 Denbigh case study

The Denbigh case study presented in Chapter 5 (§§ 5.3, 5.4, and 5.5) for several retrofit cases is now solved in a grassroots scenario. The objective is to address integrated batch process development and plant design for the production of specialty chemical S through the Denbigh reaction system (Denbigh, 1958), seeking for the flexibility of the reactor network to handle an uncertain demand. In broad terms, the solution provides: (i) a flexible plant design which maximizes the expected profit and (ii) the optimal master recipes which define the process synthesis and allocation for each demand scenario within the flexible plant.

6.3.1 Stochastic problem statement

This example tackles the design of a flexible reactor network which performs well under all demand scenarios and ensures optimal demand order satisfaction for the demand probability space. The objective function is defined as the maximization of the expected profit for the production of specialty chemical S with a maximum time horizon of 144 hours, given the demand of final product $\xi^s_{Demand_\mathrm{S}}$ and probability w^s in the forecasted scenarios $s \in \{1, ..., N_S\}$. In particular, uncertainty is modeled through five demand scenarios, which comprise an estimated demand of $21\,tn$ of product S and variations of $\pm 25\%$ and $\pm 50\%$, all of them with the same probability of 0.2. Additionally, Table 6.1 summarizes the economic parameters to be considered. A period of 1 year has been considered to define the amortization cost.

$\hat{c}_j$ $[c€/kWh]$	$\bar{c}_{j,A}$ $[€/batch]$	$\bar{c}_{j,B}$ $[€/m^3 batch]$	$\bar{c}_{j,C}$ $[€/h\,batch]$	$\check{c}_j$ $[€/h]$	$\hat{p}_\mathrm{A}$ $[c€/kg]$	$\hat{p}_\mathrm{S}$ $[c€/kg]$	$\hat{p}_{penalty}$ $[c€/kg]$
2.5	5	10	0.21	8.22	4.8	43.1	$2\,\hat{p}_\mathrm{S}$

Table 6.1: Economic parameters in grassroots Denbigh example: unitary processing costs $\hat{c}_j$, occupation costs $\bar{c}_{j,A}$, $\bar{c}_{j,B}$, and $\bar{c}_{j,C}$, and base amortization cost $\check{c}_j$ of $j \in U$, price of raw material A $\hat{p}_\mathrm{A}$ and final product S $\hat{p}_\mathrm{S}$, and penalty of the product shortfall.

To solve this problem, plant flexibility is faced through the optimization of the process synthesis and allocation decisions in each demand scenario s. It involves the same DOF as those included into the problem statement of Denbigh example in retrofit scenarios in Chapter 5 (p. 117). Additionally, decisions related to flexible plant design are included, namely the sizing of all the required processing units $j \in U$.

6.3.2 SEN superstructure

In this example, the superstructure is enlarged as new processing units are incorporated to the plant solution. The general superstructure is presented in Figure 6.3.

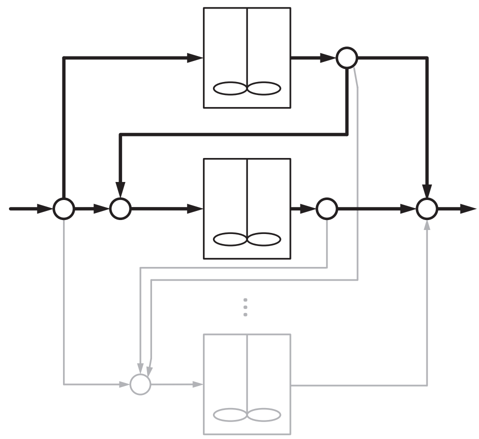


Figure 6.3: SEN superstructure of the grassroots Denbigh example.

6.3.3 Stochastic optimization model

The problem to maximize the expected profit with uncertainty is defined through an equivalent two-sage stochastic minimization problem according to prior Eq. 6.2. In the first stage, the capacities of the units to be acquired constitute the set of decision variables $u_1 \in U_1$, which have the same value in the whole demand probability space. The second stage involves the rest of DOF, namely the process synthesis and plant allocation decisions $u_2 \in U_2$.

Regarding the objective function, it is also partitioned into two terms Φ_1 and Φ_2. The former includes total amortization costs, which only depend on first-stage decisions $u_1 \in U_1$ and is independent to the uncertain demand $\xi^s_{Demand_\mathrm{S}}$ and to decisions $u_2 \in U_2$. The latter is composed of the total revenue of product S, the raw material expenses, total occupation and processing costs in batch units $j \in U$, and the penalty associated to product shortfall. This second term Φ_2 is subject to the value of the uncertain demand $\xi^s_{Demand_\mathrm{S}}$ and to the first stage solution regarding $u_1 \in U_1$. Summarizing, the formulation of the objective function reads as:

$$\begin{aligned}
&\underset{u_1 \in \{Size^j\}}{\text{minimize}}\ \Phi_1(u_1, p) + \sum_{s=1}^{N_s} w^s\, Q(u_1, \xi^s_{Demand_\mathrm{S}}),\\
&\text{with } Q(u_1, \xi^s_{Demand_\mathrm{S}}) = \\
&\quad \underset{\substack{u_2 \in \{u_k^{dyn}(t), u^{stat},\\ u^{int}, u^{Bool}\} \setminus u_1}}{\text{minimize}}\ \Phi_2(z_k(t), y_k(t), u_1, u_2, \gamma, p, \xi^s_{Demand_\mathrm{S}}),
\end{aligned} \tag{6.3}$$

being

$$\begin{aligned}
\Phi_1 =\ & \textstyle\sum_j Cost_{j,a,total},\\
\Phi_2 =\ & -Revenues_{\mathrm{S},total} + Cost_{\mathrm{A},total} + \textstyle\sum_j Cost_{j,o,total}\\
& + \textstyle\sum_j Cost_{j,p,total} + Penalty.
\end{aligned} \tag{6.4}$$

There, $u_k^{dyn}(t)$ are the dynamic control variables, comprising input and output flow rates $F^j_{1,k}(t)$ and $F^j_{2,k}(t)$ and reaction temperature $\theta^j_k(t)$ in batch reactors $j \in U$. u^{stat} are the time-invariant decision variables, namely the duration of batch operations t_l. u^{int} represent other integer decisions apart from equipment capacities $Size^j$, particularly the number of batches NB_{S}. Finally, u^{Bool} are the Boolean variables, including the selection of active batch units Y_j out of the installed ones in each plant solution, the task-unit assignment $W_{j,q}$, and the equipment configuration X^1_ψ. Additionally, differential and algebraic variables $z(t)$ and $y(t)$ and deterministic problem parameters p are part of the problem.

The extensive MLDO problem of this case study is provided in Appendix A. It includes the detailed DAE systems which represent process performance at each unit procedure as well as the complementary logical propositions to model synthesis and allocation decisions. If a unit is selected to be installed, its capacity $Size^j$ is set to be greater than zero. In particular, $Size^j$ is defined as a discrete decision variable whose value is defined using increments of $0.25\,m^3$ up to $10\,m^3$, in order to facilitate the equipment purchase. Additionally, if a unit is selected ($Y_j = true$) in the optimal master recipe in a particular demand scenario, its volume $\upsilon^j_k(t)$ is constrained by the abovementioned capacity according to:

$$\begin{bmatrix} Y_j \\ \upsilon^j_k(t) \leq Size^j, \quad t \in [0,1], \forall k \in K_j \end{bmatrix}, \quad \forall j \in U. \tag{6.5}$$

6.3.4 Problem solution

The heuristic procedure in Algorithm 6.2.1 is applied to design the flexible plant that gives the best response to the demand scenarios defined in Table 6.2. In this process, the MLDO problem is optimized to calculate the master recipe that maximizes the profit at each demand scenario $s \in \{1, ..., N_S\}$ in the plant solution P_p, $p \in \{1, ..., N_P\}$ under evaluation.

6.3.5 Results and discussion

Step 1: Demand scenarios

The values for the uncertain demand $\xi^s_{Demand_{\text{S}}}$ and probability w^s of each scenario $s \in \{1, ..., N_S\}$, $N_S = 5$ are summarized in Table 6.2, following and ascendent order in the demand value.

Scenario s	1	2	3	4	5
$\xi^s_{Demand_{\text{S}}}$ $[tn]$	10.5	15.75	21	26.25	31.5
w^s	0.2	0.2	0.2	0.2	0.2

Table 6.2: Uncertain demand value $\xi^s_{Demand_{\text{S}}}$ and probability w^s for scenarios $s \in \{1, ..., N_S\}$, $N_S = 5$ in grassroots Denbigh example.

Step 2(a): First iteration

The plant solutions obtained at the first iteration $p = 0$ of the heuristic Algorithm 6.2.1 are presented in Table 6.3 for each of the demand scenarios $s \in \{1, ..., N_S\}$. The KPIs associated to each solution are also provided therein. They correspond to the performance of the optimal master recipe that generates each plant solution for each demand $\xi^s_{Demand_{\text{S}}}$. For instance, the total revenue increases progressively from plant P_1 to P_5 since the corresponding demand goes up from $\xi^1_{Demand_{\text{S}}} = 10.5\,tn$ to $\xi^5_{Demand_{\text{S}}} = 31.5\,tn$.

It can be observed that all plant solutions correspond to the installation of a unique processing unit, with a suitable capacity to fulfill the production targets with a zero product shortfall. While the demand value increases, so does the equipment capacity from an optimal value of $Size^{U_1} = 1\,m^3$ in demand scenario 1 to $Size^{U_1} = 3\,m^3$ in demand scenario 5. Eventually, all scenarios meet solutions with the same number of batches $NB_{\mathrm{S}} = 23$ –except for scenario 2, whose optimal number of batches is 28– and increasing batch sizes, from $Batch_{\mathrm{S}} = 457\,kg/batch$ in scenario 1 to $1,370\,kg/batch$ in scenario 5.

Additionally, the maximum time horizon of 144 hours is reached in all cases, since larger utilization times allow to reduce: (i) capacity requirements and, as a result, amortization costs –which are directly related to equipment capacity–, (ii) heating requirements and, as a result, processing costs, and (iii) selectivity and, as a result, raw material costs. In contrast, temperature ranges are slightly different for the different scenarios, being clear its effect on the selectivity. The lower the temperature profile, the better the selectivity of product S. The optimal highest temperature rises gradually following a monotonically increasing behavior as long as the batch size goes up –except for the solution of scenario 2 which has a clear different pattern. This may be caused by the higher production requirements or by the reactor scale-up. Numerical errors associated to the discretization of the MLDO model could also explain this tendency.

Step 2(b): Following iterations

Next, each of the obtained plant solutions P_p, $p \in \{1, ..., N_P\}$ enters the iterative loop in step 3 of the heuristic procedure. There, each plant is used as a base case on which to evaluate the installation of additional equipment items. The problem is equivalent to a

Scenario s	1	2	3	4	5
Demand $[tn]$	10.5	15.75	21	26.25	31.5
Installed units U	U_1	U_1	U_1	U_1	U_1
Size of units U $[m^3]$	1	1.25	2	2.5	3
Plant solution	P_1	P_2	P_3	P_4	P_5
Equipment configuration	α	α	α	α	α
No. Batches	23	28	23	23	23
Batch size $[kg/batch]$	457	563	913	1,141	1,370
Total processing time $[h]$	144	144	144	144	144
Batch processing time $[h/batch]$	6.26	5.14	6.26	6.26	6.26
Batch cycle time $[h/batch]$	6.26	5.14	6.26	6.26	6.26
Shortfall of product S $[kg]$	0	0	0	0	0
Total profit [€]	**2,313**	**3,704**	**5,103**	**6,520**	**7,945**
Total revenue	4,523	6,785	9,046	11,308	13,569
Raw material cost	848	1,285	1,710	2,142	2,573
Processing cost in U	394	612	783	980	1,179
Occupation cost in U	360	505	590	705	820
Amortization in U	608	679	859	961	1,052
Penalty	0	0	0	0	0
Profit per batch [€$/batch$]	101	132	222	283	345
Profitability [€$/h$]	16	26	35	45	55
Selectivity of S $[kmol\ \mathrm{S}/kmol\ total]$	0.594	0.589	0.590	0.589	0.588
Total energy consumption $[kWh]$	15,764	24,463	31,331	39,208	47,171
Temperature range in U [°C]	$[50, 86.9]$	$[50, 109.6]$	$[50, 88.6]$	$[50, 90.7]$	$[50.0, 93.5]$

Table 6.3: Plant solutions obtained at iteration $p = 0$ in step 2 of the heuristic approach for each demand scenario $s \in \{1, ..., N_S\}$ in grassroots Denbigh example. Items in bold indicate the objective function.

retrofit problem where amortization is calculated for new and for default units in the base plant solution. The number of plants N_P is upgraded at each iteration, provided that new solutions are found.

For illustrative purposes, iterations $p = 1$ and $p = 2$ with base plants P_1 and P_2 are here presented. The former is composed of one unit U_1 with a capacity of $1\,m^3$. It has been obtained at iteration $p = 0$ with scenario $s_1^0 = 1$, which has a demand $\xi^1_{Demands_S}$ of $10.5\,tn$ of product S, and is now used to root the rest of forecasted scenarios $s \in \{s_1^0{+}1, ..., N_S\}{=}\{2, ..., 5\}$. Table 6.4 summarizes the optimal solutions for each scenario at this iteration. The same plant P_1 with no variations is maintained for $\xi^2_{Demands_S}$ and $\xi^3_{Demands_S}$, adapting the master recipe to drive the optimal process in the aforesaid reaction unit U_1. In contrast, extended systems P_6 and P_7 are obtained for the two higher demand values $\xi^4_{Demands_S}$ and $\xi^5_{Demands_S}$, incorporating an additional unit U_2 with a capacity of $1\,m^3$ and $1.75\,m^3$ respectively.

As a result of enforcing the installation of unit U_1 with a predefined capacity of $1\,m^3$, the optimal profit is reduced in all the demand scenarios $s \in \{2, ..., 5\}$ at this iteration $p = 1$ with regard to previous one $p = 0$, as it can be observed by comparing Tables 6.3 and 6.4. Let us direct the attention to the demand scenarios 2 and 3 where plant P_1 is not modified. Their higher production demands $\xi^2_{Demands_S}$ and $\xi^3_{Demands_S}$, with regard to $\xi^1_{Demands_S}$ for which this plant was designed, lead the process optimization to more

Scenario s	2	3	4	5
Demand $[tn]$	15.75	21	26.25	31.5
Installed units U	U_1	U_1	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$
Size of units U $[m^3]$	1	1	$\{1,\ 1\}$	$\{1,\ 1.75\}$
Plant solution	P_1	P_1	P_6	P_7
Equipment configuration	α	α	π	π
No. Batches	36	54	29	25
Batch size $[kg/batch]$	437	389	905	1,260
Total processing time $[h]$	144	144	144	144
Batch processing time $[h/batch]$	4.00	2.67	4.97	5.76
Batch cycle time $[h/batch]$	4.00	2.67	4.97	5.76
Shortfall of product S $[kg]$	0.92	0	0	0
Total profit [€]	**3,662**	**4,728**	**6,018**	**7,427**
Total revenue	6,784	9,046	11,308	13,569
Raw material cost	1,327	1,991	2,138	2,547
Processing cost in U	632	895	{518, 518}	{442, 775}
Occupation cost in U	555	825	{450, 450}	{390, 578}
Amortization in U	608	608	{608, 608}	{608, 804}
Penalty	1	0	0	0
Profit per batch $[€/batch]$	102	88	208	297
Profitability $[€/h]$	25	33	42	52
Selectivity of S $[kmol\ \mathrm{S}/kmol\ total]$	0.569	0.506	0.590	0.594
Total energy consumption $[kWh]$	25,267	35,796	41,418	48,670
Temperature range in U [°C]	$[50, 110]$	$[50, 110]$	$[50, 110]$ $[50, 110]$	$[50, 108.6]$ $[50, 109.5]$

Table 6.4: Plant solutions obtained at iteration $p = 1$ in step 3 of the heuristic approach for each demand scenario $s \in \{s_1^0{+}1, ..., N_S\}$, $s_1^0 = 1$ in grassroots Denbigh example. Items in bold indicate the objective function.

extreme conditions because a larger number of batches should be processed in the same time horizon within the same processing capacity. For instance, 36 and 54 batches are required respectively in these scenarios to be able to fulfill the demand, reducing the available batch processing time from 6.26 h ($s = 1$) to 4.00 h ($s = 2$) and 2.67 h ($s = 3$) per batch. As a result, reaction temperatures reach the upper bound of 110°C in both cases, higher than their optimal solutions at iteration $p = 0$ (109.6°C and 88.6°C respectively). The processing time reduction and the temperature increase go in hand with a huge diminution in the selectivity of product S, becoming a 3.4% lower in scenario 2 and a 14.2% lower in scenario 3. Furthermore, this loss of efficiency in the process causes that the size of the batches processed in the same plant P_1 is reduced despite the total demand increases, obtaining batches of 457, 438, and 389 $kg/batch$ of product S for scenarios 1, 2, and 3 respectively.

In contrast, in the solution of demand scenarios 4 and 5 , the installation of a second unit U_2 operating in parallel allows to keep a process efficiency similar to the obtained at iteration $p = 0$. For example, the selectivity is over the 0.59 in both cases, batch processing times are close to 5 $h/batch$ (*i.e.* 4.97 h and 5.76 h in demand scenarios 4 and 5 respectively), and batch sizes are not reduced so much, less than a 20% in both scenarios. Nevertheless, analyzing the percentage of profit deterioration with regard to the previous iteration, similar values are obtained in scenarios 3, 4, and 5 –namely a 7.3%, 7.7%, and 6.5% respectively. The conclusion is that, given a underspecified reactor capacity, similar

Scenario s	3	4	5
Demand $[tn]$	21	26.25	31.5
Installed units U	U_1	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$
Size of units U $[m^3]$	1.25	$\{1.25,\ 1.25\}$	$\{1.25,\ 1.5\}$
Plant solution	P_2	P_8	P_9
Equipment configuration	α	π	π
No. Batches	40	23	25
Batch size $[kg/batch]$	525	1,141	1,260
Total processing time $[h]$	144	144	144
Batch processing time $[h/batch]$	3.60	6.26	5.76
Batch cycle time $[h/batch]$	3.60	6.26	5.76
Shortfall of product S $[kg]$	0	0	0
Total profit [€]	**4,985**	**6,005**	**7,417**
Total revenue	9,046	11,308	13,569
Raw material cost	1,822	2,127	2,547
Processing cost in U	845	$\{491,\ 491\}$	$\{552,\ 663\}$
Occupation cost in U	715	$\{418,\ 418\}$	$\{453,\ 515\}$
Amortization in U	679	$\{679,\ 679\}$	$\{679,\ 744\}$
Penalty	0	0	0
Profit per batch [€$/batch$]	125	261	297
Profitability [€$/h$]	35	42	51
Selectivity of S $[kmol$ S$/kmol\ total]$	0.553	0.593	0.594
Total energy consumption $[kWh]$	33,784	39,276	48,578
Temperature range in U [°C]	$[50, 109.6]$	$[50, 86.7]$	$[50, 107.6]$
		$[50, 86.7]$	$[50, 108.2]$

Table 6.5: Plant solutions obtained at iteration $p = 2$ in step 3 of the heuristic approach for each demand scenario $s \in \{s_2^0{+}1, ..., N_S\}$, $s_2^0 = 2$ in grassroots Denbigh example. Items in bold indicate the objective function.

processing conditions can be maintained by increasing the number of processing unit. However, the economic savings are often countervailed by the higher amortization costs.

Similar result are obtained at iteration $p = 2$ with plant P_2 as base solution, which is composed of one unit U_1 with a capacity of $1.25\,m^3$. This solution has been obtained at iteration $p = 0$ with the second demand scenario $s_2^0 = 2$, therefore it is now used to root the rest of forecasted scenarios $s \in \{s_2^0{+}1, ..., N_S\}{=}\{3, ..., 5\}$. In this case, the same plant solution P_2 with no modifications is the optimal one for $\xi^3_{Demands_{\mathrm{S}}}$, whereas extended systems P_8 and P_9 are obtained for $\xi^4_{Demands_{\mathrm{S}}}$ and $\xi^5_{Demands_{\mathrm{S}}}$, incorporating an additional unit U_2 with a capacity of $1.25\,m^3$ and $1.5\,m^3$ respectively. The master recipes obtained for each scenario are summarized in Table 6.5 for this iteration. Pursing an exhaustive search, the remaining plant solutions P_p, $p \in \{3, ..., N_P\}$ would be used as base plant solutions following the same methodology. Let us note that N_P is upgraded at iterations $p = 0$, 1, and 2, since new plant elements have been incorporated improving the base solution for particular scenarios. Then, N_p rises from 0 to 5 in iteration $p = 0$, from 5 to 7 in iteration $p = 1$, and from 7 to 9 in iteration $p = 2$.

Up to this point, the solution of each demand scenario $s \in \{1, ..., N_S\}$ and rooting on each base plant P_p, $p \in \{1, ..., N_P\}$ is a deterministic optimization problem which provides an optimal solution according to the MLDO features discussed in previous chapters. Global optimality can not be guaranteed, but the chances to do so are supported through the use of IFS solutions.

Step 3: Evaluation of plant alternatives

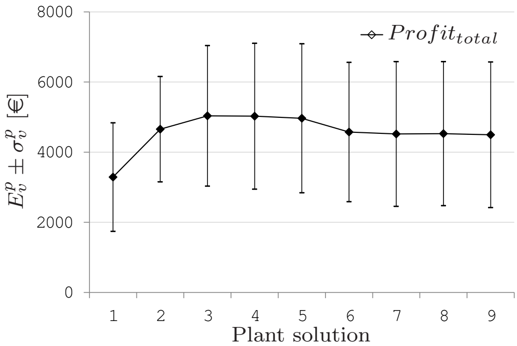
In order to determine which is the flexible plant solution, the expected profit of each plant alternative is evaluated, understood as the weighted average of all possible values taking into account the whole probability space of the uncertain demand. For that purpose, process synthesis and allocation decisions are optimized in the master recipe for each plant solution P_p, $p \in \{1, ..., 9\}$ –characterized by the capacity $Size^j$ of installed processing units $j \in U$– and for each demand scenario $s \in \{1, ..., 5\}$. Next, the expectancy of plant solution P_p, is calculated according to:

$$E^p_v = \sum_{s=1}^{N_S} w^s \; v(P_p, \xi^s_{Demands_{\mathrm{S}}}), \tag{6.6}$$

where E^p_v represents the expected value of v, referred to: total profit ($Profit_{total}$), total costs ($Cost_{total}$), product revenue ($Revenue_{\mathrm{S},total}$), raw material expenses ($Cost_{\mathrm{A},total}$), total processing, occupation, and amortization costs in batch units ($Cost_{p,total}$, $Cost_{o,total}$, and $Cost_{a,total}$ respectively), and shortfall penalty ($Penalty$). The standard deviations σ^p_v of the profit and the individual contributions v are also calculated for each plant solution P_p. This is an indicator of the risk associated to each solution, and is determined by:

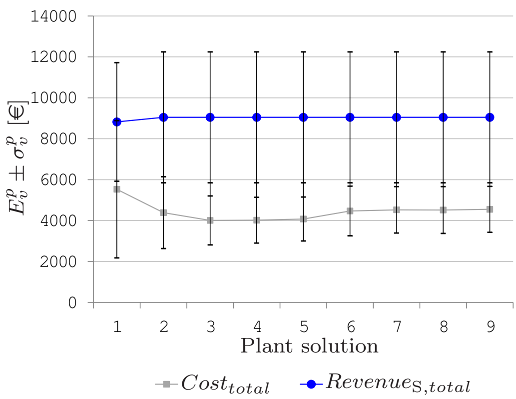
$$\sigma^p_v = \sqrt{\frac{1}{N_S}\sum_{s=1}^{N_S}(v(P_p, \xi^s_{Demands_{\mathrm{S}}}) - E^p_v)} \,. \tag{6.7}$$

Figure 6.4 summarizes the obtained expectancies and standard deviations. Two differentiated plant behaviors to deal with uncertainty are identified in sub-figures (a) and (b). On the one hand, the expected profit rises from plants P_1 to P_5, composed of a single unit U_1, as long as the reactor size increases from $1\,m^3$ to $3\,m^3$. Such gradual improvement is due to a reduction in the total costs. First, plant P_1 is distinguished of the other solutions by the huge penalty costs associated to product shortfall in the larger demand



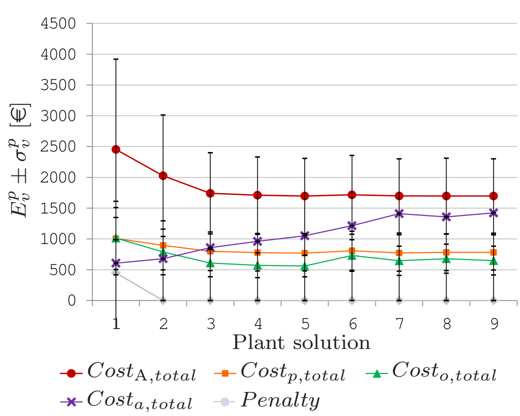
Plant solution	$Profit_{total}$ [€]
P_1	3,289±1,548
P_2	4,656±1,503
P_3	5,036±2,005
P_4	5,026±2,080
P_5	4,967±2,125
P_6	4,575±1,987
P_7	4,519±2,064
P_8	4,529±2,054
P_9	4,496±2,077

(a)



Plant solution	$Cost_{total}$ [€]	$Revenues_{S,total}$ [€]
P_1	5,532±3,353	8,821±2,898
P_2	4,390±1,754	9,046±3,198
P_3	4,010±1,196	9,046±3,198
P_4	4,021±1,118	9,046±3,198
P_5	4,079±1,074	9,046±3,198
P_6	4,471±1,212	9,046±3,198
P_7	4,527±1,134	9,046±3,198
P_8	4,517±1,144	9,046±3,198
P_9	4,550±1,122	9,046±3,198

(b)



Plant solution	$Cost_{A,total}$ [€]	$Cost_{p,total}$ [€]	$Cost_{o,total}$ [€]	$Cost_{a,total}$ [€]	$Penalty$ [€]
P_1	2,454 ±1,466	1,007 ±503	1,014 ±597	608	450 ±899
P_2	2,026±987	896±398	789±371	679	0
P_3	1,741±659	800±313	610±224	859	0
P_4	1,711±621	777±297	572±201	961	0
P_5	1,697±611	769±289	560±175	1,052	0
P_6	1,716±640	808±316	731±256	1,215	0±1
P_7	1,698±603	773±296	645±237	1,411	0
P_8	1,697±614	782±296	679±236	1,359	0
P_9	1,697±604	781±285	649±233	1,423	0

(c)

Figure 6.4: Expectancy E_v^p and standard deviation σ_v^p of variables v of each plant solution P_p in grassroots Denbigh example. v are referred to: (a) total profit ($Profit_{total}$), (b) total costs ($Cost_{total}$) and product revenue ($Revenues_{S,total}$), and (c) raw material expenses ($Cost_{A,total}$), total processing, occupation, and amortization costs in batch units ($Cost_{p,total}$, $Cost_{o,total}$, and $Cost_{a,total}$), and shortfall penalty ($Penalty$).

scenario $\xi^5_{Demands_S}$ in the given time horizon of 144 hours, reflected in a expected penalty of 450 ± 899€ in this solution. In next plant solutions P_2 to P_5, there is no penalty. Moreover, raw material, processing, and occupation costs decrease, as is illustrated in Figure 6.4c. Consequently, the total cost is reduced globally, despite the increase in amortization costs. On the other hand, plants P_6 to P_9, which comprise two processing units U_1 and U_2, provide similar results among them, since the costs compensate each other in the different solutions. A likely explanation of these results is the fact that the total volumes ($Size^{U_1}+Size^{U_2}$) are very close in all these plants, with a value of $2\,m^3$ in P_6, of $2.5\,m^3$ in P_8, and of $2.75\,m^3$ in P_7 and P_8. Thus, they have similar processing volumes and occupation costs.

Step 4: Best flexible plant

According to the expected profit maximization objective, the best plant solution is plant P_3, with a value of $5,036$€. In contrast, risk minimization could be evaluated by minimizing the standard deviation of the total expenses. In this case, the best solution of those evaluated would be P_5, with a value of $\sigma^p_{Cost_{total}} = 1,074$€. As it can be observed in Figure 6.4a, the value of the expected profit in plant solution P_3 is very alike to the value of other solutions like P_4 and P_5. This fact indicates that a similar performance can be achieved by different plants for a given structure, provided that the processing capacity in the solution space fulfills the production levels in all plausible scenarios.

Clearly, a factor of paramount importance to achieve such flexibility in several plant solutions is the support of plant design by the dynamic optimization of master recipes, involving process synthesis and plant allocation decisions. Additionally, the fulfillment of the complete demand is crucial in problems where product shortfall have a huge economic impact as in this example, where the penalty cost $\hat{p}_{penalty}$ is defined as twice the selling price $\hat{p}_S$. Let us bear in mind that a huge uncertainty margin is considered, which ranges from -50% to $+50\%$ of the estimated product demand.

The characterization of the master recipes for each demand scenarios $s \in \{1, ..., 5\}$ in the best flexible plant P_3 is summarized in Table 6.6 as an example. It can be observed that batch cycle times and processing conditions are adapted in order to provide a compromise between high product selectivity and low occupation costs. This way, reaction temperature goes up gradually along the different demand scenarios (from a constant profile set in 50°C in $s = 1$ to a dynamic profile with a highest temperature of 110°C in $s = 5$). At the same time, batch processing time is reduced (from $11.12\,h/batch$ in $s = 1$ to $3.89\,h/batch$ in $s = 5$) in order to produce larger number of batches (from 12 for $s = 1$ to 37 in $s = 5$) with a similar batch size (between 851 and $926\,kg/batch$).

Plant solutions with two processing units U_1 and U_2 do not improve the global solution, as is illustrated in Figure 6.4a. This is principally due to their higher investment costs. For instance, plant solution P_6 has a total capacity ($Size^{U_1}+Size^{U_2} = 2\,m^3$) equivalent to plant solution P_3 ($Size^{U_1} = 2\,m^3$). However, the sum of amortization costs increases from 859€ in plant P_3 to $1,215$€ in plant 6, as is shown in Figure 6.4c. Table 6.7 provides the optimal master recipes in plant P_6 for comparative purposes. In broad terms, it can be observed that a very similar number of batches and processing conditions are defined in plants P_3 and P_6 in each demand scenario. However, taking a close look at Figure 6.4, the costs are higher in plant P_6 compared to plant P_3, except for raw material cost –which is slightly lower due to higher selectivity in various scenarios in P_6– and the penalty –which is equal to zero in both cases. To determine the reasons why occupation and processing costs increase from a plant with one reactor of $2\,m^3$ to a plant with two reactors of $1\,m^3$ each one, a closer study of particular contributions in all demand scenarios should be

Scenario s	1	2	3	4	5
Demand $[tn]$	10.5	15.75	21	26.25	31.5
Installed units U	U_1	U_1	U_1	U_1	U_1
Size of units U $[m^3]$	2	2	2	2	2
Plant solution	P_3	P_3	P_3	P_3	P_3
Equipment configuration	α	α	α	α	α
No. Batches	12	17	23	30	37
Batch size $[kg/batch]$	875	926	913	875	851
Total processing time $[h]$	133.48	144	144	144	144
Batch processing time $[h/batch]$	11.12	8.47	6.26	4.80	3.89
Batch cycle time $[h/batch]$	11.12	8.47	6.26	4.80	3.89
Shortfall of product S $[kg]$	0	0	0	0	0
Total profit [€]	**2,140**	**3,647**	**5,103**	**6,488**	**7,804**
Total revenue	4,523	6,785	9,046	11,308	13,569
Raw material cost	842	1,264	1,710	2,174	2,714
Processing cost in U	368	574	783	1,021	1,252
Occupation cost in U	314	440	590	765	940
Amortization in U	859	859	859	859	859
Penalty	0	0	0	0	0
Profit per batch $[€/batch]$	178	215	222	216	211
Profitability $[€/h]$	16	25	35	45	54
Selectivity of S $[kmol$ S$/kmol\ total]$	0.599	0.598	0.590	0.580	0.558
Total energy consumption $[kWh]$	14,719	22,970	31,331	40,837	50,079
Temperature range in U [°C]	50	$[50, 74.4]$	$[50, 88.6]$	$[50, 110]$	$[50, 110]$

Table 6.6: KPIs for the optimal master recipes in the best plant solution P_3 in each demand scenario $s \in \{1, ..., 5\}$ in grassroots Denbigh example, including the optimal profit values achieved. Items in bold indicate the objective function.

addressed. This way, Table 6.7 shows that the optimal processing modes in plant P_6 for all demand $s \in \{1, ..., 5\}$ is parallel configuration π. As a result, occupation costs increase in P_6 with a total value of 731 € which is higher than occupation costs of 610 € in one single unit in P_3, due to the fixed term in the evaluation of occupation costs.

