Simultaneous Design and Control of Nonlinear Chemical Processes: A State-of-the-Art Review

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Extended Abstract

Currently, chemical process design and process control are separate disciplines assisting process development at different stages. Design and control decisions are made separately despite the common objective of dissipating the impact of disturbances and uncertainty to ensure robust plant operations. Nowadays, it is broadly accepted that this is not a desirable situation since this approach can lead to processes that are difficult to control. As a consequence, different ways to take controllability issues into account in the process design stage have been developed and reported in the literature during past two decades. This paper presents the state-of-art review of: (i) methods which enable to screen alternative designs for controllability; and (ii) methods which integrate the design of the process and the control system.

The paper first focuses on the methodologies available in the open literature to take controllability of process systems into account. The evaluation of open and closed-loop controllability indicator of different process designs allows the comparison and classification of alternatives in terms of operational characteristics. The controllability of alternatives that might have acceptable steady-state economics but poor control performance can be rejected in an early stage of the design. The controllability is quantified using indices like the Relative Gain Array (RGA), Disturbance Cost (DC), Disturbance Condition Number (DCN), and Singular Value Decomposition (SVD) based indices. The development of majority of controllability indices is based on the concepts of functional and structural controllability and switchability, on the dynamic resilience of the system and on open and closed–loop stability analysis. The brief overview of available indices with their limitations is systematically presented in the first part of the paper.

The rest of the paper focuses on the second class of methods based on the simultaneous design and control problem using dynamic process models. These methods can be classified into two categories: (i) In the first category (presented in a tabular form in the paper), the authors attempt to design economically optimal processes that can operate in an efficient dynamic mode within an envelope around the nominal point. These methods give insight into the trade-offs between economic benefits and the operability of the plant. (ii) The second class of methods consider a single economics-based performance index, while representing the system operation and system specifications with dynamic rather than steady state models. Thus, dynamic optimization is employed in order to determine the most economic design that satisfies all the operability constraints. Optimization algorithm developed so far in literature does not guarantee to find the exact global optimum. The paper finally concludes with the research gaps and useful suggestions to guide the future work for the formulation and solution of challenging simultaneous design and control problems.

Keywords: Nonlinear chemical processes; Design and control; Dynamic process models; Dynamic optimization.

1. Introduction

The design of a continuous chemical process is usually carried out at steady state for a given operating range, with the assumption that a control system can be designed to maintain the process at the desired operating level and within the design constraints. However, unfavorable process static and dynamic characteristics would limit the effectiveness of the control system, leading to a process that is unable to meet its design specifications. Moreover, alternative designs are judged on the basis of economics alone, without taking controllability and resiliency into account. This may lead to the elimination of easily controlled, but slightly less economical, alternatives in favor of slightly more economical designs that may be extremely difficult to control. It is becoming increasingly evident that design on the basis of steady state economics alone is risky, because the resulting plants are often difficult to control (i.e., inflexible, with poor disturbance-rejection properties), resulting in off-spec product, excessive use of fuel, and associated profitability losses.

Consequently, there is a growing recognition of the need to consider the controllability and resiliency (C & R) of a chemical process during design stage [1-2]. Controllability can be defined as the ease wit h which a continuous plant can be held at a specific steady state.

Resiliency measures the degree to which a processing system can meet its design objectives despite external disturbances and uncertainties in its design parameters. Clearly, it would be greatly advantageous to be able to predict how well a given process meets these dynamic performance requirements as early as possible in the design stage.

During the last 35 years a trend towards simultaneously considering the design and control aspects of a process has resulted in a development of large number of methodologies for addressing the issue. These methods can be classified according to [3] in: (i) methods which enable to screen alternative designs for controllability; and (ii) methods which integrate the design of the process and the control system.

