Game Theoretic Approach to Multiobjective Designs: Focus on Inherent Safety

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A method for designing processes that are inherently safer—with the primary focus on disturbances having the potential for unbounded hazardous responses—is introduced. In cases where safety is not threatened (as in isothermal fermentation reactors), but product quality can rapidly degrade, this method provides designs that ensure high product quality (as in pharmaceutical processes). Using game theory, the method accounts for the trade-offs in profitability, controllability, safety and/or product quality, and flexibility. For nonlinear processes that are hard to control; that is, have an unstable and/or nonminimum-phase steady state, over a wide range of operating conditions, extended bifurcation diagrams are introduced. When a steady state is nonminimum phase, the process may exhibit inverse response. The steady states of processes are classified on the basis of instability and nonminimum-phase behavior to segregate the operating regimes into distinct zones. Locally optimal designs, one corresponding to each zone, are obtained first. These are compared with other locally optimal designs at alternate operating conditions, and/or process reconfigurations, to obtain the globally optimal design using game theory. Four indices—profitability, controllability, safety and/or product quality, and flexibility—characterize the optimality of a design. A novel index for safe operation and/or product quality at a steady state is formulated as a function of the eigenvalues of the Jacobian of the process model and the Jacobian of the process zero dynamics, providing a quantitative measure of instability and nonminimum-phase behavior. The application of the proposed method to an isothermal, continuous stirred-tank reactor (CSTR) with van der Vusse reactions, an exothermic CSTR, and an anaerobic fermentor with substrate and product inhibition is presented.
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Introduction

Profitability, controllability, and flexibility are important objectives in the design of chemical processes.[1,2] Trade-offs between these objectives have been the focus of designs that account for controllability[3-6] and designs in the face of uncertainty.[7-10] Focusing on controllability, Brengel and Seider[3] proposed coordinated design and control optimizations using nonlinear model predictive control (MPC) algorithms for a fermentation process. Luyben and Floudas[4] analyzed the interaction of design and control for a binary distillation column using open-loop controllability measures. Subramanian and

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coworkers[5] developed techniques for operability analysis of CSTRs, which help designers consider control in the early stages of design. Recently, Chawankul and coworkers[6] discussed the integration of design and control for a distillation column using internal model control (IMC). Turning to flexibility, an index and algorithms for calculating operational flexibility of chemical process designs were introduced by Swaney and Grossmann.[7,8] Morari[9] discussed both flexibility and resiliency of process systems. Pistikopoulos and Grossmann[10] introduced optimal retrofit designs that improve process flexibility.[10] Finally, Chacon-Mondragon and Himmelblau[11] discussed the integration of process flexibility with control in process design.

In addition, tight safety requirements in hazardous chemical operations and regulations in pharmaceutical processes have forced designers to account for safety and/or product quality during process design. Recently, the focus has been on inherently safer process designs[12,13] and on six-sigma methodology for high-quality product designs.[14,15] Kletz[16] introduced the term *inherently safer design* (ISD) and classified the strategies to minimize risk into four categories: (1) inherent, (2) passive, (3) active, and (4) procedural. The term *inherent* implies permanent properties of the strategies; that is, properties that characterize all instances of the strategies. Examples of a few inherent strategies are to:

(1) intensify or minimize the amount of hazardous material present at any given time

(2) substitute less hazardous materials for more hazardous ones

(3) attenuate or moderate such variables as the operating pressure, temperature, and concentration

(4) simplify the plant to achieve processes that are easier to operate and maintain, with fewer chances of malfunctions

(5) limit the effects of potential hazards.

In this work, a design is considered inherently safe with respect to hazards arising from sizable disturbances when the process responses do not deviate significantly from steady-state operation, even when they increase exponentially. Herein, ISDs result from strategies of types (3) and (4), with a focus on instability hazards related to process control. These also help to decrease the likelihood of safety incidents arising from other hazards, such as toxicity, flammability, reactivity, and radioactivity, of chemicals in the process.

To achieve greater profitability, process designs have been created in regions involving complex nonlinearities where process controllers continue to face stiff challenges. These involve steady-state multiplicity, limit cycles, chaos, and parametric sensitivity, which are manifestations of the nonlinearities. In addition, many process designs have unstable and/or nonminimum-phase steady states. In many cases, operation is more profitable at an unstable steady state, or at a stable steady state in the close proximity of an unstable steady state, often involving nonminimum-phase behavior (inverse response to typical disturbances). For these types of processes, controller designs have been more challenging,[17-19] with increasing attention devoted to the control of processes that exhibit nonminimum-phase behavior. In a recent paper, the concept of *switchability* is introduced; that is, the ease of switching from one process at a nonminimum-phase steady state to another, when high controllability is more difficult to achieve.[20] The switchability of reactor–separator systems is explored, although bifurcation analysis is not applied to identify instability over broad operating conditions. Furthermore, little attention has been devoted to the modification of process designs to avoid nonminimum-phase behavior, as well as to safety and/or product quality measures. The latter are closely related to the magnitude of positive eigenvalues associated with the process and its zero dynamics. At smaller magnitudes, the rate of exponential change in response to disturbances is low and thus the process is inherently safer and/or the product quality deviates less rapidly from its set point. Given the nonlinearities and parametric sensitivities of process designs, the incentives to achieve designs that account for the trade-offs among profitability, controllability, safety and/or product quality, and flexibility measures are gaining importance.

To achieve this, a method is introduced herein that accounts for these four measures. Inherently safer designs, having increased product quality, are developed to replace designs that exhibit unstable and/or nonminimum-phase behavior, such that the same level of profitability is maintained, but the instability and/or nonminimum-phase behavior are eliminated. The methods of bifurcation analysis are used to characterize the complex nonlinearities and to examine the causes of steady-state multiplicity, nonminimum-phase behavior, input multiplicity, output multiplicity, and isola formation. Solution diagrams are divided into four zones, in *extended bifurcation diagrams*, which identify the stability and minimum-phase character of the steady states. An optimal design is obtained in each zone by accounting for trade-offs in profitability, controllability, safety and/or product quality, and flexibility. This is accomplished by formulating an optimization problem for each zone.

The four objectives are compared in all of the zones, which are obtained by changing the operating conditions, process designs, and process configurations. Then, the globally optimal design is obtained using game theory,[21-23] which provides the global optimum of this discrete multiobjective problem by comparison of several designs with discrete objective function values. It also allows the designer to alter the *key criterion* and determine its impact on the globally optimal design. When the safety and/or product quality measure is weighted more heavily, inherently safer designs, having higher product quality, are achieved.

In the nonlinear analysis of chemical and biochemical reactors, singularity theory has been used effectively to characterize regions in parameter space over which many kinds of solution diagrams exist.[24] The multiobjective optimization method using game theory, introduced herein, permits the designer to characterize zones in the parameter space with simple measures of profitability, controllability, safety and/or product quality, and flexibility. Then, these measures are used to focus on one objective, such as safety and/or product quality, with emphasis on one or more of the other objectives. Like singularity theory, this analysis divides the parameter space into operating regimes (zones) that are well represented in the multiobjective optimization.

This article is organized as follows. Initially, the focus is on the strategy of zone segregation. This is followed by a description of the optimization method for obtaining both the locally and the globally optimal designs. Then, the proposed method is demonstrated for an isothermal CSTR involving the van der Vusse reactions, an exothermic CSTR, and an anaerobic fer-

Table 1. Zone Matrix: Classification of Process Dynamics

	Minimum Phase (MP)	Nonminimum Phase (NMP)
Stable (S)	Zone I (S-MP)	Zone II (S-NMP)
Unstable (US)	Zone III (US-MP)	Zone IV (US-NMP)

mentor having substrate and product inhibition. Finally, conclusions are presented.

Strategy of Zone Segregation

When designing processes that can exhibit instability and/or nonminimum-phase behavior over a wide range of operating conditions, it is an objective to seek stable and/or minimum-phase designs having comparable profitability levels, if possible. Unstable designs are those that have an unstable steady state; that is, a right-half plane (RHP) eigenvalue of the process Jacobian evaluated at the steady state. Nonminimum-phase behavior is observed when a *zero* of the process transfer function lies in the RHP. Finite zeros of a process are calculated from the zero dynamics of the process.[25-27] They are the eigenvalues of the Jacobian of the process zero dynamics. Clearly, instability and nonminimum-phase behavior, individually or combined, limit the degree of achievable control quality; they have an adverse effect on the safety and/or product quality of process designs. Thus, a quantitative index is formulated as a function of the eigenvalues to represent the safety and/or product quality characteristics.

Bifurcation diagrams and singularity theory are used extensively to study nonlinear chemical, biochemical, and polymer processes.[24,28-31] Also, bifurcation analysis of nonlinear systems under conventional PID (proportional-integral-derivative) control[32] and input–output linearizing feedback control[33] is used to examine performance as a function of controller tuning parameters. Although designs at maximum product concentration appear on most bifurcation diagrams of nonlinear systems, measures of their profitability, controllability, safety and/or product quality, and flexibility are not identified explicitly. Because bifurcation diagrams are compact, relative to the results of dynamic simulations, extensions to represent these measures are helpful and are introduced next.

Extended bifurcation diagram

In the extended bifurcation diagram (EBD) introduced herein, the operating regimes are characterized by the stability and minimum-phase behavior of their steady states. For a particular set of operating conditions, an open-loop process is in one of four zones as the primary bifurcation parameter varies. Table 1 classifies the four zones in terms of stability and minimum-phase behavior. Zone I corresponds to stable, minimum-phase operation; zone II, stable, nonminimum-phase operation; zone III, unstable, minimum-phase operation; and zone IV, unstable, nonminimum-phase operation. Note that the inherent safety and/or product quality of the designs decrease in the transitions from zones I to IV. Inherent safety and/or product quality are measured in terms of the eigenvalues of the process and its zero dynamics (as defined later in Eq. 7), for which it is assumed that operation in zones with instability and nonminimum-phase behavior gives lower product quality (with more off-specification product) than operation in zones having stable and minimum-phase behavior. Also, this zone classification can be extended to include periodic solution branches, although this is not addressed herein.

In the optimization method presented in the following sections, alternative designs are explored that shift the operating zones toward those having inherently safer and/or higher product quality operations. The elimination or reduction of instability and nonminimum-phase behavior is achieved through changes in the operating conditions, as well as through process redesigns and reconfigurations. At first, *process operation changes*, such as inlet changes involving feed concentrations and/or cooling water temperatures, are considered. When insufficient to achieve the desired zone, *process redesign* is attempted, involving such actions as changing the reactor volume and heat-transfer area. Finally, *process reconfiguration* is used such as by adding or removing recycle streams and placing reactors in parallel or series, with or without recycle. These configurations are selected to give robust performance in the presence of uncertainty and variability in the process and kinetic parameters.