According to the master recipes in plants P_3 and P_6, it seems that the optimal operating mode in all the demand scenarios is the same, occupying the maximum number of available processing units. However, this is not the case in all plant solutions. For example, single unit operation is defined in the two-reactor plant P_7. In this solution, the capacity of processing units is asymmetrical with $1\,m^3$ and $1.75\,m^3$ in reactors U_1 and U_2 respectively. The KPIs for each demand scenario $s \in \{1, ..., 5\}$ are summarized in Table 6.8 for this plant solution P_7. As a result of having processing units with different sizes, it can be observed that occupation costs are reduced with regard to plant P_6, decreasing to 645 €. The reason is that the production level in the two lowest demand scenarios can be fulfilled within a single reactor operating at low temperatures (50°C and 69.8°C in scenarios 1 and 2 respectively) and high batch processing times ($11.04\,h$ and $7.20\,h$ in scenarios 1 and 2 respectively). To sum up, the occupation costs are reduced from 386 € to 308 € in scenario 1 and from 540 € to 465 € in scenario 2. Nevertheless, amortization costs have risen with regard to plant P_6, from $1,215$ € to $1,411$ €, more than the occupation costs savings. It is presumed that solutions with more than one processing units would be the optimal ones if longer amortization periods where considered, thus reducing the amortization load. In these case, the installation of several processing units with different

Scenario s	1	2	3	4	5
Demand $[tn]$	10.5	15.75	21	26.25	31.5
Installed units U	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$
Size of units U $[m^3]$	{1, 1}	{1, 1}	{1, 1}	{1, 1}	{1, 1}
Plant solution	P_6	P_6	P_6	P_6	P_6
Equipment configuration	π	π	π	π	π
No. Batches	12	17	23	29	36
Batch size $[kg/batch]$	875	926	913	905	875
Total processing time $[h]$	122.23	144	144	144	144
Batch processing time $[h/batch]$	10.19	8.47	6.26	4.97	4.00
Batch cycle time $[h/batch]$	10.19	8.47	6.26	4.97	4.00
Shortfall of product S $[kg]$	0	0	0	0	2
Total profit [€]	**1,712**	**3,193**	**4,627**	**6,018**	**7,323**
Total revenue	4,523	6,785	9,046	11,308	13,568
Raw material cost	837	1,254	1,696	2,138	2,655
Processing cost in U	{187, 187}	{291, 291}	{394, 394}	{518, 518}	{632, 632}
Occupation cost in U	{193, 193}	{270, 270}	{360, 360}	{450, 450}	{555, 555}
Amortization in U	{608, 608}	{608, 608}	{608, 608}	{608, 608}	{608, 608}
Penalty	0	0	0	0	2
Profit per batch [€$/batch$]	143	188	201	208	203
Profitability [€$/h$]	14	22	32	42	51
Selectivity of S $[kmol$ S$/kmol\ total]$	0.602	0.604	0.595	0.590	0.570
Total energy consumption $[kWh]$	14,926	23,289	31,527	41,418	50,538
Temperature range in U [°C]	50	$[50, 75.7]$	$[50, 86.9]$	$[50, 110]$	$[50, 110]$
	50	$[50, 75.7]$	$[50, 86.9]$	$[50, 110]$	$[50, 110]$

Table 6.7: KPIs for the optimal master recipes in plant solution P_6 in each demand scenario $s \in \{1, ..., 5\}$ in grassroots Denbigh example, including the optimal profit values achieved. Items in bold indicate the objective function.

sizes would be affordable, and savings due to the occupation of a less number of units with a more appropriated size for each demand scenario could be met.

Final remarks

One of the principal features of the obtained results is the similarity in the performance of most of the plant solutions with a same number of reactors. Besides, the complete demand fulfillment is accomplished in most of the cases, except for P_1 in demand scenario $s = 5$. Such high success in the ratio of demand fulfillment solutions is due to the adaptation of process synthesis and allocation decisions, which permit to operate in optimal conditions according to the trade-off between economic performance and plant flexibility considered in the objective function. Even in the case of plant solution P_1, which is the one with smaller capacity –*i.e.* one reactor U_1 with a capacity of $1\,m^3$–, the complete demand is fulfilled for all the demand values but $\xi^5_{Demands_\text{S}} = 31.5\,tn$, with a production level over the 98% with regard to the design demand $\xi^1_{Demands_\text{S}} = 10.5\,tn$. This way, the integrated process development approach proposed in this thesis is proved to have an crucial role in the achievement of plant flexibility through the simultaneous solution of process synthesis and plant allocation decisions, such as reference trajectories of the feed-forward control or the selection of the operating mode.

Scenario s	1	2	3	4	5
Demand $[tn]$	10.5	15.75	21	26.25	31.5
Installed units U	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$	$\{U_1,\ U_2\}$
Size of units U $[m^3]$	$\{1,\ 1.75\}$	$\{1,\ 1.75\}$	$\{1,\ 1.75\}$	$\{1,\ 1.75\}$	$\{1,\ 1.75\}$
Plant solution	P_7	P_7	P_7	P_7	P_7
Equipment configuration	β	β	π	π	π
No. Batches	13	20	17	21	25
Batch size $[kg/batch]$	808	788	1,235	1,250	1,260
Total processing time $[h]$	143.54	144	144	144	144
Batch processing time $[h/batch]$	11.04	7.20	8.47	6.86	5.76
Batch cycle time $[h/batch]$	11.04	7.20	8.47	6.86	5.76
Shortfall of product S $[kg]$	0	0	0	0	0
Total profit [€]	**1,594**	**3,058**	**4,526**	**5,987**	**7,427**
Total revenue	4,523	6,785	9,046	11,308	13,569
Raw material cost	841	1,279	1,697	2,129	2,547
Processing cost in U	{0, 368}	{0, 571}	{277, 467}	{351, 611}	{442, 775}
Occupation cost in U	{0, 308}	{0, 465}	{270, 398}	{330, 488}	{390, 578}
Amortization in U	{608, 804}	{608, 804}	{608, 804}	{608, 804}	{608, 804}
Penalty	0	0	0	0	0
Profit per batch $[€/batch]$	123	153	266	285	297
Profitability $[€/h]$	11	21	31	42	52
Selectivity of S $[kmol\ \mathrm{S}/kmol\ total]$	0.599	0.592	0.595	0.592	0.594
Total energy consumption $[kWh]$	14,739	22,850	29,764	38,492	48,670
Temperature range in U			$[50, 52.9]$	$[50, 74.3]$	$[50, 108.6]$
$[^\circ\mathrm{C}]$	50	$[50, 69.8]$	$[50, 53.0]$	$[50, 75.1]$	$[50, 109.5]$

Table 6.8: KPIs for the optimal master recipes in plant solution P_7 in each demand scenario $s \in \{1, ..., 5\}$ in grassroots Denbigh example, including the optimal profit values achieved. Items in bold indicate the objective function.

6.4 Acrylic fiber production system

The aim of this example is to direct attention toward industrial-sized polymerization processes. In particular, the simultaneous batch process development and plant design in grassroots scenarios is addressed to produce acrylic fiber with a specific composition and quality. Further synthesis decisions are considered with regard to previous examples, namely the selection of process stages, equipment technology, and chemicals, as well as the potential solvent recovery and reuse.

6.4.1 Process description

Polymerization has been historically an area of application where PSE tools have been widely used through the combination of polymer science, chemistry, and technology, with process engineering principles (Giudici, 2000). A significant amount of work has been devoted to the modeling and simulation of polymerization reaction systems, which are characterized by complex interactions between productivity indicators –*e.g.* conversion, batch time, or profit– and polymer properties –*e.g.* polydispersity or molecular weight distribution. In particular, polymer quality is strongly related to measures like the chain length or the mass average number and these should be calculated as a function of intermediate products. However, these are ruled by complex reaction mechanisms and equations systems that include phenomena like the life and dead polymers moments. Furthermore, physicochemical phenomena like the auto-acceleration and the Trommsdorf effect may occur depending on processing conditions such as the viscosity and temperature in the polymerization reaction. As a result, the design, operation and control of polymerization reactors constitute challenging problems, where the choice of the trajectories of reactor temperature and monomer feed rate is crucial to determine the compromise between productivity and polymer quality (Giudici, 2000, Embiruçu et al., 1996).

Despite most of the research has been focused on the polymerization reaction, downstream tasks also contribute to the optimization of overall economic and environmental production targets. For instance, the effect of cleaning technologies in polymerization processes was proved by Capón-García et al. (2011a) solving the optimal scheduling of polymer manufacturing facilities. Gol'dfein & Zyubin (1990) and Bajaj et al. (1996) indicated that the polymer-solvent separation stage could be dismissed if the achieved conversion was high. Gol'dfein & Zyubin (1990) also detected that the variety of organic and aqueous solvents that can be used in polymerization processes have a different environmental impact depending ton the molecular composition of the solvent. The interactions between consecutive process stages and their effect over global targets motivates the study of the trade-offs in process synthesis, plant allocation, and plant design decisions by using a unique optimization model to simultaneously evaluate structural and performance degrees of freedom.

Acrylic fiber production

Acrylic fibers are synthetic fibers composed of at least 85% of acrylonitrile (AN) monomer and the rest of another comonomer such as vinyl acetate (VA), methyl acrylate (MA), methyl methacrylate (MMA), vinyl chloride (VC), or vinylidene chloride (VDC). The production of acrylic fiber comprises a primary stage to produce the copolymer in bulk format and a secondary stage to transform it into spun format. Specifically, the principal features of the manufacturing process are defined according to the related state-of-the-art literature. The gathered information to define the complete production process is following summarized:

- Polymer production processes are composed of two stages, namely the primary process for bulk polymer generation and the secondary process for obtaining the polymer in spun form;
- The principal tasks in acrylic fiber production are polymerization reaction, polymer separation, washing and filtration, polymer repulping, filtering, spun generation, second washing, and separation of solvent and washing (Grau et al., 1996, Capón-García et al., 2011a, EPA, 1995);
- Two methods are used to synthesize acrylic fiber in industry, namely suspension and solution copolymerization technologies; either batch or continuous operation may be employed (EPA, 1995);
- There is the possibility of avoiding solvent separation after the solution copolymerization reaction, provided that high conversion rates are achieved (Gol'dfein & Zyubin, 1990, Bajaj et al., 1996);
- The operational information and dynamic models of copolymerization reaction is provided by Butala et al. (1988) and of separation systems by Haggblom (1991), Luyben (1992), Oldenburg et al. (2003), Muntean et al. (2011);
- Washing water of final product can be recovered and reused (EPA, 1995).

The general block representation of the process is presented in Figure 6.5, taking into account prior considerations and the additional recirculation of solvent and suspension medium.

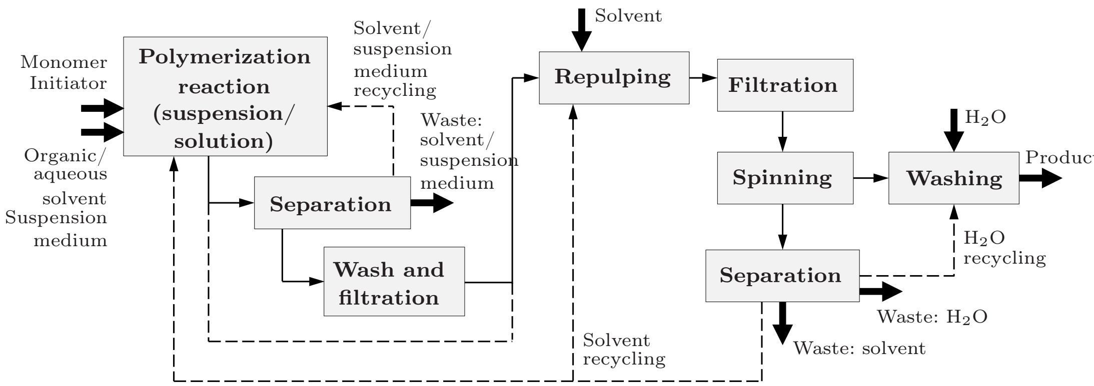


Figure 6.5: Process stages in acrylic fiber production system: general processing scheme (solid lines) and potential processing alternatives (dashed lines).

6.4.2 Problem statement

The target is to produce an acrylic fiber composed of 85% of AN and 15% of VA in bulk format. Moreover, the desired copolymer properties are associated to a maximum polydispersity variation of 0.1 and a maximum deviation in the composition of 0.025. For the sake of completeness, the modeling strategy is detailed for the entire process including spun production, in case that the problem should be extended for further study. A single-product campaign is assumed to produce batches of 200 kg of final product. The problem statement of this problem is defined as follows:

Given:

- **Planning data:** final product, intermediates, and raw materials, expected demand of final product, and maximum time horizon;
- **Plant diagram:** SEN superstructure of potential equipment units to be installed, pipelines and connection nodes like mixers and splitters;
- **Task network alternatives:** mandatory and optional tasks, alternative solvents involved into the process –*i.e.* organic solvent dimethylformamide (DMF) or aqueous solvent sodium thiocyanate (NaSCN(aq))–, allowed technologies, and possible reuse of intermediates;
- **Batch process operation:** potential task-unit assignments, batch operations and phases within each unit procedure, phase to phase switching conditions, and set of limiting processing conditions in particular units;
- **Process dynamics:** DAE systems to represent the process behavior in each unit procedure, initial conditions, and set of process and control variables;
- **Data related to performance evaluation:** decision criteria and data to evaluate the objective function, namely the direct cost of raw materials and resources ($\hat{p}_{\text{AN}}$, $\hat{p}_{\text{VA}}$, $\hat{p}_{\text{AIBN}}$, $\hat{p}_{\text{DMF}}$, and $\hat{p}_{\text{NaSCN(aq)}}$, $\hat{p}_{\text{H}_2\text{O}}$), equipment amortization and processing costs in processing units ($\check{c}_j$ and $\hat{c}_j$ respectively), and costs associated to waste treatment ($\hat{p}_{\text{waste}}$);

the goal is to determine:

- **Process synthesis decisions:** selection of separation stage, technological specification of copolymerization reaction –*i.e.* solution or suspension polymerization–, selection of solvents involved –*i.e.* DMF or NaSCN(aq)–, reference trajectories of the feed-forward control variables –*i.e.* monomer feed rate and temperature in the reaction stage and heat supplied in the separation stage–, duration of the batch operations that compose each task, recirculation of intermediate mixtures –*i.e.* solvent, suspension medium, unreacted monomer, and initiator–, and material transfer synchronization between tasks –*i.e.* synchronization of flow rates, compositions, and starting and final times;
- **Allocation of manufacturing facilities decisions:** task-equipment assignment –*i.e.* unit procedure selection–, selection of processing and storage units, and equipment configuration –*i.e.* operating mode in single or series operation–;
- **Plant design decisions:** sizing of processing units;

such that the total cost is minimized and copolymer quality restrictions are fulfilled. In particular, the total cost considers the equipment amortization, the processing costs, the raw material expenses, and the costs associated to the waste disposal. For the sake of simplicity, a deterministic demand is assumed in this example.

6.4.3 Superstructure representation

The following process stages or tasks are subject to be included into the process model and are thus represented in the superstructure: (1) copolymerization reaction, (2) recovery of unreacted monomer, solvent, and suspension medium after reaction, (3) washing and filtration, (4) repulping, (5) filtering, (6) wet spinning, (7) second washing and filtration, and (8) second recovery of solvent after spinning. For each process stage, several subtasks and configurations are allowed, which determine the required equipment pieces and their synchronization.

Nine alternative disjunctions are considered for plant and process synthesis in this case study. For instance, either solution or suspension copolymerization technologies can be selected. In solution polymerization, organic or aqueous solvent can be used. After the polymerization reaction stage, there is the possibility to separate the solvent from the copolymer or to transfer directly the solved copolymer to the repulping stage. The rest of disjunctions are summarized in Table 6.9. All in all, each alternative leads to a particular cost profile in the objective function. For example, the use of organic solvent drastically increases the waste treatment expenses.

The SEN superstructure of the complete process including primary and secondary stages is presented in Figure 6.6. It contains all the structural alternatives. In particular, the superstructure is composed of the following equipment items, which are potentially required, and the corresponding connections: solution and suspension polymerization reactors R_{11} and R_{12}, evaporator and condenser E_2, washing and filtering units F_3, F_5, F_{71} and F_{72}, repulping unit R_4, spinneret S_6, distillation columns C_{81} and C_{82}, and buffer tanks T_2, T_3, T_4, T_{81} and T_{82}.

6.4.4 Optimization model

The problem is formulated as a MLDO according to the proposed modeling strategy. First, the disjunctive alternatives presented in Table 6.9 are expressed through logical

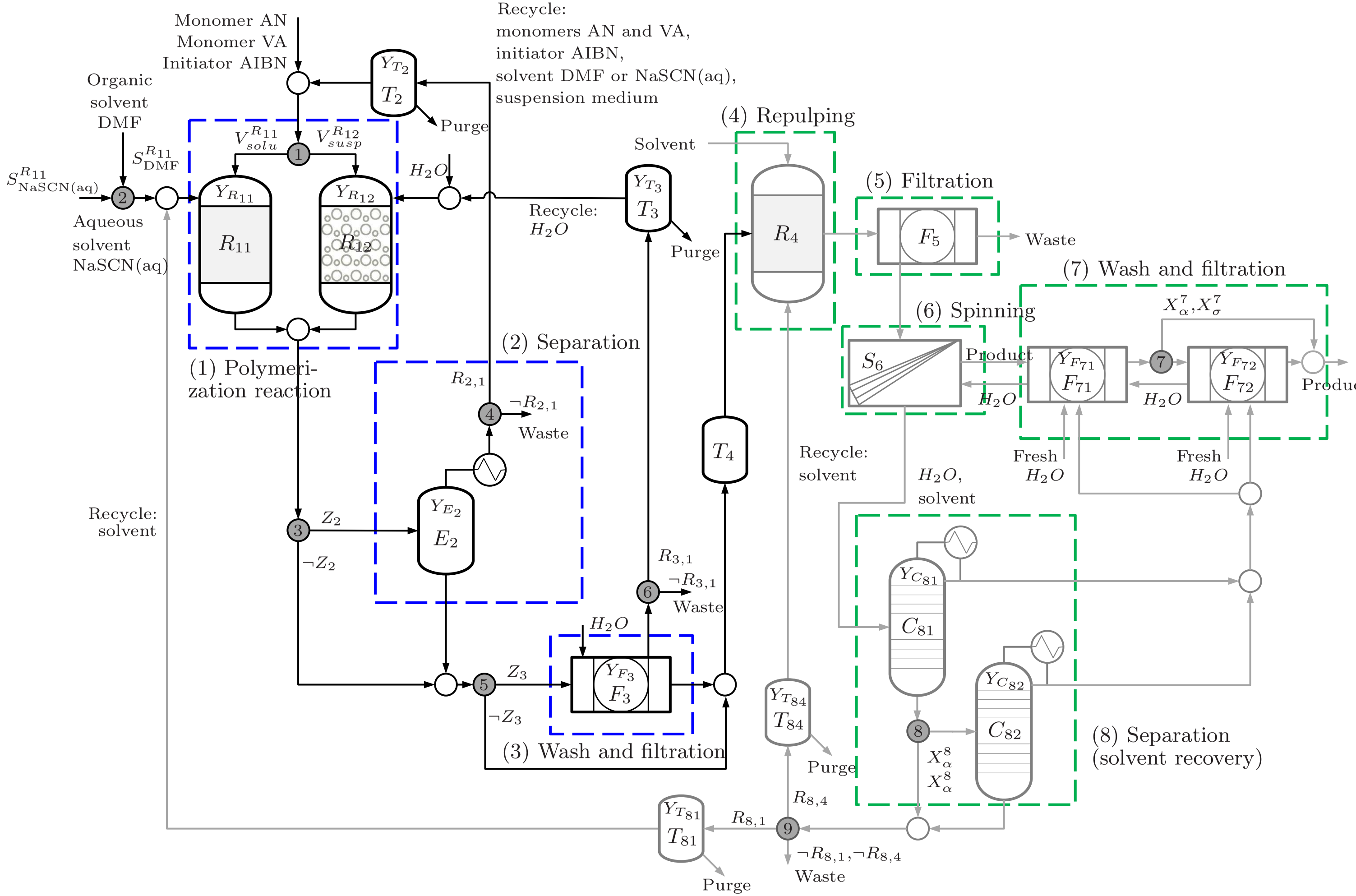


Figure 6.6: Superstructure of the acrylic fiber example, composed of the following equipment pieces: solution and suspension polymerization reactors R_{11} and R_{12}, evaporator and condenser E_2, washing and filtering units F_3, F_5, F_{71} and F_{72}, repulping unit R_4, spinneret S_6, distillation columns C_{81} and C_{82}, and buffer tanks T_2, T_3, T_4, T_{81} and T_{84}. Stages that correspond to the primary part of the process for bulk polymer generation are framed by blue dashed lines, and correspond to the states included in the optimization problem. Stages corresponding to the secondary part of the process for spun production, not solved in this example, are framed by green dashed lines.

Disjunction		Associated Booleans
1	Solution or suspension copolymerization technologies	$V_{solu}^{R_{11}}$, $V_{susp}^{R_{12}}$
2	Organic (DMF) or aqueous (NaSCN(aq)) solvent in solution polymerization	$S_{\mathrm{DMF}}^{R_{11}}$, $S_{\mathrm{NaSCN(aq)}}^{R_{11}}$
3	Selection of separation stage 2	Z_2
4	Recirculation of solvent recovered in separation stage 2 to copolymerization reaction stage 1	$R_{2,1}$
5	Selection of washing and filtration stage 3	Z_3
6	Recirculation of washing water in washing and filtration stage 3 to copolymerization reaction stage 1	$R_{3,1}$
7	Operating mode in process stage 7: single unit F_{71} or series F_{71} followed by F_{72}	X_α^7, X_σ^7
8	Operating mode in process stage 8: single unit C_{81} or series C_{81} followed by C_{82}	X_α^8, X_σ^8
9	Recirculation of solvent recovered in separation stage 8 to polymerization stage 1 or repulping stage 4	$R_{8,1}$ $R_{8,4}$

Table 6.9: Process development disjunctions in the acrylic fiber example.

propositions relating logical decisions to each other, namely the selection of process stages (Z_i), technological alternatives (V_λ^j), and chemicals (S_c^j), the potential solvent recovery and reuse (R_n), and the operating modes (X_ψ^i). These decisions are additionally related to potential processing and storage units (Y_j), and to task-unit assignments ($W_{j,q}$), which determine the processing order of batch unit procedures. Overall, the following equations are defined:

1. The selection of solution ($V_{solu}^{R_{11}}$) or suspension ($V_{susp}^{R_{12}}$) copolymerization technologies and the corresponding reactors R_{11} ($Y_{R_{11}}$) or R_{12} ($Y_{R_{12}}$) is defined by:

$$\begin{gathered} V_{solu}^{R_{11}} \veebar V_{susp}^{R_{12}}, \\ V_{solu}^{R_{11}} \Leftrightarrow Y_{R_{11}}, \\ V_{susp}^{R_{12}} \Leftrightarrow Y_{R_{12}}. \end{gathered} \tag{6.8}$$

2. The selection of organic ($S_{\mathrm{DMF}}^{R_{11}}$) or aqueous ($S_{\mathrm{NaSCN(aq)}}^{R_{11}}$) solvent in solution copolymerization is determined by:

$$V_{solu}^{R_{11}} \Leftrightarrow S_{\mathrm{DMF}}^{R_{11}} \veebar S_{\mathrm{NaSCN(aq)}}^{R_{11}}. \tag{6.9}$$

3. The possibility of dismissing separation stage 2 ($\neg Z_2$) is conditioned by the selection of solution polymerization technology and by the achievement of a conversion in the solution copolimerization reactor ($\chi_{R_{11}}$) greater than the established minimum input conversion in repulping stage 4 (χ_4^{L}). This is represented by the following equations, which include the installation of the separation unit E_2 (Y_{E_2}):

$$\begin{gathered} \neg Z_2 \Rightarrow V_{solu}^{R_{11}} \wedge \left(\chi_{R_{11}} \geq \chi_4^{\mathrm{L}}\right), \\ Z_2 \Leftrightarrow Y_{E_2}. \end{gathered} \tag{6.10}$$

4. The recirculation of the solvent or the suspension medium recovered in separation stage 2 toward reaction stage 1 ($R_{2,1}$) is associated to the installation of buffer tank T_2 (Y_{T_2}) through the proposition:

$$R_{2,1} \Leftrightarrow Y_{T_2}. \tag{6.11}$$

5. The selection of washing and filtration stage 3 (Z_3) and corresponding equipment item F_3 (Y_{F_3}) is associated to the definition of previous separation task 2, and is represented by the following equations:

$$\begin{aligned} Z_2 &\Leftrightarrow Z_3, \\ Z_3 &\Leftrightarrow Y_{F_3}. \end{aligned} \tag{6.12}$$

6. The recirculation of the washing water in filtration stage 3 toward reaction stage 1 ($R_{3,1}$) is associated to the installation of buffer tank T_3 (Y_{T_3}) through the proposition:

$$R_{3,1} \Leftrightarrow Y_{T_3}. \tag{6.13}$$

7. The operating modes considered in process stage 7 include the use of one single unit F_{71} (X_α^7) or series configuration where unit F_{71} is followed by F_{72} (X_σ^7), and are formulated by:

$$\begin{aligned} X_\alpha^7 &\veebar X_\sigma^7, \\ X_\alpha^7 &\Leftrightarrow Y_{F_{71}}, \\ X_\sigma^7 &\Leftrightarrow Y_{F_{71}} \wedge Y_{F_{72}}. \end{aligned} \tag{6.14}$$

8. The operating modes considered in process stage 8 include the use of one single unit C_{81} (X_α^8) or series configuration where unit C_{81} is followed by C_{82} (X_σ^8), and are formulated by:

$$\begin{aligned} X_\alpha^8 &\veebar X_\sigma^8, \\ X_\alpha^8 &\Leftrightarrow Y_{C_{81}}, \\ X_\sigma^8 &\Leftrightarrow Y_{C_{81}} \wedge Y_{C_{82}}. \end{aligned} \tag{6.15}$$

9. The recirculation of the solvent recovered in separation stage 8 toward reaction stage 1 ($R_{8,1}$) or toward repulping stage 4 ($R_{8,4}$) is associated to the acquisition of buffer tanks T_{81} ($Y_{T_{81}}$) or T_{84} ($Y_{T_{84}}$) through propositions:

$$\begin{aligned} R_{8,1} &\Leftrightarrow Y_{T_{81}}, \\ R_{8,4} &\Leftrightarrow Y_{T_{84}}. \end{aligned} \tag{6.16}$$

Regarding the process performance, those tasks whose control variables have a critical impact on the cost function are: (1) the copolymerization reaction, (2) the recovery of unreacted monomer, solvent, and suspension medium after reaction, and (8) the recovery of solvent after spinning and washing the final spun. A large ratio of solvent to be separated and reused can partially mitigate its environmental impact and waste disposal cost. On the contrary, low conversions in the polymerization reaction may result in higher processing costs in the following separation stage. For that reason, dynamic models are used to describe the performance of these process stages (1, 2, and 8) and the dynamic trajectories of their control variables and batch times are optimized. In contrast, process stages that are not critically contributing to the objective function and processing trade-offs may be represented by steady-state assumptions or other approximations in order to reduce the problem complexity. Further details regarding the dynamic models of the copolymerization and separation stages are provided in Appendix C as well as their synchronization.

Finally, the objective function is defined as follows:

$$\underset{\substack{u_k^{dyn}(t),u^{stat}\\ u^{int},u^{Bool}}}{\text{minimize}}\ \Phi = Cost_{\mathrm{M}_1} + Cost_{\mathrm{M}_2} + Cost_{\mathrm{I}} + Cost_{\mathrm{S}} + Cost_a + Cost_p + Cost_{\mathrm{waste}}, \tag{6.17}$$

where $u_k^{dyn}(t)$ are the profiles of input and output flow rates ($F^j_{in1,k}(t)$, $F^j_{in2,k}(t)$, and $F^j_{out,k}(t)$, $\forall k$) and the cooling temperature profile ($\theta^j_{cool,k}(t)$, $\forall k$) in the copolymerization reaction stage 1 associated to units $j \in \{R_{11}, R_{12}\}$, as well as the heat supplied in separation stage 2 associated to the evaporator $j \in \{E_2\}$ ($Q^j_{heat,k}(t)$, $\forall k$). Additionally, u^{stat} refers to the composition of raw materials during the load operation ($c^j_{c,in1,k}$, $c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{I}\}$, $k \in \{1\}$) and the composition of monomer M_1 during the reaction operation ($c^j_{\mathrm{M}_1,in1,k}$, $k \in \{2\}$) in copolymerization reaction stage 1, and to the duration of batch operations (t_l, $\forall l$). Finally, u^{int} refers to the size of installed processing units ($Size^j$), and u^{Bool} comprises qualitative decisions ($Z_i, V^j_\lambda, S^j_c, R_n, X^i_\psi, Y_j, W_{j,q}$). The complete MLDO model is provided in Appendix C.

6.4.5 Problem solution

The MLDO problem is solved through the proposed direct-simultaneous approach. Particularly, 8 finite elements and 3 collocation points in normalized Legendre roots are used in the full discretization step. Moreover, a piece-wise constant function is used to define the profiles of the control variables. The obtained MINLP is solved using the OA solver DICOPT in GAMS optimization framework. CONOPT and CPLEX are used in the NLP and MILP subproblems respectively. The resulting optimization model is large in size, as observed in Table 6.10 where the number of equations, continuous and integer variables, and non-zero elements in the MINLP model are presented. It is also worth noting the high rate of non-linear terms. These difficulties are overcome by the providing IFS that serve as initial point in the optimization algorithms.

	No. equations	No. continuous variables	No. binaries	Non-zero elements	Non-linear terms	Solution time
2 reaction technologies	4,805	3,080	6	21,566	10,357	44 s.
" & 1 separator	7,371	5,831	8	30,941	14,979	206 s.
" & 2 storage tanks	18,466	10,121	8	58,760	18,857	357 s.
" & recirculation[1]	18,532	10,121	10	58,883	18,889	258 s.

[1] Recirculation of un-reacted monomers and solvent or suspension medium.

Table 6.10: MINLP model characterization in the acrylic fiber example for different subsystems with an increasing degree of complexity.

6.4.6 Results and discussion

The primary part of the copolymerization process to obtain 200 kg of copolymer with a composition of 85% of AN and 15% of VA in bulk format is optimized. The following stages are included in the problem: (1) copolymerization reaction, (2) separation of solvent or suspension medium, and (3) washing and filtration.

First, six subsystems are addressed to obtain initial feasible solutions that can be provided to the MINLP. The subsystems refer to the two optional technologies and the two considered solvents in the solution polymerization, and to the recirculation or not of the bottoms flow in the separation stage. To solve each subproblem, the Boolean variables corresponding to prior decisions are fixed, and the logical propositions are solved in a preliminary step. This way, the remaining logical variables are determined and the MINLP problem becomes a NLP, thus avoiding the combinatorial part of the problem. The three subproblems are:

- Solution polymerization technology using organic solvent DMF: $V_{solu}^{R_{11}}= true$ and $S_{\mathrm{DMF}}^{R_{11}}=true$ for $R_{2,1}=true$ and for $R_{2,1}=false$;
- Solution polymerization technology using aqueous solvent NaSCN(aq): $V_{solu}^{R_{11}}= true$ and $S_{\mathrm{NaSCN(aq)}}^{R_{11}}=true$ for $R_{2,1}=true$ and for $R_{2,1}=false$;
- Suspension polymerization technology: $V_{susp}^{R_{12}}=true$ for $R_{2,1}=true$ and for $R_{2,1}=false$.

The complete set of Booleans for each case are summarized in Table 6.11.

Subsystem	$V_{solu}^{R_{11}}$	$V_{susp}^{R_{12}}$	$S_{\mathrm{DMF}}^{R_{11}}$	$S_{\mathrm{NaSCN(aq)}}^{R_{11}}$	Z_2	$R_{2,1}$	$Y_{R_{11}}$	$Y_{R_{12}}$	Y_{E_2}	Y_{T_2}
1	**T**	F	**T**	F	T	**F**	T	F	T	F
2	**T**	F	**T**	F	T	**T**	T	F	T	T
3	**T**	F	F	**T**	T	**F**	T	F	T	F
4	**T**	F	F	**T**	T	**T**	T	F	T	T
5	F	**T**	F	F	T	**F**	F	T	T	F
6	F	**T**	F	F	T	**T**	F	T	T	T

Table 6.11: Boolean variables for the three subsystems of the acrylic fiber example solved in the preliminary step to calculate IFS. In bold, variables fixed originally. T: *true*, F: *false*.