In the first class of methods, the open literature focuses on the controllability of process systems. The evaluation of open and closed-loop controllability indicators of different process designs allows the comparison and classification of alternatives in terms of operational characteristics. The measures include resiliency indices [4], disturbance condition numbers [5], the relative gain array [6] and the relative disturbance array [7]. This method is rather easy to integrate in existing design procedures, however the indices are often calculated based on either steady state or linear dynamic models, which introduces significant approximations and restricts further its applicability, and the relation between the indices and the *closed-loop* performance is often unclear. This issue becomes evident by the large number of papers where the authors verify their findings through closed-loop dynamic simulations.

The second class of methods is based on the simultaneous optimization of both the process and the controller Design, which are parameterized by means of a so-called superstructure. Alternative designs can now be compared based on, for example, the Integrated Squared Error (ISE) for specific disturbance scenarios [8]. Because of the computational complexity the application of this approach is limited to small case-studies with specific assumptions on the control system to be applied.

2. Tools for controllability & resiliency (C & R) analysis

This section will focus on the available methods for controllability evaluation. The evaluation of controllability indices was first introduced by [9], who defined the controllability as 'the ability of the process to achieve and maintain the desired steady state value'. It implies that the process performance depends on the availability of both measured and manipulated variables. The concept is thus referred to as 'input-output controllability'.

The term 'State controllability' is first introduced by [10], implies that 'A state is termed controllable if there exist a input which can achieve the desired state in a given time' [11] gives a thorough discussion of the issues of state controllability and also defines the term 'functional controllability'

2.1 Integral controllability

Integral controllability has been studied by Morari and co-workers [12-13]. If multi-loop SISO controllers are used, integral controllability is an important criterion in variable pairing. [14] eliminated pairings with negative Morari indexes of integral controllability (MIC) to ensure integral controllability. The MIC's are the eigenvalues of the $G^+(O)$ matrix (the plant steady-state gain matrix with the signs adjusted so that all diagonal elements have positive signs). If all of the individual loops are integrally controllable, a negative value of any of the eigenvalues of $G^+(O)$ means that the variable pairing will produce an unstable closed-loop system if each loop is detuned at an arbitrary rate. It should be noticed that for 3 x 3 or higher order systems, there are instances for which no variable pairing will give MIC's that are all positive.

2.2 Singular value analysis

The singular values of a matrix are a measure of how close the matrix is to being “singular” i.e to having a determinant that is zero. The N singular values of a real N x N matrix are defined as the square root of the eigenvalues of the matrix formed by multiplying the original matrix by its transpose,

$$\sigma_{i[\underline{A}]} = \sqrt{\lambda_{i[\underline{A}^T \underline{A}]}} \qquad i = 1, 2, \ldots\ldots\ldots, N$$

Minimum singular value was introduced as a controllability index by [4]. A smaller minimum singular value implies that large input magnitudes may be needed, and such plants are undesirable [4].

The SVD on G and G_d is useful for examining which manipulated input combinations have the largest effect and which disturbances give the largest output variations. It can also be used to predict directional sensitivity of a process. The process gain matrix is decomposed into three matrices,

$$G = U \sum V^T$$

where U is the left singular vector matrix, $\sum$ the diagonal matrix of singular values, ordered, and V the right singular vector matrix. The left and right singular vector matrices are both orthonormal matrices; that is, each column of the matrix is orthogonal to all other columns and the columns each are unit length. The diagonal singular value matrix is ordered so that the largest singular value is in the (1, 1) position. Note that the standard notation for *SVD* is to use U to represent the left singular vector matrix. When performing singular value analysis, it is important to scale the inputs and outputs to cover the same range.

“Condition number” is another important controllability index based on singular value analysis. It is defined as the ratio between the largest singular value and the smallest nonzero singular value. Plants with large condition number are called ill-conditioned, and require widely different input magnitudes depending on the direction of the desired output (i.e. the plant is sensitive to unstructured input uncertain). Note that the condition number is scaling dependent.