Example: isothermal CSTR with van der Vusse reactions

Consider an isothermal CSTR with the van der Vusse reactions (A $\rightarrow$ B $\rightarrow$ C and 2A $\rightarrow$ D, where B is the desired product).[34] The mole balances for species A and B lead to

$$\frac{dC_A}{dt} = -k_1 C_A - k_3 C_A^2 + \frac{F}{V}(C_{Af} - C_A) \tag{1}$$

$$\frac{dC_B}{dt} = k_1 C_A - k_2 C_B - \frac{F}{V} C_B \tag{2}$$

Their dedimensionalized forms are

$$\frac{dx_1}{d\tau} = Da(1 - x_1) + \beta\, Da(1 - x_1)^2 - \frac{x_1}{V_d} \tag{3}$$

$$\frac{dx_2}{d\tau} = Da(1 - x_1) - \gamma\, Da\, x_2 - \frac{x_2}{V_d} \tag{4}$$

Table 2. Dimensionless Parameters of the Isothermal CSTR with van der Vusse Reactions

$x_1 = \dfrac{C_{Af} - C_A}{C_{Af}}$	$x_2 = \dfrac{C_B}{C_{Af}}$	$Da = k_1 \dfrac{V_o}{F}$	$\tau = \dfrac{t}{V_o/F}$
$V_d = \dfrac{V}{V_o}$	$\gamma = \dfrac{k_2}{k_1} = 2$	$\beta = \dfrac{k_3 C_{Af}}{k_1}$	$k_1 = 0.0138\ s^{-1}$ ($0.833\ min^{-1}$)
$k_2 = 0.0278\ s^{-1}$ ($1.667\ min^{-1}$)	$k_3 = 10.02\ m\ s^{-1}\ kmol^{-1}$ ($0.167\ L\ min^{-1}\ mol^{-1}$)	$V_o = 10\ m^3$	$C_{Af} = 10\ kmol/m^3$

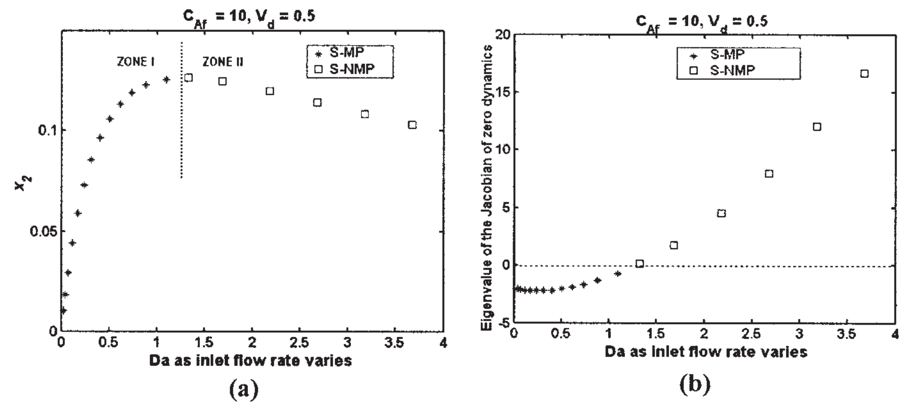

Figure 1. x_2 and the eigenvalue of the zero-dynamics Jacobian for the CSTR with the van der Vusse reactions as a function of *Da*.

where the parameters and dimensionless variables are defined in Table 2. The controlled variable, x_2, is the dimensionless concentration of B (C_B/C_{Af}), and the zero dynamics equation is

$$\dot{\eta}_1 = \frac{y_{sp1}(1-\eta_1)}{(1-\eta_1-\gamma y_{sp1})V_d}[1+\beta(1-\eta_1)] - \frac{\eta_1}{V_d} \quad (5)$$

Figure 1a shows the steady-state dimensionless concentration of the desired product (x_2) as a function of Damköhler number (*Da*). Bifurcation analysis reveals that all of the steady states of the process are stable. However, as seen in Figures 1a and 1b, the real part of the eigenvalue of the process zero dynamics changes from negative to positive, corresponding to a change from minimum- to nonminimum-phase behavior, as *Da* increases. When the nonminimum-phase behavior is ignored, the reactor design at two *Da* values provides the same concentration of the desired product. The significance of the nonminimum-phase behavior on the profitability, controllability, safety and/or product quality, and flexibility, and in turn the globally optimal design is considered in the next sections.

Method of Design Optimization

In this section, local optimization in each zone is discussed before game theory is introduced for global optimization.

Local design optimization

First, quantitative indices corresponding to the four objectives are defined. Then, the zones are defined and the approach to determining the locally optimal design in each zone, as a function of the process parameters and operating conditions, is discussed.

Quantitative indices

The performance of a design within a zone is measured by four quantitative indices for profitability, controllability, safety and/or product quality, and flexibility, as defined below:

Profitability Index (PI). In the early stages of design, it is sufficient to use the venture profit:

$$\text{Venture profit} = (1-t)(S-C) - i \times C_{TCI} \quad (6)$$

where t is the total income tax rate (federal plus state), S is the annual sales, C is the annual cost of manufacture, i is the effective annual interest rate, and C_{TCI} is the total capital investment.[35]

Controllability Index (CI). Again, in the early stages of design, a rough measure of controllability is sufficient. Here, the condition number (ratio of the largest to smallest eigenvalues) of the dimensionless process steady-state gain matrix (Jacobian) is used.[4] Note that a measure of the "closed-loop" controllability cannot be calculated early in process design because the controllers have not been designed.

Safety and/or Product Quality Index (S/Q). The *S*/*Q* index is introduced herein as

$$S/Q = w \times \text{Re}\{\text{RHP } \lambda_{\text{process}}\} + \text{Re}\{\text{RHP } \lambda_{\text{zero dynamics}}\} \quad (7)$$

where Re{RHP λ_{process}} is the sum of the real parts of the right-half plane (RHP) eigenvalues of the process Jacobian and Re{RHP $\lambda_{\text{zero dynamics}}$} is sum of the real parts of the RHP eigenvalues of the zero dynamics Jacobian; w is the weighting factor, herein assumed to be 2, thereby doubling the weight of the process eigenvalues compared with the zero dynamics eigenvalues. Clearly, as the magnitude of the eigenvalues in the RHP increases, it becomes more difficult to achieve inherently safe operation and/or high product quality.

Note that the condition number is just one formulation for the controllability index. This and other controllability measures are not suitable measures of the inherent safety of a process because they do not account for the sign of the eigenvalues in the process. For this reason, it is important to define the *S*/*Q* index and to weight it significantly in multiobjective design optimization, which also considers a controllability index, as described in the section on global design optimization.

Flexibility Index (FI). *FI* is a measure of the distance of a design from the bounds on the bifurcation parameter in a zone; that is, *FI* increases as it becomes more difficult to shift to another zone in the face of parametric uncertainty. *FI* will be defined by Eq. 8, in the subsection on zone-specific optimal designs, after the zones are defined in the subsection on zone classification.

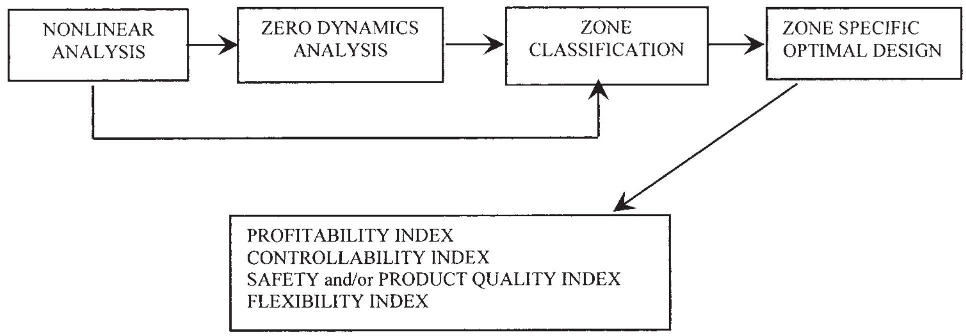

Figure 2. Local design optimization.

Algorithm

Figure 2 shows the steps in the local optimization of a process design. These are described next:

Nonlinear Analysis. The AUTO software[36] is used to perform nonlinear (bifurcation) analysis for a process model to obtain the steady-state and periodic solution branches as the primary bifurcation parameter varies. The eigenvalues of the Jacobian of the process along the solution branches are computed.

Zero Dynamics Analysis. The algorithm to obtain the zero dynamics of a process is provided elsewhere.[25-27] It is implemented herein using geometric control software[37] developed with *Mathematica*. Given a process model, the software derives an analytical model–based controller for the process. The eigenvalues of the Jacobian of the zero dynamics equations are obtained using this software. When these eigenvalues are positive, the steady state has nonminimum-phase behavior.

Zone Classification. The real parts of the eigenvalues of the Jacobians of the process and zero dynamics identify the zone for every design on the solution diagram; that is, each design is classified in one of the four zones in Table 1. This gives the *extended bifurcation diagram* (EBD), with the number of zones for a particular process model identified. For example, Figure 3a shows a sketch of a steady-state solution branch (A–B–C–D–E) of x_c, a process variable of a typical nonlinear system, as a function of *Da*. Note that designs on branch A–B–C have stable steady states and those on branch C–D–E have unstable steady states. Furthermore, the designs on branch A–B–C are subclassified into zone I (stable, minimum phase: branch A–B) and zone II (stable, nonminimum phase: branch B-C) using the eigenvalues of the zero dynamics equations. Similarly, branch C–D–E is subclassified into zone III (unstable, minimum phase: branch C–D) and zone IV (unstable, nonminimum phase: branch D—E). Note also that often zones of the same type appear more than once, with any EBD branch having at least one of the four zones.

Zone-Specific Optimal Designs. Initially, the feasible regions for each zone are modified given the operating constraints associated with the process. For example, as shown in Figure 3b, when the inequality constraint, $x_c \geq b$, applies, the bounds on the primary bifurcation parameter are adjusted for each zone. Branches A_F–B, B–C_{F1}, C_{F2}–D, and D–E_F are the feasible regions for zones I–IV, respectively. The branch C_{F1}–C of zone II and C–C_{F2} of zone III are not in the feasible region. Thus, only the branches B–C_{F1} and C_{F2}–D are searched to find the locally optimal designs in zones II and III, respectively. Note that bounding constraints, such as bounds on the inlet and coolant flow rates, and reactor volume, appear in the three case studies. For general inequality constraints, involving multiple process variables, designs computed by AUTO are removed from a zone when one or more constraints are violated.

Next, the designs (points on a solution branch computed by AUTO) are examined. Note that the number of designs in each zone depends on the step length (h) of the primary bifurcation parameter. The designs computed by AUTO are shown schematically for zone i in Figure 4a, where the primary bifurcation parameter, Da, is bounded by Da_{l_i} and Da_{u_i}, with $x_c = b$ defining Da_{l_i}. The solid circles denote designs computed by AUTO, with designs k and $k + 1$ surrounding the midpoint of

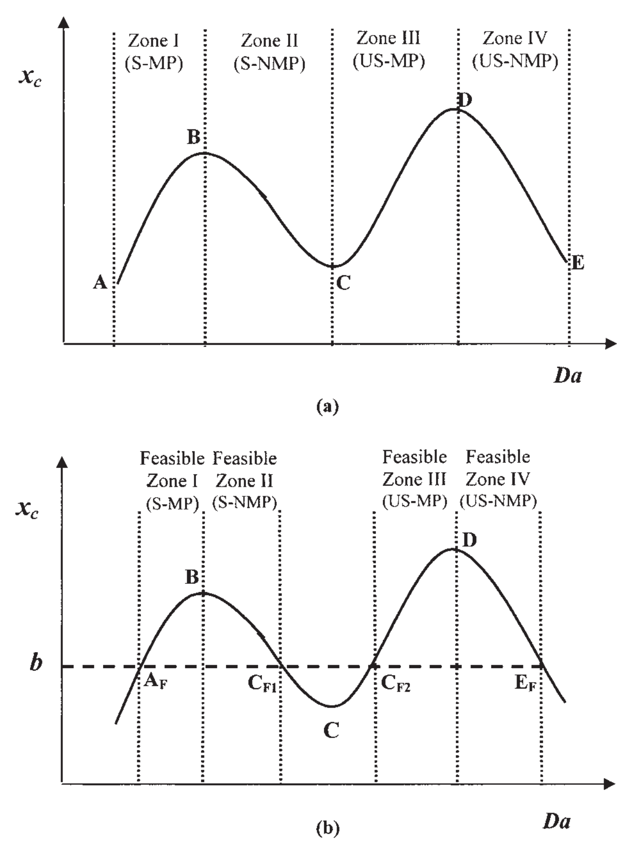

Figure 3. Zone classification.

(a) Without constraints; (b) With a lower-bound constraint.

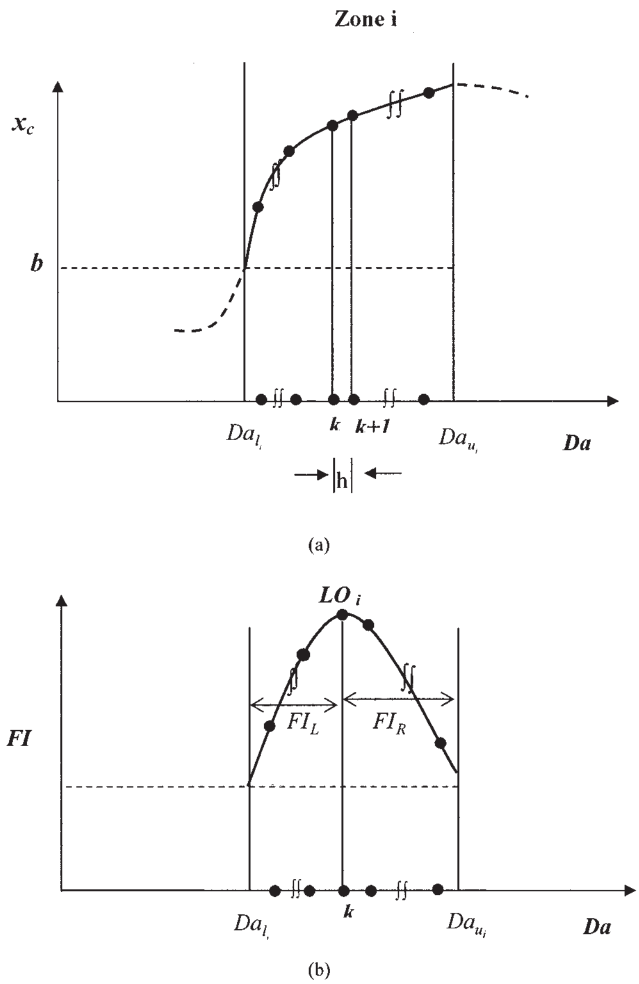

Figure 4. (a) A typical feasible zone; (b) *FI* in the feasible zone.

the zone. Note also that the dependent variable(s), x_c, varies nearly linearly within a zone, in the absence of turning points.