In Figure 6.7 the objective function values obtained for the six NLP subsystems are presented for comparative purposes. The results for the MINLP considering the complete system are also shown for the case where recirculation from separated solvent or suspension medium in stage 2 to copolymerization reaction stage 1 is not allowed $R_{2,1}=false$ and when it is allowed $R_{2,1}=\{true, false\}$. It is fair to note that the optimal solution among the three alternatives –*i.e.* solution polymerization with organic solvent, with aqueous solvent, or suspension polymerization– depends on decisions on other process stages, namely the recirculation. When recirculation it is not considered, the best alternative is suspension polymerization (subsystem 5). In contrast, solution polymerization with aqueous solvent (solution 4) is selected when the recirculation of solvent and unreacted monomer are allowed, which are used in a subsequent batch. The proposed modeling approach integrates all these degrees of freedom and allows the consideration of the alternatives simultaneously to obtain the optimal solution.

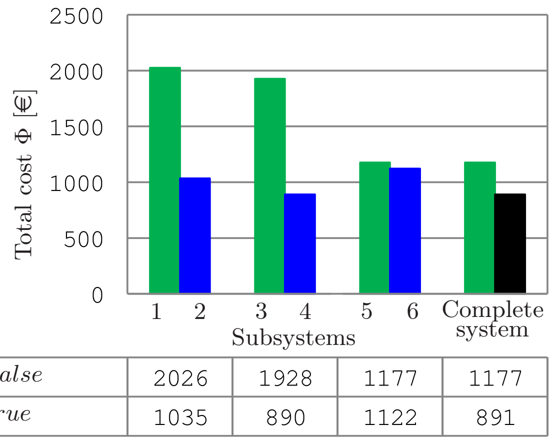


Figure 6.7: Total cost for the six subsystems and for the complete system with $R_{2,1}$=*false* and without $R_{2,1}$=*true* recirculation in the acrylic fiber example. In black, optimal solution.

The contributions to the cost calculation in the objective function are summarized in Table 6.12 for the six subsystems, including the optimal solution. Essentially, it can be noted that the heaviest cost weight is related to raw material, emphasizing the solvent cost compared to the suspension medium. This way, solutions with recirculation replace a great part of the raw material costs. For the economic scenario considered, these costs are much higher than cooling water, and even heat costs in the separation stage. In fact, this is the reason why solutions with recirculation are much better than solutions without recirculation in all cases, even for the case of suspension polymerization. These solutions are consistent, since recirculation is the only mean to promote solvent savings without detriment of the reaction effectiveness. The solution would presumably be different if sec-

			Subsystems 1	2	3	4	5	6	Complete system
Φ Total cost		[€]	**2026**	**1035**	**1928**	**890**	**1177**	**1122**	**890**
R_{11} or R_{12}	Total cost in R_{11} or R_{12}	[€]	**1958**	**967**	**1829**	**772**	**1089**	**1011**	**835**
	Amortization	[€]	228	225	167	197	238	234	197
	Water consumption cost	[€]	5	5	4	4	11	11	4
	Cost of monomer AN	[€]	637	322	689	315	346	377	315
	Cost of monomer VA	[€]	328	214	373	123	51	56	123
	Cost of initator	[€]	251	168	101	96	441	333	96
	Cost of solvent or suspension medium	[€]	510	33	494	36	1	0	36
E_2	Total cost in E_2	[€]	**67**	**68**	**99**	**119**	**88**	**111**	**119**
	Amortization	[€]	13	10	14	15	23	21	15
	Energy cost	[€]	33	37	53	71	21	46	71
	Cost of waste disposal	[€]	21	21	31	33	43	45	33

Table 6.12: Contributions to the cost calculation associated to potential units R_{11}, R_{12}, and E_2, in the acrylic fiber example considering: subsystem alternatives 1 to 6 (NLP problems) and the complete system (MINLP problem).

ondary stage would be considered in the problem, since the option of avoiding separation stage and reusing solvent in the repulping task would be more relevant.

The optimal processing scheme is illustrated in Figure 6.8. It is characterized by the control and processing variable profiles shown in Figure 6.9. The optimal trajectories for the monomer dosage and the temperature in the polymerization task follow a monotonically increasing piece-wise constant function, whereas the vapor flow in the evaporation is set in the upper bound in most of the time. One relevant feature is that the evolution of the compositions along time show a big excess of monomers. This excessive consumption is also supported by the recirculation of the distillate after the separation stage, since all the monomers are light components and are complete recovered. The results obtained also prove that the optimal time for the polymerization reaction task is much longer than the duration of the separation stage. Therefore, it would be necessary to consider the use of more polymerization reactors with a parallel out-of-phase configuration to reduce the cycle time.

To conclude, the major strength of the proposed methodology is the holistic evaluation of the decision criteria. In particular, trade-offs between the various process stages within the complete process is considered in the optimization, as well as the interactions between synthesis and allocation degrees of freedom. Additionally, the optimization model permits the evaluation and comparison of processing alternatives according to multiple points of view, like processing, economic, or sustainable production policies. The defined system, which is a sub-part of the complete process for acrylic fiber production, has been successfully solved with regard to the isolated solution of particular structures. However,

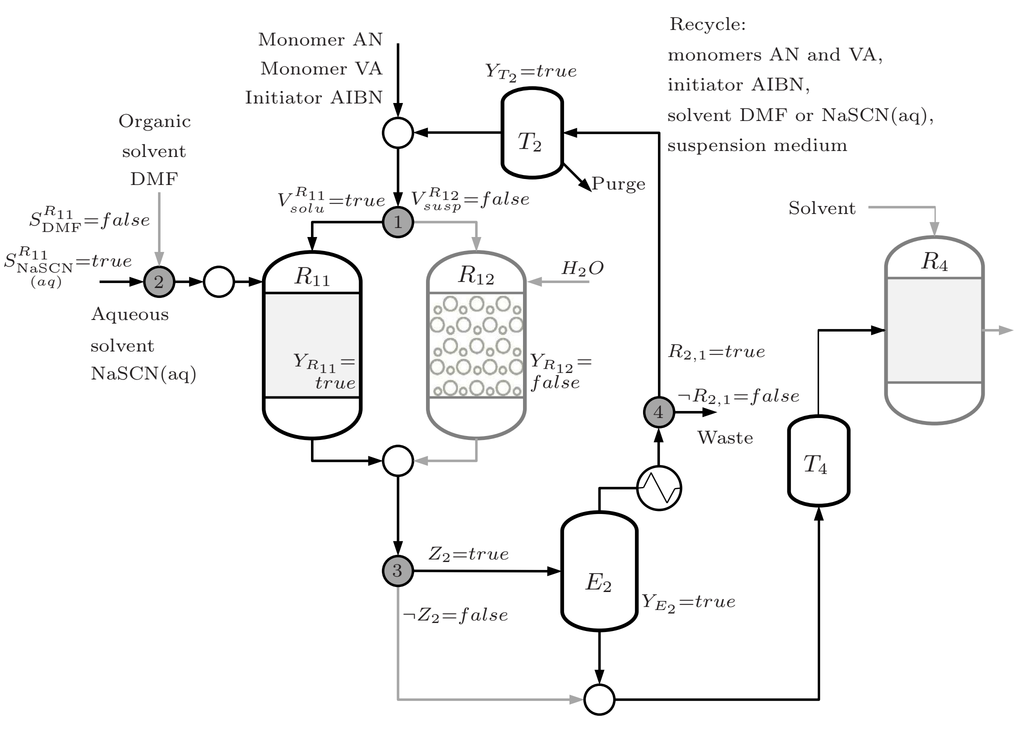


Figure 6.8: Optimal structure and corresponding logical variables in the acrylic fiber example.

to fully exploit the methodology, it would be necessary to consider not only the primary production stage, but the complete system. Additionally, further degrees of freedom have been detected, which should be incorporated into the model, as it is the use of several reactors and their arrangement in parallel out-of-phase configuration, provided that the reduction of the cycle time can be and additional objective in the production of several batches with a limited time horizon.

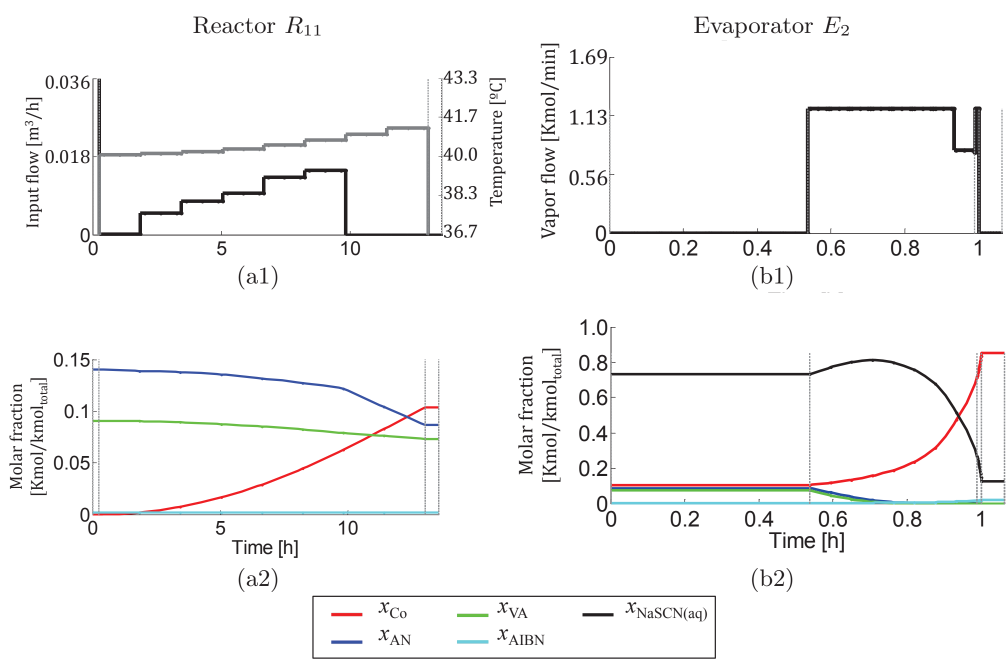


Figure 6.9: Control and process variable profiles in the optimal solution in the suspension polymerization reactor R_{11} and in the evaporator E_2 in the acrylic fiber example: (a1) AN dosage (black line) and temperature (grey line) in R_{11}, (b1) vapor flow in E_2, and (a2-b2) molar compositions of copolymer x_{Co}, monomers AN x_{AN} and VA x_{VA}, initiator x_{AIBN}, and aqueous solvent $x_{\mathrm{NaSCN(aq)}}$ in R_{11} and E_2 respectively.

6.5 Concluding remarks

This chapter has posed two principal targets. First, flexibility of the batch plant has been pursued through the incorporation of uncertainty in product demand, in order to reflect changing market conditions and variations of the plausible customer orders. Second, the integrated solution of plant design and batch process development has been exploited as a challenge to avoid suboptimal solutions in grassroots designs and to enhance future flexibility.

On the one hand, the Denbigh example (§ 6.3) demonstrates that an important role is played by process development decisions in the flexible plant design. Degrees of freedom like the reference trajectories of the feed-forward control variables or the selection of the operating mode permit the adaptation of master recipes, in order that the entire range of uncertain demand can be fulfilled in every plant solution. Overall, the integrated solution of plant design and process development allows to fully exploit the degrees of freedom associated to the different sub-problems, as opposed to the use of predefined recipes. The results also indicate that physical plant restrictions barely represent a determinant factor in the plant performance, provided that reasonable demand levels are defined. In particular, the results of this example are characterized by the similarity in the performance of most of the plant solutions with a same number of reactors, even considering a wide demand uncertainty space, between the -50% and the +50% of an estimated value.

On the other hand, the industrial-size example for acrylic fiber production (§ 6.4) deals with the holistic evaluation of process development with additional degrees of freedom, namely the selection of process stages, technological alternatives, and chemicals, as well as the potential solvent recovery and reuse. In fact, this problem has permitted to study the trade-offs among decisions associated to consecutive process stages. This way, the influence of recirculating an intermediate flow toward the polymerization reaction is shown: The decision on incorporating such recycle determines the optimal value of other decisions like the technological alternative and the solvent selection. Essentially, the huge advantage of the proposed MLDO-based strategy is illustrated, namely the possibility to consider all the processing alternatives simultaneously and avoid enumeration methods or heuristics which could skip the optimal solution.

Chapter 7

Conclusions

"The chief enemy of creativity is 'good' sense."
Pablo Picasso (1881 – 1973)

The fast development of sustainable processes and their agile introduction into production systems are crucial elements for competitiveness in specialty chemical industry. Plant flexibility and insights into physicochemical properties of the process are complementary elements to ensure a feasible and efficient operation in changing frameworks. To give a response to these challenges, this thesis has proposed an optimization-based approach to tackle the problem of batch process development. Particularly, synthesis of conceptual processing schemes and plant allocation sub-problems have been integrated in a single model in order to address their simultaneous optimization, while taking into account the physical plant characterization.

The proposed approach relies on the combination of optimization-based tools from three very well established areas of research in PSE, complementing each other: logic-based modeling and optimization –extensively applied to synthesis of continuous processes–, Multistage Dynamic Optimization –predominant tool in the optimal design of individual batch units–, and Mixed-Integer Programming –historically applied to batch plant design and scheduling problems.

The complex mathematical implications of an integrated model which cover a wide range of decisions justify partly the general reluctance to use such integrative approaches, where the optimization step may become an especially demanding activity. However, hurdles in solution procedures should not hamper the promising results obtained and the enormous incentives that motivate further research in modeling and optimization tools for integrated batch process development. Special emphasis is placed on the plant flexibility and adaptability gained through the proposed approach.

Overall, this thesis addresses the main challenges associated the application of advanced model-based optimization tools to this problem is feasible and rewarding, provided that the detail level in the process performance representation is properly handled. This chapter summarizes the contributions of this thesis and the further research directions that can be followed on the basis of the results obtained.

7.1 Thesis contributions

In the academic context, the problem of batch process development has been framed by three well established research fields: synthesis of conceptual processing schemes, design of individual processing units with dynamic reference trajectories, and scheduling and design of multiproduct and multipurpose facilities. Generally, each of these problems is solved independently through *divide and conquer strategies*, loosing a significant part of the interaction among the decisions made. For instance, batch plant design problems often assume fixed time and cost values, which restrict the allocation problem by dismissing a number of solutions that could be obtained modifying processing conditions in a sensible range. Another example is the influence between neighboring units, which is not taken into account when batch unit procedures are optimized separately.

This thesis contributes to the integration of batch process development sub-problems –*i.e.* batch process synthesis, plant allocation, and plant design– with several achievements in both retrofit and grassroots design scenarios, as is following detailed.

Previous step: homogenization of the terminology

The first challenge in the development of this thesis has been the definition and classification of published references in the context of batch process development problem. Doctoral dissertations by Allgor (1997), Ahmad (1997), Ali (1999), Cavin (2003), Papaeconomou (2005) and foundations provided by Rippin (1993), Reklaitis (1990), Stephanopoulos et al. (1999), and Stephanopoulos & Reklaitis (2011) are valued in this regard. In this context:

- This work contributes to highlight the degrees of freedom to be considered in the development of batch processes and their relation to each of the sub-problems. To do so, the terminology has been homogenized according to the definitions provided by Standard S88 (ANSI/ISA-88) and to the widespread terms used by the PSE research community devoted to batch processing.

Modeling strategy for integrated batch process development

Going a step further, the principal novelty of this study is the proposed modeling strategy, which combines specific modeling approaches typically applied to different problems. In particular, an emphasis is placed on the following methods: logic-based modeling in Generalized Disjunctive Programming (GDP) –extensively applied to synthesis of continuous processes–, multistage Dynamic Optimization (DO) –predominant strategy in the optimal design of individual batch units–, and mixed-integer modeling –historically applied to batch plant design and scheduling problems. This way, an integrated model has been developed, based on: the representation of synthesis and allocation alternatives in a SEN superstructure, the formulation of the dynamic performance of batch tasks, the consideration of physical plant decisions and constraints, and the synchronization of unit procedures as a function of the selected processing scheme. Overall, the problem is formulated as a Mixed-Logic Dynamic Optimization (MLDO) problem. To the author's knowledge, no strategy based on GDP and DO including material transfer profiles has been reported hitherto in the context of batch process development.

In general, cautious steps have been taken by the scientific community toward the use of optimization-based approaches which address a big number of decisions simultaneously in a single formulation. The reasons are the mathematical complexity of the resulting problem and the risk of obtaining mathematically intractable problems. However, the proposed modeling strategy presents outstanding advantages:

- First, the SEN superstructure is characterized by covering a broad spectrum of processing alternatives, since the characterization of the connection flows are subject to the equipment configuration and the task-unit assignment. Moreover, it facilitates the consideration of constraints associated to the physical plant.
- Additionally, each processing element in the SEN is associated to a single-stage or a multistage model. These allow the representation of dynamic process performance and the transition between batch operations and phases of the allocated batch and semi-continuous unit procedures.
- The concurrent models of the different unit procedures are defined by the internal characterization of each unit, by the DAE system associated to the allocated tasks, and by the profiles of input variables defined in previous tasks.
- Moreover, the optimization of dynamic profiles through DO techniques allows to enlarge the attainable region of the process with respect to the use of fixed set-points, pursuing the improvement of the process efficiency.
- The use of mixed-logic modeling allows to restrict the problem size through the incorporation of qualitative information and decisions into the mathematical model.
- Finally, the introduction of synchronization constraints ensures batch integrity in all processing alternatives, controlling the input conditions in each unit procedure.

Technical issues

The practical progress in the aforesaid combination of modeling approaches has been achieved by fulfilling two main issues concerning modeling techniques:

- At first place, it has been fundamental to formulate the several problem elements with a strategy that makes possible the use of current optimization tools. For instance, one difficulty is that static and dynamic variables associated to the multistage and single-stage models of the different unit procedures have to be synchronized depending on structural decisions.
- Second, bearing in mind the increased problem complexity, the optimization strategy has been supported by a consistent mathematical formulation. For that purpose, the disjunctive multistage modeling approach and the bypass strategy by Oldenburg & Marquardt (2008) have been extended to cover coexisting multistage and single-stage models, their interconnection, and synchronization.

Successful solution procedures

Several approaches to solve the integrated MLDO have been proposed and tested. Specifically, a direct-simultaneous approach, a Differential Genetic Algorithm, and their combination in a hybrid strategy have been proved successful in a preliminary study, providing optimal and near-optimal solutions. Given the problem complexity, getting reliable solutions is a crucial achievement of this research work, especially taking into account that the proposed approaches rely on available mathematical platforms and commercial solvers. In particular, the contributions of the studied approaches are:

- In the direct-simultaneous strategy (§ 4.2.1), the MLDO problem is first transformed into a MIDO one. Then, the problem is further transformed into a MINLP through full discretization of the control and process variables. This can be solved using a number of well-established solvers, like the decomposition algorithm OA (Duran & Grossmann, 1986a) used in this contribution. Due to the mathematical features of the problem, global optimality can not be guaranteed. Thus, a strategy to provide several initial feasible solutions (IFSs) is used to support this approach and increase the chances of finding the global optimum (§ 4.2.1, p. 94, and § 5.2.2, p. 115). This solution method is used in the examples of Chapters 5 and 6 which illustrate the integrated batch process development in retrofit (§§ 5.3, 5.4, 5.5, and 5.6) and grassroots scenarios (§§ 6.3 and 6.4).

- In contrast, the proposed stochastic and hybrid approaches lead to physically feasible solutions with no need of IFSs, what represents a crucial advantage in front of the prior deterministic method. Moreover, the DGA strategy (§ 4.3.2) provides near-optimal solutions compared to the deterministic reference ones. By means of the hybrid approach (§ 4.3.3), the DGA solutions are further improved up to the reference by fixing integer decision variables and using a direct-simultaneous method to solve the dynamic part of the model. To do so, the resulting DO model is transformed into a NLP, avoiding the combinatorial part of the problem. These results are a promising first step to deal with current limitations in computational performance of standard deterministic solvers and to rise the expectations of future solution of industrial-size problems.

Interactions among batch process synthesis, plant allocation, and plant design problems

The promising results obtained in the examples of integrated batch process development corroborate the advantages of the holistic evaluation of the decision criteria in both retrofit and grassroots scenarios. In particular, the proposed strategies allow to fully exploit the degrees of freedom associated to the different sub-problems, as opposed to the use of predefined recipes:

- The optimization of dynamic profiles in the recipe design for emergent pollutants through Advanced Oxidation Processes leads to reductions of nearly the 80% in the treatment cost compared to typical recipes (§ 5.6).
- Again compared to the use of fixed recipes, improvements between the 21% and 121% in the objective function are achieved in all the retrofit scenarios of Denbigh case study to produce specialty chemical S (§§ 5.3 and 5.4). This is accomplished thanks to a better use of the plant capabilities, even though the installation of new equipment is not evaluated in these particular examples.
- Moreover, if equipment re-sizing is contemplated, the objective function further improves with regard to the problem solution with no plant modifications although only slightly, a 0.85% in the considered example (§ 5.5).

Additionally, the proposed optimization-based strategy helps to quantify the interactions between synthesis and allocation sub-problems. Otherwise, the evaluation of compromised solutions would be an arduous activity. For instance:

- A greater influence on structural decisions has been identified in the retrofit Denbigh example, compared to the effect of optimizing dynamic profiles (§ 5.3). This last optimization provided an improvement of 12% by optimizing the dynamic profiles with a predefined configuration, whereas it went as far as a 24% when qualitative decisions has been considered as degrees of freedom with constant variable profiles. Moreover, the simultaneous optimization of the structural decisions and dynamic control profiles leads to further improved results, with an improvement of the 25% due to the synergism between both kinds of decisions.

Regarding the integration of batch process development and flexible plant design, the results indicate that physical plant restrictions barely represent a determinant factor in the plant performance, provided that reasonable demand levels are defined:

- The results of the grassroots Denbigh example (§ 6.3) are characterized by the similarity in the performance of most of the plant solutions with a same number of reactors, even considering a wide demand uncertainty space, between the −50% and the +50% of an estimated value. Such flexibility in most of the plants is gained through the adaptation of process synthesis and allocation decisions, which lead to an operation in optimal conditions according to each economic scenario. The exception are those plants of smaller processing capacities, which are unable to fulfill larger demands and have a huge load in shortfall penalties.

Finally, the trade-offs among decisions associated to consecutive process stages is studied in the industrial-size acrylic fiber example (§ 6.4). There:

- The influence of recirculating an intermediate flow toward the polymerization reaction is shown. In particular, the decision on incorporating such recycle determines the optimal value of other decisions, like the technological alternative and the solvent selection.
- The huge advantage of the proposed MLDO-based strategy in this regard is the possibility to consider all the processing alternatives simultaneously and avoid enumeration methods or heuristics which could skip optimal solutions.
- The extension of the solved primary polymerization stage –to include the secondary stage– would serve to evaluate further compromises among neighboring tasks.

Modeling detail in dynamic transfer profiles

This work incorporates a further level of detail into the problem of batch process development which has not been previously addressed in batch process and plant design or scheduling problems. Besides equipment configuration and dynamic control profiles optimization, as done in previous contributions from the state of the art, synchronization of material transfer operations using dynamic flow rate profiles has been also integrated:

- However, most of the examples with the Denbigh case study (SS 5.3, 5.4), as well as the acrylic fiber example (§ 6.4), show a small influence of dynamic variables in transference stages . In fact, transfer stages are usually defined to be as fast as possible, with input and output flow rate profiles ranging between the extreme values and no temperature variation.

These complementary degrees of freedom in the exploitation of batch plants adaptability permit a wider improvement margin in the objective function, however it can not concluded that effort is justified. In contrast, the simplification of these batch operations by optimizing uniquely their duration and constant profiles of the control variables would likely lead to equally good solutions.

The flexibility resulting from the proposed modeling strategy allows to select the most appropriated level of detail to be used for each unit procedure and for each material transfer profile. Thus, it is possible to exploit this flexibility through different modeling aspects from the simpler algebraic model to the more complex partial differential algebraic system, from single-stage to multistage models, and from material transfer synchronization within a dynamic time interval to static conditions in a unique temporal slot.

Tool for comparative purposes

In addition, the resulting optimization model has the potential to easily incorporate changes affecting the economic scenarios, the decision criteria, or the production policy.

This capability also enables the prompt evaluation of synthesis alternatives combination or the study of multiple objectives, through a unique and versatile model that includes all these options. As a mater of fact, this philosophy is the basis of the proposed heuristic approach for flexible plant design (§ 6.2.2):

- Solutions obtained for different production policies and economic scenarios have been evaluated in the different examples with the Denbigh case study along this thesis, illustrating the potential to adapt the optimal master recipe according to in-time needs.

Integrative approach

A final remark is worth regarding the reluctance to address the problem of batch process development using integrative models that cover a wide range of decisions:

- Mathematical implications and size of the problem, with a high number of combinatorial decisions and non-linear functions, justify the cautious efforts. The solution of such problem is a tough activity, and tested solution procedures are still far from being robust. The efforts of this research work can not only but agree that detailed dynamics and structural decisions should be only combined in the same problem if potential synergies exist between both types of decisions.
- However, less than discourage new contributions, this thesis aims at motivating the further study of solution strategies to address this problem, since it has been demonstrated that PSE tools can be successfully applied to the solution of batch integrated batch process development problem, which is definitively a bottleneck for the fast introduction of optimal processing schemes into production systems to improve a firm's value.

7.2 Future work

Hence, much work remains to be done in this research field, in order to enhance the benefits of combining PSE tools and the adaptability potential of batch plants based on MLDO. Particularly, the incorporation of additional degrees of freedom in the optimization model and the refinement of solution strategies are highlighted, among other issues:

- At first place, this thesis develops a modeling strategy and the guidelines to represent the basic elements that constitute the process and recipe design problem. However, there are still synthesis and operational alternatives which are candidates to be included in the formulation, like the replication of units working in parallel using out-of-phase parallel unit procedures, or the consideration of multi-product and multi-purpose production campaigns. The incorporation of these decisions can be done according to the proposed modeling strategy, analyzing the corresponding constraints to be formulated and the practical issues for the implementation.
- Secondly, solution procedures here proposed can be improved by introspecting optimization tools which are robust and more efficient according to the mathematical features of the optimization model. For example, solution strategies like benders decomposition for mixed-integer problems, or the use of sandwich constraints for bilinear terms, could improve the computational times and the solution reliability, and should be explored. Especially, it is highlighted the need of establishing global search procedures, in order that the modeling effort to pose a holistic formulation with all decisions evaluated simultaneously is fully exploited and the global optimum is not hampered by a misbehaving solution strategy.

- Additionally, once the design problem solution is robust, it can be considered the on-line implementation to improve the operation. Some works integrating scheduling and process control functions in batch plants operation are already considering these issues.
- Furthermore, many experts have underlined the importance of extending process design problems to be combined with process control –with the goal of obtaining stable and controllable plants– and with product design problems –with the purpose of developing products whose posterior manufacture is competitive from an economical and sustainable point of view.
- Besides, the multi-objective evaluation of sustainable, environmental benign, and economic objectives represents a challenge to exploit the process and recipe design. This approach was introduced in the Advanced Oxidation Process example (§ 5.6), but could be further developed.
- Moreover, internal uncertainty could be also considered to mitigate the calculation error for model inaccuracy.
- Finally, the determination of an appropriated level of complexity in procedural unit models is a crucial determinant of the success to find a compromise between a rigorous process representation and computational load. This problem could be also further explored.

Appendix A

Model of the Denbigh case study

This appendix details the Denbigh case study used in different examples throughout this thesis to illustrate integrated batch process development problems. For instance, this case study has been used to study the solution of retrofit and grassroots scenarios, of different objective functions, and of diverse economic situations in Chapters 5 and 6. The process description is here given together with the symbols used to denote physicochemical parameters and variables. Moreover, the comprehensive MLDO model of this case study is provided in consonance to the formulation proposed in Chapter 3, including the specific set elements and parameters of the modeling strategy. Its reformulation into MIDO and MINLP models should be made afterwards as was explained in Chapter 4.

A.1 Problem description

The Denbigh case study consists of a competitive reaction system first proposed by Denbigh (1958) to study temperature control profiles. The reaction mechanism is defined by:

$$\begin{tikzcd} \mathrm{A} \arrow[r, "1"] \arrow[d, "2"'] & \mathrm{R} \arrow[r, "3"] \arrow[d, "4"'] & \mathrm{S} \\ \mathrm{T} & \mathrm{U}. & \end{tikzcd} \tag{A.1}$$

Later, this example was adopted as a benchmark case study and used by several authors to study process synthesis in continuous, semi-batch, and batch systems. In this thesis, the problem parameters defined by Schweiger & Floudas (1999a) have been used to calculate activation energies $E_{a,r}$ and standard kinetic constants $k_{0,r}$, assuming that those authors worked at a nominal temperature T_{nom} of 80°C. In addition, reaction enthalpy $\triangle h_r$ data have been defined in order to incorporate energy balances into the problem. To do so, all reactions are considered endothermic and reference heats of formation and combustion (Perry & Gree, 1999, Tables 2-220 and 2-221) have been taken into account to provide consistent orders of magnitude. To sum up, the kinetic data used in the Denbigh case study are presented in Table A.1. Like in the work by Schweiger & Floudas (1999a), a molar density ρ of 6 $kmol/m^3$ is assumed for all the chemical compounds A, R, S, T, and U, as well as a molecular weight MW of 130 $kg/kmol$.

The process is implemented in a SEN superstructure like the one represented in Figure 3.1 (p. 54), which may exist or be newly-constructed depending on each example. The only difference between both situations is the base amortization cost $\check{c}_j$, which is zero in the case of existing units and non-zero otherwise.

The operation of each batch reactor is defined by three operations, *i.e.* load, hold, and unload, and by the input and output flow rates and reaction temperature as control variables in each stage. To back numerical methods, the initial volume $\upsilon_1^{j,0}$ in batch reactors is defined as a 0.1% of the maximum capacity $Size^{\mathrm{U}}$ rather than zero. Likewise, final volume $\upsilon_{|k_j|}^{j}(1)$ is constrained in the optimization model such that it is lower than the initial volume $\upsilon_1^{j,0}$ with a maximum difference between initial and final volumes of the 0.075% of the maximum capacity. This way, both values can be approximated to zero while avoiding indeterminate forms and tight restrictions. The associated mathematical error by doing so is minimal in comparison to the full-discretization errors. A minimum occupied volume in batch reactors is also defined in the end of hold operation υ_1^{L}.

Finally, economic decision criteria are evaluated subject to the economic parameters summarized in Table A.2, which may differ for each particular problem example.

Reaction r	$E_{a,r}$ $[kcal/kmol]$	$k_{0,r}$ $[h^{-1}]$ or $[m^3/(kmol\ h)]$	$k_{nom,r}$ $[h^{-1}]$ or $[m^3/(kmol\ h)]$	c_r	n_r	$\triangle h_r$ $[kcal/kmol]$
1	1000	4.16	1	A	2	$42{\cdot}10^3$
2	2580	23.75	0.6	A	1	$38{\cdot}10^3$
3	1800	7.81	0.6	R	1	$40{\cdot}10^3$
4	1210	0.56	0.1	R	2	$44{\cdot}10^3$

Table A.1: Kinetic constants, adapted from Schweiger & Floudas (1999a) assuming T_{nom}=80°C as nominal temperature, in the Denbigh case study: activation energy $E_{a,r}$, standard and nominal kinetic constants $k_{0,r}$ and $k_{nom,r}$, reactant c_r, reaction order n_r, and reaction enthalpy $\triangle h_r$.

Scenario	$\hat{c}_j$ $[c€/kWh]$	$\bar{c}_{j,A}$ $[€/batch]$	$\bar{c}_{j,B}$ $[€/m^3batch]$	$\bar{c}_{j,C}$ $[€/h\,batch]$	$\check{c}_j$ $[€/h]$	$\hat{p}_{\mathrm{A}}$ $[c€/kg]$	$\hat{p}_{\mathrm{S}}$ $[c€/kg]$	$\hat{p}_{\mathrm{R}}$ $[c€/kg]$	$\hat{p}_{penalty}$ $[c€/kg]$
1	2.5	5	10	0.21	0	4.8	43.1	-	$2\,\hat{p}_p$
2	2.5	5	10	0.21	0	9.6	43.1	-	$2\,\hat{p}_p$
3	10	5	10	0.21	0	4.8	43.1	-	$2\,\hat{p}_p$
4	2.5	5	10	0.21	0	4.8	-	35.8	$2\,\hat{p}_p$
5	2.5	5	10	0.21	1.03	4.8	43.1	-	$2\,\hat{p}_p$
6	2.5	5	10	0.21	8.22	4.8	43.1	-	$2\,\hat{p}_p$

Table A.2: Parameters of economic scenarios 1-6 in the Denbigh case study: unitary processing costs $\hat{c}_j$, unitary occupation costs $\bar{c}_{j,A}$, $\bar{c}_{j,B}$, and $\bar{c}_{j,C}$, and base amortization cost $\check{c}_j$ of reactors $j \in U$, price of raw material A $\hat{p}_{\mathrm{A}}$, price of final products $\hat{p}_p$, $p \in \{\mathrm{S}, \mathrm{R}\}$, and shortfall penalty $\hat{p}_{penal}$.