2.3 Disturbance cost

Lewin [15] presented the disturbance cost, DC, as an index that quantifies the disturbance resiliency properties of a linear process and discusses the incapability of the previously mentioned measures for this problem. Consider a process model,

$$y(s)=G(s)u(s)+G_d(s)d(s)$$

assuming perfect disturbance rejection by the control system and a linear dynamic model for the process,

$$u(s)=-G^{-1}(s)d'(s) \qquad \text{where } d'(s)=G_d(s)d(s)$$

Computing the norm of the actuator response, $\|u\|_2$, as a function of the disturbance direction, the relative cost of rejecting a particular disturbance, d, can be computed as a function of its direction, .i.e., a quantitative measure of the control effort to reject a given disturbance vector is the Euclidean norm. This norm, $\|u\|_2$, is the disturbance cost.

2.4 Disturbance condition number

In order to study the direction of a disturbance [5] introduced Disturbance Condition Number (DCN). For a particular disturbance it tells us how much largest the input magnitude needs to be to reject a unit disturbance, compared to if the disturbance was in the best possible direction of the plant. The Disturbance Condition Number is actually only a good indication of which setpoint vector will be difficult to track [15].

2.5 Relative gain array

The most widely used controllability measure is probably the RGA which was introduced by Bristol, 1966. In general for MIMO systems, consider a square plant $G(s)$,

$$y(s)=G(s)u(s) \tag{1}$$

The relative gain is defined as the ratio of process gain as seen by a given controller with all other loops open to the process gain as seen by a given controller with all other loops closed and can be computed as,

$$\Lambda(s)=G(s)\otimes\left(G^{-1}(s)\right)^T \tag{2}$$

where the $\otimes$ symbol indicates element-by element multiplication (Schur product). An important property of the RGA is that it is scaling independent. The elements in the RGA can be numbers that vary from very large negative values to very large positive values. The larger the values of the elements of RGA, the more sensitive the transfer function will be to errors. The closer the number is to 1, the less difference closing the other loop makes on the loop being considered.

For interactive plants which do not have large RGA elements, a decoupler may be useful. In particular, this applies to the case where the RGA-elements vary in magnitude with frequency, and it may be difficult to find a good pairing for decentralized control [16].

The problem with pairing in order of avoiding interaction is that the interaction is not necessarily always undesirable thing. Therefore, the use of the RGA to decide how to pair variables is not an effective tool for controllability analysis.

2.6 Resiliency indices

Karafyllis and Kokossis [17], introduced Disturbance Resiliency Index (DRI) as a measure for the integration of design and control. The measure reflects on the ability of the process to reject disturbances and prevent saturation in the manipulated variables. The measure is defined mathematically and a set of properties and theorems are proved to enable its use. For a large number of systems and networks, the application of the theory yields analytical expressions one can study and analyze. In other cases, it yields bounding expressions that one can embed in optimization formulations and mathematical models.
The new measure quantifies the disturbance resiliency properties of a process. It applies to linear and nonlinear systems as opposed to all the previously mentioned measures and resiliency indices that apply to linear systems. Compared to the works of [18-19], it has the advantage of a clear extension to the dynamical properties of the system.

Table 1

Controllability and Resiliency Analysis

Authors	**Work outline**
1. Lim et. al. (1972)	Process controllability analysis for counter current, heat exchangers and packed absorbers.
2. Saboo and Morari (1984)	Systematic design procedure for resilient heat exchange networks
3. Yu and Luyben (1986)	Relative gain array for feedback control system with integral action.
4. Skogestad and Morari (1987)	Introduced “disturbance condition number” to quantify the effect of disturbance direction on closed-loop performance.
5. Skogestad et. al. (1992)	Demonstrated tools for controllability analysis on FCC reactor.
6. Lewin and Bogle (1996)	C & R analysis for a non-linear industrial polymerization reactor.