Having defined feasible zones, before proceeding, the flexibility index, *FI*, is defined as

$$FI = \frac{FI_R + FI_L}{2} - |FI_R - FI_L| \qquad (8)$$

where the RHS flexibility of a design, FI_R, is the absolute value of the difference between the upper bound and the design value of the primary bifurcation parameter in the zone. Similarly, the LHS flexibility, FI_L, is defined as the absolute value of the difference between the lower bound and the design value. The first term is half the width of a zone; that is, the maximum flexibility when a design is at the midpoint of the zone $[(Da_{l_i} + Da_{u_i})/2]$. The second term penalizes the flexibility index as a design moves from the center point. Thus, in a zone, *FI* is maximized for design *k*, computed by AUTO, closest to the midpoint, as shown schematically in Figure 4b. Note that *FI* differs from the flexibility index defined by Grossmann and coworkers,[7,8] which is advantageous for multidimensional, closed, feasible spaces. *FI* in Eq. 8 is sufficient for solution branches within a zone (in the absence of singular points).

Because the gradients of *FI* exceed those of the other indices in each zone, the locally optimal design in zone *i* is selected where *FI* is maximized; that is, the design at which $|FI_L - FI_R|$ is minimized. This corresponds to design *k* in Figure 4b, denoted by LO_i, which is located closest to the middle of the zone. In the face of design uncertainties, these designs (LO_i) are less likely to shift from their current zone to other zones, where the shift is accompanied by significant changes in the four indices (*PI*, *CI*, *S*/*Q*, and *FI*).

It is also possible to formulate a nonlinear program involving a weighted-sum objective function,[38] involving the four indices, with *FI* weighted more heavily, and resulting in a similar locally optimal design. However, considering that gradients in *FI* greatly exceed those for the other three indices, it is sufficient to maximize *FI* in zone *i*. In our experience, within each zone, the variations in *PI*, *CI*, and *S*/*Q* are small and, thus, it is sufficient to select the design having the maximum *FI*. This design usually does not have the maximum venture profit, but it is inherently safer and/or exhibits higher product quality; that is, the frequencies of accidents and off-specification products are reduced. The locally optimal design for zone *j* is represented as the set $\{PI_{LO_j}, CI_{LO_j}, S/Q_{LO_j}, FI_{LO_j}\}$. Note that only *FI* is used to obtain the locally optimal design in zone *j*; however, all four indices are used to calculate the globally optimal design.

In summary, as discussed in the section on strategy of zone segregation, alternative designs that shift the operating zones toward operations having inherently safer and/or higher product quality are explored through: (1) process operation changes, (2) process redesigns, and/or (3) process reconfigurations. Then, for each zone, an optimal design, with its four indices, is computed. Given the local optima for all possible zones, LO_1, LO_2, . . . , LO_n, and associated indices, the global optimum is determined, as described next.

Global Design Optimization

Having determined an optimal design for each zone, with four index values, location of the global optimum requires compromises that can be implemented using game theory. The latter is a multiobjective optimization technique in which multiple discrete objective functions, with varying magnitudes, are compared for competitive designs.

Game theory formulation

Game theory[21-23] is a branch of mathematical analysis used to study decision making in conflicting situations. It involves the prediction of outcomes for a group of interacting players, where the action of a single player directly affects the payoffs of the other players. In this section, game theory is applied for multiobjective process design.

The elements of a game are: (1) several players, (2) actions/strategies, and (3) payoffs (objective functions), which for multiobjective process design, are:

- *Players*: (1) profitability, (2) controllability, (3) safety and/or product quality, and (4) flexibility.
- *Actions/Strategies*: assigned to each player involving operating zones and process parameters—these are simply the parameter moves among the feasible operating zones.

Table 3. Game Matrix: Description of Elements of the Game

Players	(I) **Profitability**	(II) **Controllability**	(III) **Safety and/or Product Quality**	(IV) **Flexibility**
Actions/strategies	Shift in operating zones (Classified as a function of the primary bifurcation parameter)	Adjust the manipulated variables	Redesign process Reconfigure process	Accommodate disturbance variables and/or uncertain parameters
Payoffs (Objective function)	Maximize venture profit **(Profitability index)**	Minimize dimensionless condition number **(Controllability index)**	Minimize RHP eigenvalues of the Jacobians of process and its zero dynamics **(*S*/*Q* index)**	Minimize the extent of zone change due to uncertainty **(Flexibility index)**

- *Payoff consequences*: quantitative index measures formulated for each player.

The complete game matrix (table) to obtain the globally optimal zone, in terms of the players, their actions/strategies, and objectives, is shown in Table 3. Herein, actions/strategies for the player *profitability* are moves among the four operating zones as a function of the primary bifurcation parameter, *Da*, and the *payoff* (*objective function*); that is, the profitability index (venture profit), *PI*. In this case, the goal is to maximize the venture profit. Actions/strategies for the player *controllability* move the manipulated variables from zone-to-zone and the *payoff* is the controllability index (condition number), *CI*, which is minimized. Actions/strategies for the player *safety and/or product quality* are design variations to reduce the impact of instability and nonminimum-phase behavior (such as introduction or removal of recycle, adjustments between parallel and series configurations, etc.) and the *payoff* is measured as the safety and/or product quality index (in terms of the RHP eigenvalues of the Jacobians of the process and of the zero dynamics), with the goal to minimize the *S*/*Q* index. Actions/strategies for the player *flexibility* adjust the process parameters, accounting for uncertainty in the process, and the *payoff* is the flexibility index, *FI*, with the goal to maximize *FI*.

Thus, the problem of obtaining inherently safe and/or high product quality designs is formulated as a *multiplayer*, *normal-form* (represented in table form as opposed to tree form), *simultaneous-move* (all players make a move at the same time as opposed to sequential moves where each player observes the actions/strategies of the other players before making a move), *noncooperative* [each player tries to optimize its objective function (payoff) ignoring the objective functions of the other players] game. As introduced in Appendix A, techniques to implement game theory,[21-23] that is, to find the *equilibrium* of a game (the globally optimal design), are: (1) *equilibrium in dominant actions*, (2) *pure-strategy Nash equilibrium*, and (3) *mixed-strategy Nash equilibrium*. These are used to obtain inherently safer and/or higher product quality designs, which account for the trade-offs among profitability, controllability, safety and/or product quality, and flexibility. For example, when a single locally optimal design dominates all other locally optimal designs (that is, where each player has a dominant strategy and the corresponding payoffs are maximized regardless of the actions/strategies of the other players), the globally optimal design is obtained using the *equilibrium in dominant actions* technique. When two or more locally optimal designs are equally preferred (that is, where not all players have a dominant strategy), *pure-strategy Nash equilibrium* is used. Finally, when *equilibrium in dominant actions* and *pure-strategy Nash equilibrium* are insufficient, *mixed-strategy Nash equilibrium* is used, with probabilities assigned to the locally optimal designs, and those having higher probabilities identified as globally optimal designs. GAMBIT,[39] software for game theory, is used herein to obtain globally optimal designs, given locally optimal designs for each zone. The details of its implementation are explained using three case studies in the next section.

The *equilibrium in dominant action* technique indicates the existence of a global solution. However, in the case of *pure-strategy Nash equilibrium* and *mixed-strategy Nash equilibrium*, there is more than one potential global solution. Depending on the decision maker's preference, additional criteria lead to a single globally optimal design, as needed. Like other multiobjective optimization algorithms, game theory can lead to poor solutions for multidimensional problems and may fail to identify a pareto-optimal solution, if one exists. However, the main advantage of using game theory in process design is the ease in visualizing the four indices in each zone, enabling the designer to emphasize any one (or more) of the indices, leading to different globally optimal solutions. Note that alternative MINLP (mixed-integer nonlinear programming) formulations to identify the globally optimal zone involve difficulties in: (1) calculating the *S*/*Q* index in GAMS and (2) formulating comparisons of designs obtained through process redesign and reconfiguration. The latter comparisons are easily formulated using game theory.

Case Studies

Figure 5 identifies the zones for the three reactors examined herein. For the isothermal CSTR with the van der Vusse reactions, zones I and II are observed as the primary bifurcation parameter, *Da*, is varied. For the CSTR with the exothermic reactions, $A \rightarrow B \rightarrow C$, zones I, II, and III are exhibited as a function of the dimensionless feed flow rate. Furthermore, when a recycle stream is added, using the same model, zones II and IV are observed. Finally, for an anaerobic fermentor with a continuous culture of *Klebsiella pneumoniae*, having both product and substrate inhibition, all four zones are exhibited as a function of the dimensionless substrate feed concentration. Note that both the number and the complexity of the zones increase with process complexities and nonlinearities. Next, consider determining globally optimal designs, with a focus on inherent safety and product quality for the second case study and high product quality for the first and third case studies. Appendix B provides an algorithm to summarize the different steps involved in obtaining a global-optimal solution using the

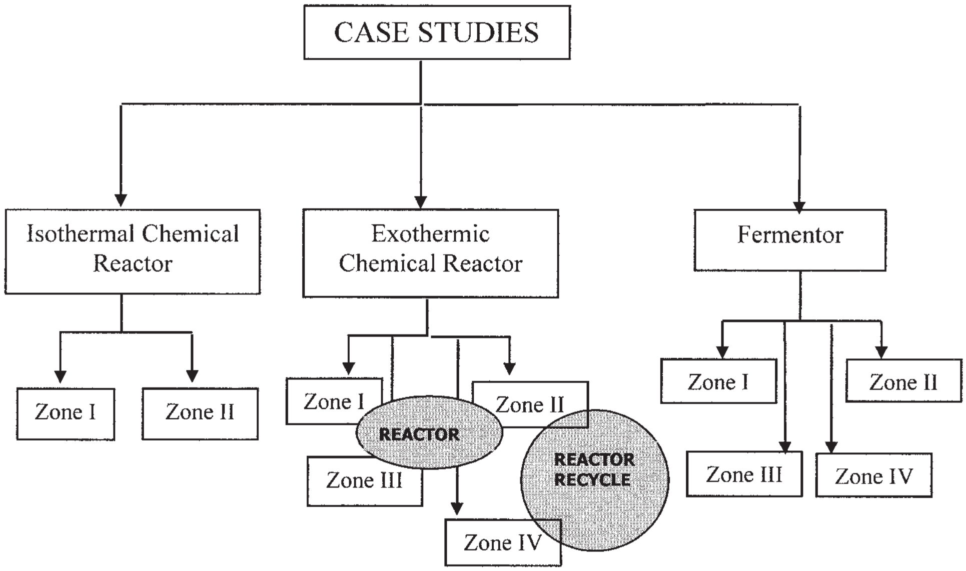

Figure 5. Summary of zones for three reactors.

proposed approach, details of which can be seen in the following case studies.

Example I: Isothermal CSTR with van der Vusse reactions

The process model and the zero dynamics for an isothermal CSTR with the van der Vusse reactions are shown in the section on strategy of zone segregation. In this study, EBDs are obtained to select high product quality designs from among four reactor volumes at three feed concentrations, as a function of the primary bifurcation parameter, *Da*.

The players are *profitability*, *flexibility*, and *product quality*. Note that controllability does not vary significantly from zone I to zone II and, consequently, is not included. Game theory is applied with three objectives to: (1) maximize *PI* (by adjusting *Da* from 0 to 5.0), (2) minimize *S*/*Q* (by adjusting the reactor volume, V_d = {0.5, 1, 1.5, 2}), and (3) maximize *FI* (by adjusting the concentration of A in the feed, C_{Af} = {7, 10, 13 kmol/m^3}). The feasible region within each zone is modified to satisfy the constraint that the dimensionless concentration of B exceeds 0.1.