A.2 Notation

The sets and parameters of the Denbigh case study to solve integrated batch process development problems are defined in Table A.3. Tables A.4, A.5, and A.6 summarize Boolean u^{Bool}, integer u^{int}, time-invariant u^{stat}, and dynamic $u_k^{dyn}(t)$ decision variables, as well as differential $z_k(t)$, algebraic $y_k(t)$, and time-invariant γ variables and process parameters p associated to batch units $j \in U$, to storage tanks $j \in T$, and to the general process. Parameters involved in PC and EPC constraints are also included therein.

Set	Elements in Denbigh case study	Set	Elements in Denbigh case study
U	$U{=}\{U_1,U_2\}$	$N_i^{in}{\subseteq}N_i$	$N_1^{in}{=}\{1\}$
T	$T{=}\{T_{raw},T_{prod}\}$	$N_j^{in}{\subset}N$	$N_{U_1}^{in}{=}\{2\}$, $N_{U_2}^{in}{=}\{7\}$, $N_{T_{prod}}^{in}{=}\{9\}$,
Sp	$Sp{=}\{Sp_1,Sp_2\}$		$N_{Mx_1}^{in}{=}\{3,6\}$, $N_{Mx_2}^{in}{=}\{5,8\}$, $N_{Sp_1}^{in}{=}\{1\}$,
Mx	$Mx{=}\{Mx_1,Mx_2\}$		$N_{Sp_2}^{in}{=}\{4\}$
J	$J{=}\{U_1,U_2,T_{raw},T_{prod},Sp_1,Sp_2,$ $Mx_1,Mx_2\}$	$N_j^{out}{\subset}N$	$N_{U_1}^{out}{=}\{4\}$, $N_{U_2}^{out}{=}\{8\}$, $N_{T_{raw}}^{out}{=}\{1\}$, $N_{Mx_1}^{out}{=}\{7\}$, $N_{Mx_2}^{out}{=}\{9\}$, $N_{Sp_1}^{out}{=}\{2,3\}$,
PS	$PS{=}\{1\}$		$N_{Sp_2}^{out}{=}\{5,6\}$
$J_i{\subseteq}J$	$J_1{=}J$	$N_{i,\psi}^0{\subseteq}N$	$N_{1,\alpha}^0{=}N_{1,\beta}^0{=}N_{1,\pi}^0{=}\{6\}$,$N_{1,\sigma}^0{=}\{3,5\}$
Ψ_i	$\Psi_1{=}\{\alpha,\beta,\pi,\sigma\}$, α:single U_1, β:single U_2, π:parallel, σ:series U_1-U_2	M_j	$M_{U_1}{=}M_{U_2}{=}\{1,2\}$
		$M_j^{in}{\subseteq}M_j$	$M_{U_1}^{in}{=}M_{U_2}^{in}{=}\{1\}$
L	$L{=}\{1,\ldots,5\}$	$M_j^{out}{\subseteq}M_j$	$M_{U_1}^{out}{=}M_{U_2}^{out}{=}\{2\}$
$L^a{\subseteq}L$	$L_\alpha{=}L_\beta{=}L_\pi{=}\{1,\ldots,3\}$,$L_\sigma{=}\{1,\ldots,5\}$	Q	$Q{=}\{1,2\}$
K_j	$K_{U_1}{=}K_{U_2}{=}$ $\{1,\ldots,3\}$	$L_j^0{\subseteq}L$	$L_{U_1}^0{=}L_{U_2}^0{=}\{1,3\}$
$I_j{\subseteq}K_j$	$I_{U_1}{=}I_{U_2}{=}\{1\}$	$D_{i,\psi}{\subseteq}U_i$	$D_{1,\alpha}{=}D_{1,\beta}{=}D_{1,\pi}{=}\{U_1,U_2\}$,
$O_j{\subseteq}K_j$	$O_{U_1}{=}O_{U_2}{=}\{3\}$		$D_{1,\sigma}{=}\{U_1\}$
N	$N{=}\{1,\ldots,9\}$	C	$C{=}\{$A,R,S,T,U$\}$
$N_i{\subseteq}N$	$N_1{=}N$	$P{\subset}C$	$P{=}\{$S,R$\}$
Parameter	**Value in Denbigh case study**	**Parameter**	**Value in Denbigh case study**
$L^{\max}$	$L^{\max}{=}5$	$DOF_{i,\psi}$	$DOF_{1,\alpha}{=}DOF_{1,\beta}{=}DOF_{1,\pi}{=}4$,
$l_{j,q}^0$	$l_{U_1,1}^0{=}l_{U_2,2}^0{=}1$, $l_{U_1,2}^0{=}l_{U_2,2}^0{=}3$		$DOF_{1,\sigma}{=}3$

Table A.3: Sets and parameters in the Denbigh case study to solve integrated batch process development problems.

Type	Description	Variable/ parameter		Value/ bounds
u^{Bool}	Equipment selection	Y_j	-	$\{true,false\}$
	Task-unit assignment	$W_{j,q}$	-	$\{true,false\}$
u^{int}	Capacity of unit j	$Size^j$	$[m^3]$	[0, 10]
$u_k^{dyn}(t)$	Input flow rate	$F_{1,k}^j(t)$	$[m^3/h]$	[0, 7.7]
	Output flow rate	$F_{2,k}^j(t)$	$[m^3/h]$	[0, 7.7]
	Reaction temperature	θ_k^j	[°C]	[50, 110]
$z_k(t)$	Reactor volume	$\upsilon_k^j(t)$	$[m^3]$	[0, 2.5]
	- Initial reactor volume	$\upsilon_1^{j,0}$	$[m^3]$	0.01
	Molar amount of compound c	$\eta_{c,k}^j(t)$	$[kmol]$	[0, 15]
	- Initial molar amount of compound c	$\eta_{c,1}^{j,0}$	$[kmol]$	0.1
$y_k(t)$	Molar fraction of compound c in input flow	$x_{c,1,k}^j(t)$	$[kmol/kmol]$	[0, 1]
	Molar fraction of compound c in output flow	$x_{c,2,k}^j(t)$	$[kmol/kmol]$	[0, 1]
	Rate of reaction r	$RX_{r,k}^j(t)$	$[kmol/m^3h]$	$[0, \infty]$
γ	Duration of stage k of unit j	t_k^j	$[h]$	[0, 2.5]
	Starting time of unit j	$t^{j,s}$	$[h]$	[0, 144]
	Final time of unit j	$t^{j,end}$	$[h]$	[0, 144]
	Total time of unit j	$T^{j,f}$	$[h]$	[0, 7.5]
	Processing cost in unit j	$Cost_{j,p}$	$[€/batch]$	$[0, \infty]$
	Occupation cost in unit j	$Cost_{j,o}$	$[€/batch]$	$[0, \infty]$
	Amortization cost in unit j	$Cost_{j,a}$	$[€/batch]$	$[0, \infty]$
	Heating energy consumed in unit j	Q_h^j	$[kcal/batch]$	$[0, \infty]$
p	Molar density	ρ	$[kmol/m^3]$	6
	Stoichiometric coefficient of c in reaction r	$\nu_{r,c}$	$[kmol/kmol]$	(Eq. A.1)
	Activation energy of reaction r	$E_{a,r}$	$[kcal/kmol]$	
	Standard kinetic constant of reaction r	$k_{0,r}$	$[h^{-1}]$ or	
	Reactant in reaction r	c_r	-	(Table A.1)
	Order of reaction r	n_r	[ ]	
	Enthalpy of reaction r	$\triangle h_r$	$[kcal/kmol]$	
	Ideal gas constant	R	$[kcal/°\mathrm{K}\,kmol]$	1.987
	Specific heat in the reaction mixture	c_p	$[kcal/°\mathrm{K}/, kg]$	1.1
	Temperature of input flow	θ_1^{in}	[°C]	25
	Heating cost	$\hat{c}_j$	$[€/kcal]$	
	Fixed occupation cost	$\bar{c}_{j,A}$	$[€/batch]$	
	Size-dependent occupation cost	$\bar{c}_{j,B}$	$[€/m^3\,batch]$	(Table A.2)
	Time-dependent occupation cost	$\bar{c}_{j,C}$	$[€/h\,batch]$	
	Base amortization cost	$\check{c}_j$	$[€/h]$	
	Size power in amortization function	n	[ ]	0.5
	Base equipment capacity	$Size^0$	$[m^3]$	3.8
PC	Lower bound of input/output flow rates	F^{L}	$[m^3/h]$	1.9
	Upper bound of input/output flow rates	F^{U}	$[m^3/h]$	7.7
EPC	Lower bound of final volume in stage 1	υ_1^{L}	$[m^3]$	0.25
	Upper bound of final volume in last stage	$\upsilon_{\lvert K_j \rvert}^{\mathrm{U}}$	$[m^3]$	$\upsilon_1^{j,0}$
	Lower bound of final volume in last stage	$\upsilon_{\lvert K_j \rvert}^{\mathrm{L}}$	$[m^3]$	$0.25\,\upsilon_1^{j,0}$

Table A.4: Variables and process parameters associated to batch units $j \in U$ in the Denbigh case study.

Type	Description	Variable/ parameter		Value/ bounds
$z_k(t)$	Molar amount of compound c	$\eta^{j}_{c,l}(t)$	$[kmol]$	[0 500]
	- Initial molar amount of compound c	$\eta^{T_{raw},0}_{\mathrm{A},1}$	$[kmol]$	500
		$\eta^{T_{raw},0}_{c,1}$, $c{\neq}\mathrm{A}$	$[kmol]$	0
		$\eta^{T_{prod},0}_{c,1}$	$[kmol]$	0
γ	Cost of raw material A	$Cost_{\mathrm{A}}$	$[€/batch]$	$[0, \infty]$
	Revenue of product S	$Revenue^{T_{prod}}_{\mathrm{S}}$	$[€/batch]$	$[0, \infty]$
p	Molar fraction of compound c in T_{raw}	$x_{\mathrm{A},1}$	$[kmol/kmol]$	1
		$x_{c,1}$, $c{\neq}\mathrm{A}$	$[kmol/kmol]$	0
	Molar density	ρ	$[kmol/m^3]$	6
	Molecular weight	MW	$[kg/kmol]$	130
	Cost of raw material A	$\hat{p}_{\mathrm{A}}$	$[€/kg]$	(Table A.2)
	Price of final product S	$\hat{p}_{\mathrm{S}}$	$[€/kg]$	

Table A.5: Variables and process parameters associated to storage tanks $j \in T$ in the Denbigh case study.

Type	Description	Variable/ parameter		Value/ bounds
u^{Bool}	Operating mode ψ selection	X^1_{ψ}	-	$\{true,false\}$
u^{int}	Number of batches of product p	NB_p	$[batch]$	[1, 160]
u^{stat}	Duration of mathematical stage l	t_l	$[h]$	[0, 2.5]
$y_l(t)$	Flow rate of pipeline $n \in \{1, ..., 9\}$	$F_{n,l}(t)$	$[m^3/h]$	[0, 15.4]
	Molar fraction of compound c in flow n	$x_{c,n,l}(t)$	$[kmol/kmol]$	[0, 1]
γ	Starting time of the recipe	t^s	$[h]$	[0, 144]
	Final time of the recipe	t^{end}	$[h]$	[0, 144]
	Batch processing time	T^f	$[h/batch]$	[0, 144]
	Batch cycle time	T^{cycle}	$[h/batch]$	[0, 144]
	Total processing time	T^{total}	$[h]$	[0, 144]
	Total profit	$Profit$	$[€]$	$[0, \infty]$
	Profitability	$Profitability$	$[€/h]$	$[0, \infty]$
	Total selectivity of product p	ς^{p}_{total}	$[kmol/kmol]$	[0, 1]
	Batch production size	$Batch_{\mathrm{S}}$	$[kg/batch]$	[0, 31.5]
	Unaccomplished demand of product S	$Shortfall_{\mathrm{S}}$	$[tn]$	[0, 31.5]
p	Demand of product S	$Demand_{\mathrm{S}}$	$[tn]$	{10.5,15.75, 21,26.25,31.5}
	Demand of product R	$Demand_{\mathrm{R}}$	$[tn]$	21
EPC	Lower bound of stage l duration	t^{L}	$[h]$	0.05
	Upper bound of stage l duration	t^{U}	$[h]$	10
	Time horizon, maximum processing time for all NB_p batches	$Horizon$	$[h]$	144

Table A.6: General variables and process parameters at Level 0 in the Denbigh case study.

A.3 MLDO model

A.3.1 Batch procedures at Level 1

Models of batch units

The following disjunction defines the multistage models of batch units $j \in U$ and corresponds to Eqs. 3.5 and 3.6 of the formulation proposed in Chapter 3. Summarizing, batch units $j \in U$ are batch reactors where the Denbigh reaction system is carried out and are represented by:

$$\begin{bmatrix} Y_j \\ \dot{\upsilon}_k^j(t) = \left(F_{1,k}^j(t) - F_{2,k}^j(t)\right) t_k^j,\ t \in [0,1], \forall k \in K_j, \\ \dot{\eta}_{c,k}^j(t) = \left(F_{1,k}^j(t)\,\rho\, x_{c,1,k}^j(t) - F_{2,k}^j(t)\,\rho\, x_{c,2,k}^j(t) + \sum_{r=1}^{4} \nu_{r,c}\, RX_{r,k}^j(t)\, \upsilon_k^j(t)\right) t_k^j, \\ \qquad t \in [0,1], \forall c \in C, k \in K_j, \\ \upsilon_{k+1}^{j,0} = \upsilon_k^j(1), \eta_{c,k+1}^{j,0} = \eta_{c,k}^j(1),\ \forall c \in C, k \in \{1,...,|K_j|-1\}, \\ \upsilon_k^j(0) = \upsilon_k^{j,0}, \eta_{c,k}^j(0) = \eta_{c,k}^{j,0},\ \forall c \in C, k \in K_j, \\ RX_{r,k}^j(t) = k_{0,r}\, exp^{-E_{a,r}/R\,\theta_k^j(t)} (\eta_{c_r,k}^j(t)/\upsilon_k^j(t))^{n_r}, \\ t \in [0,1], \forall r \in \{1,...,4\}, k \in K_j, \\ x_{c,2,k}^j(t) = \eta_{c,k}^j(t) / \sum_{c\in C} \eta_{c,k}^j(t),\ \ t \in [0,1], \forall c \in C, k \in K_j, \\ Q_h^j = \sum_{k\in K_j} \left(\int_0^1 c_p\,(\theta_k^j(t) - \theta_1^{in})\, F_{1,k}^j(t)\, dt\, t_k^j + \sum_{r=1}^{4} \triangle h_r\, RX_{r,k}^j(t)\right), \\ Cost_{j,p} = \hat{c}_j\, Q_h^j, \\ Cost_{j,o} = \bar{c}_{j,A} + \bar{c}_{j,B}\, Size^j + \bar{c}_{j,C} \sum_{k\in K_j} t_k^j \\ \upsilon_k^j(t) \le Size^j,\ \ t \in [0,1], \forall k \in K_j \\ F^{\mathrm{L}} \le F_{1,k}^j(t) \le F^{\mathrm{U}},\ t \in [0,1], \forall k \in I_j,\ F_{1,k}^j(t) = 0,\ t \in [0,1], \forall k \in K_j \backslash I_j, \\ F^{\mathrm{L}} \le F_{2,k}^j(t) \le F^{\mathrm{U}},\ t \in [0,1], \forall k \in O_j,\ F_{2,k}^j(t) = 0,\ t \in [0,1], \forall k \in K_j \backslash O_j, \\ \upsilon_1^{\mathrm{L}} \le \upsilon_1^j(1),\ \ \upsilon_{|K_j|}^{\mathrm{U}} \ge \upsilon_{|K_j|}^j(1), \\ T^{j,f} = \sum_{k\in K_j} t_k^j,\ \ t^{j,end} = t^{j,s} + T^{j,f} \end{bmatrix}$$

$$\veebar \begin{bmatrix} \neg Y_j \\ \dot{\upsilon}_k^j(t) = 0, \dot{\eta}_{c,k}^j(t) = 0,\ \ t \in [0,1], \forall c \in C, k \in K_j, \\ \upsilon_{k+1}^{j,0} = \upsilon_k^j(1), \eta_{c,k+1}^{j,0} = \eta_{c,k}^j(1),\ \ \forall c \in C, k \in \{1,...,|K_j|-1\}, \\ \upsilon_k^j(t) = \upsilon_k^{j,0}, \eta_{c,k}^j(t) = \eta_{c,k}^{j,0},\ \ t \in [0,1], \forall c \in C, k \in K_j, \\ F_{m,k}^j(t) = 0,\ x_{c,m,k}^j(t) = 0,\ \ t \in [0,1], \forall c \in C, m \in \{1,2\}, k \in K_j, \\ RX_{r,k}^j(t) = 0,\ \ t \in [0,1], \forall r \in \{1,...,4\}, k \in K_j, \\ Q_j = 0,\ Cost_{j,p} = 0,\ Cost_{j,o} = 0, \\ T^{j,f} = 0,\ t^{j,end} = 0,\ t^{j,s} = 0 \end{bmatrix},\ \forall j \in U. \tag{A.2}$$

The amortization cost is not calculated inside the disjunctive equation, since a processing unit $j{\in}U$ can be acquired by defining a capacity $Size^j$ greater to zero, with its corresponding investment cost, but it may not be necessarily selected in a particular master recipe. Therefore, this cost is independent to Y_j according to:

$$Cost_{j,a} = \frac{\check{c}_j \left(Size^j/Size^0\right)^n Horizon}{NB_{\mathrm{S}}}. \tag{A.3}$$

A.3.2 Synchronization

The synchronization of unit procedures is lead through the definition of task-unit assignment, which are related to unit selection by Eq. 3.10 of the formulation. This equation reads as:

$$Y_j \Leftrightarrow \underset{q\in Q}{\veebar} W_{j,q}, \quad \forall j \in U. \tag{A.4}$$

The task-unit assignment controls the relation between times and input and output variables across the two modeling Levels 0 and 1 defined in Eqs. 3.11 to 3.14 of the formulation. In this particular case study, where $l^0_{j,1}$=1 and $l^0_{j,2}$=3, $N^{in}_{U_1}$={2}, $N^{out}_{U_1}$={4}, $N^{in}_{U_2}$={7}, and $N^{out}_{U_2}$={8}, these equations become:

$$\begin{bmatrix} W_{U_1,1} \\ t^{U_1,s} = t^s, \\ t_l = t^{U_1}_l,\ \forall l \in \{1,...,|K_{U_1}|\}, \\ F_{2,l}(t) = F^{U_1}_{1,l}(t),\ x_{c,2,l}(t) = x^{U_1}_{c,1,l}(t), \\ F_{4,l}(t) = F^{U_1}_{2,l}(t),\ x_{c,4,l}(t) = x^{U_1}_{c,2,l}(t), \\ t \in [0,1], \forall l \in \{1,...,|K_{U_1}|\}, \\ F_{2,l}(t) = 0,\ x_{c,2,l}(t) = 0, \\ F_{4,l}(t) = 0,\ x_{c,4,l}(t) = 0, \\ t \in [0,1], \forall l \in L\backslash\{1,...,|K_{U_1}|\} \end{bmatrix} \veebar \begin{bmatrix} W_{U_1,2} \\ t^{U_1,s} = t^s + \sum_{l=1}^2 t_l, \\ t_l = t^{U_1}_{l-2},\ \forall l \in \{3,...,|K_{U_1}|+2\}, \\ F_{2,l}(t) = F^{U_1}_{1,l-2}(t),\ x_{c,2,l}(t) = x^{U_1}_{c,1,l-2}(t), \\ F_{4,l}(t) = F^{U_1}_{2,l-2}(t),\ x_{c,4,l}(t) = x^{U_1}_{c,2,l-2}(t), \\ t \in [0,1], \forall l \in \{3,...,|K_{U_1}|+2\}, \\ F_{2,l}(t) = 0,\ x_{c,2,l}(t) = 0, \\ F_{4,l}(t) = 0,\ x_{c,4,l}(t) = 0, \\ t \in [0,1], \forall l \in L\backslash\{3,...,|K_{U_1}|+2\} \end{bmatrix}$$
$$\veebar \begin{bmatrix} \neg Y_{U_1} \\ F_{2,l}(t) = 0,\ x_{c,2,l}(t) = 0, \\ F_{4,l}(t) = 0,\ x_{c,4,l}(t) = 0, \\ t \in [0,1], \forall l \in L \end{bmatrix} \tag{A.5}$$

and

$$\begin{bmatrix} W_{U_2,1} \\ t^{U_2,s} = t^s, \\ t_l = t^{U_2}_l,\ \forall l \in \{1,...,|K_{U_2}|\}, \\ F_{7,l}(t) = F^{U_2}_{1,l}(t),\ x_{c,7,l}(t) = x^{U_2}_{c,1,l}(t), \\ F_{8,l}(t) = F^{U_2}_{2,l}(t),\ x_{c,8,l}(t) = x^{U_2}_{c,2,l}(t), \\ t \in [0,1], \forall l \in \{1,...,|K_{U_2}|\}, \\ F_{7,l}(t) = 0,\ x_{c,7,l}(t) = 0, \\ F_{8,l}(t) = 0,\ x_{c,8,l}(t) = 0, \\ t \in [0,1], \forall l \in L\backslash\{1,...,|K_{U_2}|\} \end{bmatrix} \veebar \begin{bmatrix} W_{U_2,2} \\ t^{U_2,s} = t^s + \sum_{l=1}^2 t_l, \\ t_l = t^{U_2}_{l-2},\ \forall l \in \{3,...,|K_{U_2}|+2\}, \\ F_{7,l}(t) = F^{U_2}_{1,l-2}(t),\ x_{c,7,l}(t) = x^{U_2}_{c,1,l-2}(t), \\ F_{8,l}(t) = F^{U_2}_{2,l-2}(t),\ x_{c,8,l}(t) = x^{U_2}_{c,2,l-2}(t), \\ t \in [0,1], \forall l \in \{3,...,|K_{U_2}|+2\}, \\ F_{7,l}(t) = 0,\ x_{c,7,l}(t) = 0, \\ F_{8,l}(t) = 0,\ x_{c,8,l}(t) = 0, \\ t \in [0,1], \forall l \in L\backslash\{3,...,|K_{U_2}|+2\} \end{bmatrix}$$
$$\veebar \begin{bmatrix} \neg Y_{U_2} \\ F_{7,l}(t) = 0,\ x_{c,7,l}(t) = 0, \\ F_{8,l}(t) = 0,\ x_{c,8,l}(t) = 0, \\ t \in [0,1], \forall l \in L \end{bmatrix}. \tag{A.6}$$

A.3.3 Process stages

Operating mode or configuration

Equipment selection and task-unit assignment depend on the operating mode or equipment configuration according to Eqs. 3.17 to 3.20. These logical propositions read as:

$$X^1_\alpha \quad \Leftrightarrow \quad W_{U_1,1} \wedge \neg Y_{U_2}, \tag{A.7}$$
$$X^1_\beta \quad \Leftrightarrow \quad W_{U_2,1} \wedge \neg Y_{U_1}, \tag{A.8}$$
$$X^1_\pi \quad \Leftrightarrow \quad W_{U_1,1} \wedge W_{U_2,1}, \tag{A.9}$$
$$X^1_\sigma \quad \Leftrightarrow \quad W_{U_1,1} \wedge W_{U_2,2}. \tag{A.10}$$

The selected configuration also enforces a specific flow distribution, as determined by Eq. 3.21. In this case study, the flow distribution is defined by the following disjunction:

$$\begin{bmatrix} X_\alpha^1 \vee X_\beta^1 \vee X_\pi^1 \\ F_{6,l}(t) = 0,\ t \in [0,1], \forall l \in L \end{bmatrix} \quad \underline{\vee} \quad \begin{bmatrix} X_\sigma^1 \\ F_{n,l}(t) = 0,\ t \in [0,1], \forall n \in \{3,5\}, l \in L \end{bmatrix}. \tag{A.11}$$

A.3.4 Plant elements at Level 0

Models of plant elements with semi-continuous procedures

Time relations at Level 0 are defined by Eqs. 3.22 and 3.23, which read as follows:

$$\begin{array}{c} T^f = \sum_{l \in L} t_l, \quad t^{end} = t^s + T^f, \\ t^{\mathrm{L}} \le t_l \le t^{\mathrm{U}},\ \forall l \in \{1, ..., |L^a|\}, \\ \text{bypass stages: } t_l = 0,\ \forall l \in \{|L^a|+1, ..., |L|\}. \end{array} \tag{A.12}$$

Additionally, the flow sheet model involves mass balances in mixers and splitters from Eqs. 3.24 to 3.27. According to the definitions of the input and output flows N_j^{in} and N_j^{out} in connecting units $j \in Mx \cup Sp$ in this case study, global mass balances are defined by:

$$\begin{array}{c} F_{3,l}(t) + F_{6,l}(t) = F_{7,l}(t),\ t \in [0,1], \forall l \in L, \\ F_{5,l}(t) + F_{8,l}(t) = F_{9,l}(t),\ t \in [0,1], \forall l \in L, \\ F_{1,l}(t) = F_{2,l}(t) + F_{3,l}(t),\ t \in [0,1], \forall l \in L, \\ F_{4,l}(t) = F_{5,l}(t) + F_{6,l}(t),\ t \in [0,1], \forall l \in L, \end{array} \tag{A.13}$$

and component balances are defined by:

$$\begin{array}{c} F_{3,l}(t) x_{c,3,l}(t) + F_{6,l}(t) x_{c,6,l}(t) = F_{7,l}(t) x_{c,7,l}(t),\ t \in [0,1], \forall c \in C, l \in L, \\ F_{5,l}(t) x_{c,5,l}(t) + F_{8,l}(t) x_{c,8,l}(t) = F_{9,l}(t) x_{c,9,l}(t),\ t \in [0,1], \forall c \in C, l \in L \\ x_{c,1,l}(t) = x_{c,n,l}(t),\ t \in [0,1], \forall c \in C, n \in \{2,3\}, l \in L, \\ x_{c,4,l}(t) = x_{c,n,l}(t),\ t \in [0,1], \forall c \in C, n \in \{5,6\}, l \in L. \end{array} \tag{A.14}$$

Finally, the following disjunction defines the multistage models at Level 0 of semi-continuous storage tanks $j \in T$, which supply raw material and collect the mixture containing final product, and corresponds to Eq. 3.28 of the formulation in Chapter 3:

$$\begin{array}{c} \dot{\eta}_{c,l}^{T_{raw}}(t) = (-F_{1,l}(t)\ \rho\ x_{c,1,l}(t))\, t_l,\ t \in [0,1], \forall c \in C, l \in \{1, ..., |L^a|\}, \\ \dot{\eta}_{c,l}^{T_{prod}}(t) = (F_{9,l}(t)\ \rho\ x_{c,9,l}(t))\, t_l,\ t \in [0,1], \forall c \in C, l \in \{1, ..., |L^a|\}, \\ \eta_{c,l+1}^{j,0} = \eta_{c,l}^{j}(1),\ \forall c \in C, l \in \{1, ..., |L|-1\}, j \in T, \\ \eta_{c,l}^{j}(0) = \eta_{c,l}^{j,0},\ \forall c \in C, l \in\in \{1, ..., |L^a|\}, j \in T, \\ x_{c,1,l}(t) = x_{c,1},\ t \in [0,1], \forall c \in C, l \in \{1, ..., |L^a|\}, \\ Cost_{\mathrm{A}} = \hat{p}_{\mathrm{A}}(\eta_{\mathrm{A},1}^{T_{raw},0} - \eta_{\mathrm{A},|L|}^{T_{raw}}(1)), \\ Revenues_{\mathrm{S}} = \hat{p}_{\mathrm{S}}(\eta_{\mathrm{S},|L|}^{T_{prod}}(1) - \eta_{\mathrm{S},1}^{T_{prod},0}), \\ \text{bypass stages: } \dot{\eta}_{c,l}^{j}(t) = 0,\ \eta_{c,l}^{j}(t) = \eta_{c,l}^{j,0},\ x_{c,1,l}(t) = 0, \\ t \in [0,1], \forall c \in C, l \in \{|L^a|+1, ..., |L|\}, j \in T. \end{array} \tag{A.15}$$

A.3.5 Batching

The number of batches is considered as a degree of freedom in this case study, according to Eq. 3.32 of the formulation. Particularly, this equation relates the number of batches, the batch size, and the total amount of product S obtained and reads as:

$$NB_{\mathrm{S}}\ Batch_{\mathrm{S}} \ge Demand_{\mathrm{S}} - Shortfall_{\mathrm{S}}. \tag{A.16}$$

This equation indicates that the accomplishment of the full demand can be relaxed. As is defined next section (§ A.3.6), the product shortfall will have an associated penalty cost.

A.3.6 Objective function and key performance indicators

Several objective functions have been defined in the different examples of the Denbigh case study along the thesis, such as the profit, the profitability, or the total processing costs. Additionally, other indicators or KPI have been provided to render an extensive assessment of the process performance, like the product selectivity, the total processing time, or the batch cycle time. Their calculation is following detailed:

Total processing cost in $j\in U$:	$Cost_{j,p,total} = NB_{\mathrm{S}}\; Cost_{j,p},$	(A.17)
Total occupation cost in $j\in U$:	$Cost_{j,o,total} = NB_{\mathrm{S}}\; Cost_{j,o},$	(A.18)
Total amortization cost in $j\in U$:	$Cost_{j,a,total} = NB_{\mathrm{S}}\; Cost_{j,a},$	(A.19)
Total raw material cost:	$Cost_{\mathrm{A},total} = NB_{\mathrm{S}}\; Cost_{\mathrm{A}},$	(A.20)
Total revenue:	$Revenues_{\mathrm{S},total} = NB_{\mathrm{S}}\; Revenues_{\mathrm{S}},$	(A.21)
Shortfall penalty:	$Penalty = \hat{p}_{penal} Shortfall_{\mathrm{S}},$	(A.22)
Total profit:	$Profit_{total} = Revenues_{\mathrm{S},total} - Cost_{\mathrm{A},total} - \sum_{j\in U}(Cost_{j,p,total}+Cost_{j,o,total}+Cost_{j,a,total}) - Penalty,$	(A.23)
Batch cycle time:	$T^{cycle} = \max_{j\in U} NB_{\mathrm{S}}\; T^{j,f},$	(A.24)
Total processing time:	$T^{total} = NB_{\mathrm{S}}\; T^{cycle},$	(A.25)
Profitability:	$Profitability = Profit_{total}/T^{total},$	(A.26)
Selectivity of product S:	$\varsigma^{\mathrm{S}}_{total} = \eta^{T_{prod}}_{\mathrm{S},\lvert L\rvert}(1) \Big/ \sum_{c\in C} \eta^{T_{prod}}_{c,\lvert L\rvert}(1).$	(A.27)

Finally, the maximum processing time is also constrained as follows:

$$T^{total} \leq Horizon. \tag{A.28}$$

Degrees of freedom in the optimization model

The total number of decisions variables is reduced according to the degrees of freedom of each problem, such that the number of actual control variables in practice is set. This way, the consistency of the search strategy of the solution method is improved. In this case study, the flow rates of batch units at Level 1 which behave as control variables are subject to the following definitions, according to Eqs. 3.34 and 3.35:

$$F^{j}_{2,k}(t) \in u^{dyn}_{k}(t), \quad t \in [0,1], \forall k \in \{3\}, \forall j \in \{U_1, U_2\}, \tag{A.29}$$

$$\begin{bmatrix} X^1_\alpha \vee X^1_\beta \vee X^1_\pi \\ F^{j}_{1,k}(t) \in u^{dyn}_{k}(t), \quad t \in [0,1], \forall k \in \{1\}, \forall j \in \{U_1, U_2\} \end{bmatrix} \veebar \begin{bmatrix} X^1_\sigma \\ F^{j}_{1,k}(t) \in u^{dyn}_{k}(t), \quad t \in [0,1], \forall k \in \{1\}, \forall j \in \{U_1\} \end{bmatrix}. \tag{A.30}$$

Moreover, the logical propositions in Eqs. 3.10, and 3.17-3.20 remove six degrees of freedom related to logical variables and therefore permit the reduction of the ten Boolean decisions $u^{Bool}=\{Y_j, W_{j,q}, X^1_\psi\}$ to four, namely the selection of the processing mode X^1_ψ.