7. Lewin (1999)	Presented a review on integration of design and control.
8. Kuhlmann and Bogle (2001)	Controllability Evaluation for Non-minimum Phase-Processes with Multiplicity.
9. Seferlis and Grievink (2001)	A method is developed that screens process flowsheet and control system configurations within an optimization framework.
10. Karafyllis and Kokossis (2002) Solovyey and Lewin (2004)	The paper introduces a new measure for the integration of design and control: a disturbance resiliency index. Showed applications on steady state resiliency index
11. Meeuse and Tousain (2002)	Introduced a new approach to compare alternative process designs in the presence of stochastic disturbances on a distillation column.
12. Segovia-Hernandez et. al. (2008)	Controllability analysis of alternate schemes to complex column arrangements with thermal coupling for the separation of ternary mixtures was demonstrated.
13. Perales et. al. (2008)	Controllability analysis and decentralized control of a wet limestone flue gas desulfurization plant.

3. Simultaneous process design and control system

In the early stages of simultaneous design and control, major efforts were towards the controllability analysis under the limitations of linear and steady state systems. Thus, the systematic efforts in the area appear in the literature which aims to avoid the limitations of controllability indicators, resulted in two general categories of methods [19]:

1) Methods which attempt to design economically optimal processes that can operate in an efficient dynamic mode within an envelope around the nominal point. The problem is often presented as multi-objective optimization problem, with conflicting goals: an economic index of performance and a dynamic measure (e.g. integral square error). The methods though gives the insight into the trade-offs between economic benefits and the operability of the plant. However, their drawback is their inability to determine precisely the importance of the two competing objectives and to treat systematically the dynamic behaviour of the plant.

2) Methods which consider a single economics-based performance index, while representing the system operation and system specifications with dynamic rather than steady state models. Thus, dynamic optimization is employed in order to determine the most economic design that satisfies all the operability constraints.

Walsh and Perkins [21] and Narraway and Perkins [22] were among the first to consider general mathematical programming techniques for the simultaneous design and control problem using dynamic process models. Dimitriadis and Pistikopoulos [23] applied the ideas reported in [18] to systems described by sets of differential and algebraic equations. On the basis of the aforementioned methodologies, a unified framework is proposed by [24] on process design for obtaining integrated process and control system designs under uncertainty. Alternative formulations and solution procedures were reported in [25] and [26]. The main drawback of these methodologies stems from the fact that the combined design and control problem, a mixed integer dynamic optimization (MIDO) problem, is solved as a mixed integer nonlinear programming (MINLP) problem by transforming the system of differential and algebraic equations into algebraic equations by using either full discretization or integration. In the former case, the size of the resulting MINLP is explosive, and in the latter case, extensive dual information is needed to formulate a (mixed integer linear) master problem that is ever increasing in size.

The Mixed Integer Dynamic Optimization algorithms reported in literature are based on complete discretization[24], on an adjoint-based approach [27], and on an outer approximation [28]. None of these methods is guaranteed to find the exact global optimum of the underlying optimization problem [2]. Therefore, the need for new global mixed integer dynamic optimization algorithms becomes extremely important in preventing the generation of economically unfavorable designs.

Recently, Angira [29], Angira & Santosh [30], Babu & Angira [31], Angira & Babu [32] used evolutionary algorithms for solving the nonlinear, mixed integer nonlinear and dynamic optimization problems encountered in chemical engineering. But these techniques are not applied and tested on Mixed Integer Dynamic Optimization problems that arise from the simultaneous process design and control.

Table 2

Simultaneous design and control

Authors	**Work outline**
I. Lim et. al. (1972)	Integration of design and control, simultaneous optimization of process design and process control
II. Luyben and Floudas	Used ε-constraint method in GBD framework, MOOP is solved