EBDs for four reactor volumes at a particular value of the feed concentration (C_{Af} = 10 kmol/ m^3) are shown in Figure 6a. Similarly, EBDs at V_d = 1 and at the three feed concentrations are shown in Figure 6b. The nonminimum-phase behavior (RHP eigenvalues of zero dynamics) increases with the reactor volume, as seen in Figure 6a. However, the impact of changes in the feed concentration on the nonminimum-phase behavior is not as significant, as seen in Figure 6b. Locally optimal designs in each zone are obtained; that is, a total of 24 designs (two for each pair of feed concentration and reactor volume), which are shown in Table 4. The entries in each cell of the table are the set {normalized *PI* (that is, profitability of a design divided by 10^y, where $z \times 10^y$ is the maximum profitability of the designs in the parameter space), *S*/*Q*, *FI*} plus the primary bifurcation parameter, *Da*.

To obtain the globally optimal design using game theory, dominant actions, if any, for each player are identified first. For the player *profitability*, the *PI* in two rows, for zone I and zone II, at each of the C_{Af}, are compared in Table 4. Clearly, the best profitabilities are in zone I regardless of the actions of the other players; thus, zone I is the dominant action for profitability. Similarly, for the player *product quality*, *S*/*Q* is compared for the four actions, V_d = {0.5, 1, 1.5, 2} (in the four columns), at each C_{Af}. Note that smaller values of *S*/*Q* are preferred. Therefore, V_d = 2 is preferred in zone II; but, the preference in zone I is not observed (*S*/*Q* is not defined). Because the dominant action for *profitability* is operation in zone I, designs in zone II are not considered when selecting the global optimum. Thus, it is important to select one V_d as the dominant action for the player *product quality* in zone I. This can be accomplished by: (1) formulating an alternate *S*/*Q* index, such as the LHP eigenvalues of the zero dynamics, which are smallest for V_d = 0.5, giving a higher product quality design (thus, V_d = 0.5 is the dominant action in zone I—which differs from the dominant action in zone II, V_d = 2); (2) using *FI* to select the dominant action among V_d = {0.5, 1, 1.5, 2}, giving V_d = 0.5, which has the maximum *FI*; and (3) using a modified *S*/*Q* index:

$$S/Q_n = w_1 \frac{S/Q}{\max(S/Q)} + w_2 \frac{FI}{\max(FI)}, \qquad w_1 = -1, w_2 = 1 \tag{9}$$

that is, a normalized, weighted index, S/Q_n. The latter permits the selection of the best *S*/*Q* index influenced by the trade-offs in *FI*, giving V_d = 0.5 as the dominant action for zone I, as well as zone II (weak dominance).

From the analysis thus far, using option (3) for the *S*/*Q* index, components of the *equilibrium in dominant actions* solution are (zone I, V_d = 0.5). Furthermore, for the player *flexibility*, *FI* is compared for C_{Af} = {7, 10, 13 kmol/m^3} at actions for the player's *profitability* and *product quality* equal to (zone I, V_d = 0.5). As seen in Table 4 and Figure 6b, all of the indices change far less with C_{Af} than with *Da* and V_d. Furthermore, both solutions (zone I, V_d = 0.5, C_{Af} = 10

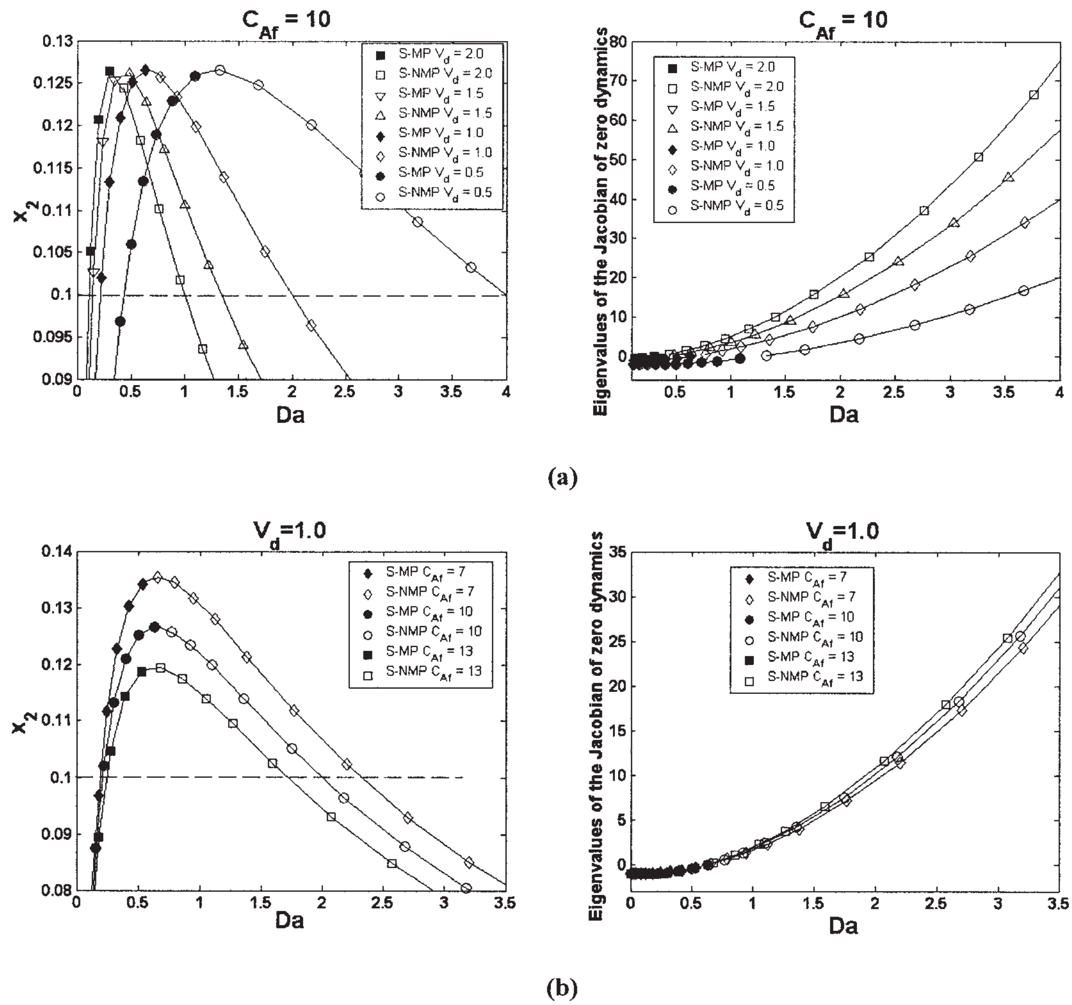

Figure 6. Extended bifurcation diagram and eigenvalues of zero dynamics for isothermal CSTR with van der Vusse reactions.

(a) V_d varies; (b) C_{Af} varies.

Table 4. Locally Optimal Designs for Example 1*

		Product Quality			
C_{Af} = 7	Zone	V_d = 0.5	V_d = 1.0	V_d = 1.5	V_d = 2.0
Profitability	I	{0.3, **[0.45], 0.73} (0.83)	{0.3, **[0.17], 0.27} (0.42)	{0.32, **[0.12], 0.2} (0.26)	{0.19, **[0.1], 0.17} (0.32)
	II	{0.057, 9.68 [0], 1.61} (3.0)	{0.07, 4.0 [0.1], 0.84} (1.33)	{0.078, 2.04 [0.05], 0.43} (0.84)	{0.082, 1.42 [0.05], 0.33} (0.61)
C_{Af} = 10	Zone	V_d = 0.5	V_d = 1.0	V_d = 1.5	V_d = 2.0
Profitability	I	{0.32, **[0.38], 0.61} (0.74)	{0.3, **[0.21], 0.33} (0.4)	{0.33, **[0.11], 0.19} (0.24)	{0.20, **[0.09], 0.16} (0.30)
	II	{0.09, 4.54 [0.34], 1.3} (2.12)	{0.088, 2.33 [0.13], 0.6} (1.1)	{0.075, 2.07 [0.05], 0.43} (0.81)	{0.08, 1.4 [0.05], 0.32} (0.59)
C_{Af} = 13	Zone	V_d = 0.5	V_d = 1.0	V_d = 1.5	V_d = 2.0
Profitability	I	{0.31, **[0.37], 0.6} (0.72)	{0.29, **[0.18], 0.29} (0.39)	{0.23, **[0.12], 0.18} (0.33)	{0.2, **[0.09], 0.15} (0.28)
	II	{0.084, 4.83 [0.15], 1.04} (2.16)	{0.088, 2.23 [0.1], 0.53} (1.05)	{0.011, 0.96 [0.1], 0.33} (0.62)	{0.078, 1.39 [0], 0.23} (0.57)

*Entries in each cell: {normalized *PI*, *S/Q* [S/Q_n], *FI*}
(Da)

**Not defined.

Table 5. Dimensionless Variables and Parameters of Example II

$x_1 = \frac{C_A}{C_{Afo}}$	$x_2 = \frac{C_B}{C_{Afo}}$	$x_3 = \frac{T - T_{fo}}{T_{fo}} \gamma$	$x_4 = \frac{T_c - T_{fo}}{T_{fo}} \gamma$
$x_{1f} = \frac{C_{Af}}{C_{Afo}} = 1$	$x_{2f} = \frac{C_{Bf}}{C_{Afo}} = 0$	$x_{3f} = \frac{T_f - T_{fo}}{T_{fo}} \gamma = 0$	$x_{4f} = \frac{T_{cf} - T_{fo}}{T_{fo}} \gamma = -1$
$\zeta_1(x_3) = \exp \frac{x_3}{1 + \frac{x_3}{\gamma}}$	$\zeta_2(x_3) = \exp \frac{\psi x_3}{1 + \frac{x_3}{\gamma}}$	$\tau = \frac{Q_o}{V} t$	$q = \frac{Q}{Q_o}$
$q_c = \frac{Q_c}{Q_o}$	$\delta = \frac{UA}{\rho C_p Q_o} = 0.78$	$\delta_1 = \frac{V}{V_c} = 10$	$\delta_2 = \frac{\rho C_p}{\rho_c C_{pc}} = 0.952$
$S = \frac{k_2(T_{fo})}{k_1(T_{fo})} = 1.015$	$\phi = \frac{V}{Q_o} k_1(T_{fo}) = 0.06$	$\beta = \frac{-\Delta H_A C_{Afo} \gamma}{\rho C_p T_{fo}} = 8$	$\alpha = \frac{-\Delta H_B}{-\Delta H_A} = 0.19$
$\gamma = \frac{E_1}{RT_{fo}} = 27.85$	$\psi = \frac{E_2}{E_1} = 0.32$		

kmol/m^3) and (zone I, $V_d = 0.5$, $C_{Af} = 7$ kmol/m^3) provide high product quality designs with comparable profits. Note that a single solution can be obtained using a weighted-sum, multiobjective function, with weighting factors for *PI*, S/Q_n, and *FI* selected by the designer. GAMBIT selects (zone I, $V_d = 0.5$, $C_{Af} = 7$ kmol/m^3) as an *equilibrium in dominant action* solution when S/Q_n is used. This is a globally optimal, high product quality solution.