Appendix B

Model of the photo-Fenton case study

This appendix provides further information regarding the photo-Fenton case study. This was presented in Chapter 5 to illustrate the development of a batch PCT remediation process to be implemented in a existing AOPs treatment plant, given two objective functions. The process description is here given together with the specific set elements and parameters of the proposed modeling strategy and the symbols used to denote physico-chemical parameters and variables. The problem is formulated according to the MLDO modeling strategy proposed in Chapter 3. However, qualitative decisions have not been considered in this example, thus the mixed-logic part of the formulation is not required. As a result, the problem becomes a DO model. Following the direct-simultaneous solution procedure explained in Chapter 4, the DO should be discretized to obtain a NLP problem that is optimized using deterministic solvers.

B.1 Problem description

Advanced Oxidation Processes (AOPs) are treatment technologies aimed at degrading and mineralizing recalcitrant organic matter from wastewater through reaction with hydroxyl radical ($^{\bullet}OH$). Recently, these technologies have been proposed as a solution to treat emerging contaminants, especially pharmaceuticals and personal care products (Pignatello et al., 2007). AOPs' reactions can be further promoted by iron catalysts (Fe^{2+}) and UV irradiation, giving rise to photo-Fenton systems. Research on AOPs modeling and simulation have proved that operational variables such as reagent dosage, pollutant load, pH, and UV source, determine the accomplishment of degradation targets.

In this case study, the model proposed by Cabrera Reina et al. (2012) is adapted to predict the kinetic behavior of the process variables, namely the concentrations of PCT, H_2O_2, Fe^{2+}, Fe^{3+}, dissolved oxygen, $^{\bullet}$OH radical (R), and TOC, including dummy intermediates. Hence, the Fenton-like reaction is added to the model (Kusic et al., 2006). In addition, the TOC consumption is represented by phantom degradation rate that is calculated using an approximated degradation constant and a first reaction order with regard to the TOC and $^{\bullet}$OH radical concentrations. The reaction scheme reads as:

$$
\begin{array}{ll}
\text{Photo-Fenton reactions:} & Fe^{2+} + H_2O_2 \xrightarrow{1} Fe^{3+} + R \\
 & Fe^{3+} + hv \xrightarrow{2} Fe^{2+} + R \\
\text{Inefficient reactions:} & R + H_2O_2 \xrightarrow{3} O_2 \\
 & R + R \xrightarrow{4} O_2 \\
\text{Efficient reactions:} & R + M + O_2 \xrightarrow{5} R + MX_1 \\
 & R + M \xrightarrow{6} R + MX_1 \\
 & R + MX_1 \xrightarrow{7} R + MX_2 \\
 & R + MX_1 \xrightarrow{8} O_2 \\
 & R + MX_2 \xrightarrow{9} O_2 \\
\text{Fenton-like reaction:} & Fe^{3+} + H_2O_2 \xrightarrow{10} Fe^{2+}.
\end{array}
\tag{B.1}
$$

The kinetic constants and expressions are summarized in Table B.1. Reaction rates are calculated assuming that the order of reaction with respect to each reactive corresponds to the stoichiometric coefficients.

The remediation of a PCT effluent with a volume of 15 L and concentration of 0.52 mM of PCT is pursued. The objective is to minimize the batch processing time and treatment expenses, while accomplishing an elimination of the 99.9% of substrate and 90% of TOC within a maximum time horizon of 10 hours. Moreover, the process should be implemented in an existing AOPs plant with a reactor capacity of 15 L and lamp intensity of 36 W/m^2. The installation or expansion of the existing equipment is not considered. As for the boundaries of the decision variables, the initial concentration of Fe^{2+} is set between 0 and 0.179 mM –which satisfies the legal iron concentration allowed in effluents (DOGC, 2003)– and the concentration of H_2O_2 is constrained to a typical concentrations range between 0 and 45 mM during all the process.

Further decision variables that can be formulated through the proposed MLDO-based approach for the development of AOPs processes are: the batch size, the potential installation of other lamp intensities, the potential combination of the photo-Fenton process with other primary or secondary wastewater treatment operations, the installation of ad-

Reaction r	Reaction rate r_r	k_r $[mM^{-1}h^{-1}]$
1	$r_1{=}k_1\,C_{Fe^{2+}}\,C_{H_2O_2}$	8.81^a
2	$r_2{=}k_2\,C_{Fe^{3+}}\,C_I$	5.63^a
3	$r_3{=}k_3\,C_R\,C_{H_2O_2}$	75.8^a
4	$r_4{=}k_4\,C_R^2$	42.8^a
5	$r_5{=}k_5\,C_M\,C_R\,C_{O_2}$	9643^a
6	$r_6{=}k_6\,C_M\,C_R$	257^a
7	$r_7{=}k_7\,C_{MX_1}\,C_R$	2865^a
8	$r_8{=}k_8\,C_{MX_1}\,C_R$	271^a
9	$r_9{=}k_9\,C_{MX_2}\,C_R$	107^a
10	$r_{10}{=}k_{10}\,C_{Fe^{3+}}\,C_{H_2O_2}$	0.02^b
11	$r_{11}{=}k_{11}\,C_{TOC}\,C_R$	0.7375

Table B.1: Kinetic constants k_r and expressions to calculate the reaction rates r_r in the photo-Fenton case study. Sources: [a]Cabrera Reina et al. (2012), [b]Pignatello (1992).

ditional equipment, the use of other operating modes –*i.e.* in parallel or series–, or the potential recirculation of intermediate flows.

B.2 Notation

Table B.2 summarizes the time-invariant u^{stat} and dynamic $u_k^{dyn}(t)$ decision variables, as well as differential $z_k(t)$, algebraic $y_k(t)$, and time-invariant γ variables and process parameters p associated to the photo-Fenton case study. Parameters involved in EPC constraints are also included therein.

B.3 MLDO model of the photo-Fenton case study

B.3.1 Objective function and constraints

This case study poses a bi-objective optimization problem to minimize the treatment expenses and the processing time. According to the definition of MO problems, the decision criteria read as:

$$\underset{u^{dyn}(t),u^{stat}}{\text{minimize}} \quad \begin{aligned} &\Phi_1 = Cost_{\mathrm{Fe}^{2+}} + Cost_{\mathrm{H_2O_2}} + Cost_{\epsilon}, \\ &\Phi_2 = t^{end}. \end{aligned} \tag{B.2}$$

The treatment cost comprises the cost of reagents Fe^{2+} and H_2O_2 and the cost of electricity consumption in the lamp, which are defined as follows:

$$Cost_{\mathrm{Fe}^{2+}} = \hat{p}_{\mathrm{Fe}^{2+}} C^0_{\mathrm{Fe}^{2+}}\ \upsilon, \tag{B.3}$$

$$Cost_{\mathrm{H_2O_2}} = \hat{p}_{\mathrm{H_2O_2}} (C^0_{\mathrm{H_2O_2}}\ \upsilon + \int_{t^s}^{t^{end}} q(t)\, dt), \tag{B.4}$$

$$Cost_{\epsilon} = \hat{p}_{\epsilon}\, I\, A_w\, t^{end}. \tag{B.5}$$

The optimization model also includes constraints to guarantee the accomplishment of minimum yields χ_{PCT} and χ_{TOC} in the final PCT and TOC reduction:

$$\frac{C^0_{\mathrm{PCT}} - C_{\mathrm{PCT}}(t^{end})}{C^0_{\mathrm{PCT}}}\, 100 \geq \chi_{\mathrm{PCT}}, \tag{B.6}$$

$$\frac{C^0_{\mathrm{TOC}} - C_{\mathrm{TOC}}(t^{end})}{C^0_{\mathrm{TOC}}}\, 100 \geq \chi_{\mathrm{TOC}}. \tag{B.7}$$

B.3.2 Batch procedure in the photo-reactor

In this case study, equipment selection is not a decision variable due to the availability of one unique processing unit. Then, the definition of its corresponding batch unit procedure does not require to be controlled by an equipment Boolean Y_j, since it should be selected in all solutions. Overall, the batch model in the photo-reactor is defined by the mass balances of the compounds O_2, R, M, MX_1, MX_2, CO_2, Fe^{2+}, Fe^{3+}, H_2O_2, and TOC, defined by the following set of differential equations:

Type	Description	Variable/ parameter		Value/ bounds
$u_k^{dyn}(t)$	H_2O_2 input rate rate	$q(t)$	$[mmol/h]$	[0, 1,000]
u^{stat}	Initial concentration of H_2O_2	$C^0_{H_2O_2}$	$[mM]$	[0, 45]
	Initial concentration of Fe^{2+}	$C^0_{Fe^{2+}}$	$[mM]$	[0, 0.179]
	Final time	t^{end}	$[h]$	[0, 10]
	Total amount of H_2O_2 introduced	$N_{H_2O_2}$	$[mmol]$	[0, 661.5]
	Initial dosage time	t^i	$[h]$	[0, 10]
	Fraction of $N_{H_2O_2}$ completed at time t^i	F^i	$[mmol/mmol]$	[0, 1]
	Continuous dosage span	$\triangle t^{add}$	$[h]$	[0, 10]
$z_k(t)$	Concentration of O_2, $C^0_{O_2}$=0.25	$C_{O_2}(t)$	$[mM]$	[0, 1]
	Concentration of R, C^0_R=0	$C_R(t)$	$[mM]$	[0, 1]
	Concentration of M, C^0_M=0.52	$C_M(t)$	$[mM]$	[0, 3.125]
	Concentration of MX_1, $C^0_{MX_1}$=0	$C_{MX_1}(t)$	$[mM]$	[0, 1]
	Concentration of MX_2, $C^0_{MX_2}$=0	$C_{MX_2}(t)$	$[mM]$	[0, 1]
	Concentration of CO_2, $C^0_{CO_2}$=0	$C_{CO_2}(t)$	$[mM]$	[0, 1]
	Concentration of Fe^{2+}	$C_{Fe^{+2}}(t)$	$[mM]$	[0, 0.179]
	Concentration of Fe^{3+}, $C^0_{Fe^{+3}}$=0	$C_{Fe^{+3}}(t)$	$[mM]$	[0, 0.179]
	Concentration of H_2O_2	$C_{H_2O_2}(t)$	$[mM]$	[0, 45]
	Concentration of TOC, C^0_{TOC}=4.16	$C_{TOC}(t)$	$[mM]$	[0, 25]
$y_k(t)$	Rate of reaction $r\in\{1, ..., 11\}$	$r_r(t)$	$[mM/h]$	[0, ∞]
γ	Capacity of the photo-reactor	$Size$	$[L]$	15
	Lamp intensity	I	$[W/m^2]$	36
	Reaction volume	v	$[L]$	15
	Starting time	t^s	$[h]$	0
	Cost of reagent H_2O_2	$Cost_{H_2O_2}$	$[€/batch]$	[0, ∞]
	Cost of reagent Fe^{2+}	$Cost_{Fe^{2+}}$	$[€/batch]$	[0, ∞]
	Cost of electricity	$Cost_{\epsilon}$	$[€/batch]$	[0, ∞]
p	Kinetic constant of reaction $r\in\{1, ..., 11\}$	k_r	$[mM^{-1}h^{-1}]$	(Table B.1)
	Price of reagent H_2O_2	$\hat{p}_{Fe^{2+}}$	$[€/mol]$	3.17
	Price of reagent Fe^2	$\hat{p}_{Fe^{2+}}$	$[€/mol]$	12.62
	Price of electricity	$\hat{p}_{\epsilon}$	$[c€/kWh]$	14.56
	Stoichiometric coefficients in O_2 balance	g_1	[ ]	0.75^a
		g_2	[ ]	0.47^a
		c_1	[ ]	0.10^a
	Saturation concentration of O_2	$C^{sat}_{O_2}$	$[mM]$	0.250
	Global coefficient of mass transfer of O_2	k_{la}	$[h^{-1}]$	2.7
	Irradiation surface	A_w	$[m^2]$	0.018^b
EPC	Minimum final yield in PCT elimination	χ_{PCT}	[%]	99.9
	Minimum final yield in TOC elimination	χ_{TOC}	[%]	90

Table B.2: Variables and process parameters in the photo-Fenton case study. Sources: [a]Cabrera Reina et al. (2012), [b]Yamal-Turbay et al. (2012).

$$\dot{C}_{\mathrm{O_2}} = (g_1\, r_3) + (g_2\, r_4) - (c_1\, r_5) + (k_{la}\, (C^{sat}_{\mathrm{O_2}} - C^{sat}_{\mathrm{O_2}})), \tag{B.8}$$
$$\dot{C}_{\mathrm{R}} = r_1 + r_2 - r_3 - 2\, r_4 - r_5 - r_6 - r_7 - r_8 - r_9, \tag{B.9}$$
$$\dot{C}_{\mathrm{M}} = -r_5 - r_6, \tag{B.10}$$
$$\dot{C}_{\mathrm{MX_1}} = r_5 + r_6 - r_7 - r_8, \tag{B.11}$$
$$\dot{C}_{\mathrm{MX_2}} = r_7 - r_9, \tag{B.12}$$
$$\dot{C}_{\mathrm{CO_2}} = r_8 + r_9, \tag{B.13}$$
$$\dot{C}_{\mathrm{Fe^{2+}}} = -r_1 + r_2 + r_{10}, \tag{B.14}$$
$$\dot{C}_{\mathrm{Fe^{3+}}} = r_1 - r_2 - r_{10}, \tag{B.15}$$
$$\dot{C}_{\mathrm{H_2O_2}} = -r_1 - r_3 - r_{10} + q(t)/v, \tag{B.16}$$
$$\dot{C}_{\mathrm{TOC}} = -r_{11}. \tag{B.17}$$

The rates of reactions $r \in \{1, ..., 11\}$ are calculated according to the algebraic expressions of Table B.1, namely:

$$r_1 = k_1\, C_{\mathrm{Fe^{2+}}}\, C_{\mathrm{H_2O_2}} \tag{B.18}$$
$$r_2 = k_2\, C_{\mathrm{Fe^{3+}}}\, C_I \tag{B.19}$$
$$r_3 = k_3\, C_{\mathrm{R}}\, C_{\mathrm{H_2O_2}} \tag{B.20}$$
$$r_4 = k_4\, C_{\mathrm{R}}^2 \tag{B.21}$$
$$r_5 = k_5\, C_{\mathrm{M}}\, C_{\mathrm{R}}\, C_{\mathrm{O_2}} \tag{B.22}$$
$$r_6 = k_6\, C_{\mathrm{M}}\, C_{\mathrm{R}} \tag{B.23}$$
$$r_7 = k_7\, C_{\mathrm{MX_1}}\, C_{\mathrm{R}} \tag{B.24}$$
$$r_8 = k_8\, C_{\mathrm{MX_1}}\, C_{\mathrm{R}} \tag{B.25}$$
$$r_9 = k_9\, C_{\mathrm{MX_2}}\, C_{\mathrm{R}} \tag{B.26}$$
$$r_{10} = k_{10}\, C_{\mathrm{Fe^{3+}}}\, C_{\mathrm{H_2O_2}} \tag{B.27}$$
$$r_{11} = k_{11}\, C_{\mathrm{TOC}}\, C_{\mathrm{R}} \tag{B.28}$$

The predefined dosage protocol proposed by Yamal-Turbay et al. (2012) to define the addition of H_2O_2 to the photo-Fenton reaction can be reformulated into the following piecewise function, where the input rate $q(t)$ of H_2O_2 is expressed as a function of the static variables t^i, F^i, $N_{\mathrm{H_2O_2}}$, and $\triangle t^{add}$:

$$q(t) = \begin{cases} 0 & t \leq t^i \\ \frac{(1-F^i)\; N_{\mathrm{H_2O_2}}}{\triangle t^{add}} & t^i \leq t \leq t^i + \triangle t^{add} \\ 0 & t^i + \triangle t^{add} \leq t. \end{cases} \tag{B.29}$$

Appendix C

Model of the acrylic fiber case study

This appendix provides further information regarding the acrylic fiber production case study. This was presented in § 6.4 to illustrate the solution of integrated batch process development in a grassroots scenario. The process description is here given together with the physicochemical parameters and variables of the process and economic data. Overall, the problem is formulated according to the MLDO modeling strategy and formulation proposed in §§ 3.2 and 3.3. The MLDO should be next reformulated as a MIDO and discretized to obtain a MINLP problem, following the direct-simultaneous solution procedure explained in § 4.2. The resulting MINLP can be optimized using conventional deterministic solvers.

C.1 Problem description

Polymerization reaction systems are characterized by complex interactions between productivity indicators –*e.g.* conversion, batch time, or profit– and polymer properties –*e.g.* polydispersity or molecular weight distribution. In particular, polymer quality is strongly related to measures like the chain length or the mass average number and these should be calculated as a function of intermediate products. However, these are ruled by complex reaction mechanisms and equations systems that include phenomena like the life and dead polymers moments. Furthermore, physicochemical phenomena like the auto-acceleration and the Trommsdorf effect may occur depending on processing conditions such as the viscosity and temperature in the polymerization reaction. As a result, the choice of the trajectories of reactor temperature and monomer feed rate in polymerization reactors is crucial to determine the compromise between productivity and polymer quality (Giudici, 2000, Embiruçu et al., 1996). In addition to polymerization reaction, downstream tasks also contribute to the optimization of overall economic and environmental production targets. For instance, the selection of solvents, cleaning technologies, and recirculation schemes are determinant decisions in the global performance of polymerization systems (Gol'dfein & Zyubin, 1990, Bajaj et al., 1996, Capón-García et al., 2011a).

C.1.1 Acrylic fiber production

Acrylic fibers are synthetic fibers composed of at least 85% of acrylonitrile (AN) monomer and the rest of another comonomer such as vinyl acetate (VA), methyl acrylate (MA), methyl methacrylate (MMA), vinyl chloride (VC), or vinylidene chloride (VDC). In particular, the target in this case study is to produce an acrylic fiber composed of 85% of AN and 15% of VA in batches of 200 kg of final product. The desired copolymer properties are associated to a maximum polydispersity variation of 0.1 and a maximum deviation in the composition of 2.5%.

Essentially, the production of acrylic fiber comprises a primary stage to produce the copolymer in bulk format and a secondary stage to transform it into spun format. The general block representation of the process is provided in Figure C.1, taking into account prior considerations and the additional recirculation of solvent and suspension medium. To sum up, the following process stages or tasks are subject to be included into the process model and are thus represented in the superstructure: (1) copolymerization reaction, (2) recovery of unreacted monomer, solvent, and suspension medium after reaction, (3) washing and filtration, (4) repulping, (5) filtering, (6) wet spinning, (7) second washing and filtration, and (8) second recovery of solvent after spinning.

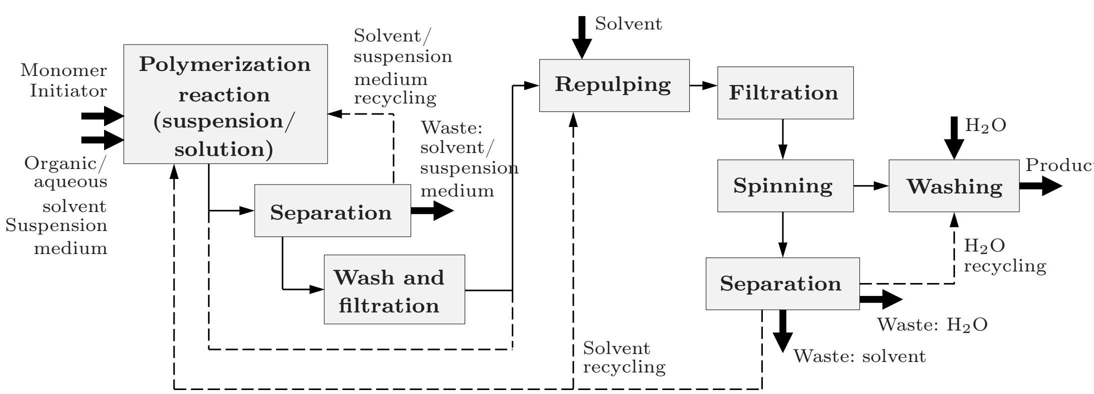


Figure C.1: Process stages in acrylic fiber production system: general processing scheme (solid lines) and potential processing alternatives (dashed lines).

This block diagram is used to detail the SEN superstructure of potential processing schemes in this example, presented in § 6.4 (Figure 6.6). It includes the following equipment items: solution and suspension polymerization reactors R_{11} and R_{12}, evaporator and condenser E_2, washing and filtering units F_3, F_5, F_{71} and F_{72}, repulping unit R_4, spinneret S_6, distillation columns C_{81} and C_{82}, and buffer tanks T_2, T_3, T_4, T_{81} and T_{82}.

Copolymerization reaction

Two polymerization technologies are used to synthesize acrylic fiber in industry, namely suspension and solution copolymerization technologies (EPA, 1995). On the one hand, solution polymerization is can be driven either in an organic solvent –such as dimethylformamide (DMF), here considered– or in an aqueous solvent –such as sodium thiocyanate (NaSCN(aq)), here studied. On the other, water is the suspension medium in suspension polymerization. In this case, the system is composed by two physical phases: an organic phase (I) composed by the monomers, polymer, and initiator, and the aqueous phase (II) which only contains soluble monomers, namely AN in this case study.

The reaction mechanism of both technologies can be defined by radical polymerization and terminal model, with three reaction mechanism steps, namely initiation, propagation, and termination by combination. The radical initiator considered is azobisisobutyronitrile (AIBN), often used in polymerization processes. According to Butala et al. (1988), this reaction system is defined as follows:

$$
\begin{aligned}
&\text{Initiation:} && \mathrm{I} \longrightarrow 2\mathrm{R}, \\
& && \mathrm{R} + \mathrm{M}_1 \xrightarrow{k_d} \mathrm{P}_{10}, \\
& && \mathrm{R} + \mathrm{M}_2 \xrightarrow{k_d} \mathrm{Q}_{01}, \\
&\text{Propagation:} && \mathrm{P}_{n,m} + \mathrm{M}_1 \xrightarrow{k_{p11}} \mathrm{P}_{n+1,m}, \\
& && \mathrm{P}_{n,m} + \mathrm{M}_2 \xrightarrow{k_{p12}} \mathrm{Q}_{n,m+1}, \\
& && \mathrm{Q}_{n,m} + \mathrm{M}_1 \xrightarrow{k_{p21}} \mathrm{P}_{n+1,m}, \\
& && \mathrm{Q}_{n,m} + \mathrm{M}_2 \xrightarrow{k_{p22}} \mathrm{Q}_{n,m+1}, \\
&\text{Termination:} && \mathrm{P}_{n,m} + \mathrm{P}_{r,q} \xrightarrow{k_{tc11}} \mathrm{M}_{n+r,m+q}, \\
& && \mathrm{P}_{n,m} + \mathrm{Q}_{r,q} \xrightarrow{k_{tc12}} \mathrm{M}_{n+r,m+q}, \\
& && \mathrm{Q}_{n,m} + \mathrm{Q}_{r,q} \xrightarrow{k_{tc22}} \mathrm{M}_{n+r,m+q},
\end{aligned}
\tag{C.1}
$$

where I represents the initiator (AIBN), R represents free radicals, M_1 and M_2 refer to monomers AN and VA respectively. $\mathrm{P}_{n,m}$ denotes a growing copolymer chain with n units of monomer M_1 and m units of monomer M_2, and monomer M_1 on the end. Equally, $\mathrm{Q}_{n,m}$ denotes a growing copolymer chain with monomer M_2 on the end. Finally, $\mathrm{M}_{n,m}$ represents inactive polymer –also known as dead polymer. Moreover, the dynamic control variables are the M_1 (AN) monomer dosage and the reaction temperature in both suspension and solution technologies. The following assumptions are also considered in the model:

- The polymer properties are tracked through the number and weight average chain length and the polydispersity, by computing the dead and live polymer moments;
- The chain transfer to monomer or solvent is disregarded;
- The termination is defined by combination of polymer chains;
- The heat of copolymerization of AN and VA is calculated through algebraic interpolation of their individual heats of polymerization $\triangle h_{\mathrm{M}_1}$ and $\triangle h_{\mathrm{M}_2}$;
- AN equilibrium between the organic and aqueous phases is considered in suspension polymerization by means of the global partition coefficient φ, as is following detailed.
- Gel and glass effects due to the high viscosity in the polymer (organic) phase in suspension polymerization are dismissed.

The kinetic data associated to the abovementioned reaction mechanism depend on the used solvent or suspension medium S and have been gathered from literature on polymerization processes, as summarized in Table C.1. Other process parameters are presented in Table C.2. Some of them are also subject to the solvent or suspension medium S, namely the selection of DMF, NaSCN(aq), or water.

		Solution S = DMF		Solution S = NaSCN(aq)		Suspension S = H_2O	
Reaction r		$k_{0,r,\mathrm{S}}$ $[\frac{m^3}{kmol\,s}]$	$E_{a,r,\mathrm{S}}$ $[\frac{kcal}{kmol}]$	$k_{0,r,\mathrm{S}}$ $[\frac{m^3}{kmol\,s}]$	$E_{a,r,\mathrm{S}}$ $[\frac{kcal}{kmol}]$	$k_{0,r,\mathrm{S}}$ $[\frac{m^3}{kmol\,s}]$	$E_{a,r,\mathrm{S}}$ $[\frac{kcal}{kmol}]$
Initiator decomposition	d	$6.02{\cdot}10^{15(a)}$	$31730^{(a)}$	$6.02{\cdot}10^{15(a)}$	$31730^{(a)}$	$6.02{\cdot}10^{15(a)}$	$31730^{(a)}$
Chain propagation	$p11$	$1.37{\cdot}10^{6(b)}$	$3869^{(c)}$	$1.59{\cdot}10^{7(d)}$	$4108^{(e)}$	$1.59{\cdot}10^{7(d)}$	$4108^{(e)}$
	$p12$	$3.38{\cdot}10^{5(b,g)}$	$3869^{(c)}$	$3.92{\cdot}10^{6(d,g)}$	$4108^{(e)}$	$3.92{\cdot}10^{6(d,g)}$	$4108^{(e)}$
	$p21$	$5.25{\cdot}10^{8(f,g)}$	$6300^{(f)}$	$5.25{\cdot}10^{8(f,g)}$	$6300^{(f)}$	$5.25{\cdot}10^{8(f,g)}$	$6300^{(f)}$
	$p22$	$3.20{\cdot}10^{7(f)}$	$6300^{(f)}$	$3.20{\cdot}10^{7(f)}$	$6300^{(f)}$	$3.20{\cdot}10^{7(f)}$	$6300^{(f)}$
Termination by combination	$tc11$	$3.84{\cdot}10^{11(b)}$	$3702^{(c)}$	$2.46{\cdot}10^{13(d)}$	$5398^{(e)}$	$2.46{\cdot}10^{13(d)}$	$5398^{(e)}$
	$tc12$	$8.67{\cdot}10^{11(a,b,f)}$	$3451^{(c,f)}$	$6.93{\cdot}10^{12(a,d,f)}$	$4299^{(e,f)}$	$6.93{\cdot}10^{12(a,d,f)}$	$4299^{(e,f)}$
	$tc22$	$3.70{\cdot}10^{9(f)}$	$3200^{(f)}$	$3.70{\cdot}10^{9(f)}$	$3200^{(f)}$	$3.70{\cdot}10^{9(f)}$	$3200^{(f)}$

Table C.1: Kinetic constants in the acrylic fiber case study: pre-exponential factor $k_{0,r,\mathrm{S}}$ and activation energy $E_{a,r,\mathrm{S}}$ of reaction r in solvent or suspension medium S. References: [a]Butala et al. (1988), [b]Brandrup et al. (1999, page II/81 Ref. 88), [c]Brandrup et al. (1999, page II/417 Ref. 32), [d]Brandrup et al. (1999, page II/81 Ref. 54), [e]Brandrup et al. (1999, page II/417 Ref. 25), [f]Machado et al. (2004), and [g]Mayo et al. (1948).

Parameter p_S		Solution S = DMF	Solution S = NaSCN(aq)	Suspension S = H_2O
Density of S	ρ_S $[kg/m^3]$	$948^{(a)}$	1000	1000
Specific heat of S	$c_{p,\mathrm{S}}$ $[kcal/kg°\mathrm{C}]$	$0.478^{(a)}$	1.000	1.000
Molecular weight of S	MW_S $[kg/kmol]$	73.09	18	18
Parameter p				
Ideal gas constant	R $[kcal/kmol°\mathrm{C}]$		1.987	
Molecular weight of M_1	MW_{M_1} $[kg/kmol]$		53.06	
Molecular weight of M_2	MW_{M_2} $[kg/kmol]$		86.09	
Molecular weight of I	MW_I $[kg/kmol]$		164.21	
Density of M_1	ρ_{M_1} $[kg/m^3]$		810	
Density of M_2	ρ_{M_2} $[kg/m^3]$		$939^{(b)}$	
Density of P_1	ρ_{P_1} $[kg/m^3]$		1184	
Density of P_2	ρ_{P_2} $[kg/m^3]$		1190	
Density of I	ρ_I $[kg/m^3]$		1100	
Heat of copolymerization of M_1	$\triangle h_{\mathrm{M}_1}$ $[kcal/kmol]$		$16800^{(c)}$	
Heat of copolymerization of M_2	$\triangle h_{\mathrm{M}_2}$ $[kcal/kmol]$		$22490^{(c)}$	
Overall heat transfer coefficient	h_c $[kcal/m^2 s°\mathrm{C}]$		$6.5^{(a)}$	
Heat transfer area per reactor volume	A_c $[m^2/m^3]$		1	
Density of cooling water	ρ_{cool} $[kg/m^3]$		1000	
Specific heat of cooling water	$c_{p,cool}$ $[kcal/kg°\mathrm{C}]$		1.000	
Reactivity ratio of monomer M_1	$r_1 = k_{p11}/k_{p12}$ [ ]		4.05	
Reactivity ratio of monomer M_2	$r_2 = k_{p22}/k_{p21}$ [ ]		0.061	

Table C.2: Process parameters in the copolymerization stage in the acrylic fiber case study: p independent and p_S dependent on the solvent or suspension medium S, where I = AIBN, M_1 = AN, M_2 = VA, S $\in$ {DMF, NaSCN(aq), H_2O}. References: [a]Butala et al. (1988), [b]Machado et al. (2004), [c]Miyama & Fujimoto (1961).

Regarding the global partition coefficient φ, this variable is associated to the equilibrium of AN between the organic and aqueous phases. It is defined as:

$$\varphi = \frac{\eta_{\mathrm{M}_1,II}}{\eta_{\mathrm{M}_1,I}}, \tag{C.2}$$

where $\eta_{\mathrm{M}_1,I}$ and $\eta_{\mathrm{M}_1,II}$ are the molar amounts of AN in organic phase (I) and aqueous phase (II) respectively. The definition of φ roots in the correlation proposed by Lu et al. (2006) for suspension copolymerization of AN and styrene at 50°C:

$$\left(\frac{A_s}{S}\right) \Big/ \left(\frac{A_w}{W}\right) \left(0.089 - \frac{A_w}{W}\right) = 0.35 + 5.2\,\frac{A_w}{W}, \tag{C.3}$$

where A_s and A_w are the mass of AN and S and W are the total mass of organic and aqueous phases respectively. This correlation can be reformulated into the following form:

$$1/\varphi \left(0.089 - \frac{MW_{\mathrm{M}_1}}{\rho_{\mathrm{H_2O}}} \left(\frac{\eta_{\mathrm{M}_1,II}}{\upsilon_{II}}\right)\right) \frac{\upsilon_{II}}{\upsilon_I} = 0.35 + 5.2\,\frac{MW_{\mathrm{M}_1}}{\rho_{\mathrm{H_2O}}} \left(\frac{\eta_{\mathrm{M}_1,II}}{\upsilon_{II}}\right), \tag{C.4}$$

where MW_{M_1} is the molecular weight of AN, $\rho_{\mathrm{H_2O}}$ is the density of aqueous phase, and υ_I and υ_{II} are the volumes of organic and aqueous phases respectively. This expression allows computing the inverse of the global partition coefficient $1/\varphi$ as a function of the concentration of AN in the aqueous phase ($\eta_{\mathrm{M}_1,II}/\upsilon_{II}$) and volumes υ_I and υ_{II}. In this example, such correlation is approximated to an exponential function in the processing range of $(\eta_{\mathrm{M}_1,II}/\upsilon_{II}) \in [0,\, 17]\; kmol/m^3$ to simplify the mathematical model. Particularly, the approximation used in the model has the following form:

$$1/\varphi \frac{\upsilon_{II}}{\upsilon_I} = a\; exp^{\left(b\left(\frac{\eta_{\mathrm{M}_1,II}}{\upsilon_{II}}\right)\right)}, \tag{C.5}$$

where parameters a and b have a value of 0.2 and 0.0877 respectively. The influence of the reaction temperature on the partition coefficient is dismissed.