	(1994)	using cutting plane method.
III.	Pistikopoulos et. al. (1996)	Unified process design framework to cope with process uncertainties and time varying disturbances, the problem is posed as a mixed integer stochastic optimal control formulation.
IV.	Schweiger and Floudas (1999)	Superstructure is mathematically modeled using differential and algebraic constraints, optimal control problem, involves the application of a control parametrization approach where the selected control variables are discretized in terms of time-invariant parameters
V.	Kookos and Perkins (2001)	Introduces a new algorithm for the solution of the simultaneous process and control design problem using bounding scheme.
VI.	Seferlis and Grievink (2001)	The steady-state disturbance rejection characteristics of the nonlinear process models are considered in conjunction with economic criteria
VII.	Pistikopoulos et. al. (2002)	Systems involving both discrete and continuous decisions, are simultaneously optimized for realistic dynamic models, resulting MIDO problem is solved using rigorous algorithm.
VIII.	Bandoni et. al. (2004)	MIDO approach to perform the simultaneous design and control of styrene polymerization reactors is used, and The gPROMS/gOPT package was successfully used to solve the MIDO.
IX.	Pistikopoulos et. al. (2004)	Presented a good review on optimization based simultaneous process and control design.
X.	Budman et. al. (2005)	The paper presents a method for integrating process control at the design stage. An MPC strategy, designed together with the design of the process, was used to define a robust variability cost in the face of model uncertainty.
XI.	Pajula and Ritala (2006)	How the control structure design is affected by measurement uncertainty and how the corresponding dynamic problem is defined and solved with rather regular tools is illustrate through a case study.
XII.	Flores-Tlacuahuac and Biegler (2007)	Three MINLP formulations based on a nonconvex formulation, the conventional Big-M formulation and generalized disjunctive programming (GDP) is made and compared with the outer

		approximation and NLP branch and bound algorithms.
	Flores-Tlacuahuac and Biegler (2008)	Work addresses the simultaneous process control and design problem of polymerization reactors during dynamic grade transition operation
XIII.	Banga et. al. (2008)	Propose a global optimization algorithm, based on extensions of the metaheuristic Tabu Search, in order to solve this challenging class of problems in an efficient and robust way.

4. The Future

Based on the detailed review of the available literature, the following gaps in the existing research are identified:

(i) a systematic study aiming to avoid the limitations of controllability indicators particularly for nonlinear dynamic systems

(ii) the incorporation of advanced control techniques such as model predictive control, is a leading industrial advanced control technology and should be implemented in a process design framework with the prospect of improving the process performance and

(iii) a global optimization technique for a rigorous and efficient solution of the simultaneous process design and control optimization problem.

The research gaps mentioned above are the key challenges that lie ahead in simultaneous design and control of non linear chemical processes.

5. References:

1. Downs J.J. and Vogel E.F. (1990). "A plant wide industrial process control problem." *American Institute of Chemical Engineering Annual mtg.* Chicago, USA.
2. Pistikopoulos E.N. and Van Schijndel J.M.G. (1999). "Towards the integration of process design, process control & process operability - current status & future trends." *In Foundations of Computer-Aided Process Design*, Snowmass, Colorado, USA.
3. Lewin. D.R. (1999). "Interaction of design and control." *Proceedings of 7th Mediterranean conference on control and automation (MED 99)*, Hafia, Israel.
4. Morari M. (1983). "Flexibility and resiliency of process systems." *Computers and Chemical Engineering,* 7, 423.