Example II: Exothermic CSTR with reactions A → B → C

This CSTR involves the exothermic reactions A → B → C and has jacket dynamics.[40,41] Mole balances on A and B, and energy balances for the reactor and its jacket are, respectively,

$$\frac{dC_A}{dt} = \frac{Q}{V}(C_{Af} - C_A) - k_1(T)C_A \tag{10}$$

$$\frac{dC_B}{dt} = \frac{Q}{V}(C_{Bf} - C_B) - k_2(T)C_B + k_1(T)C_A \tag{11}$$

$$\frac{dT}{dt} = \frac{Q}{V}(T_f - T) + k_1(T)C_A \frac{(-\Delta H_A)}{\rho C_p} + k_2(T)C_B \frac{(-\Delta H_B)}{\rho C_p} - \frac{UA}{\rho C_p V}(T - T_c) \tag{12}$$

$$\frac{dT_C}{dt} = \frac{Q_c}{V_c}(T_{cf} - T_c) + \frac{UA}{\rho C_{pc} V_c}(T - T_c) \tag{13}$$

Using the dimensionless parameters and variables in Table 5, the model in dimensionless form is

$$\frac{dx_1}{d\tau} = q(x_{1f} - x_1) - x_1\zeta_1(x_3)\phi \tag{14}$$

$$\frac{dx_2}{d\tau} = q(x_{2f} - x_2) + x_1\zeta_1(x_3)\phi - x_2\phi\zeta_2(x_3)S \tag{15}$$

$$\frac{dx_3}{d\tau} = q(x_{3f} - x_3) + \beta\phi[x_1\zeta_1(x_3) + \alpha x_2 S\zeta_2(x_3)] + \delta(x_4 - x_3) \tag{16}$$

$$\frac{dx_4}{d\tau} = \delta_1[q_c(x_{4f} - x_4) + \delta\delta_2(x_4 - x_3)] \tag{17}$$

Here, the controlled variables are the dimensionless concentration of B, x_2, and the dimensionless jacket temperature, x_4, and the manipulated variables are the dimensionless feed and coolant flow rates, q and q_c. The zero dynamics equations are

$$\dot{\eta}_1 = -\frac{\zeta_1(\eta_2)(-x_{2f} + y_{sp1})\phi\eta_1 - (-x_{1f} + \eta_1)[\zeta_2(\eta_2)Sy_{sp1}\phi - \zeta_1(\eta_2)\phi\eta_1]}{y_{sp1} - x_{2f}} \tag{18}$$

$$\dot{\eta}_2 = \frac{(y_{sp1} - x_{2f})\{-\beta\phi[\zeta_2(\eta_2)Sy_{sp1}\alpha + \zeta_1(\eta_2)\eta_1] - \delta(y_{sp2} - \eta_2)\}}{y_{sp1} - x_{2f}} - \frac{[\zeta_2(\eta_2)Sy_{sp1}\phi - \zeta_2(\eta_2)\phi\eta_1](\eta_2 - x_{3f})}{y_{sp1} - x_{2f}} \tag{19}$$

Depending on the heat of reaction, these reactors exhibit several steady states, both stable and unstable, and the system may have a RHP zero(s). Analyzing the dimensionless, nonlinear reactor model and its zero dynamics, the eigenvalues of the Jacobians of the process model and zero dynamics are used to obtain the EBDs, in which zones I, II, and III are found as the primary bifurcation parameter (dimensionless feed flow rate) is varied. Similarly, EBDs are obtained for a reactor–recycle system, with 20% of the unreacted A in the reactor effluent recycled. Because the reactor–recycle system is more

Table 6. Locally Optimal Designs for Example II*

	Zone	Controllability $q_c = 0.1$	$q_c = 0.2$	$q_c = 0.3$	$q_c = 0.4$
Profitability	I	{1.94, 31.8, **[0.25], 0.27} (2.24)	{1.58, 22.5, **[0.21], 0.23} (1.90)	{1.24, 16.23, **[0.16], 0.18} (1.57)	{0.88, 11.6, **[0.12], 0.13} (1.2)
	II	{0.96, 28.7, 3.88 [0.4], 0.82} (1.18)	{0.89, 20.3, 1.9 [0.45], 0.68} (1.1)	{0.74, 14.94, 0.99 [0.41], 0.55} (0.96)	{0.51, 10.6, 0.44 [0.37], 0.45} (0.75)
	III	NA†	{0.82, 28.56, 11.28 [−0.58], 0.46} (1.7)	{0.63, 16.75, 5.64 [−0.13], 0.41} (1.34)	{0.43, 9.13, 1.03 [0.25], 0.38} (0.97)
	IV	NA	NA	NA	NA

*Entries in each cell: {normalized *PI, S/Q* [S/Q_n], *FI*}
(q)

**Not defined.
†NA, not applicable.

Table 7. Locally Optimal Designs for the Reactor–Recycle System in Example II*

	Zone	Controllability $q_c = 0.1$	$q_c = 0.2$	$q_c = 0.3$	$q_c = 0.4$
Profitability	I	NA†	NA	NA	NA
	II	{0.67, 24.15, 1.00 [0.64], 0.8} (1.32)	{0.78, 18.94, 0.74 [0.84], 1.0} (1.48)	{0.84, 15.63, 0.63 [0.94], 1.1} (1.56)	{0.65, 13.2, 0.6 [0.87], 1.02} (1.25)
	III	NA	NA	NA	NA
	IV	NA	NA	{1.6, 18.46, 6.53 [−0.44], 0.15} (2.68)	{1.57, 15.42, 9.74 [−0.5], 0.4} (2.65)

*Entries in each cell: {normalized *PI, S/Q* [S/Q_n], *FI*}
(q)

†NA, not applicable.

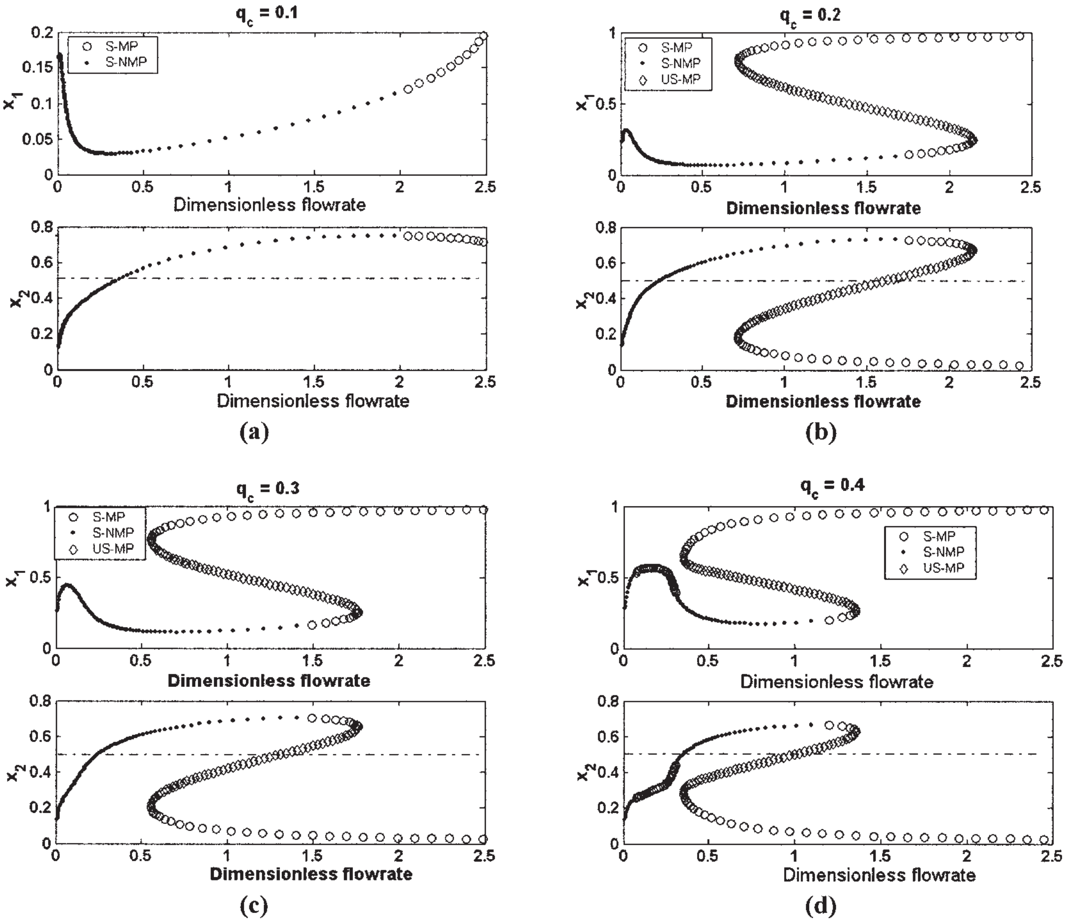

Figure 7. Extended bifurcation diagram for the reactor in Example II.

complex, having more severe nonlinearities, it often exhibits zones II and IV as the feed flow rate is varied. It is shown that nonminimum-phase behavior increases when recycle is added to the exothermic CSTR. This is consistent with the observation that recycle introduces nonminimum-phase behavior.[42]

The players for this game are *profitability*, *controllability*, *safety and product quality*, and *flexibility*. Game theory is applied with four objectives to: (1) maximize *PI* (by adjusting the dimensionless, feed flow rate *q*, from 0 to 3.0), (2) minimize *CI* (by adjusting the dimensionless, cooling water flow rate, $q_c = \{0.1, 0.2, 0.3, 0.4\}$), (3) minimize *S*/*Q* (by adjusting the flow rate of a recycle stream from zero to finite recycle), and (4) maximize *FI* (by adjusting C_{Af}, the concentration of A in the feed, and T_f, the feed temperature).

The feasible region within each zone is modified to satisfy the constraint that the dimensionless concentration of B, x_2, exceeds 0.5. The locally optimal designs are obtained for all existing zones, corresponding to the full range of operating conditions reported in Tables 6 and 7 for the reactor and the reactor–recycle system, respectively. The entries in each cell of the table are the set {normalized *PI*, *CI*, *S*/*Q* [S/Q_n], *FI*} plus the primary bifurcation parameter, *q*. The EBDs of the reactor and reactor–recycle systems, showing the dimensionless concentrations of A and B, x_1 and x_2, at four coolant flow rates are in Figures 7a–7d and Figures 8a–8d, respectively. For the reactor system, zones I and II exist for $q_c = 0.1$, and zones I, II, and III exist for $q_c = 0.2$, 0.3, and 0.4. Similarly, for the reactor–recycle system, zone II exists for $q_c = 0.1$ and 0.2, and zones II and IV exist for $q_c = 0.3$ and 0.4.

To obtain the globally optimal solution, locally optimal designs are compared with emphasis on inherent safety. To reduce the dimensionality of the optimization, the impact of small variations in C_{Af} and T_f are assumed to have negligible impact on the optimal solution, as in Example 1. Consequently, only one strategy for the player *flexibility* is considered. Furthermore, S/Q_n is used for the player *safety and product quality* because it accounts for the trade-offs between *FI* and *S*/*Q* because *q*, q_c, and the design configuration vary.

From Table 6, for the reactor system, the dominant action for the player *profitability* is zone I (normalized *PI* is maximized for all controllability actions [$q_c = \{0.1, 0.2, 0.3, 0.4\}$]). However, from Table 7, for the reactor–recycle system, the dominant action for the player *profitability* is zone IV. For the player *controllability*, the preferred action is $q_c = 0.4$ for both the reactor and reactor–recycle system; that is, *CI* is minimized for profitability actions (zone I, . . . , zone IV). Identification of the dominant strategy for the player *safety and product quality* by comparing S/Q_n is not straightforward because the zones for the reactor and reactor–recycle systems differ significantly. Nevertheless, the existence of zone I for the reactor system,

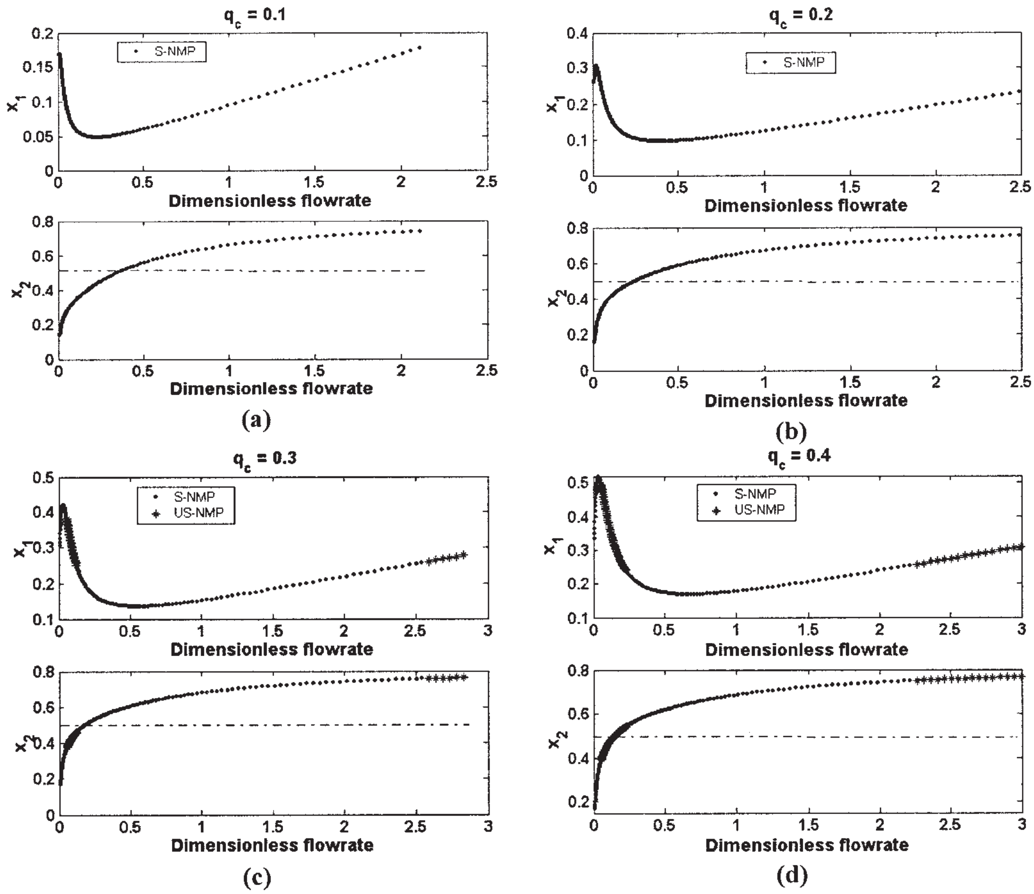

Figure 8. Extended bifurcation diagram for the reactor–recycle system in Example II.

coupled with the existence of zone IV for the reactor–recycle system, give the reactor system a weak dominance over the reactor–recycle system. However, for zone II only, S/Q_n of the reactor–recycle system dominates over that for the reactor system. Thus, for improved safety and flexibility, the designer may select a reactor–recycle design in zone II. For the other zones, the reactor system is the dominant action for the player *safety and product quality*.