Separation stage

The separation stage is lead using a energy separation system composed of an evaporator and a condenser. The dynamic equations system is defined according to Haggblom (1991), Luyben (1992), Oldenburg et al. (2003), and Muntean et al. (2011).

The vapor pressure ($p^j_{v,c,k}(t)$) is calculated by means of the Antoine equation for the light components of the separation mixture, namely monomers M_1 and M_2 as well as the solvent S. The Antoine coefficients are summarized in Table C.3. Regarding the heavy components I and Co, their values are defined with a value of 0.81 bar (OECD Screening Information Dataset, 1999) and 0.10 bar respectively.

Watson correlation to estimate the latent heats of vaporization of light components $c \in \{\mathrm{M}_1,\mathrm{M}_2,\mathrm{S}\}$. The data have been extracted from Aspen HYSIS thermodynamics according to Watson's correlation defined by:

$$log(h_{v,c}) = log(A_{h,c}) + log(1 - \theta/\theta c_c) B_{h,c}, \tag{C.6}$$

where h_v is the unit of the heat of vaporization defined in $kJ/kmol$, θ is the temperature of the system and θc_c is the critical temperature defined in °C, and $A_{h,c}$ and $B_{h,c}$ are the coefficients, which are specific for each component c. The coefficients for the light components are defined in Table C.4.

c	A_c	B_c	C_c
M_1 = AN	4.06661	1255.939	-41.853
M_2 = VA	4.34032	1299.069	-46.183
S = DMF	3.93068	1337.716	-82.648
S = NaSCN(aq)[1] S = H_2O	5.08354	1663.125	-45.622

[1] Approximated to coefficients of H_2O

Table C.3: Antoine coefficients to compute the vapor pressure $p_{v,c}$ of light compounds $c \in \{M_1, M_2, S\}$ in the acrylic fiber case study. Data source: NIST database (URL: http://webbook.nist.gov/chemistry/name-ser.html, accessed 10/09/2012).

c	$A_{h,c}$	$B_{h,c}$	θc_c [°C]
M_1 = AN	41550	0.2733	262.9
M_2 = VA	47700	0.3765	251.9
S = DMF	59217	0.37996	373.9
S = NaSCN(aq)[1] S = H_2O	52053	0.3199	374.1

[1] Approximated to coefficients of H_2O

Table C.4: Watson coefficients to compute the latent heat of vaporization $h_{v,c}$ and critical temperature θc_c of light compounds $c \in \{M_1, M_2, S\}$ in the acrylic fiber case study. Data source: Aspen HYSIS thermodynamics.

Economic data

The raw material prices, unitary processing costs, amortization base, and waste disposal expenses in the copolymerization reaction stage and the separation stage are summarized in Table C.5.

$\hat{p}_I$ [€/kg]	$\hat{p}_{M_1}$ [€/kg]	$\hat{p}_{M_2}$ [€/kg]	$\hat{p}_{S(S=DMF)}$ [€/kg]	$\hat{p}_{S(S=NaSCN(aq))}$ [€/kg]	$\hat{p}_{S(S=H_2O)}$ [c€/kg]	$\hat{c}_{j,cool}$ [c€/kg]	$\hat{c}_{j,heat}$ [c€/kWh]	$\check{c}_j$ [c€/s]	$\hat{p}_{waste}$ [€/kg]
8.11	1.76	0.91	0.57	1.22	0.181	0.181	17.4	0.404	0.85

Table C.5: Economic data in the acrylic fiber case study: $\hat{p}_c$ price of raw material $c \in$ {I, M_1, M_2, S} where I = AIBN, M_1 = AN, M_2 = VA, S $\in$ {DMF, NaSCN(aq), H_2O}, $\hat{c}_{j,cool}$ processing cost associated to cooling water, $\hat{c}_{j,heat}$ processing cost associated to heating energy, $\check{c}_j$ base amortization cost, and $\hat{p}_{waste}$ expenses of waste disposal.

C.2 Notation

Tables C.6, C.8, C.9, and C.7 summarize the Boolean u^{Bool}, integer u^{int}, time-invariant u^{stat} and dynamic $u_k^{dyn}(t)$ decision variables, as well as differential $z_k(t)$, algebraic $y_k(t)$, and time-invariant γ variables and process parameters p associated to the acrylic fiber case study.

Figure C.2 presents the flow indexes in Levels 0 and 1 used in the balances. The input flows to the polymerization reactors from raw material and from buffer tank T_2 are here separated with regard to the SEN superstructure in Figure 6.6 (§ 6.4.3) in order to facilitate the optimization of the control trajectories of flow rate and composition of raw material input.

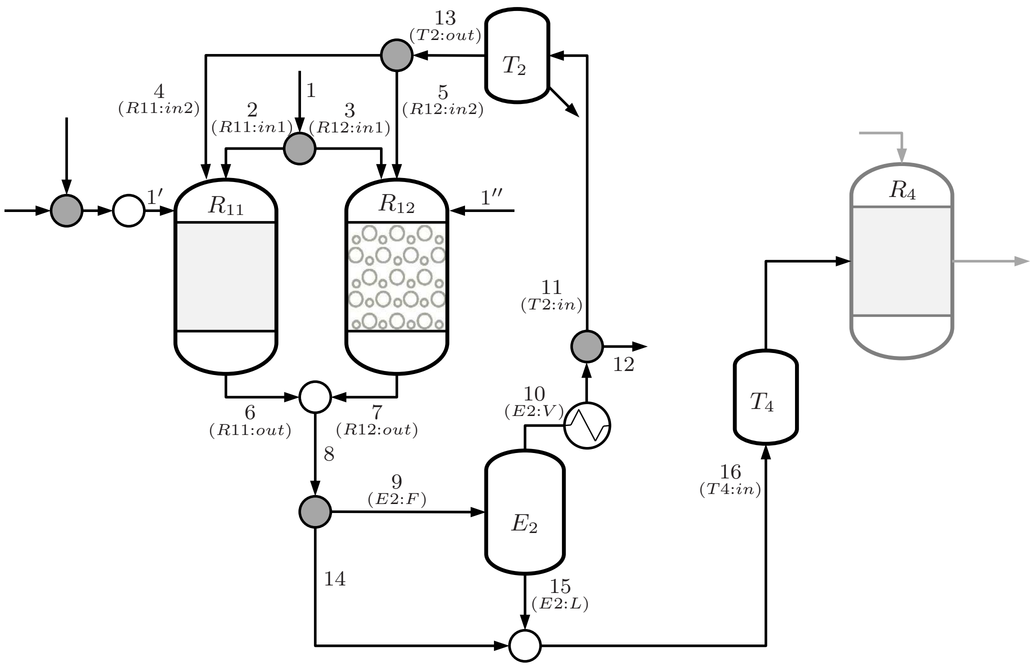


Figure C.2: Flow indexes in Levels 0 and 1 in the acrylic fiber case study. In parenthesis the indexes associated to particular equipment items.

Type	Description	Variable/ parameter		Value/ bounds
u^{Bool}	Process stage selection	Z_i	-	$\{true, false\}$
	Technological alternative selection	V_λ^j	-	$\{true, false\}$
	Chemicals selection	S_c^j	-	$\{true, false\}$
	Potential solvent recovery and reuse	R_n	-	$\{true, false\}$
	Operating mode ψ selection	X_ψ^i	-	$\{true, false\}$
	Selection of processing and storage units	Y_j	-	$\{true, false\}$
	Task-unit assignment	$W_{j,q}$	-	$\{true, false\}$
u^{stat}	Duration of mathematical stage l	t_l	$[h]$	$[0, 15]$
p	Batch production size	$Batch$	$[kg]$	200
	Base equipment capacity	$Size^0$	$[m^3]$	3.8
	Size power in amortization funcion	n	[ ]	0.5

Table C.6: General variables and process parameters at Level 0 in the acrylic fiber case study.

Type	Description	Variable/ parameter		Value/ bounds
$z_k(t)$	Total molar amount	$H_l^j(t)$	$[kmol]$	$[0, 10]$
	- Initial total molar amount	$H_1^{j,0}$	$[kmol]$	0
	Molar amount of $c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}$	$\eta_{c,l}^j(t)$	$[kmol]$	$[0, 10]$
	- Initial molar amount of $c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}$	$\eta_{c,1}^{j,0}$	$[kmol]$	0
$y_k(t)$	Molar flow rate in input flow *in*	$F_{in,l}^j(t)$	$[kmol/h]$	$[0, 72]$
	Molar flow rate in output flow *out*	$F_{out,l}^j(t)$	$[kmol/h]$	$[0, 72]$
	Molar fraction in input flow *in*	$x_{c,in,l}^j(t)$	$[\frac{kmol}{kmol\ total}]$	$[0, 1]$
	Molar fraction in the tank and output flow *out*	$x_{c,l}^j(t)$	$[\frac{kmol}{kmol\ total}]$	$[0, 1]$

Table C.7: Variables associated to buffer tanks $j \in \{T_2, T_4\}$ in the acrylic fiber case study.

Type	Description	Variable/ parameter		Value/ bounds
$u_k^{dyn}(t)$	Molar flow rate of input flow *in*1 (raw material)	$F^j_{in1,k}(t)$	$[kmol/h]$	$[0,72]$
	Molar flow rate of input flow *in*2 (from buffer tank T_2)	$F^j_{in2,k}(t)$	$[kmol/h]$	$[0,72]$
	Molar flow rate of output flow *out*	$F^j_{out,k}(t)$	$[kmol/h]$	$[0,72]$
	Cooling temperature	$\theta^j_{cool,k}(t)$	$[^\circ\mathrm{C}]$	$[20,80]$
u^{stat}	Molar fraction of compound $c \in \{\mathrm{I,M_1,M_2}\}$ in input flow *in*1 (raw material)	$x^j_{c,in1,k}$	$[\frac{kmol}{kmol\ total}]$	[ ]
$z_k(t)$	Molar amount of compound $c\in\{\mathrm{I,M_1,M_2,S,P,Q}\}$	$\eta^j_{c,k}(t)$	$[kmol]$	$[0,10]$
	- Initial molar amount of I	$\eta^{j,0}_{\mathrm{I},1}$	$[kmol]$	0.0062
	- Initial molar amount of $\mathrm{M_1}$	$\eta^{j,0}_{\mathrm{M_1},1}$	$[kmol]$	0.05
	- Initial molar amount of $\mathrm{M_2}$	$\eta^{j,0}_{\mathrm{M_2},1}$	$[kmol]$	0.034
	- Initial molar amount of S	$\eta^{j,0}_{\mathrm{S},1}$	$[kmol]$	0.01
	- Initial molar amount of P	$\eta^{j,0}_{\mathrm{P},1}$	$[kmol]$	10^{-8}
	- Initial molar amount of Q	$\eta^{j,0}_{\mathrm{Q},1}$	$[kmol]$	10^{-8}
	Reaction temperature	$\theta^j_k(t)$	$[^\circ\mathrm{C}]$	$[25,100]$
	- Initial reaction temperature	$\theta^{j,0}_1$	$[^\circ\mathrm{C}]$	40
$y_k(t)$	Molar fraction of $c \in \{\mathrm{I,M_1,M_2,S,P,Q}\}$ in the reactor	$x^j_{c,k}(t)$	$[\frac{kmol}{kmol\ total}]$	[ ]
	Molar fraction of $c \in \{\mathrm{I,M_1,M_2,S,P,Q}\}$ in input flow *in*2 (from buffer tank T_2)	$x^j_{c,in2,k}(t)$	$[\frac{kmol}{kmol\ total}]$	[ ]
	Volume of the reaction system	$\upsilon^j_k(t)$	$[m^3]$	$[0,10]$
	Converted monomer $c \in \{\mathrm{M_1,M_2}\}$	$\chi^j_{c,k}(t)$	$[kmol]$	$[0,10]$
	Copolymerization reaction rate	$RX^j_k(t)$	$[kmol/m^3\ s]$	[ ]
	Heat of copolymerization	$\triangle H^j_k(t)$	$[kcal/kmol]$	[ ]
	Initiator decomposition rate constant	$k^j_{d,k}(t)$	$[s^{-1}]$	[ ]
	Propagation rate constants, i,i'=1, 2	$k^j_{pii',k}(t)$	$[m^3/kmol\ s]$	[ ]
	Termination by combination rate constant, i,i'=1, 2	$k^j_{tcii',k}(t)$	$[m^3/kmol\ s]$	[ ]
	Instantaneous mole fraction of $\mathrm{M_1}$ in copolymer	$F^j_{1,k}(t)$	$[\frac{kmol\ \mathrm{M_1}}{kmol\ total}]$	$[0,1]$
	Flow rate of cooling water	$F^j_{cool,k}(t)$	$[m^3/h]$	[ ]
	Cooling energy consumption	$Q^j_{cool,k}(t)$	$[kcal/s]$	[ ]
γ	Duration of stage k of unit j	t^j_k	$[h]$	$[0.0125,15]$
	Density of the reaction mixture	ρ^j	$[kg/m^3]$	
	Specific heat in the reaction mixture	c^j_p	$[kcal/kg^\circ\mathrm{C}]$	
	Pre-exponential factor of reaction $r\in\{d,pii',tcii'\}$,i,i'=1, 2	$k^j_{0,r}$	$[m^3/kmol\ s]$	
	Activation energy of reaction $r\in\{d,pii',tcii'\}$, i,i'=1, 2	$E^j_{a,r}$	$[kcal/kmol]$	
	Total converted monomer $c \in \{\mathrm{M_1,M_2}\}$	$\chi^j_{c,total}$	$[kmol]$	
	Total consumption of compound $c \in \{\mathrm{M_1,M_2,I,S}\}$	$Cons^j_c$	$[kmol]$	
p	Temperature in input flow *in*1 (raw material)	$\theta^j_{in1,k}$	$[^\circ\mathrm{C}]$	25
	Temperature in input flow *in*2 (from buffer tank T_2)	$\theta^j_{in2,k}$	$[^\circ\mathrm{C}]$	25
	Initial temperature of cooling water	$\theta^j_{cool,0}$	$[^\circ\mathrm{C}]$	18
	Set-point of $F^j_{1,k}(t)$	$F^{SP}_{\mathrm{M_1}}$	$[\frac{kmol\ \mathrm{M_1}}{kmol\ total}]$	0.85
	Maximum deviation of $F^j_{1,k}(t)$	$F^{\sigma}_{\mathrm{M_1}}$	$[\frac{kmol\ \mathrm{M_1}}{kmol\ total}]$	0.025
PC	Lower bound of input/output flow rates	$F^{j,\mathrm{L}}$	$[kmol/h]$	18
	Upper bound of input/output flow rates	$F^{j,\mathrm{U}}$	$[kmol/h]$	72
	Lower bound of reaction temperature	θ^{L}	$[^\circ\mathrm{C}]$	40
	Upper bound of reaction temperature	θ^{U}	$[^\circ\mathrm{C}]$	80

Table C.8: Variables and process parameters associated to copolymerization stage 1 in solution and suspension copolymerization reactors $j \in \{R_{11}, R_{12}\}$ in the acrylic fiber case study.

Type	Description	Variable/ parameter		Value/ bounds
$y_k(t)$	Volume of phase I in the reaction system	$\upsilon^j_{I,k}(t)$	$[m^3]$	$[0, 10]$
	Volume of phase II in the reaction system	$\upsilon^j_{II,k}(t)$	$[m^3]$	$[0, 10]$
	Molar amount of M_1 in phase I	$\eta^j_{\mathrm{M}_1,I,k}(t)$	$[kmol]$	$[0, 10]$
	Molar amount of M_1 in phase II	$\eta^j_{\mathrm{M}_1,II,k}(t)$	$[kmol]$	$[0, 10]$
	Global partition coefficient of M_1	$\varphi^j_k(t)$	$[kmol\, II/kmol\, I]$	
p	Parameters to evaluate the global partition	a	$[\,]$	0.2
	coefficient of M_1 according to Eq. C.5	b	$[\,]$	0.0877

Table C.9: Additional variables and process parameters associated to copolymerization stage 1 in suspension copolymerization reactor $j \in \{R_{12}\}$ in the acrylic fiber case study.

Type	Description	Variable/ parameter		Value/ bounds
$u^{dyn}_k(t)$	Heating energy supplied	$Q^j_{heat,k}(t)$	$[kcal/h]$	$[\,]$
$z_k(t)$	Holdup	$H^j_k(t)$	$[kmol]$	[0,10]
	- Initial holdup	$H^{j,0}_1$	$[kmol]$	0
	Molar amount of $c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}$	$\eta^j_{c,k}(t)$	$[kmol]$	[0,10]
	- Initial molar amount of $c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}$	$\eta^{j,0}_{c,1}$	$[kmol]$	0
$y_k(t)$	Molar flow rate of input flow F	$F^j_{F,k}(t)$	$[kmol/h]$	[0,72]
	Molar flow rate of output flow L (bottoms)	$F^j_{L,k}(t)$	$[kmol/h]$	[0,72]
	Molar flow rate of output flow V (distillate)	$F^j_{V,k}(t)$	$[kmol/h]$	[0,72]
	Molar fraction of $c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}$ in input flow F	$z^j_{c,F,k}(t)$	$[\frac{kmol}{kmol\, total}]$	[0,1]
	Molar fraction of $c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}$ in liquid phase	$x^j_{c,k}(t)$	$[\frac{kmol}{kmol\, total}]$	[0,1]
	Molar fraction of $c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}$ in vapor phase	$y^j_{c,k}(t)$	$[\frac{kmol}{kmol\, total}]$	[0,1]
	Temperature in the separation unit	$\theta^j_k(t)$	$[^\circ\mathrm{K}]$	$[\,]$
	Total pressure in the separation unit	P^j_{total}	$[bar]$	$[\,]$
	Vapor pressure of light components $c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{S}\}$	$p^j_{v,c,k}(t)$	$[bar]$	$[\,]$
	Specific heat of vaporization of $c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}$	$h^j_{v,c,k}(t)$	$[kcal/kmol]$	$[\,]$
	Heat of vaporization	$\triangle h^j_{v,k}(t)$	$[kcal/kmol]$	$[\,]$
γ	Duration of stage k of unit j	t^j_k	$[h]$	[0.0125,10]
	Amount of waste material	$Waste^j$	$[kmol]$	$[\,]$
p	Percentage of waste	P_{waste}	$[\%(kmol)]$	2%
	Antoine coefficients of $c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{S}\}$	$A_c,\ B_c,\ C_c$	$[\,]$	(Table C.3)
	Vapor pressure of heavy components $c \in \{\mathrm{Co}, \mathrm{I}\}$	$p_{v,\mathrm{I}}$	$[bar]$	0.81
		$p_{v,\mathrm{Co}}$	$[bar]$	0.10
	Watson coefficients of $c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{S}\}$	$A_{h,c},\ B_{h,c}$	$[\,]$	(Table C.4)
	Critical temperature of $c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{S}\}$	θc_c	$[^\circ\mathrm{K}]$	
PC	Lower bound of input/output flow rates	$F^{j,\mathrm{L}}$	$[kmol/h]$	0.72
	Upper bound of input/output flow rates	$F^{j,\mathrm{U}}$	$[kmol/h]$	72

Table C.10: Variables and process parameters associated to separation stage 2 in evaporation unit $j \in \{E_2\}$ in the acrylic fiber case study.

C.3 MLDO model of the acrylic fiber case study

C.3.1 Objective function and production targets

The objective function considers several economic terms. Particularly, it includes: equipment amortization ($Cost_{j,a}$) and processing costs ($Cost_{j,p}$) of units $j \in \{R_{11}, R_{12}, E_2, T_2\}$, raw material expenses ($Cost_{\mathrm{M}_1}$, $Cost_{\mathrm{M}_2}$, $Cost_{\mathrm{I}}$, and $Cost_{\mathrm{S}}$), and costs associated to the waste disposal ($Cost_{\mathrm{waste}}$), becoming:

$$\underset{\substack{u_k^{dyn}(t), u^{stat} \\ u^{int}, u^{Bool}}}{\text{minimize}} \; \Phi = Cost_{\mathrm{M}_1} + Cost_{\mathrm{M}_2} + Cost_{\mathrm{I}} + Cost_{\mathrm{S}} + Cost_a + Cost_p + Cost_{\mathrm{waste}}, \tag{C.7}$$

where $u_k^{dyn}(t)$ are the profiles of input and output flow rates ($F^j_{in1,k}(t)$, $F^j_{in2,k}(t)$, and $F^j_{out,k}(t)$, $k \in \{1, 2, 3\}$) and the cooling temperature profile ($\theta^j_{cool,k}(t)$, $k \in \{1, 2, 3\}$) in the copolymerization reaction stage 1 associated to units $j \in \{R_{11}, R_{12}\}$, as well as the heat supplied in separation stage 2 associated to the evaporator $j \in \{E_2\}$ ($Q^j_{heat,k}(t)$, $k \in \{1, 2, 3, 4\}$). Additionally, u^{stat} refers to the composition of raw materials during the load operation ($c^j_{c,in1,k}$, $c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{I}\}$, $k \in \{1\}$) and the composition of monomer M_1 during the reaction operation ($c^j_{\mathrm{M}_1,in1,k}$, $k \in \{2\}$) in copolymerization reaction stage 1, and to the duration of batch operations (t_l, $\forall l$). Finally, u^{int} refers to the size of installed processing units ($Size^j$), and u^{Bool} comprises qualitative decisions ($Z_i, V^j_\lambda, S^j_c, R_n, X^i_\psi, Y_j, W_{j,q}$). Each contribution of the objective function is following detailed:

$$\begin{aligned}
&Cost_{\mathrm{M}_1} = \hat{p}_{\mathrm{M}_1} MW_{\mathrm{M}_1} \sum_{\substack{j\in\{R_{11},\\ R_{12},T_2\}}} Cons^j_{\mathrm{M}_1}, && Cost_{\mathrm{M}_2} = \hat{p}_{\mathrm{M}_2} MW_{\mathrm{M}_2} \sum_{\substack{j\in\{R_{11},\\ R_{12},T_2\}}} Cons^j_{\mathrm{M}_2},\\
&Cost_{\mathrm{I}} = \hat{p}_{\mathrm{I}}\, MW_{\mathrm{I}} \sum_{\substack{j\in\{R_{11},\\ R_{12}\}}} Cons^j_{\mathrm{I}}, && Cost_{\mathrm{S}} = \sum_{\substack{j\in\{R_{11},\\ R_{12},T_2\}}} (\hat{p}^j_{\mathrm{S}}\, MW_{\mathrm{S}}\, Cons^j_{\mathrm{S}}),\\
&Cost_a = \sum_{\substack{j\in\{R_{11},R_{12},\\ E_2,T_2,T_4\}}} Cost_{j,a}, && Cost_p = \sum_{\substack{j\in\{R_{11},\\ R_{12},E_2\}}} Cost_{j,p},\\
&Cost_{\mathrm{waste}} = \hat{p}_{waste} \sum_{j\in\{E_2\}} Waste^j.
\end{aligned} \tag{C.8}$$

Additionally, the process is subject to several production targets. First, the product demand, which corresponds to the batch size $Batch$ of $200\,kg$, should be fulfilled in the selected polymerization reactor R_{11} or R_{12}. The following restriction guarantees the accomplishment of the demand:

$$\begin{bmatrix} Y_j \\ Batch \leq \chi^j_{\mathrm{M}_1,total} MW_{\mathrm{M}_1} + \chi^j_{\mathrm{M}_2,total} MW_{\mathrm{M}_2}, \\ \chi^j_{c,total} = \eta^{j,0}_{c,1} - \eta^j_{c,3}(1) + \sum_{k=1}^{3} \int_0^1 \Big(F^j_{in1,k}(t) x^j_{c,in1,k}(t) \\ + F^j_{in2,k}(t) x^j_{c,in2,k}(t) - F^j_{out,k}(t) x^j_{c,k}(t) \Big)\, t^j_k dt,\, c\in\{\mathrm{M}_1, \mathrm{M}_2\} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ \chi^j_{c,total} = 0, \\ c \in \{\mathrm{M}_1, \mathrm{M}_2\} \end{bmatrix}, \quad j \in \{R_{11}, R_{12}\}. \tag{C.9}$$

Second, the set-point instantaneous copolymer composition $F^{SP}_{\mathrm{M}_1}$ with a value of 85% of M_1 (AN) should be pursued along the chain growth, with a maximum deviation $F^\sigma_{\mathrm{M}_1}$ in the composition of 2.5%. This is defined in the selected reaction unit R_{11} or R_{12} by:

$$\begin{bmatrix} Y_j \\ -F^\sigma_{\mathrm{M}_1} \leq F^{SP}_{\mathrm{M}_1} - F^j_{\mathrm{M}_1,k}(t) \leq F^\sigma_{\mathrm{M}_1},\ t \in [0, 1], \forall k \in K_j \end{bmatrix}, j \in \{R_{11}, R_{12}\}. \tag{C.10}$$

C.3.2 Batch procedures at Level 1

Copolymerization reaction in batch units

The following disjunctions define the multistage models of batch units $j \in \{R_{11}, R_{12}\}$ and correspond to Eqs. 3.5 and 3.6 of the formulation proposed in § 3.3. On the one hand, batch unit R_{11} is the copolymerization reactor where solution polymerization takes place and is represented by:

$$\begin{bmatrix} Y_j \\ \begin{aligned} \dot\eta^j_{\mathrm{I},k}(t) =& \Big(F^j_{in1,k}(t)\,x^j_{\mathrm{I},in1,k} + F^j_{in2,k}(t)\,x^j_{\mathrm{I},in2,k}(t) - F^j_{out,k}(t)\,x^j_{\mathrm{I},k}(t) - k^j_{d,k}(t)\,\eta^j_{\mathrm{I},k}(t)\Big)\,t^j_k, \\ \dot\eta^j_{\mathrm{M}_1,k}(t) =& \Big(F^j_{in1,k}(t)\,x^j_{\mathrm{M}_1,in1,k} + F^j_{in2,k}(t)\,x^j_{\mathrm{M}_1,in2,k}(t) - F^j_{out,k}(t)\,x^j_{\mathrm{M}_1,k}(t) \\ & -(k^j_{p11,k}(t)\,\eta^j_{\mathrm{P},k}(t) + k^j_{p21,k}(t)\,\eta^j_{\mathrm{Q},k}(t))\eta^j_{\mathrm{M}_1,k}(t)/\upsilon^j_k(t)\Big)\,t^j_k, \\ \dot\eta^j_{\mathrm{M}_2,k}(t) =& \Big(F^j_{in1,k}(t)\,x^j_{\mathrm{M}_2,in1,k} + F^j_{in2,k}(t)\,x^j_{\mathrm{M}_2,in2,k}(t) - F^j_{out,k}(t)\,x^j_{\mathrm{M}_2,k}(t) \\ & -(k^j_{p22,k}(t)\,\eta^j_{\mathrm{Q},k}(t) + k^j_{p12,k}(t)\,\eta^j_{\mathrm{P},k}(t))\eta^j_{\mathrm{M}_2,k}(t)/\upsilon^j_k(t)\Big)\,t^j_k, \\ \dot\eta^j_{\mathrm{S},k}(t) =& \Big(F^j_{in1,k}(t)\,x^j_{\mathrm{S},in1,k} + F^j_{in2,k}(t)\,x^j_{\mathrm{S},in2,k}(t) - F^j_{out,k}(t)\,x^j_{\mathrm{S},k}(t)\Big)\,t^j_k, \\ \dot\theta^j_k(t) =& \Big(\tfrac{F^j_{in1,k}(t)}{\upsilon^j_k(t)}(\theta^j_{in1,k}-\theta^j_k(t)) + \tfrac{F^j_{in2,k}(t)}{\upsilon^j_k(t)}(\theta^j_{in2,k}-\theta^j_k(t)) \\ & +\tfrac{\triangle H^j_k(t)\,RX^j_k(t)}{\rho^j\,c^j_p} - \tfrac{h_c A_c}{\rho^j\,c^j_p}(\theta^j_k(t)-\theta^j_{cool,k}(t))\Big)\,t^j_k, \\ \dot\eta^j_{\mathrm{P},k}(t) =& \Big(k^j_{d,k}(t)\,\eta^j_{\mathrm{I},k}(t) + k^j_{p21,k}(t)\tfrac{\eta^j_{\mathrm{M}_1,k}(t)\eta^j_{\mathrm{Q},k}(t)}{\upsilon^j_k(t)} - k^j_{p12,k}(t)\tfrac{\eta^j_{\mathrm{M}_2,k}(t)\eta^j_{\mathrm{P},k}(t)}{\upsilon^j_k(t)} \\ & -k^j_{tc11,k}(t)\,\tfrac{(\eta^j_{\mathrm{P},k}(t))^2}{\upsilon^j_k(t)} - k^j_{tc12,k}(t)\tfrac{\eta^j_{\mathrm{P},k}(t)\eta^j_{\mathrm{Q},k}(t)}{\upsilon^j_k(t)} - F^j_{out,k}(t)\,x^j_{\mathrm{P},k}(t)\Big)\,t^j_k, \\ \dot\eta^j_{\mathrm{Q},k}(t) =& \Big(k^j_{d,k}(t)\,\eta^j_{\mathrm{I},k}(t) + k^j_{p12,k}(t)\tfrac{\eta^j_{\mathrm{M}_2,k}(t)\eta^j_{\mathrm{P},k}(t)}{\upsilon^j_k(t)} - k^j_{p21,k}(t)\tfrac{\eta^j_{\mathrm{M}_1,k}(t)\eta^j_{\mathrm{Q},k}(t)}{\upsilon^j_k(t)} \\ & -k^j_{tc22,k}(t)\tfrac{(\eta^j_{\mathrm{Q},k}(t))^2}{\upsilon^j_k(t)} - k^j_{tc12,k}(t)\tfrac{\eta^j_{\mathrm{P},k}(t)\eta^j_{\mathrm{Q},k}(t)}{\upsilon^j_k(t)} - F^j_{out,k}(t)\,x^j_{\mathrm{P},k}(t)\Big)\,t^j_k, \end{aligned} \\ k^j_{r,k}(t) = k^j_{0,r}exp^{-E^j_{a,r}/R\,\theta^j_k(t)},\ \forall r\in\{d,pii',tcii'\}, i,i'=1,2, \\ x^j_{c,k}(t) = \eta^j_{c,k}(t)/\textstyle\sum_{c'}(\eta^j_{c',k}(t)),\ \forall c\in\{\mathrm{I},\mathrm{M}_1,\mathrm{M}_2,\mathrm{S},\mathrm{P},\mathrm{Q}\}, \\ \chi^j_{c,k}(t)=\eta^{j,0}_{c,1}-\eta^j_{c,k}(t)+\sum_{k'=1}^{k-1}\int_0^1(F^j_{in1,k'}(t)x^j_{c,in1,k'}(t)+F^j_{in2,k'}(t)x^j_{c,in2,k'}(t)-F^j_{out,k'}(t)x^j_{c,k'}(t))t^j_{k'}dt \\ +\int_0^t(F^j_{in1,k}(t)c^j_{c,in1,k}(t)+F^j_{in2,k}(t)c^j_{c,in2,k}(t)-F^j_{out,k}(t)c^j_{c,k}(t))t^j_k dt,\quad c\in\{\mathrm{M}_1,\mathrm{M}_2\}, \\ \upsilon^j_k(t)=\eta^j_{\mathrm{M}_1,k}(t)\tfrac{MW_{\mathrm{M}_1}}{\rho_{\mathrm{M}_1}}+\eta^j_{\mathrm{M}_2,k}(t)\tfrac{MW_{\mathrm{M}_2}}{\rho_{\mathrm{M}_2}}+\eta^j_{\mathrm{I},k}(t)\tfrac{MW_{\mathrm{I}}}{\rho_{\mathrm{I}}}+\chi^j_{\mathrm{M}_1,k}(t)\tfrac{MW_{\mathrm{P}_1}}{\rho_{\mathrm{P}_1}}+\chi^j_{\mathrm{M}_2,k}(t)\tfrac{MW_{\mathrm{P}_2}}{\rho_{\mathrm{P}_2}}, \\ \triangle H^j_k(t) = \triangle h_{\mathrm{M}_1}F^j_{\mathrm{M}_1,k}(t) + \triangle h_{\mathrm{M}_2}(1-F^j_{\mathrm{M}_1,k}(t)), \\ Q^j_{cool,k}(t) = h_c\,A_c\,\upsilon^j_k(t)(\theta^j_k(t)-\theta^j_{cool,k}(t)) \\ F^j_{cool,k}(t) = Q^j_{cool}(t)/\rho_{cool}\,c_{p,cool}(\theta^j_{cool,k}(t)-\theta^j_{cool,0}) \\ RX^j_k(t) = \Big(k^j_{p11,k}(t)\,\eta^j_{\mathrm{P},k}(t)\,\eta^j_{\mathrm{M}_1,k}(t) + k^j_{p21,k}(t)\,\eta^j_{\mathrm{Q},k}(t)\,\eta^j_{\mathrm{M}_1,k}(t) \\ +k^j_{p22,k}(t)\,\eta^j_{\mathrm{Q},k}(t)\,\eta^j_{\mathrm{M}_2,k}(t) + k^j_{p12,k}(t)\,\eta^j_{\mathrm{P},k}(t)\,\eta^j_{\mathrm{M}_2,k}(t)\Big)/\upsilon^j_k(t), \\ F^j_{\mathrm{M}_1,k}(t) = \frac{r_1(\eta^j_{\mathrm{M}_1,k}(t))^2+\eta^j_{\mathrm{M}_1,k}(t)\,\eta^j_{\mathrm{M}_2,k}(t)}{r_1(\eta^j_{\mathrm{M}_1,k}(t))^2+2\,\eta^j_{\mathrm{M}_1,k}(t)\,\eta^j_{\mathrm{M}_2,k}(t)+r_2(\eta^j_{\mathrm{M}_2,k}(t))^2}, \\ t\in[0,1], k\in\{1,2,3\} \end{bmatrix}$$

$$\veebar \begin{bmatrix} \neg Y_j \\ \dot\eta^j_{c,k}(t) = 0, c\in\{\mathrm{M}_1,\mathrm{M}_2,\mathrm{I},\mathrm{S},\mathrm{P},\mathrm{Q}\},\ \dot\theta^j_k(t)=0, \\ k^j_{r,k}(t)=0, r\in\{d,pii',tcii'\}, i,i'=1,2,\ RX^j_k(t)=0,\ F^j_{\mathrm{M}_1,k}(t)=0, \\ x^j_{c,k}(t)=0, c\in\{\mathrm{I},\mathrm{M}_1,\mathrm{M}_2,\mathrm{S},\mathrm{P},\mathrm{Q}\},\ \chi^j_{c,k}(t)=0, c\in\{\mathrm{M}_1,\mathrm{M}_2\}, \\ \upsilon^j_k(t)=0,\ \triangle H^j_k(t)=0,\ Q^j_{cool,k}(t)=0,\ F^j_{cool,k}(t)=0, \\ t\in[0,1], k\in\{1,2,3\} \end{bmatrix}. \tag{C.11}$$