5. Skogestad S. and Morari M. (1987). "Effect of disturbance directions on closed loop performance." *Industrial & Engineering Chemistry Research,* 26:2029–2035.
6. Bristol E.H. (1966). "On a new measure of interactions for multivariable process control." *IEEE Trans. Automat. Control,* AC-11, 133-134.
7. Stanley G., Marino-Galarraga M., and McAvoy T. J. (1985). "Shortcut operability analysis. 1. The relative disturbance gain." *Ind. Eng. Chem. Process Des. Dev.,* 24(4): 1181-1188.
8. Schweiger C. and Floudas C. "Optimization framework for the synthesis of chemical reactor networks." *Industrial & Engineering Chemistry Research,* 38:744–766.
9. Ziegler J.G. and Nichols N.B. (1943). "Process lags in automatic control circuits." *Transactions ASME,* 65:433-444.
10. Kalman R. E. (1960). "A New Approach to Linear Filtering and Prediction Problems." Transactions of the ASME–Journal of Basic Engineering, 82 (Series D): 35-45.
11. Rosenbrock H. H. (1970). "State space and multivariable theory", Nelson, London.
12. Grosdidier P., Morari M., and Holt B. R. (1985). "Closed-Loop properties from Steady-State Gain Information." *Ind. Eng. Chem. Fundam.,* 24, 221.
13. Saboo A. K., Morari M., and Woodcock D. C. (1985). "Design of Resilient Processing Plants–VIII, A Resilience Index for Heat Exchanger Networks." *Chemical Engineering Science,* 40:1553-1565.
14. Yu C. and Luyben W. L. (1986). "Robustness with respect to integral controllability." Industrial Engineering and Chemistry Research, 26(5):1043-1045.
15. Lewin, D. R. (1996). "A simple tool for disturbance resiliency diagnosis and feedforward control design." *Computers and Chemical Engineering,* 20, 13–25.
16. Skogestad S. and Hovd M. (1990). "Use of frequency dependent RGA for control structure selection." *Proceedings of American control conference (ACC)* 2133-2139 San Diego USA.
17. Karafyllis I. and Kokossis A. (2002). "On a new measure for the integration of process design and control: The disturbance resiliency index." *Chemical Engineering Science.* 57:873–886.
18. Halemane K.P. and Grossmann I.E. (1983). "Optimal process design under uncertainty." *Journal of American Institute of Chemical Engineers*, 29:425-433.
19. Grossmann, I., Halemane, K., & Swaney, R. (1983). "Optimization strategies for flexible chemical processes." *Computers and Chemical Engineering,* 7(4), 439–462.
20. Sakizlis V., Perkins J.D. and Pistikopoulos E.N. (2004). "Recent advances in optimization-based simultaneous process and control design." *Computers & Chemical Engineering,* 28:2069-2086.
21. Walsh S. and Perkins J.D. (1996). "Operability and control in process synthesis and design." In Anderson J. L. (Ed.), *Advances in chemical engineering—Process synthesis.* New York: Academic Press; p. 301–402.

22. Narraway L. and Perkins J.D. (1993). “Selection of process control structure based on linear dynamic economics.” *Industrial & Engineering Chemistry Research*, 32:2681–2692.
23. Dimitriadis V. and Pistikopoulos E.N. (1995). “Flexibility analysis of dynamic systems.” *Industrial & Engineering Chemistry Research,* 34:4451–4462.
24. Mohideen M., Perkins J.D. and Pistikopoulos E. N. (1996a). “Optimal design of dynamic systems under uncertainty.” *Journal of American Institute of Chemical Engineers,* 42:2251–2272.
25. Bahri P., Bandoni J. A. and Romagnoli J. A. (1997). “Integrated flexibility and controllability analysis in design of chemical processes.” *Journal of American Institute of Chemical Engineers*, 43:997–1015.
26. Schweiger C. and Floudas C. (1999). “Optimization framework for the synthesis of chemical reactor networks.” *Industrial & Engineering Chemistry Research,* 38:744–766.
27. Sakizlis V., Bansal V., Ross R., Perkins J.D. and Pistikopoulos E.N. (2001). “An adjoint-based algorithm for mixed integer dynamic optimization.” *R. Gani & S. Jorgensen (Eds.), ESCAPE-11*, Kolding, Denmark, 9:273–278.
28. Bansal V., Sakizlis V., Ross R., Perkins J.D. and Pistikopoulos E.N. (2003). “New algorithms for mixed integer dynamic optimization.” *Computers and Chemical Engineering,* 27:647–668.
29. Angira R. (2005). “Evolutionary computation for optimization of selected non-linear chemical processes [PhD Thesis]”. *Birla Institute of Technology & Science,* Pilani.
30. Angira R. and Alladwar S. (2007). “Optimization of dynamic systems: A trigonometric differential evolution approach.” *Computers & Chemical Engineering,* 31:1055-1063.
31. Babu B.V. and Angira R. (2006). “Modified differential evolution for optimization of nonlinear chemical processes.” *Computers & Chemical Engineering,* 30:989-1002.
32. Angira R. and Babu B.V. (2006). “Optimization of process synthesis and design problems: A modified differential evolution approach.” *Chemical Engineering Science,* 61:4707-4721.
33. Lee H. H., Koppel L. B. and Lim H. C. (1972). “Integrated approach to class of countercurrent design and control of a processes.” *Ind. Eng. Chem. Process Des. Dev.,* 11(3), 376-382.
34. Saboo A. K. and Morari M. (1984). “Design of resilient processing plants-IV: some new results on heat exchange network synthesis.” *Chemical Engineering Science,* 39(3), 579-592.
35. Wolf E. A., Skogestad S., Hovd M. and Mathisen K. W. (1992). “A procedure for controllability analysis.” *IFAC workshop on integration between process design and process control,* Imperial college, London.
36. Lewin D. R. and Bogle D. (1996). “Controllability Analysis of an Industrial Polymerization Reactor.” *Computers and Chemical Engineering,* 20:S871-S876.