Therefore, when ignoring zone II, the components (zone I, q_c = 0.4, reactor system) is the globally optimal solution obtained by the *equilibrium in dominant actions* technique. Note that S/Q_n has been used to select the reactor or reactor–recycle design, but has not been used to select designs having the best S/Q_n in a zone. For zone I, *FI* and thus S/Q_n decrease with q_c; thus, the action $q_c = 0.1$ is inherently safer than $q_c = 0.4$. Furthermore, within zone I, when the player *safety and product quality* is emphasized, the components (zone I, $q_c = 0.1$, reactor system) is the optimal solution, which also has the maximum *PI*.

Using S/Q_n, GAMBIT gives three *profiles* (that is, solutions): (1) {zone I, $q_c = 0.4$, reactor system}, (2) {zone IV, $q_c = 0.4$, reactor–recycle system}, and (3) a solution using the *mixed-strategy Nash equilibrium* technique, in which probabilities are assigned by GAMBIT to profiles (1) and (2). Given the desire to focus on the player *safety and product quality*, although the *PI* in zone I of the first profile is less than the *PI* in zone IV of the second profile, the second profile cannot be globally optimal because the player *safety and product quality* prefers zone I. Beginning with the first profile of GAMBIT, to obtain an inherently safer design, S/Q_n is searched in zone I, giving the design at $q_c = 0.1$.

Table 8. Dimensionless Variables and Parameters of the Anaerobic Fermentor

$x = \dfrac{X}{X_m}$	$y = \dfrac{C_S}{C_S^*}$	$z = \dfrac{C_p}{C_p^*}$	$\tau = t\mu_{\max}$
$u = \dfrac{\mu}{\mu_{\max}}$	$d = \dfrac{D}{\mu_{\max}}$	$y_o = \dfrac{C_{So}}{C_{So}^*}$	$\alpha_1 = \dfrac{K_S^*}{C_S^*} = 0.01$
$\alpha_2 = \dfrac{K_p^*}{C_S^*} = 0.025$	$\alpha_3 = \dfrac{K_S}{C_S^*} = 0.00014$	$\beta_1 = \dfrac{m_s}{\Delta q_S^m} = 0.0286$	$\beta_2 = \dfrac{m_p}{\Delta q_p^m} = 0.0083$
$\gamma_1 = \dfrac{\mu_{\max}}{Y_s^m \Delta q_S^m} = 2.3929$	$\gamma_2 = \dfrac{Y_p^m \mu_{\max}}{\Delta q_p^m} = 0.5583$	$\phi_1 = \dfrac{X_m \Delta q_S^m}{C_S^* \mu_{\max}} = 0.1306$	$\phi_2 = \dfrac{X_m \Delta q_p^m}{C_S^* \mu_{\max}} = 0.8955$

Table 9. Locally Optimal Designs for the Anaerobic Fermentor*

Profitability	Controllability				
Zone	$d = 0.1$	$d = 0.2$	$d = 0.3$	$d = 0.4$	$d = 0.5$
I	{0.83, 5123.3, **[0.33], 0.11} (0.39)	{1.55, 7.56, **[0.24], 0.079} (0.36)	{2.07, 1188.9, **[0.15], 0.05} (0.32)	{2.5, 378.6, **[0.09], 0.03} (0.29)	{2.76, 55.064, **[0.026], 0.0085} (0.25)
II	{0.74, 1.58, 0.36 [0.67], 0.33} (0.56)	{1.3, 3.29, 0.5 [0.21], 0.22} (0.47)	{1.72, 10.47, 0.3 [0.12], 0.13} (0.38)	NA	NA
III	NA†	NA	NA	{2.68, 572.66, 0.49 [−0.3], 0.05} (0.26)	{2.85, 208.85, 0.59 [−0.44], 0.032} (0.24)
IV	{0.97, 218.40, 1.1 [−0.7], 0.1} (0.39)	{1.77, 348.18, 1.0 [−0.68], 0.074} (0.35)	{2.37, 1637.1, 0.82 [−0.58], 0.056} (0.32)	NA	NA

*Entries in each cell: {normalized *PI*, *S/Q* [S/Q_n], *FI*} (y_o)

**Not defined.

†NA, not applicable.

Example III: anaerobic fermentor

Bioreactors are known to exhibit oscillatory behavior over a wide range of operating conditions, which sometimes adversely affects the product quality. Thus, it is often an objective to eliminate the limit cycle behavior. However, at times it is desirable to induce and/or stabilize oscillations to increase the metabolites produced by the cell. Thus, design for stability and consistency of bioprocesses has become more important considering tighter regulations on product quality.

In this example, an anaerobic fermentor is designed for high product quality. A continuous culture of *K. pneumoniae* is grown on glycerol.[43] The fermentation products are ethanol, acetic acid, and 1,3-propanediol, with 1,3-propanediol being the main product. At high concentrations, the latter, as well as the glycerol substrate, may exert feedback inhibition on the growth of the cells. This process exhibits characteristics of *metabolic overflow*, in which high extracellular substrate concentrations lead to an excessive uptake of intermediate metabolite(s). The latter strongly affect the dynamic behavior of the cells, often exhibiting sustained oscillations and steady-state multiplicity. Cell, substrate, and product mass balances are, respectively,

$$\frac{dX}{dt} = X(\mu - D) \tag{20}$$

$$\frac{dC_s}{dt} = D(C_{so} - C_s) - Xq_s \tag{21}$$

$$\frac{dC_p}{dt} = Xq_p - DC_p \tag{22}$$

where

$$\mu = \mu_{\max} \frac{C_s}{C_s + K_s}\left(1 - \frac{C_s}{C_s^*}\right)\left(1 - \frac{C_p}{C_p^*}\right) \tag{23}$$

$$q_s = m_s + \frac{\mu}{Y_s^m} + \Delta q_s^m \frac{C_s}{C_s + K_s^*} \tag{24}$$

$$q_p = m_p + Y_P^m \mu + \Delta q_p^m \frac{C_s}{C_s + K_p^*} \tag{25}$$

Note that Eqs. 23–25 describe the specific growth rate of the cells, the specific substrate consumption rate, and the specific growth rate of the product. Using the dimensionless variables and parameters in Table 8, the model becomes

$$\frac{dx}{d\tau} = x(u - d) \tag{26}$$

$$\frac{dy}{d\tau} = d(y_o - y) - x\phi_1\left(\beta_1 + \gamma_1 u + \frac{y}{y + \alpha_1}\right) \tag{27}$$

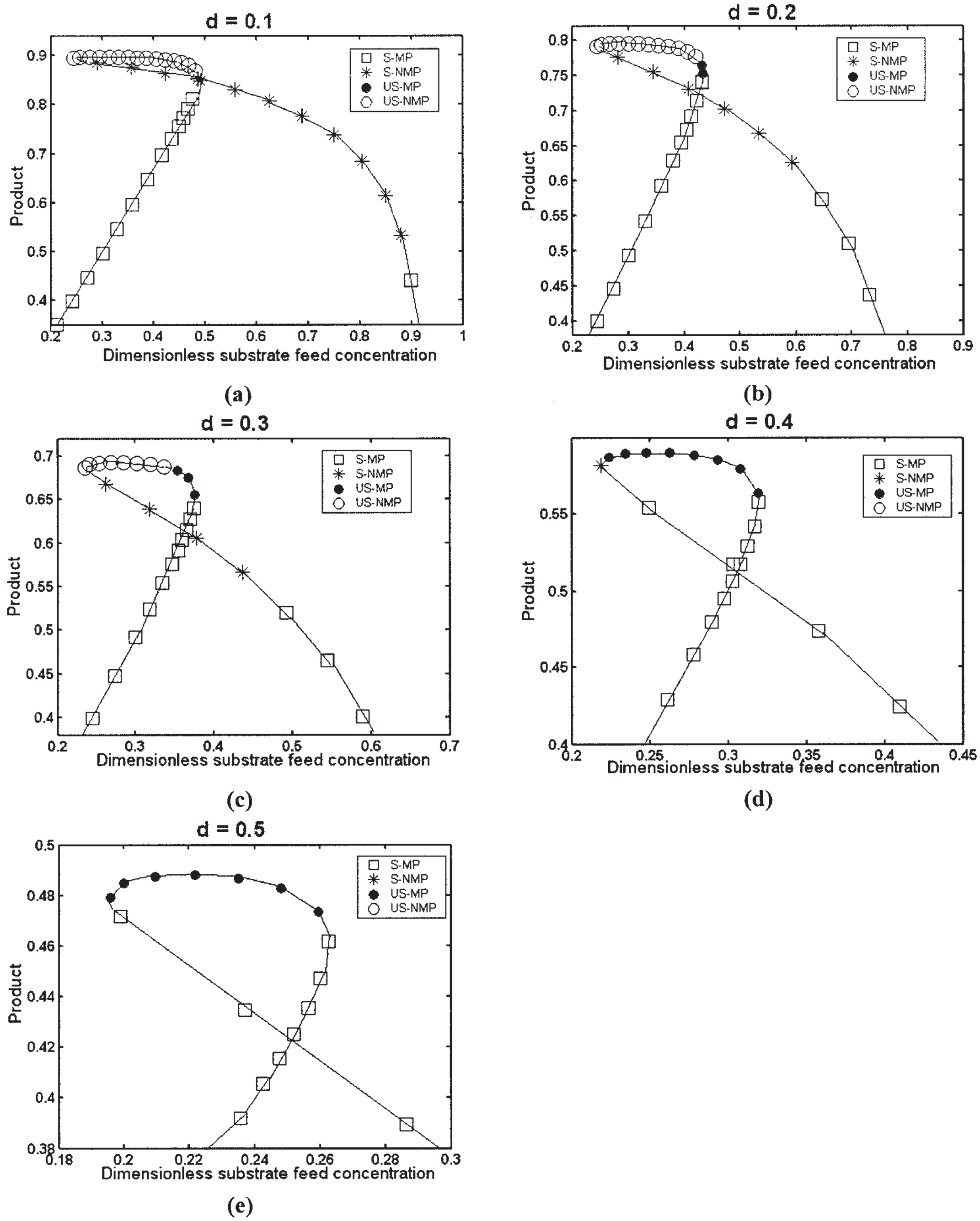

Figure 9. Extended bifurcation diagram for the anaerobic fermentor.

$$\frac{dz}{d\tau} = x\phi_2\left(\beta_2 + \gamma_2 u + \frac{y}{y + \alpha_2}\right) - zd \tag{28}$$

$$u = \frac{y}{y + \alpha_3}(1 - y)(1 - z) \tag{29}$$

Here, the controlled variables are the dimensionless cell and substrate concentrations, x and y, and the manipulated variables are the dimensionless dilution rate, d, and the substrate feed concentration, y_o, respectively. The zero dynamics are

$$\dot{\eta}_1 = \frac{y_{sp1}y_{sp2}\phi_2}{y_{sp2} + \alpha_2} + y_{sp1}\beta_2\phi_2 + \frac{y_{sp2}}{y_{sp2} + \alpha_3}(y_{sp1}\gamma_2\phi_2 - y_{sp1}y_{sp2}\gamma_2\phi_2 - \eta_1 + y_{sp2}\eta_1) + \frac{y_{sp2}}{y_{sp2} + \alpha_3}[y_{sp1}y_{sp2}\gamma_2\phi_2\eta_1 - y_{sp1}\gamma_2\phi_2\eta_1 + (\eta_1)^2 - y_{sp2}(\eta_1)^2] \tag{30}$$

By analyzing the dimensionless, anaerobic fermentor model, the eigenvalues of the Jacobian of the process model and its zero dynamics are used to obtain the EBDs. Zones I, II, III, and

IV appear as the primary bifurcation parameter (dimensionless, substrate feed concentration, y_o) is varied. The players for this game are the *profitability*, *controllability*, *product quality*, and *flexibility*. Game theory is applied with four objectives to: (1) maximize *PI* (by adjusting the dimensionless, substrate feed concentration, y_o, from 0 to 1), (2) minimize *CI* (by adjusting the dimensionless dilution rate, $d = \{0.1, 0.2, 0.3, 0.4, 0.5\}$), (3) minimize *S/Q*, and (4) maximize *FI* (by adjusting $\mu_{\max}$, the maximum specific-growth rate).