On the other, batch unit R_{12} is the copolymerization reactor where suspension polymerization takes place and is represented by:

$$
\left[\begin{array}{c}
Y_j \\
\dot{\eta}^j_{\mathrm{I},k}(t) = \Big(F^j_{in1,k}(t)\,x^j_{\mathrm{I},in1,k} + F^j_{in2,k}(t)\,x^j_{\mathrm{I},in2,k}(t) - F^j_{out,k}(t)\,x^j_{\mathrm{I},k}(t) - k^j_{d,k}(t)\,\eta^j_{\mathrm{I},k}(t)\Big)\,t^j_k, \\
\dot{\eta}^j_{\mathrm{M}_1,k}(t) = \Big(F^j_{in1,k}(t)\,x^j_{\mathrm{M}_1,in1,k} + F^j_{in2,k}(t)\,x^j_{\mathrm{M}_1,in2,k}(t) - F^j_{out,k}(t)\,x^j_{\mathrm{M}_1,k}(t) \\
-(k^j_{p11,k}(t)\,\eta^j_{\mathrm{P},k}(t) + k^j_{p21,k}(t)\,\eta^j_{\mathrm{Q},k}(t))\eta^j_{\mathrm{M}_1,I,k}(t)/\upsilon^j_{I,k}(t)\Big)\,t^j_k, \\
\dot{\eta}^j_{\mathrm{M}_2,k}(t) = \Big(F^j_{in1,k}(t)\,x^j_{\mathrm{M}_2,in1,k} + F^j_{in2,k}(t)\,x^j_{\mathrm{M}_2,in2,k}(t) - F^j_{out,k}(t)\,x^j_{\mathrm{M}_2,k}(t) \\
-(k^j_{p22,k}(t)\,\eta^j_{\mathrm{Q},k}(t) + k^j_{p12,k}(t)\,\eta^j_{\mathrm{P},k}(t))\eta^j_{\mathrm{M}_2,k}(t)/\upsilon^j_{I,k}(t)\Big)\,t^j_k, \\
\dot{\eta}^j_{\mathrm{S},k}(t) = \Big(F^j_{in1,k}(t)\,x^j_{\mathrm{S},in1,k} + F^j_{in2,k}(t)\,x^j_{\mathrm{S},in2,k}(t) - F^j_{out,k}(t)\,x^j_{\mathrm{S},k}(t)\Big)\,t^j_k, \\
\dot{\theta}^j_k(t) = \Big(\frac{F^j_{in1,k}(t)}{\upsilon^j_{I,k}(t)}(\theta^j_{in1,k}-\theta^j_k(t)) + \frac{F^j_{in2,k}(t)}{\upsilon^j_{I,k}(t)}(\theta^j_{in2,k}-\theta^j_k(t)) \\
+\frac{\triangle H^j_k(t)\,RX^j_k(t)}{\rho^j\,c^j_p} - \frac{h_c A_c}{\rho^j\,c^j_p}(\theta^j_k(t) - \theta^j_{cool,k}(t))\Big)\,t^j_k, \\
\dot{\eta}^j_{\mathrm{P},k}(t) = \Big(k^j_{d,k}(t)\,\eta^j_{\mathrm{I},k}(t) + k^j_{p21,k}(t)\frac{\eta^j_{\mathrm{M}_1,I,k}(t)\eta^j_{\mathrm{Q},k}(t)}{\upsilon^j_{I,k}(t)} - k^j_{p12,k}(t)\frac{\eta^j_{\mathrm{M}_2,k}(t)\eta^j_{\mathrm{P},k}(t)}{\upsilon^j_{I,k}(t)} \\
-k^j_{tc11,k}(t)\frac{(\eta^j_{\mathrm{P},k}(t))^2}{\upsilon^j_{I,k}(t)} - k^j_{tc12,k}(t)\frac{\eta^j_{\mathrm{P},k}(t)\eta^j_{\mathrm{Q},k}(t)}{\upsilon^j_{I,k}(t)} - F^j_{out,k}(t)\,x^j_{\mathrm{P},k}(t)\Big)\,t^j_k, \\
\dot{\eta}^j_{\mathrm{Q},k}(t) = \Big(k^j_{d,k}(t)\,\eta^j_{\mathrm{I},k}(t) + k^j_{p12,k}(t)\frac{\eta^j_{\mathrm{M}_2,k}(t)\eta^j_{\mathrm{P},k}(t)}{\upsilon^j_{I,k}(t)} - k^j_{p21,k}(t)\frac{\eta^j_{\mathrm{M}_1,I,k}(t)\eta^j_{\mathrm{Q},k}(t)}{\upsilon^j_{I,k}(t)} \\
-k^j_{tc22,k}(t)\frac{(\eta^j_{\mathrm{Q},k}(t))^2}{\upsilon^j_{I,k}(t)} - k^j_{tc12,k}(t)\frac{\eta^j_{\mathrm{P},k}(t)\eta^j_{\mathrm{Q},k}(t)}{\upsilon^j_{I,k}(t)} - F^j_{out,k}(t)\,x^j_{\mathrm{P},k}(t)\Big)\,t^j_k, \\
k^j_{r,k}(t) = k^j_{0,r}exp^{-E^j_{a,r}/R\,\theta^j_k(t)},\ \forall r \in \{d, pii', tcii'\}, i, i' = 1, 2, \\
x^j_{c,k}(t) = \eta^j_{c,k}(t)/\sum_{c'}(\eta^j_{c',k}(t)),\ \forall c \in \{\mathrm{I}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{S}, \mathrm{P}, \mathrm{Q}\}, \\
\chi^j_{c,k}(t) = \eta^{j,0}_{c,1} - \eta^j_{c,k}(t) + \sum_{k'=1}^{k-1}\int_0^1 (F^j_{in1,k'}(t)x^j_{c,in1,k'}(t) + F^j_{in2,k'}(t)x^j_{c,in2,k'}(t) - F^j_{out,k'}(t)x^j_{c,k'}(t))t^j_{k'}dt \\
+\int_0^t (F^j_{in1,k}(t)c^j_{c,in1,k}(t) + F^j_{in2,k}(t)c^j_{c,in2,k}(t) - F^j_{out,k}(t)c^j_{c,k}(t))t^j_k dt,\ \ c \in \{\mathrm{M}_1, \mathrm{M}_2\}, \\
\upsilon^j_{I,k}(t) = \eta^j_{\mathrm{M}_1,I,k}(t)\frac{MW_{\mathrm{M}_1}}{\rho_{\mathrm{M}_1}} + \eta^j_{\mathrm{M}_2,k}(t)\frac{MW_{\mathrm{M}_2}}{\rho_{\mathrm{M}_2}} + \eta^j_{\mathrm{I},k}(t)\frac{MW_{\mathrm{I}}}{\rho_{\mathrm{I}}} + \chi^j_{\mathrm{M}_1,k}(t)\frac{MW_{\mathrm{P}_1}}{\rho_{\mathrm{P}_1}} + \chi^j_{\mathrm{M}_2,k}(t)\frac{MW_{\mathrm{P}_2}}{\rho_{\mathrm{P}_2}}, \\
\upsilon^j_{II,k}(t) = \upsilon^j_k(t) - \upsilon^j_{I,k}(t), \\
\triangle H^j_k(t) = \triangle h_{\mathrm{M}_1} F^j_{\mathrm{M}_1,k}(t) + \triangle h_{\mathrm{M}_2}(1 - F^j_{\mathrm{M}_1,k}(t)), \\
Q^j_{cool,k}(t) = h_c\,A_c\,\upsilon^j_k(t)(\theta^j_k(t) - \theta^j_{cool,k}(t)) \\
F^j_{cool,k}(t) = Q^j_{cool}(t)/\rho_{cool}\,c_{p,cool}(\theta^j_{cool,k}(t) - \theta^j_{cool,0}) \\
RX^j_k(t) = \Big(k^j_{p11,k}(t)\,\eta^j_{\mathrm{P},k}(t)\,\eta^j_{\mathrm{M}_1,I,k}(t) + k^j_{p21,k}(t)\,\eta^j_{\mathrm{Q},k}(t)\,\eta^j_{\mathrm{M}_1,I,k}(t) \\
+k^j_{p22,k}(t)\,\eta^j_{\mathrm{Q},k}(t)\,\eta^j_{\mathrm{M}_2,k}(t) + k^j_{p12,k}(t)\,\eta^j_{\mathrm{P},k}(t)\,\eta^j_{\mathrm{M}_2,k}(t)\Big)/\upsilon^j_{I,k}(t), \\
F^j_{\mathrm{M}_1,k}(t) = \frac{r_1(\eta^j_{\mathrm{M}_1,I,k}(t))^2 + \eta^j_{\mathrm{M}_1,I,k}(t)\,\eta^j_{\mathrm{M}_2,k}(t)}{r_1(\eta^j_{\mathrm{M}_1,I,k}(t))^2 + 2\,\eta^j_{\mathrm{M}_1,I,k}(t)\,\eta^j_{\mathrm{M}_2,k}(t) + r_2(\eta^j_{\mathrm{M}_2,k}(t))^2}, \\
\text{AN equilibrium: } 1/\varphi^j_k(t) = a\,exp\left(b\left(\eta^j_{\mathrm{M}_1,II}(t)/\upsilon^j_{II,k}(t)\right)\right)\frac{\upsilon^j_{I,k}(t)}{\upsilon^j_{II,k}(t)}, \\
\eta^j_{\mathrm{M}_1,I,k}(t) = \eta^j_{\mathrm{M}_1,k}(t)\frac{1/\varphi^j_k(t)}{1+1/\varphi^j_k(t)},\ \ \eta^j_{\mathrm{M}_1,II,k}(t) = \eta^j_{\mathrm{M}_1,k}(t) - \eta^j_{\mathrm{M}_1,I,k}(t), \\
t \in [0,1], k \in \{1,2,3\}
\end{array}\right]
$$

$$
\veebar \left[\begin{array}{c}
\neg Y_j \\
\dot{\eta}^j_{c,k}(t) = 0, c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}, \mathrm{P}, \mathrm{Q}\},\ \dot{\theta}^j_k(t) = 0, \\
k^j_{r,k}(t) = 0, r \in \{d, pii', tcii'\}, i, i' = 1, 2,\ RX^j_k(t) = 0,\ F^j_{\mathrm{M}_1,k}(t) = 0, \\
x^j_{c,k}(t) = 0, c \in \{\mathrm{I}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{S}, \mathrm{P}, \mathrm{Q}\},\ \chi^j_{c,k}(t) = 0, c \in \{\mathrm{M}_1, \mathrm{M}_2\}, \\
\upsilon^j_{I,k}(t) = 0,\ \upsilon^j_{II,k}(t) = 0,\ \eta^j_{\mathrm{M}_1,I,k}(t) = 0,\ \eta^j_{\mathrm{M}_1,II,k}(t) = 0, \\
\triangle H^j_k(t) = 0,\ Q^j_{cool,k}(t) = 0,\ F^j_{cool,k}(t) = 0, \\
t \in [0,1], k \in \{1,2,3\}
\end{array}\right]. \qquad \text{(C.12)}
$$

The total consumption of raw materials and solvent $c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}$ in copolymerization reaction stage 1 is calculated from the material inputs in each potential equipment unit $j \in \{R_{11}, R_{12}\}$ as follows:

$$\begin{bmatrix} Y_j \\ Cons_c^j = \eta_{c,1}^{j,0} + \sum_{k=1}^{3} \int_0^1 \Big(F_{in1,k}^j(t) x_{c,in1,k}^j(t) + \\ F_{in2,k}^j(t) x_{c,in2,k}^j(t) \Big) \, t_k^j \, dt, \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ Cons_c^j = 0 \end{bmatrix}, \quad c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}. \tag{C.13}$$

Apart from the costs of raw material consumption defined in Eq. C.8, copolymerization stage also involves: (i) amortization costs $Cost_{j,a}$ associated to the purchase of the polymerization reactors and (ii) processing costs $Cost_{j,p}$ associated to the consumption of cooling water for the energy balance. These costs are defined for each potential equipment unit $j \in \{R_{11}, R_{12}\}$ as follows:

$$\begin{bmatrix} \neg Y_j \\ Size^j = 0 \end{bmatrix}, \tag{C.14}$$

$$Cost_{j,a} = \check{c}_j (Size^j / Size^0)^n \sum_{k=1}^{3} t_k^j, \tag{C.15}$$

$$\begin{bmatrix} Y_j \\ Cost_{j,p} = \hat{c}_{j,cool} \sum_{k=1}^{3} \int_0^1 \Big(F_{cool,k}^j(t) \; \rho_{cool} \Big) \, t_k^j \; dt \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ Cost_{j,p} = 0 \end{bmatrix}. \tag{C.16}$$

The operation is also subject to the following constraints in reactors $j \in \{R_{11}, R_{12}\}$:

$$\begin{bmatrix} Y_j \\ x_{c,in1,k}^j = 0, \;\; c \in \{\mathrm{M}_2, \mathrm{I}, \}, k \in \{2,3\} \\ \theta^{\mathrm{L}} \le \theta_k^j(t) \ge \theta^{\mathrm{U}}, \;\; t \in [0,1], k \in \{1,2,3\}, \\ \theta_{cool,k}^j(t) \le \theta_k^j(t), \;\; t \in [0,1], k \in \{1,2,3\}, \\ F^{j,\mathrm{L}} \le F_{in1,k}^j(t) \le F^{j,\mathrm{U}}, \;\; t \in [0,1], k \in \{1\}, \\ F_{in1,k}^j(t) = 0, \;\; t \in [0,1], k \in \{3\}, \\ F^{j,\mathrm{L}} \le F_{in1,k}^j(t) \le 0.05 \, F^{j,\mathrm{U}}, \;\; t \in [0,1], k \in \{2\}, \\ F^{j,\mathrm{L}} \le F_{in2,k}^j(t) \le F^{j,\mathrm{U}}, \;\; t \in [0,1], k \in \{1\}, \\ F_{in2,k}^j(t) = 0, \;\; t \in [0,1], k \in \{2,3\}, \\ F^{j,\mathrm{L}} \le F_{out,k}^j(t) \le F^{j,\mathrm{U}}, \;\; t \in [0,1], k \in \{3\}, \\ F_{out,k}^j(t) = 0, \;\; t \in [0,1], k \in \{1,2\}, \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ x_{c,in1,k}^j = 0, c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{I}\}, \forall k, \\ \theta_k^j(t) = 0, \;\; t \in [0,1], \forall k \\ F_{m,k}^j(t) = 0, \;\; t \in [0,1], \forall k \\ m \in \{in1, in2, out\}, \\ t_k^j = 0, \; \forall k \end{bmatrix} \tag{C.17}$$

The definition of the parameters that depend on the technology and solvent selection in polymerization reactors $j \in \{R_{11}, R_{12}\}$ are controlled through the disjunction:

$$\begin{bmatrix} V_{solu}^j \\ \begin{bmatrix} S_{\mathrm{DMF}}^j \\ \rho^j = \rho_{\mathrm{DMF}}, \\ c_p^j = c_{p,\mathrm{DMF}}, \\ MW_{\mathrm{S}}^j = MW_{\mathrm{DMF}}, \\ \hat{p}_{\mathrm{S}}^j = \hat{p}_{\mathrm{DMF}}, \\ k_{0,r}^j = k_{0,r,\mathrm{DMF}}, \\ E_{a,r}^j = E_{a,r,\mathrm{DMF}}, \\ r \in \{d, pii', tcii'\}, i, i' = 1,2 \end{bmatrix} \veebar \begin{bmatrix} S_{\mathrm{NaSCN(aq)}}^j \\ \rho^j = \rho_{\mathrm{NaSCN(aq)}}, \\ c_p^j = c_{p,\mathrm{NaSCN(aq)}}, \\ MW_{\mathrm{S}}^j = MW_{\mathrm{NaSCN(aq)}}, \\ \hat{p}_{\mathrm{S}}^j = \hat{p}_{\mathrm{NaSCN(aq)}}, \\ k_{0,r}^j = k_{0,r,\mathrm{NaSCN(aq)}}, \\ E_{a,r}^j = E_{a,r,\mathrm{NaSCN(aq)}}, \\ r \in \{d, pii', tcii'\}, i, i' = 1,2 \end{bmatrix} \end{bmatrix} \veebar \begin{bmatrix} V_{susp}^j \\ \rho^j = \rho_{\mathrm{H_2O}}, \\ c_p^j = c_{p,\mathrm{H_2O}}, \\ MW_{\mathrm{S}}^j = MW_{\mathrm{H_2O}}, \\ \hat{p}_{\mathrm{S}}^j = \hat{p}_{\mathrm{H_2O}}, \\ k_{0,r}^j = k_{0,r,\mathrm{H_2O}}, \\ E_{a,r}^j = E_{a,r,\mathrm{H_2O}}, \\ r \in \{d, pii', tcii'\}, i, i' = 1,2 \end{bmatrix}. \tag{C.18}$$

Separation in batch evaporation unit

The following disjunctions define the multistage model of batch evaporator $j \in \{E_2\}$ and correspond to Eqs. 3.5 and 3.6 of the formulation proposed in § 3.3:

$$\begin{bmatrix} Y_j \\ \dot{H}^j_k(t) = \Big(F^j_{F,k}(t) - F^j_{L,k}(t) - F^j_{V,k}(t)\Big)\, t^j_k, \\ \dot{\eta}^j_{\mathrm{Co},k}(t) = \Big(F^j_{F,k}(t)\, z^j_{\mathrm{Co},F,k}(t) - F^j_{L,k}(t)\, x^j_{\mathrm{Co},k}(t) - F^j_{V,k}(t)\, y^j_{\mathrm{Co},k}(t)\Big)\, t^j_k, \\ \dot{\eta}^j_{\mathrm{M_1},k}(t) = \Big(F^j_{F,k}(t)\, z^j_{\mathrm{M_1},F,k}(t) - F^j_{L,k}(t)\, x^j_{\mathrm{M_1},k}(t) - F^j_{V,k}(t)\, y^j_{\mathrm{M_1},k}(t)\Big)\, t^j_k, \\ \dot{\eta}^j_{\mathrm{M_2},k}(t) = \Big(F^j_{F,k}(t)\, z^j_{\mathrm{M_2},F,k}(t) - F^j_{L,k}(t)\, x^j_{\mathrm{M_2},k}(t) - F^j_{V,k}(t)\, y^j_{\mathrm{M_2},k}(t)\Big)\, t^j_k, \\ \dot{\eta}^j_{\mathrm{S},k}(t) = \Big(F^j_{F,k}(t)\, z^j_{\mathrm{S},F,k}(t) - F^j_{L,k}(t)\, x^j_{\mathrm{S},k}(t) - F^j_{V,k}(t)\, y^j_{\mathrm{S},k}(t)\Big)\, t^j_k, \\ \eta^j_{\mathrm{I},k}(t) = H^j_k(t) - \eta^j_{\mathrm{Co},k}(t) - \eta^j_{\mathrm{M_1},k}(t) - \eta^j_{\mathrm{M_2},k}(t) - \eta^j_{\mathrm{S},k}(t), \\ log_{10}(p^j_{v,c,k}(t)) = A_c - \frac{B_c}{(\theta^j_k(t) + C_c)},\, c \in \{\mathrm{M_1}, \mathrm{M_2}\}, \\ log_{10}(p^j_{v,\mathrm{S},k}(t)) = A^j_{\mathrm{S}} - \frac{B^j_{\mathrm{S}}}{(\theta^j_k(t) + C^j_{\mathrm{S}})}, \\ x^j_{c,k}(t) = \eta^j_{c,k}(t)/H^j_k(t),\ c \in \{\mathrm{Co}, \mathrm{M_1}, \mathrm{M_2}, \mathrm{I}, \mathrm{S}\}, \\ y^j_{c,k}(t) = x^j_{c,k}(t)\, p^j_{v,c,k}(t)/P^j_{total},\ c \in \{\mathrm{M_1}, \mathrm{M_2}, \mathrm{S}\}, \\ y^j_{c,k}(t) = x^j_{c,k}(t)\, p_{v,c}/P^j_{total},\ c \in \{\mathrm{Co}, \mathrm{I}\}, \\ 1 = \sum_{c \in \{\mathrm{Co},\mathrm{M_1},\mathrm{M_2},\mathrm{I},\mathrm{S}\}} y^j_{c,k}(t), \\ log(h^j_{v,c,k}(t)\, 4.1868\, kJ/kcal) = log(A_{h,c}) + log(1 - \frac{\theta^j_k(t) - 273}{\theta c_c - 273}) B_{h,c},\ c \in \{\mathrm{M_1}, \mathrm{M_2}\}, \\ log(h^j_{v,\mathrm{S},k}(t)\, 4.1868\, kJ/kcal) = log(A^j_{h,\mathrm{S}}) + log(1 - \frac{\theta^j_k(t) - 273}{\theta c^j_{\mathrm{S}} - 273}) B^j_{h,\mathrm{S}}, \\ \triangle h^j_{v,k}(t) = \sum_{c \in \{\mathrm{M_1},\mathrm{M_2},\mathrm{S}\}} h^j_{v,c,k}(t)\, y^j_{c,k}(t), \\ Q^j_{heat,k}(t) = F^j_{V,k}(t)\, \triangle h^j_{v,k}(t), \\ t \in [0,1], k \in \{1, ..., 4\}, \\ Waste^j = P_{waste}/100 \sum_{k=1}^{4} \int_0^1 F^j_{F,k}(t) t^j_k\, dt \end{bmatrix}$$

$$\veebar \begin{bmatrix} \neg Y_j \\ \dot{H}^j_k(t) = 0,\ \dot{\eta}^j_{c,k}(t) = 0, c \in \{\mathrm{Co}, \mathrm{M_1}, \mathrm{M_2}, \mathrm{I}, \mathrm{S}\}, \\ p^j_{v,c,k}(t) = 0, c \in \{\mathrm{M_1}, \mathrm{M_2}, \mathrm{S}\},\ h^j_{v,c,k}(t) = 0, c \in \{\mathrm{M_1}, \mathrm{M_2}, \mathrm{S}\}, \\ x^j_{c,k}(t) = 0, c \in \{\mathrm{Co}, \mathrm{M_1}, \mathrm{M_2}, \mathrm{I}, \mathrm{S}\},\ y^j_{c,k}(t) = 0, c \in \{\mathrm{Co}, \mathrm{M_1}, \mathrm{M_2}, \mathrm{I}, \mathrm{S}\}, \\ \triangle h^j_{v,k}(t) = 0,\ Q^j_{heat,k}(t) = 0, \\ t \in [0,1], k \in \{1, ..., 4\}, \\ Waste^j = 0 \end{bmatrix}. \quad \text{(C.19)}$$

The computation of the vapor pressure and heat of vaporization of the solvent or suspension media is subject to the technology and solvent selected in the copolymerization stage. To accomplish this, the value of parameters A^j_{S}, B^j_{S}, C^j_{S}, $A^j_{h,\mathrm{S}}$, $B^j_{h,\mathrm{S}}$, and θc^j_{S} in the evaporator $j \in \{E_2\}$ is defined as a function of Booleans $V^{j'}_{\lambda}$ and $S^{j'}_{c}$ in the reactors $j' \in \{R_{11}, R_{12}\}$ by means of:

$$\begin{bmatrix} V^{j'}_{solu} \\ \begin{bmatrix} S^{j'}_{\mathrm{DMF}} \\ A^j_{\mathrm{S}} = A_{\mathrm{DMF}}, \\ B^j_{\mathrm{S}} = B_{\mathrm{DMF}}, \\ C^j_{\mathrm{S}} = C_{\mathrm{DMF}}, \\ A^j_{h,\mathrm{S}} = A_{h,\mathrm{DMF}}, \\ B^j_{h,\mathrm{S}} = B_{h,\mathrm{DMF}}, \\ \theta c^j_{\mathrm{S}} = \theta c_{\mathrm{DMF}} \end{bmatrix} \veebar \begin{bmatrix} S^{j'}_{\mathrm{NaSCN(aq)}} \\ A^j_{\mathrm{S}} = A_{\mathrm{NaSCN(aq)}}, \\ B^j_{\mathrm{S}} = B_{\mathrm{NaSCN(aq)}}, \\ C^j_{\mathrm{S}} = C_{\mathrm{NaSCN(aq)}}, \\ A^j_{h,\mathrm{S}} = A_{h,\mathrm{NaSCN(aq)}}, \\ B^j_{h,\mathrm{S}} = B_{h,\mathrm{NaSCN(aq)}}, \\ \theta c^j_{\mathrm{S}} = \theta c_{\mathrm{NaSCN(aq)}} \end{bmatrix} \end{bmatrix} \vee \begin{bmatrix} V^{j'}_{susp} \\ A^j_{\mathrm{S}} = A_{\mathrm{H_2O}}, \\ B^j_{\mathrm{S}} = B_{\mathrm{H_2O}}, \\ C^j_{\mathrm{S}} = C_{\mathrm{H_2O}}, \\ A^j_{h,\mathrm{S}} = A_{h,\mathrm{H_2O}}, \\ B^j_{h,\mathrm{S}} = B_{h,\mathrm{H_2O}}, \\ \theta c^j_{\mathrm{S}} = \theta c_{\mathrm{H_2O}} \end{bmatrix}, j' \in \{R_{11}, R_{12}\}. \quad \text{(C.20)}$$

The separation stage involves the following economic weights: (i) amortization costs $Cost_{j,a}$ associated to the purchase of the evaporator and (ii) processing costs $Cost_{j,p}$

associated to the consumption of heating in the boiler. These costs are defined for the potential equipment unit $j \in \{E_2\}$ as follows:

$$\begin{bmatrix} \neg Y_j \\ Size^j = 0 \end{bmatrix}, \tag{C.21}$$

$$Cost_{j,a} = \check{c}_j (Size^j/Size^0)^n \sum_{k=1}^{4} t_k^j, \tag{C.22}$$

$$\begin{bmatrix} Y_j \\ Cost_{j,p} = \hat{c}_{j,heat} \sum_{k=1}^{4} \int_0^1 Q_{heat,k}^j(t)\, t_k^j\, dt \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ Cost_{j,p} = 0 \end{bmatrix}. \tag{C.23}$$

The operation is also subject to the following constraints in the evaporator $j \in \{E_2\}$:

$$\begin{bmatrix} Y_j \\ Q^{\mathrm{L}} \leq Q_{heat,k}^j(t) \leq Q^{\mathrm{U}},\;\; t \in [0,1], \forall\{2,3\} \\ Q^j heat, k(t) = 0,\;\; t \in [0,1], \forall\{1,4\} \\ F^{j,\mathrm{L}} \leq F_{F,k}^j(t) \leq F^{j,\mathrm{U}},\; t \in [0,1], k \in \{1\}, \\ F_{F,k}^j(t) = 0,\; t \in [0,1], k \in \{2,...4\}, \\ F^{j,\mathrm{L}} \leq F_{V,k}^j(t) + F_{L,k}^j(t) \leq F^{j,\mathrm{U}},\; t \in [0,1], k \in \{2,3,4\}, \\ F_{V,k}^j(t) = 0,\; t \in [0,1], k \in \{1,4\}, \\ F_{L,k}^j(t) = 0,\; t \in [0,1], k \in \{1,2\} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ Q_{heat,k}^j(t) = 0,\; t \in [0,1], \forall k \\ F_{m,k}^j(t) = 0,\; t \in [0,1], \forall k, \\ m \in \{F, V, L\} \\ t_k^j = 0,\; \forall k \end{bmatrix}. \tag{C.24}$$

C.3.3 Plant elements at Level 0

Buffer tanks

The following equations define the multistage models of the semi-continuous storage units $j \in \{T_2, T_4\}$, which correspond to Eq. 3.28 of the formulation proposed in § 3.3.

$$\begin{bmatrix} Y_j \\ \dot{H}_l^j(t) = \left(F_{in,l}^j(t) - F_{out,l}^j(t)\right) t_l, \\ \dot{\eta}_{c,l}^j(t) = \left(F_{in,l}^j(t)\, x_{c,in,l}^j(t) - F_{out,l}^j(t)\, x_{c,l}^j(t)\right) t_l,\; c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{S}\}, \\ \eta_{\mathrm{I},l}^j(t) = H_l^j(t) - \sum_{c \in \{\mathrm{Co},\mathrm{M}_1,\mathrm{M}_2,\mathrm{S}\}} \eta_{c,l}^j(t), \\ x_{c,l}^j(t) = \eta_{c,l}^j(t)/H_l^j(t),\;\; c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{S}\}, \\ x_{\mathrm{I},l}^j(t) = 1 - \sum_{c \in \{\mathrm{Co},\mathrm{M}_1,\mathrm{M}_2,\mathrm{S}\}} x_{c,l}^j(t), \\ t \in [0,1], l \in \{1, ..., 6\} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ \dot{H}_l^j(t) = 0, \dot{\eta}_{c,l}^j(t) = 0, c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}, \\ x_{c,l}^j(t) = 0, c \in \{\mathrm{Co}, \mathrm{M}_1, \mathrm{M}_2, \mathrm{I}, \mathrm{S}\}, \\ t \in [0,1], l \in \{1, ..., 6\} \end{bmatrix}, \tag{C.25}$$

where Y_{T_4} is always $true$ since T_4 is a mandatory item whereas Y_{T_2} can be $true$ or $false$, depending on the selection of recirculating the distillate from the evaporator E_2 or not. In fact, the particular function of tank T_2 is reducing the raw material consumption. This is because this tank, if it is installed, has the function of supplying to reaction stage 1 the unreacted monomers M_1 and M_2 and recovered solvent or suspension medium S that comes from separation stage 2. These saving in raw material requirements is quantified in Eq. C.8 through a negative consumption in this tank. This is calculated for $j \in \{T_2\}$ as follows:

$$\begin{bmatrix} Y_j \\ Cons_c^j = -\sum_{l=1}^{6} \int_0^1 F_{out,l}^j(t)\, x_{c,l}^j(t)\, t_l\, dt \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ Cons_c^j = 0 \end{bmatrix},\;\; c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{S}\}. \tag{C.26}$$

In order to facilitate the convergence in the optimization procedure, the following redundant equation is incorporated into the optimization model:

$$\left[\begin{array}{c} Y_{T_2} \\ \sum\limits_{j'\in\{R_{11},\ R_{12}\}} Cons_c^{j'} \geq -Cons_c^{T_2} \end{array}\right], \quad c \in \{\mathrm{M}_1, \mathrm{M}_2, \mathrm{S}\}. \tag{C.27}$$