37. Seider W.D., Seader J.D. and Lewin D.R. (1999). "Process design principle." New York: Wiley.
38. Kuhlmann A. and Bogle D. L. (2001). "Controllability evaluation for non-minimum phase processes with multiplicity." *Journal of American Institute of Chemical Engineers,* 47(11):2627–2632.
39. Seferlis P. and Grievink J. (2001). "Process design and control structure screening based on economic and static controllability criteria." *Computers and Chemical Engineering,* 25:177-188.
40. Meeuse F. M. and Tousain R. L. (2002). "Closed-loop controllability analysis of process designs: Application to distillation column design." *Computers and Chemical Engineering,* 26:641-647.
41. Segovia-Hernandez et. al. (2008). "Controllability analysis of alternate schemes to complex column arrangements with thermal coupling for the separation of ternary mixtures." *Computers and Chemical Engineering,* 32:3057-3066.
42. Luyben M. L. and Floudas C. A. (1994). "Analyzing the interaction of design and control-1. A multiobjective framework and application to binary distillation synthesis." *Computers and Chemical Engineering,* 18(10):933-969.
43. Kookos I. K. and Perkins J. D. (2001). "An algorithm for simultaneous process design and control." *Industrial & Engineering Chemistry Research,* 40:4079-4088.
44. Bansal V., Perkins J. D. and Pistikopoulos E. N. (2002). "A case study in simultaneous design and control using rigorous, mixed-integer dynamic optimization models." *Industrial & Engineering Chemistry Research,* 41:760-778.
45. Asteasuain M., Brandolin A., Sarmoria C., and Bandoni A. (2004). "Simultaneous design and control of a semibatch styrene polymerization reactor." *Industrial & Engineering Chemistry Research,*43:5233-5247.
46. Chawankul N., Budman H., and Douglas P. L. (2005). "Integration of design and control: A robust control approach using MPC." *Proceedings of the 44th IEEE Conference on Decision and Control, and the European Control Conference 2005,* Seville, Spain.
47. Pajula E., and Ritala R. (2006). "Measurement uncertainty in integrated control and process design-A case study." *Chemical Engineering and Processing,* 45:312-322.
48. Flores-Tlacuahuac A., and Biegler L. T. (2007). "Simultaneous mixed-integer dynamic optimization for integrated design and control." *Computers and Chemical Engineering,* 31:588-600.
49. Flores-Tlacuahuac A., and Biegler L. T. (2008). "Integrated control and process design during optimal polymer grade transition operations." *Computers and Chemical Engineering,* 32:2823-2837.
50. Exler O., Antelo L. T., Egea J. A., Alonso A. A., and Banga J. R. (2008). "A tabu search-based algorithm for mixed-integer nonlinear problems and its application to integrated process and control system design." *Computers and Chemical Engineering,* 32:1877-1891.

51. Yi, C. & Luyben, W. (1997). “Design and control of coupled reactor/ column systems. Part 1. A binary coupled reactor/rectifier system.” *Computers and Chemical Engineering,* 21(1), 24–46.