The feasible region within each zone is modified to satisfy the constraint that the dimensionless concentration of the product exceeds 0.4. The locally optimal designs, obtained for all existing zones, are reported in Table 9 for the fermentor. The entries in each cell of the table are the set {normalized *PI*, *CI*, *S/Q* [S/Q_n], *FI*} plus the primary bifurcation parameter, y_o. The EBDs of the fermentor, showing the dimensionless product concentrations, are in Figure 9 at five dimensionless dilution rates. Zones I, II, and IV exist for $d = 0.1$, 0.2, and 0.3, and zones I and III exist for $d = 0.4$ and 0.5.

To obtain the globally optimal solution using game theory, *PI* and *CI* are initially used to find dominant actions for the players *profitability* and *controllability*. Then S/Q_n is used to locate the higher product quality design among the solutions preferred by these players. From Table 9, the dominant action for the player *profitability* is toward higher zone numbers; that is, for $d = 0.1$, 0.2, and 0.3; zone IV is the dominant action and for $d = 0.4$ and 0.5; zone III is the dominant action. Similarly, the dominant action for the player *controllability* is $d = 0.1$ for zones II and IV. However, in zone I, *CI* does not follow any particular sequence. Furthermore, in zones I, III, and IV, *CI* values are very high and, consequently, are not considered. Therefore (zone II, $d = 0.1$) becomes one of the possible solutions. Furthermore, S/Q_n decreases with d and, consequently, the latter is a higher quality design as well. From Table 9, it is still possible to achieve significant improvement in *PI* with marginal reductions in *CI* and S/Q_n with the design (zone II, $d = 0.3$).

When the actions for the player's *profitability* and *controllability* are exchanged, the same locally optimal designs are obtained in different order. Clearly, zone II is the dominant action for the player *controllability*. The dominant action for the player *profitability* is toward higher d; that is, $d = 0.5$ is the dominant action for the player *profitability* in zones I and III, and $d = 0.3$ is the dominant action in zones II and IV. From this formulation ($d = 0.3$, zone II) is the *equilibrium in dominant action* solution. Furthermore, within zone II, both S/Q_n and *CI* support $d = 0.1$. Thus, there are trade-offs between (zone II, $d = 0.1$) and (zone II, $d = 0.3$) and a *mixed-strategy Nash equilibrium* is obtained for these two locally optimal designs. Considering that profitability for (zone II, $d = 0.1$) is much smaller than that for the other locally optimal designs in Table 9, and S/Q_n is reasonably good for (zone II, $d = 0.3$), the latter is the globally optimal, high product quality design. These results are also obtained by GAMBIT.

Conclusions

This article presents a novel multiobjective optimization method for designing processes that are inherently safe and/or have high product quality. *Extended bifurcation diagrams* (EBDs) are introduced to analyze nonlinear processes (having unstable steady states and/or nonminimum-phase behavior). The dynamics and nonminimum-phase behavior are well summarized using four zones in the parameter space. Game theory is used to identify the globally optimal zone by accounting for trade-offs between the four players: *profitability*, *controllability*, *safety and/or product quality*, and *flexibility*. This results in inherently safer designs, having higher product quality. Stated differently, the operating zones provide a compact representation of the extensive results from bifurcation analysis. Three reactors, having increasing complexity, are optimized to demonstrate the method.

This method can be applied and extended for more complex reaction systems, such as those that occur in polymerization reactors[30] and for distributed parameter systems. Using CFD software, such as FEMLAB and FLUENT, the impact of mixing on the inherent safety of stirred-tank reactors can be explored.

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Notation

Acronyms

AUTO = software for continuation and bifurcation analysis of differential equations
CFD = computational fluidic dynamics
CSTR = continuous stirred-tank reactor
EBD = extended bifurcation diagram
GAMBIT = software to solve problems using game theory
ISD = inherently safer design
LHP = left-half plane
LHS = left-hand side
NA = not applicable
PID = proportional–integral–derivative
RHP = right-half plane
RHS = right-hand side

Notation: General

CI = controllability index
FI = flexibility index
FI_L = left-hand side flexibility
FI_R = right-hand side flexibility
PI = profitability index
S/Q = safety and/or product quality index
S/Q_n = normalized safety and/or product quality index; see Eq. 9

Notation: Isothermal CSTR with van der Vusse reactions

C_A, C_B = concentration of species A and B, kmol/m^3
C_{Af} = feed concentration of species A, kmol/m^3
Da = Damköhler number
F = volumetric feed flow rate, m^3/s
k_1, k_2, k_3 = rate constant of first, second, and third reaction, s^{-1}, s^{-1}, m^3 kmol^{-1} s^{-1}
t = time, s
V = reactor volume, m^3
V_d = dimensionless reactor volume; see Table 2
V_o = reference reactor volume, m^3
x_1 = conversion of species A
x_2 = dimensionless concentration of species B; see Table 2
y_{sp1} = set point for the controlled variable 1, x_2

Greek: Isothermal CSTR with van der Vusse reactions

β = dimensionless constant; see Table 2
γ = ratio of second to first reaction rate constant; see Table 2
η_i = *i*th variable of zero dynamics equation
τ = dimensionless time

Notation: Exothermic CSTR with reactions A → B → C

A = heat transfer area, m^2
A_1, A_2 = Arrhenius preexponential factor for first and second reaction, s^{-1}
C_A, C_B = concentration of species A and B, $kmol/m^3$
C_{Af}, C_{Bf} = feed concentration of species A and B, $kmol/m^3$
C_p, C_{pc} = heat capacity of reaction mixture and coolant, kJ $kmol^{-1}$ K^{-1}
Da = Damköhler number
E_1, E_2 = activation energy of first and second reaction, kJ/kmol
k_1, k_2 = rate constant of first and second reaction, s^{-1}
Q = volumetric feed flow rate, m^3/s
q = dimensionless volumetric feed flow rate
Q_c = cooling-medium, volumetric flow rate, m^3/s
q_c = dimensionless, cooling-medium, volumetric flow rate; see Table 5
R = universal gas constant, kJ $kmol^{-1}$ K^{-1}
S = ratio of rate constants; see Table 5
t = time, s
T, T_c = temperature of reactor and coolant, K
T_{cf} = cooling medium feed temperature, K
T_f = feed temperature, K
T_{fo} = reference temperature of the feed stream, K
U = heat-transfer coefficient, kJ m^{-1} s^{-1} K^{-1}
V = reactor volume, m^3
V_c = cooling jacket volume, m^3
w = weighting factor for safety and/or product quality index
x_1, x_2 = dimensionless concentration of species A and B; see Table 5
x_{1f}, x_{2f} = dimensionless feed concentration of species A and B; see Table 5
x_3, x_4 = dimensionless temperature of reactor and coolant; see Table 5
x_{3f} = dimensionless, reactor feed temperature; see Table 5
x_{4f} = dimensionless, coolant feed temperature; see Table 5
y_{sp1}, y_{sp2} = set point values for controlled variables 1 and 2, x_2 and x_4

Greek letters: Exothermic CSTR with reactions A → B → C

α = heat of reaction ratio; see Table 5
β = dimensionless heat of reaction (A → B); see Table 5
δ = dimensionless heat-transfer coefficient; see Table 5
δ_1 = ratio of reactor to coolant volume; see Table 5
δ_2 = ratio of reacting mixture to coolant specific-heat capacities; see Table 5
ρ = reaction mixture density, kg/m^3
ρ_c = coolant density, kg/m^3
ϕ = Damköhler number at constant volume
ψ = ratio of second to first reaction activation energy; see Table 5
ζ_1 = dimensionless Arrhenius exponential factor (first reaction); see Table 5
ζ_2 = dimensionless Arrhenius exponential factor (second reaction); see Table 5
η_i = *i*th variable of zero dynamics equations
ΔH_A = heat of reaction of the first reaction (A → B), kJ/kmol
ΔH_B = heat of reaction of the second reaction (B → C), kJ/kmol
τ = dimensionless time; see Table 5

Notation: Anaerobic fermentor

C_p = product concentration, mol/m^3
C_p^* = maximal product concentration, mol/m^3
C_s, C_{so} = substrate concentration in reactor and feed medium, mol/m^3
C_s^* = maximum residual substrate concentration, mol/m^3
D = dilution rate, s^{-1}
d = dimensionless dilution rate; see Table 8
K_s = Monod saturation constant, mol/m^3
K_S^*, K_P^* = saturation constants for substrate and product in kinetic equations with excess terms, mol/m^3
m_s, m_p = maintenance terms of substrate consumption and product formation under substrate-limited conditions, mol kg^{-1} s^{-1}
q_s, q_p = specific rates of substrate consumption and product formation under substrate-limited conditions, mol kg^{-1} s^{-1}
Δq_S^m, Δq_P^m = maximum increment of substrate consumption rate and product formation rate under substrate-sufficient conditions, mol kg^{-1} s^{-1}
t = time, s
u = dimensionless specific growth rate; see Table 8
X, X_m = biomass and an arbitrary reference biomass concentration, kg/m^3
x = dimensionless biomass concentration; see Table 8
Y_S^m, Y_P^m = maximum growth yield and product yield, mol/kg
y, y_o = dimensionless substrate concentration in reactor and feed medium; see Table 8
y_{sp1}, y_{sp2} = set point values for controlled variables 1 and 2, x and y
z = dimensionless product concentration; see Table 8

Greek: Anaerobic fermentor

α_1, α_2, α_3 = dimensionless saturation constants; see Table 8
β_1, β_2 = dimensionless maintenance requirements of substrate consumption and product formation under substrate-limited conditions; see Table 8
ϕ_1, ϕ_2 = dimensionless maximum increment of substrate uptake rate and product formation rate under substrate-sufficient conditions; see Table 8
γ_1, γ_2 = dimensionless maximum growth yield and product yield
λ = eigenvalues
η_1 = variable of zero dynamics equation
μ, μ_{max} = specific and maximum growth rates, s^{-1}
τ = dimensionless time; see Table 8

Literature Cited

1. Sakizlis V, Perkins JD, Pistikopoulos EN. Recent advances in optimization-based simultaneous process and control design. *Comp Chem Eng.* 2004;28:2069-2086.
2. Blanco AM, Bandoni JA. Interaction between process design and process operability of chemical processes: An eigenvalue optimization approach. *Comp Chem Eng.* 2003;27:1291-1301.
3. Brengel DD, Seider WD. Coordinated design and control optimization of nonlinear processes. *Comp Chem Eng.* 1992;16:861-886.
4. Luyben ML, Floudas CA. Analyzing the interaction of design and control. 1. A multiobjective framework and application to binary distillation synthesis. *Comp Chem Eng.* 1994;18:933-969.
5. Subramanian S, Uzturk D, Georgakis C. An optimization-based approach for the operability analysis of continuously stirred tank reactors. *Ind Eng Chem Res.* 2001;40:4238-4252.
6. Chawankul N, Budman H, Douglas PL. The integration of design and control: IMC control and robustness. *Comp Chem Eng.* 2005;29:261-271.
7. Swaney RE, Grossmann IE. An index for operational flexibility in chemical process design: 1. Formulation and theory. *AIChE J.* 1985; 31:621-630.
8. Swaney RE, Grossmann IE. An index for operational flexibility in chemical process design: 2. Computational algorithms. *AIChE J.* 1985; 31:631-641.
9. Morari M. Flexibility and resiliency of process systems. *Comp Chem Eng.* 1983;7:423-437.
10. Pistikopoulos EN, Grossmann IE. Optimal retrofit design for improving process flexibility in linear-systems. *Comp Chem Eng.* 1988;12: 719-731.
11. Chacon-Mondragon OL, Himmelblau DM. Integration of flexibility and control in process design. *Comp Chem Eng.* 1996;20:447-452.
12. Hendershot DC. Inherently safer chemical process design. *J Loss Prevent Process Ind.* 1997;10:151-157.
13. Hendershot DC. Measuring inherent safety, health and environmental characteristics early in process development. *Proc Safety Prog.* 1997;16:78-79.