The acquisition of storage tanks $j \in \{T_2, T_4\}$ also involve the economic expenses associated to their amortization $Cost_{j,a}$. This is calculated like the abovementioned amortization costs for the polymerization reactors and the evaporator:

$$\left[\begin{array}{c} \neg Y_j \\ Size^j = 0 \end{array}\right], \tag{C.28}$$

$$Cost_{j,a} = \check{c}_j (Size^j/Size^0)^n \sum_{l=1}^{6} t_k^j. \tag{C.29}$$

Balance in mixers and splitters

The flow sheet model involves mass balances in mixers and splitters. According to the scheme of Figure C.2, global mass balances in connecting units $j \in Mx \cup Sp$ are defined by:

$$\begin{array}{rl} F_{6,l}(t) + F_{7,l}(t) = F_{8,l}(t), & t \in [0,1], l \in \{1,...,6\}, \\ F_{14,l}(t) + F_{15,l}(t) = F_{16,l}(t), & t \in [0,1], l \in \{1,...,6\}, \\ F_{1,l}(t) = F_{2,l}(t) + F_{3,l}(t), & t \in [0,1], l \in \{1,...,6\}, \\ F_{13,l}(t) = F_{4,l}(t) + F_{5,l}(t), & t \in [0,1], l \in \{1,...,6\}, \\ F_{8,l}(t) = F_{9,l}(t) + F_{14,l}(t), & t \in [0,1], l \in \{1,...,6\}, \\ F_{10,l}(t) = F_{11,l}(t) + F_{12,l}(t), & t \in [0,1], l \in \{1,...,6\}, \end{array} \tag{C.30}$$

and component balances are defined by:

$$\begin{array}{r} F_{6,l}(t)x_{c,6,l}(t) + F_{7,l}(t)x_{c,7,l}(t) = F_{8,l}(t)x_{c,8,l}(t), t{\in}[0,1], c{\in}\{\mathrm{M}_1,\mathrm{M}_2,\mathrm{I},\mathrm{S},\mathrm{Co}\}, l{\in}\{1,...,6\}, \\ F_{14,l}(t)x_{c,14,l}(t) + F_{15,l}(t)x_{c,15,l}(t) = F_{16,l}(t)x_{c,16,l}(t), t{\in}[0,1], c{\in}\{\mathrm{M}_1,\mathrm{M}_2,\mathrm{I},\mathrm{S},\mathrm{Co}\}, l{\in}\{1,...,6\}, \\ x_{c,1,l}(t) = x_{c,n,l}(t), \quad t \in [0,1], c \in \{\mathrm{M}_1,\mathrm{M}_2,\mathrm{I},\mathrm{S},\mathrm{Co}\}, n \in \{2,3\}, l \in \{1,...,6\}, \\ x_{c,13,l}(t) = x_{c,n,l}(t), \quad t \in [0,1], c \in \{\mathrm{M}_1,\mathrm{M}_2,\mathrm{I},\mathrm{S},\mathrm{Co}\}, n \in \{4,5\}, l \in \{1,...,6\}, \\ x_{c,8,l}(t) = x_{c,n,l}(t), \quad t \in [0,1], c \in \{\mathrm{M}_1,\mathrm{M}_2,\mathrm{I},\mathrm{S},\mathrm{Co}\}, n \in \{9,14\}, l \in \{1,...,6\}, \\ x_{c,10,l}(t) = x_{c,n,l}(t), \quad t \in [0,1], c \in \{\mathrm{M}_1,\mathrm{M}_2,\mathrm{I},\mathrm{S},\mathrm{Co}\}, n \in \{11,12\}, l \in \{1,...,6\}. \end{array} \tag{C.31}$$

C.3.4 Synchronization

In this case study the synchronization is controlled by the unit selection. The reason is that the process stages included in this formulation are associated exclusively to one single unit configuration and do not require task-unit assignment Booleans. Therefore, the equations that detail the synchronization of flow rates, compositions, and batch phase duration of unit procedures in units $j \in \{R_{11}, R_{12}, E_2, T_2, T_4\}$ read as:

$$\left[\begin{array}{c} Y_{R_{11}} \\ t_l^{R_{11}} = t_l, \ l \in \{1,...,3\}, \\ F_{in1,l}^{R_{11}}(t) = F_{2,l}(t), \ x_{c,in1,l}^{R_{11}}(t) = x_{c,2,l}(t), \\ F_{in2,l}^{R_{11}}(t) = F_{4,l}(t), \ x_{c,in2,l}^{R_{11}}(t) = x_{c,4,l}(t), \\ F_{out,l}^{R_{11}}(t) = F_{6,l}(t), \ x_{c,l}^{R_{11}}(t) = x_{c,6,l}(t), \\ t \in [0,1], l \in \{1,...,3\}, \\ F_{n,l}(t) = 0, \ x_{c,n,l}(t) = 0, \ n \in \{2,4,6\}, \\ t \in [0,1], l \in \{4,...,6\} \end{array}\right] \veebar \left[\begin{array}{c} \neg Y_{R_{11}} \\ F_{n,l}(t) = 0, \ x_{c,n,l}(t) = 0, \\ n \in \{2,4,6\}, \\ t \in [0,1], l \in \{1,...,6\} \end{array}\right], \tag{C.32}$$

$$\begin{bmatrix} Y_{R_{12}} \\ t_l^{R_{12}} = t_l,\ l \in \{1,...,3\}, \\ F_{in1,l}^{R_{12}}(t) = F_{3,l}(t),\ x_{c,in1,l}^{R_{12}}(t) = x_{c,3,l}(t), \\ F_{in2,l}^{R_{12}}(t) = F_{5,l}(t),\ x_{c,in2,l}^{R_{12}}(t) = x_{c,5,l}(t), \\ F_{out,l}^{R_{12}}(t) = F_{7,l}(t),\ x_{c,l}^{R_{12}}(t) = x_{c,7,l}(t), \\ t \in [0,1], l \in \{1,...,3\}, \\ F_{n,l}(t) = 0,\ x_{c,n,l}(t) = 0,\ n \in \{3,5,7\}, \\ t \in [0,1], l \in \{4,...,6\} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_{R_{12}} \\ F_{n,l}(t) = 0,\ x_{c,n,l}(t) = 0, \\ n \in \{3,5,7\}, \\ t \in [0,1], l \in \{1,...,6\} \end{bmatrix}, \tag{C.33}$$

$$\begin{bmatrix} Y_{E_2} \\ t_{l-2}^{E_2} = t_l,\ l \in \{3,...,6\}, \\ F_{F,l-2}^{E_2}(t) = F_{9,l}(t),\ z_{c,F,l-2}^{E_2}(t) = x_{c,9,l}(t), \\ F_{V,l-2}^{E_2}(t) = F_{10,l}(t),\ y_{c,V,l-2}^{E_2}(t) = x_{c,10,l}(t), \\ F_{L,l-2}^{E_2}(t) = F_{15,l}(t),\ x_{c,L,l-2}^{E_2}(t) = x_{c,15,l}(t), \\ t \in [0,1], l \in \{3,...,6\}, \\ F_{n,l}(t) = 0,\ x_{c,n,l}(t) = 0,\ n \in \{9,10,15\}, \\ t \in [0,1], l \in \{1,2\} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_{E_2} \\ F_{n,l}(t) = 0,\ x_{c,n,l}(t) = 0, \\ n \in \{9,10,15\}, \\ t \in [0,1], l \in \{1,...,6\} \end{bmatrix}, \tag{C.34}$$

$$\begin{bmatrix} Y_{T_2} \\ t_{l-3}^{T_2} = t_l,\ l \in \{4,5\}, \\ F_{in,l-3}^{T_2}(t){=}F_{11,l}(t),\ x_{c,in,l-3}^{T_2}(t){=}x_{c,11,l}(t),\ t{\in}[0,1], l{\in}\{4,5\}, \\ F_{11,l}(t){=}0,\ x_{c,11,l}(t){=}0,\ t{\in}[0,1], l{\in}\{1,...,6\}\backslash\{4,5\}, \\ t_{l+2}^{T_2} = t_l,\ l \in \{1\}, \\ F_{out,l+2}^{T_2}(t){=}F_{13,l}(t),\ x_{c,l+2}^{T_2}(t){=}x_{c,13,l}(t),\ t{\in}[0,1], l{\in}\{1\}, \\ F_{13,l}(t){=}0,\ x_{c,13,l}(t){=}0,\ t{\in}[0,1], l{\in}\{1,...,6\}\backslash\{1\} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_{T_2} \\ F_{n,l}(t) = 0,\ x_{c,n,l}(t) = 0, \\ n \in \{11,13\}, \\ t \in [0,1], l \in \{1,...,6\} \end{bmatrix}, \tag{C.35}$$

$$\begin{bmatrix} Y_{T_4} \\ \begin{bmatrix} Y_{E_2} \\ t_{l-4}^{T_4} = t_l,\ l \in \{5,6\}, \\ F_{in,l-4}^{T_4}(t) = F_{16,l}(t), \\ x_{c,in,l-4}^{T_4}(t) = x_{c,16,l}(t), \\ t \in [0,1], l \in \{5,6\}, \\ F_{16,l}(t) = 0,\ x_{c,16,l}(t) = 0, \\ t \in [0,1], l \in \{1,...,4\} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_{E_2} \\ t_{l-2}^{T_4} = t_l,\ l \in \{3\}, \\ F_{in,l-2}^{T_4}(t) = F_{16,l}(t), \\ x_{c,in,l-2}^{T_4}(t) = x_{c,16,l}(t), \\ t \in [0,1], l \in \{3\}, \\ F_{16,l}(t) = 0,\ x_{c,16,l}(t) = 0, \\ t \in [0,1], l \in \{1,...,6\}\backslash\{3\} \end{bmatrix} \end{bmatrix} \veebar \begin{bmatrix} \neg Y_{T_4} \\ F_{16,l}(t) = 0,\ x_{c,16,l}(t) = 0, \\ t \in [0,1], l \in \{1,...,6\} \end{bmatrix}. \tag{C.36}$$

C.3.5 Logical propositions

The logical propositions considered in this case study to define the plant and process synthesis are:

1. The selection of solution ($V_{solu}^{R_{11}}$) or suspension ($V_{susp}^{R_{12}}$) copolymerization technologies and the corresponding reactors R_{11} ($Y_{R_{11}}$) or R_{12} ($Y_{R_{12}}$) is defined by:

$$\begin{gathered} V_{solu}^{R_{11}} \veebar V_{susp}^{R_{12}}, \\ V_{solu}^{R_{11}} \Leftrightarrow Y_{R_{11}}, \\ V_{susp}^{R_{12}} \Leftrightarrow Y_{R_{12}}. \end{gathered} \tag{C.37}$$

2. The selection of organic ($S^{R_{11}}_{\mathrm{DMF}}$) or aqueous ($S^{R_{11}}_{\mathrm{NaSCN(aq)}}$) solvent in solution copolymerization is determined by:

$$V^{R_{11}}_{solu} \Leftrightarrow S^{R_{11}}_{\mathrm{DMF}} \veebar S^{R_{11}}_{\mathrm{NaSCN(aq)}}. \tag{C.38}$$

3. The possibility of dismissing separation stage 2 ($\neg Z_2$) is conditioned by the selection of solution polymerization technology and by the achievement of a conversion in the solution copolimerization reactor ($\chi_{R_{11}}$) greater than the established minimum input conversion in repulping stage 4 (χ^{L}_4). This is represented by the following equations, which include the installation of the separation unit E_2 (Y_{E_2}):

$$\begin{aligned} \neg Z_2 \Rightarrow V^{R_{11}}_{solu} \wedge \left(\chi_{R_{11}} \geq \chi^{\mathrm{L}}_4\right), \\ Z_2 \Leftrightarrow Y_{E_2}. \end{aligned} \tag{C.39}$$

4. The recirculation of the solvent or the suspension medium recovered in separation stage 2 toward reaction stage 1 ($R_{2,1}$) is associated to the installation of buffer tank T_2 (Y_{T_2}) through the proposition:

$$R_{2,1} \Leftrightarrow Y_{T_2}. \tag{C.40}$$

5. The selection of washing and filtration stage 3 (Z_3) and corresponding equipment item F_3 (Y_{F_3}) is associated to the definition of previous separation task 2, and is represented by the following equations:

$$\begin{aligned} Z_2 \Leftrightarrow Z_3, \\ Z_3 \Leftrightarrow Y_{F_3}. \end{aligned} \tag{C.41}$$

6. The recirculation of the washing water in filtration stage 3 toward reaction stage 1 ($R_{3,1}$) is associated to the installation of buffer tank T_3 (Y_{T_3}) through the proposition:

$$R_{3,1} \Leftrightarrow Y_{T_3}. \tag{C.42}$$

7. The operating modes considered in process stage 7 include the use of one single unit F_{71} (X^7_α) or series configuration where unit F_{71} is followed by F_{72} (X^7_σ), and are formulated by:

$$\begin{aligned} X^7_\alpha \veebar X^7_\sigma, \\ X^7_\alpha \Leftrightarrow Y_{F_{71}}, \\ X^7_\sigma \Leftrightarrow Y_{F_{71}} \wedge Y_{F_{72}}. \end{aligned} \tag{C.43}$$

8. The operating modes considered in process stage 8 include the use of one single unit C_{81} (X^8_α) or series configuration where unit C_{81} is followed by C_{82} (X^8_σ), and are formulated by:

$$\begin{aligned} X^8_\alpha \veebar X^8_\sigma, \\ X^8_\alpha \Leftrightarrow Y_{C_{81}}, \\ X^8_\sigma \Leftrightarrow Y_{C_{81}} \wedge Y_{C_{82}}. \end{aligned} \tag{C.44}$$

9. The recirculation of the solvent recovered in separation stage 8 toward reaction stage 1 ($R_{8,1}$) or toward repulping stage 4 ($R_{8,4}$) is associated to the acquisition of buffer tanks T_{81} ($Y_{T_{81}}$) or T_{84} ($Y_{T_{84}}$) through propositions:

$$\begin{aligned} R_{8,1} \Leftrightarrow Y_{T_{81}}, \\ R_{8,4} \Leftrightarrow Y_{T_{84}}. \end{aligned} \tag{C.45}$$

Appendix D

Comparison of solution methods: a preliminary study

In this appendix, a study is presented which compares the application of the deterministic, stochastic, and hybrid methods proposed in Chapter 4. Specifically, the direct-simultaneous, the DGA, and the DGA-NLP strategies are used to solve a preliminary example of the Denbigh reaction system (Denbigh, 1958). The example is a variation of the Denbigh examples addressed in Chapter 5 (p. 116, 126, and 137) and Chapter 6 (p. 158). It was part of the preliminary studies during the development of this thesis. The results prove that the proposed stochastic and hybrid approaches can be considered as a plausible alternative to the deterministic one, provided that a good tuning of the DGA is performed.

D.1 Denbigh case study: comparison of solution methods

The proposed strategies are applied to solve the integrated batch process development in a retrofit scenario. Particularly, a competitive reaction mechanism, the Denbigh reaction system (Denbigh, 1958), is considered to introduce the production of a specialty chemical into an existing plant through a single-product campaign. The plant diagram in corresponds to the reactor network of the motivating example 1 in Chapter 3 (Figure 3.1, p. 54), composed of two batch reactors U_1 and U_2. The objective is to produce batches of $900\,kg$ of product S maximizing the profit, which is reads as:

$$\begin{aligned} \text{minimize}\ \ \Phi_{Objective} &= -Profit \\ &= -(Revenue_{\mathrm{S}} - Cost_{\mathrm{A}} - \textstyle\sum_{j\in\{U_1,U_2\}}(Cost_{j,p} + Cost_{j,o})). \end{aligned} \quad \text{(D.1)}$$

Each contribution is defined as follows:

- Product revenue:

$$Revenue_{\mathrm{S}} = \hat{p}_{\mathrm{S}} \left(\eta_{\mathrm{S}}^{T_{prod}}(t^{end}) - \eta_{\mathrm{S}}^{T_{prod}}(t^{s}) \right), \quad \text{(D.2)}$$

  where $\hat{p}_{\mathrm{S}}$ is the selling price of product S with a value of $6.15\,€/kg$, t^s and t^{end} are the initial and final times of the batch, and $\eta_{\mathrm{S}}^{T_{prod}}(t^s)$ and $\eta_{\mathrm{S}}^{T_{prod}}(t^{end})$ are the initial and final amounts of S in storage tank T_{prod};

- Raw material cost:

$$Cost_{\mathrm{A}} = \hat{p}_{\mathrm{A}} \left(\eta_{\mathrm{A}}^{T^{raw}}(t^s) - \eta_{\mathrm{A}}^{T^{raw}}(t^{end}) \right), \tag{D.3}$$

  where $\hat{p}_{\mathrm{A}}$ is the cost of raw material A with a value of $1.54\,€/kg$, and $\eta_{\mathrm{A}}^{T^{raw}}(t^s)$ and $\eta_{\mathrm{A}}^{T^{raw}}(t^{end})$ are the initial and final amounts of raw material A in storage tank T^{raw};
- Processing cost, as a function of the processed material:

$$\begin{bmatrix} Y_j \\ Cost_{j,p} = \hat{c}_j \sum_{k=1}^{3} \int_0^1 F_{2,k}^j(t)dt\, t_k^j \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ Cost_{j,p} = 0 \end{bmatrix}, \forall j \in \{U_1, U_2\}, \tag{D.4}$$

  where $\hat{c}_j$ is the unitary processing cost with a value of $0.38\,€/kg$ in unit U_1 and $0.47\,€/kg$ in U_2, $F_{2,k}^j(t)$ is the output flow and t_k^j is the duration of stage $k{\in}K_j$, and Y_j is the equipment Boolean that indicates whether batch unit $j{\in}\{U_1, U_2\}$ is selected or not.
- Occupation cost, as a function of the batch processing time:

$$\begin{bmatrix} Y_j \\ Cost_{j,o} = \bar{c}_j \sum_{k=1}^{3} t_k^j \end{bmatrix} \veebar \begin{bmatrix} \neg Y_j \\ Cost_{j,o} = 0 \end{bmatrix}, \forall j \in \{U_1, U_2\}, \tag{D.5}$$

  where $\bar{c}_j$ is the time-dependent occupation cost with a value of $100\,€/h$ in unit U_1 and $200\,€/h$ in U_2, t_k^j is the duration of stage $k{\in}K_j$, and Y_j is the equipment Boolean that indicates whether batch unit $j{\in}\{U_1, U_2\}$ is selected or not.

The rest of the MLDO model is detailed in Appendix A, according to the modeling strategy proposed in Chapter 3. The process synthesis decisions addressed are: (i) the splitting of reaction stage into subtasks, (ii) the dynamic reference trajectories of the feed-forward control variables, which include input and output flow rates ($F_{1,k}^j(t)$ and $F_{3,k}^j(t)$) and processing temperature ($\theta_k^j(t)$) in each stage $k{\in}\{1,2,3\}$ in batch units $j{\in}\{U_1, U_2\}$, (iii) the duration of batch operations (t_l) in each potential stage $l{\in}\{1,...,5\}$ considering all the batch unit procedures, and (iv) the material transfer synchronization between tasks –*i.e.* synchronization of flow rates, compositions, and starting and final times. As for the equipment allocation problem, the selection of batch processing units (Y_j, $j{\in}\{U_1, U_2\}$) (v) is solved, together with the optimization of: (vi) task-unit assignment ($W_{j,q}$, $j{\in}\{U_1, U_2\}$, $q{\in}\{1,2\}$), and (vii) the eventual combination of equipment pieces for reaction stage, creating series σ, parallel π, or single unit α or β configurations (X_ψ^1, $\psi{\in}\{\alpha,\beta,\pi,\sigma\}$).

D.1.1 Direct-simultaneous method

The problem is first solved using the direct-simultaneous approach explained in Chapter 4 (p. 92). To sum up, the MLDO problem is reformulated into a MIDO by replacing Boolean variables $u^{Bool}{=}\{Y_j, W_{j,q}, X_\psi^1\}$ by binaries $u^{bin}{=}\{y_j, w_{j,q}, x_\psi^1\}$ and using binary multiplication and CNF reformulation (Clocksin & Mellish, 1981, Raman & Grossmann, 1991) to transform the mixed-logic problem into a mixed-integer one. Next, the model tranformed into a MINLP through full-discretization of the process and control variables, by means of orthogonal collocation on finite elements (Cuthrell & Biegler, 1989). Three collocation points and four finite elements are used in this example. Finally, the MINLP problem is implemented in GAMS and solved using Outer Approximation (OA) method (Duran & Grossmann, 1986a) by decomposing the problem into MILP and NLP subproblems that are solved iteratively in the optimization algorithm. Multiple IFS are used to initialize the search procedure. The optimal solution obtained with this approach is taken as a reference for the stochastic and hybrid approaches.

D.1.2 Stochastic DGA method

In this example, the chromosome presented in Figure 4.4 (p. 99) is used, given the batch units U=$\{U_1, U_2\}$, batch operations K_j=$\{1, 2, 3\}$ at j∈U, with input and output stages I_j=$\{1\}$ and O_j=$\{3\}$, input and output flows M_j^{in}=$\{1\}$ and M_j^{out}=$\{2\}$, model stages L=$\{1, ..., 5\}$ at Level 0, final product P=$\{S\}$, procedure orders Q=$\{1, 2\}$, equipment configurations Ψ=$\{\alpha, \beta, \pi, \sigma\}$, and reaction task PS=$\{1\}$. Moreover, N_e=4 finite elements are used for in the discretization of batch profiles where PWC control profiles are adopted, like in the deterministic approach.

The analysis of the DOF associated to qualitative decisions in this example permits to reduce the binary decision variables to the selection of equipment configuration, $x_\psi^1, \psi \in \{\alpha, \beta\, \sigma, \pi\}$. The interested reader is referred to Appendix A (p. 199) for further details. Then, binary variables y_j for selected processing units j∈U and $w_{j,q}$ for the assignment of unit j∈U to the procedure in order q∈Q depend on the equipment configuration according to the algebraic equations of Ω in Eq. 4.8 that correspond to the mixed-integer reformulation of original Eqs. 3.10 and 3.17-3.20. Otherwise, they should be included in the chromosome. Besides, the number of batches is assumed to be fixed to NB_{S}=47 in this example.

As a result, the chromosome length is 49, composed of: (i) 40 continuous variables in Part I, namely $u_{k,e}^{dyn}$=$\{F_{1,3,e}^j, F_{2,1,e}^j, \theta_{k,e}^j\}$, with j∈U, k∈K_j, and e∈$\{1, ..., N_e\}$, (ii) five continuous variables in Part II, namely u^{stat}=$\{t_l\}$, with l∈L, and (iii) four discrete variables in Part III, namely u^{bin}=$\{x_\psi^1\}$, with ψ∈Ψ. An overview of GA features is shown in Table D.1.

Parameter	Value	Parameter	Value
No. variables	49	No. crossover points	2
No. population	460	Penalization weight f_p	30
Selection	50%	Mutation rate	5%
No. elite individuals	2	σ^2 in mutation for $F_{1,3,e}^j$ and $F_{2,1,e}^j$	0.25

Table D.1: GA parameters in the preliminary Denbigh example.

To evaluate the goodness of each individual inside a population, the fitness function $\Phi_{Fitness}$ is defined including the profit objective function $\Phi_{Objective}$ and penalization of model unsupported restrictions as follows:

$$\Phi_{Fitness} = \Phi_{Objective} + f_p \cdot P. \tag{D.6}$$

In this example, the penalizations $f_p \cdot P$ to support the model inequalities are committed to ensure: the fulfillment of the demand Dem_{S}, the minimum input and output flow rates $F_{1,3,e}^j$ and $F_{2,1,e}^j$ in active units, the maximum volume $v_{|K_j|}^{\mathrm{U}}$ that ensures that batch units j∈U are empty in the final time $t^{j,end}$, lower and upper bound for stage durations t_l at Level 0, and non-negative volumes in units and storage tanks.

D.1.3 Hybrid DGA-NLP method

To apply the hybrid DGA-NLP method, presented in Figure 4.5 (p. 101), the GA features and tuning parameters presented in Table D.1 are also employed in steps (1) and (2). However, in the exploratory step (1) the four variables regarding configuration x^1_ψ are fixed to 1 alternatively for the four possible configurations $\psi \in \{\alpha, \beta, \sigma, \pi\}$. In last step (3), the NLP solver CONOPT is used.

D.1.4 Results and discussion

Figure D.1 shows the fitness function evolution for the DGA and the hybrid DGA-NLP strategies, with respect to the reference determined by the direct-simultaneous approach. The goodness of obtained solutions at the final iteration are also compared in Table D.2, bearing in mind that stochastic solutions may vary with the GA tuning.

It can be observed that the DGA method provides a solution closer to the reference optimal one, in comparison to the hybrid strategy without refinement. Indeed, the filtering DGA step (2) of the hybrid method provides no improvement over the N_{IFS} chromosomes from step (1), even though dynamic profiles are allowed in this step, providing a margin for improving the solution. A simple filter to automatically select the best out of the N_{IFS} solutions available would be likewise appropriate. Besides, the almost negligible penalizations are common to all cases. Additionally, it is worth to note in Figure D.1 how the DGA strategy converges to a good solution as rapidly as the exploratory GA in the hybrid method. Thus, apparently it should be equally efficient to solve a unique DGA with free configuration and dynamic profiles that substitutes steps (1) and (2), to afterwards refine the solution with the NLP solver in step (3).

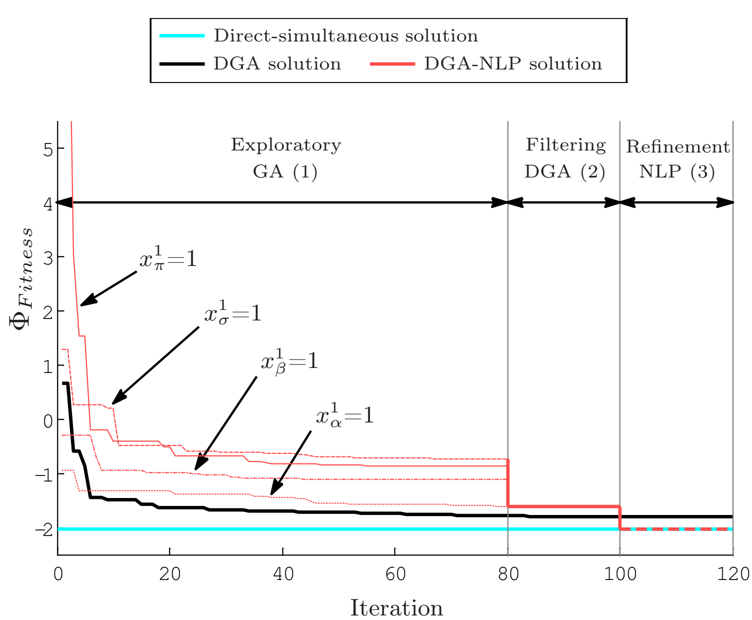


Figure D.1: Evolution of DGA throughout the solution with stochastic and hybrid methods in the preliminary Denbigh example.

Case	$\Phi_{Fitness}$	$\Phi_{Objective}$	$f_p \cdot P$	Error in $\Phi_{Fitness}$
Direct-simultaneous strategy	-2.0303	-2.0303	0	-
DGA strategy	-1.8306	-1.9083	0.0777	0.1997
Hybrid: filtering DGA	-1.6219	-1.6382	0.0164	0.4084
Hybrid: refining NLP	-2.0303	-2.0303	0	0

Table D.2: Comparison of solution goodness of tested solution strategies in the preliminary Denbigh example.

To conclude, in the tested cases, physically feasible solutions are obtained by the stochastic and hybrid methods without providing initial feasible solutions, which is a crucial advantage in front of deterministic methods. The solutions obtained with the DGA strategy are close to the reference and can be further improved up to the reference optimum by using a direct-simultaneous method for DO, which can be solved using NLP solvers with lower combinatorial complexity, as shown in the hybrid approach. These results are a promising first step to solve industrial size problems, currently limited by computational requirements of standard solvers. However, the tuning of the DGA parameters should be further studied to ensure that blind searches –without a deterministic reference solution– lead to the optimal.

Appendix E

Publications

This is a list of the works carried out so far within the scope of this thesis, in reversed chronological order. The list has been divided in manuscripts to international refereed journals, conference proceedings, and workshops. It includes works directly related to this thesis and other related work.

E.1 Journals

E.1.1 Manuscripts in progress

Moreno-Benito, M., K. Frankl, A. Espuña, & W. Marquardt. A modelling strategy for batch process and recipe design using mixed-logic dynamic optimization.

Moreno-Benito, M., A. Espuña, & L. Puigjaner. Flexible Plant Design using Mixed-Logic Dynamic Optimization.

Moreno-Benito, M., E. Yamal-Turbay, A. Espuña, M. Pérez-Moya, & M. Graells. Optimization of H_2O_2 dosage in photo-Fenton process.

E.1.2 Manuscripts submitted

Moreno-Benito, M. & A. Espuña. Stochastic and hybrid approaches to solve integrated synthesis and operation of batch processes. *Computers & Chemical Engineering.*

E.1.3 Manuscripts published

Capón-García, E., **M. Moreno-Benito**, & A. Espuna. Improved Short-Term Batch Scheduling Flexibility Using Variable Recipes. *Industrial & Engineering Chemistry Research*, 50(9):4983–4992, 2011. DOI 10.1021/ie101404b.

Muñoz, E., E. Capón-García, **M. Moreno-Benito**, A. Espuña, & L. Puigjaner. Scheduling and control decision-making under an integrated information environment. *Computers & Chemical Engineering*, 28:1195–1200, 2011. DOI 10.1016/j.comp chemeng.2011. 01.025.

E.2 Articles in conference proceedings

Moreno-Benito, M., E. Yamal-Turbay, A. Espuña, M. Pérez-Moya, & M. Graells. Optimal recipe design for Paracetamol degradation by advanced oxidation processes (AOPs) in a pilot plant. *In: Kraslawski, A. & I. Turunen (Eds.), 23rd European Symposium on Computer Aided Process Engineering*, 32:943–948, 2013. DOI 10.1016/B978-0-444-63234-0.50158-5.

Moreno-Benito, M., K. Frankl, W. Marquardt, & A. Espuña. Simultaneous Process and Recipe Design of an Acrylic Fibre Production System. *In: 2012 AIChE Annual Meeting, Pittsburgh, PA*, Paper No. 279233, 2012.

Moreno-Benito, M. & A. Espuña. Stochastic and hybrid approaches to solve integrated synthesis and operation of batch processes. *In: Bogle, D. & M. Fairweather (Eds.), 22nd European Symposium on Computer Aided Process Engineering* 30:1332–1336, 2012. DOI: 10.1016/B978-0-444-59520-1.50125-1.

Muñoz, E., E. Capón, J. M. Laínez, **M. Moreno-Benito**, A. Espuña & L. Puigjaner. Operational, Tactical and Strategical Integration for Enterprise Decision-Making. *In: Bogle, D. & M. Fairweather (Eds.), 22nd European Symposium on Computer Aided Process Engineering*, 30:397–401, 2012. DOI: 10.1016/B978-0-444-59519-5.50080-0.

Moreno-Benito, M. & A. Espuña Facing new products demand through simultaneous structural and operational decisions in the design of the control recipe. *In: Klemeš, J. J., H. L. Lam, & P. S. Varbanov (Eds.) 14th International Conference on Process Integration, Modelling and Optimization for Energy Saving and Pollution Reduction, Chemical Engineering Transactions*, 25:423–428, 2011. DOI: 10.3303/CET1125071.

Moreno-Benito, M., A. Espuña & L. Puigjaner. Integrating economic targets for simultaneous structural and operational decision-making in the design of the control recipe. *In: 2010 AIChE Annual Meeting, Salt Lake City*, Paper No. 197685, 2010.

Capón-García, E., E. Muñoz, **M. Moreno-Benito**, A. Espuña, & L. Puigjaner. Scheduling and control decision-making under an integrated information environment. *In: Pierucci, S. & G. B. Ferraris (Eds.) 20th European Symposium on Computer Aided Process Engineering* 28:1195–1200, 2010. DOI: 10.1016/S1570-7946(10)28200-7.

Gradišar, D., P. Copado, E. Muñoz, **M. Moreno-Benito**, A. Espuña, & L. Puigjaner. Communication within an integrated batch control. *In: 6th Vienna International Conference on Mathematical Modelling, Proceedings 2009 MATHMOD Vienna*, 2490–2493, 2009.

E.3 Workshops

Moreno-Benito, M., A. Espuña, & L. Puigjaner. Use of MINLP to solve structural and operational decisions at the scheduling level. *In: Exploratory Workshop on Mixed Integer Nonlinear Programming EWMINLP, Sevilla*, 2010.

Tables

Figures

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