14. Rath & Strong Management Consultants. *Design for Six Sigma Pocket Guide*. Lexington, MA: Rath & Strong Management Consultants/AON Management Consulting; 2002.
15. Wheeler JM. Getting started: Six-sigma control of chemical operations. *Chem Eng Prog.* 2002;98:76-81.
16. Kletz T. *Process Plants: A Handbook for Inherently Safer Design*. London: Taylor & Francis; 1998.
17. Kanter JM, Seider WD, Soroush M. Real-time, nonlinear control of a constrained, non-minimum-phase process. *AIChE J.* 2002;48:2247-2254.
18. Luyben WL. Tuning proportional-integral controllers for processes with both inverse response and deadtime. *Ind Eng Chem Res.* 2000; 39:973-976.
19. Doyle FJ, Ogunnaike BA, Pearson RK. Nonlinear model-based control using 2nd-order Volterra models. *Automatica.* 1995;31:697-714.
20. Kuhlmann A, Bogle IDL. Design of nonminimum phase processes for optimal switchability. *Chem Eng Process.* 2004;43:649-656.
21. Nash JF. Non-cooperative games. *Ann Math* 1951;54:286-295.
22. Nash JF. Equilibrium points in N-person games. *Proc Natl Acad Sci USA.* 1950;36:48-49.
23. Dixit A, Skeath S. *Games of Strategy*. New York, NY: Norton; 1999.
24. Balakotaiah V, Luss D. Analysis of the multiplicity patterns of a CSTR. *Chem Eng Commun.* 1982;19:185-189.
25. Kanter JM, Soroush M, Seider WD. Nonlinear controller design for input-constrained, multivariable processes. *Ind Eng Chem Res.* 2002; 41:3735-3744.
26. Kravaris C, Daoutidis P. Nonlinear state feedback-control of 2nd-order nonminimum-phase nonlinear systems. *Comp Chem Eng.* 1990;14: 439-449.
27. Kravaris C. Input output linearization—A nonlinear analog of placing poles at process zeros. *AIChE J.* 1988;34:1803-1812.
28. Seider WD, Brengel DD, Widagdo S. Nonlinear-analysis in process design. *AIChE J.* 1991;37:1-38.
29. Zhang YC, Henson MA. Bifurcation analysis of continuous biochemical reactor models. *Biotech Prog.* 2001;17:647-660.
30. Ray WH, Villa CM. Nonlinear dynamics found in polymerization processes—A review. *Chem Eng Sci.* 2000;55:275-290.
31. Ramkrishna D, Amundson NR. Mathematics in chemical engineering: A 50-year introspection. *AIChE J.* 2004;50:7-23.
32. Chang HC, Chen LH. Bifurcation characteristics of nonlinear-systems under conventional PID control. *Chem Eng Sci.* 1984;39: 1127-1142.
33. Hahn J, Monnigmann M, Marquardt W. A method for robustness analysis of controlled nonlinear systems. *Chem Eng Sci.* 2004;59: 4325-4338.
34. Kuhlmann A, Bogle D. Study on non-minimum phase behaviour and optimal operation. *Comp Chem Eng.* 1997;21:S397-S402.
35. Seider WD, Seader JD, Lewin DR. *Product and Process Design Principles: Synthesis, Analysis, and Evaluation*. Hoboken, NJ: Wiley; 2004.
36. Doedel E. AUTO: Software for continuation and bifurcation analysis problems in ordinary differential equations. http://indy.cs.concordia.ca/auto/; 1997.
37. Panjapornpon C, Soroush M, Seider WD. Software for analytical model-based controller design. Submitted to *Comp. Chem. Eng.,* 2005.
38. Rosenthal RE. Principles of multiobjective optimization. *Decision Sci.* 1985;16:133-152.
39. Turocy T, McLennan A, McKelvey RD. Gambit: Software tools for game theory. http://econweb.tamu.edu/gambit/; 2002.
40. Gamboa-Torres AE, Flores-Tlacuahuac A. Effect of process design/operation on the steady-state operability of a CSTR—Reactions A → B → C. *Chem Eng Res Des.* 2000;78:481-491.
41. Gamboa-Torres AE, Flores-Tlacuahuac A. Effect of process modeling on the nonlinear behaviour of a CSTR—Reactions A → B → C. *Chem Eng J.* 2000;77:153-164.
42. Jacobsen EW. Effect of recycle on the plant zero dynamics. *Comp Chem Eng.* 1997;21:S279-S284.
43. Xiu ZL, Zeng AP, Deckwer WD. Multiplicity and stability analysis of microorganisms in continuous culture: Effects of metabolic overflow and growth inhibition. *Biotechnol Bioeng.* 1998;57:251-261.

Table A1. Game Table for Example 1 in Appendix A

(a) **P3** Chooses: $P3_{S1}$		**P2**	
		$P2_{S1}$	$P2_{S2}$
P1	$P1_{S1}$	2, 2, 2	3, $\underline{6}$, 3
	$P1_{S2}$	$\underline{6}$, 3, 3	$\underline{4}$, $\underline{4}$, 1

(b) **P3** Chooses: $P3_{S2}$		**P2**	
		$P2_{S1}$	$P2_{S2}$
P1	$P1_{S1}$	3, 3, $\underline{6}$	1, $\underline{4}$, $\underline{4}$
	$P1_{S2}$	$\underline{4}$, 1, $\underline{4}$	$\underline{5}$, $\underline{5}$, $\underline{5}$

Appendix A: Examples of Games with Varying Complexities

Three examples are provided to illustrate aspects of game theory for *simultaneous move* games (all players make a move at the same time) and *noncooperative* games [each player tries to optimize its objective function (payoff), ignoring the objective function of the other players]. For a more complete treatment, see *Games of Strategy*.[23]

Example 1: Equilibrium in dominant actions

In this section, a simple three-player game is solved to clarify some of the basic concepts of game theory. Three players, *P1*, *P2*, and *P3*, have to select from their actions/strategies, $\{P1_{S1}, P1_{S2}\}$, $\{P2_{S1}, P2_{S2}\}$, and $\{P3_{S1}, P3_{S2}\}$, respectively. An outcome for each player (that is, a measure of overall worth) is estimated for its action/strategy against the actions/strategies of all of the remaining players. The goal is to determine the best actions/strategies for each player by comparing the outcomes (payoffs), leading to an equilibrium (optimal) solution. To find the equilibrium, game Table A1 [(a) and (b)] shows outcomes for all of the possible combinations, selected to illustrate an *equilibrium in dominant actions* solution.

The table has two rows for *P1*'s two strategies, two columns for *P2*'s two strategies, and two pages for *P3*'s two strategies [(a) and (b)]. In each cell, payoffs (outcomes) are listed for the row player first, the column player second, and the page player third; that is, *P1*, *P2*, and *P3*. To find the equilibrium solution, a dominant strategy is sought for one or more of the players; that is, a strategy that outperforms the other strategies, regardless of the actions of the opposing players.

For *P1*, the two rows of both pages of the table are compared. When *P3* chooses $P3_{S1}$, *P1* always prefers $P1_{S2}$ ($6 > 2$, $4 > 3$) and when *P3* chooses $P3_{S2}$, *P1* always prefers $P1_{S2}$ ($4 > 3$, $5 > 1$). Thus, the dominant strategy for *P1* is $P1_{S2}$ regardless of the actions of the other players. Similarly, for *P2*, the two columns of both pages of the table are compared. *P2*'s dominant strategies in both pages of the table are $P2_{S2}$ (prefers $P2_{S2}$ $\{6 > 2, 4 > 3\}$ when *P3* chooses $P3_{S1}$, and prefers $P2_{S2}$ $\{4 > 3, 5 > 1\}$ when *P3* chooses $P3_{S2}$). To check whether *P3* has a dominant strategy, careful evaluation is needed because outcomes that keep *P1* and *P2*'s behavior constant needs to be compared. Each cell across the pages of the table, for example, the top left cell in the first page (on the left) is compared with the top left cell in the second page (on the right), and so on.

Table A2. Game Table for Example 2 in Appendix A

		P2	
		$P2_{S1}$	$P2_{S2}$
P1	$P1_{S1}$	2,1	0,0
	$P1_{S2}$	0,0	1,2

P3's dominant strategy is $P3_{S2}$. Therefore, the equilibrium solution, (5, 5, 5) in this case, corresponds to ($P1_{S2}$, $P2_{S2}$, $P3_{S2}$). This outcome is an equilibrium (optimal solution) in dominant actions. However, occasionally, a pareto-optimal solution exists when all of the players prefer a solution other than the equilibrium in dominant actions. Thus, equilibrium solutions using game theory must be checked carefully.

Example 2: Nash equilibrium (pure strategy)

Consider the game table shown in Table A2. In this game, there is no dominant action for either of the players. When *P2* selects $P2_{S1}$, *P1* prefers $P1_{S1}$, and when *P2* selects $P2_{S2}$, *P1* prefers $P1_{S2}$. Thus, there is no dominant action for *P1*. Similarly, there is no dominant action for *P2*. In these situations, a Nash equilibrium is sought. An outcome is a *Nash equilibrium* when no player finds it beneficial to deviate from its strategy when all of the other players do not deviate from their strategies. Therefore, the outcome (2, 1) and (1, 2) is a Nash equilibrium. Equilibrium in dominant action is a Nash equilibrium, although the converse is not true. There is only one equilibrium in dominant action, but there can be multiple Nash equilibria.

Example 3: Mixed-strategy Nash equilibrium

Consider the game table shown in Table A3. In this example, there is neither equilibrium in dominant actions nor pure-strategy Nash equilibrium. For game tables like this, equilibria are sought through mixed-strategy Nash equilibrium. In a pure-strategy Nash equilibrium, a nonrandom strategy is used by every player, whereas in a mixed strategy, a move is chosen randomly from the set of pure strategies with assigned probabilities. In mixed strategies, rules cause players to use each of their pure strategies a fraction of the time, as defined by the probabilities. Mixed-strategy equilibrium can often be the outcome of a game that has no equilibrium in pure strategies, or when a game has many equilibria in pure strategies.

Table A3. Game Table for Example 3 in Appendix A

		P2	
		$P2_{S1}$	$P2_{S2}$
P1	$P1_{S1}$	1, 4	1, 0
	$P1_{S2}$	1, 0	1, 3

Assume that *P1* chooses $P1_{S1}$ with probability pp and $P1_{S2}$ with probability $(1 - pp)$. Similarly, *P2* plays $P2_{S1}$ with probability qq and $P2_{S2}$ with probability $(1 - qq)$. *P1*'s expected payoff when *P2* chooses $P2_{S1}$ is equal to 1 $[=1 \times pp + 1 \times (1 - pp)]$ and for $P2_{S2}$ it is also equal to 1 $[=1 \times pp + 1 \times (1 - pp)]$. This indicates that P1 does not have any preference. The expected payoff for *P2* when *P1* chooses $P1_{S1}$ is $4 \times qq + 0 \times (1 - qq)$, and when *P1* chooses $P1_{S2}$, it is $0 \times qq + 3 \times (1 - qq)$. The value of qq is obtained by equating these two payoffs; that is, $4qq = 3(1 - qq)$, which gives $qq = 3/7$. Thus, there is a mixed-strategy Nash equilibrium having probabilities 3/7 and 4/7 for $P2_{S1}$ and $P2_{S2}$, respectively. Another extension of this game occurs when *P1* also has a preference, in which case probabilities are assigned to the strategies of both players. Depending on the nature of the game table, there could be many extensions to the solutions obtained for a particular game, as the problem becomes more complex. Note that it is always possible to find a mixed-strategy solution for a finite game table.

Appendix B: Algorithm to Obtain the Global Optimum for a Process

(1) Obtain a mathematical model of the process.

(2) Compute stable and unstable branches using AUTO.

(3) Carry out zero-dynamics analysis to classify designs as minimum- or nonminimum phase.

(4) Prepare an extended bifurcation diagram by classifying designs into one of the four zones in Table 1.

(5) Obtain feasible zones by applying constraints and determine the locally optimal design in each feasible zone by maximizing *FI*. Record *PI*, *CI*, and *S*/*Q*, along with *FI*, for each locally optimal design.

(6) Define the game; that is, the players, strategies, and payoffs (objectives).

(7) For each strategy (that is, process redesign or reconfiguration), prepare an extended bifurcation diagram by repeating steps (1)–(4). Then, obtain locally optimal designs for each zone, as in step (5).

(8) For all zones obtained through process redesigns and reconfigurations, prepare the game table with locally optimal designs, displaying values for *PI*, *CI*, *S*/*Q*, and *FI*.

(9) Apply game theory solution techniques to obtain the global optimum (equilibrium of the game) from all the locally optimal designs reported in the game table.

(10) Depending on the types of solution obtained in step (9), identify one or more globally optimal designs. Finally, assign more importance to one objective over the others, to obtain a globally optimal solution.

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