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Feasibility and flexibility analysis of black-box processes part 2: Surrogate-based flexibility analysis

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HIGHLIGHTS

- Methods for feasibility and flexibility analysis of black-box processes are presented.
- A novel method for surrogate-based feasibility analysis is introduced in Part 1.
- A novel method for surrogate-based flexibility analysis is introduced in Part 2.
- Both methods are demonstrated using a pharmaceutical roller compaction case study.

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ABSTRACT

The flexibility index can be used to evaluate process robustness and can be incorporated into algorithms for optimal process design under uncertainty. Traditional approaches to evaluating the flexibility index have focused on explicit enumeration or active set strategies. These necessitate closed form expressions for process constraints and can be computationally expensive to implement for problems with a large numbers of constraints. In addition, these methods generally perform best for problems involving convex or 1-d quasi convex feasible regions with respect to the uncertain variables. In this article, a method for flexibility analysis of systems with black-box constraints will be introduced. This is the second in a series of two articles related to surrogate-based feasibility and flexibility analysis. The first article described a strategy for building surrogate models to represent the feasible region for processes with black-box constraints. In this work, surrogate feasibility functions are used to evaluate the flexibility index for processes that lack closed-form expressions for process constraints. The proposed approach can be applied to processes with stochastic uncertainties described by arbitrary distribution functions. Due to the low computational cost of evaluating surrogate feasibility functions, this method can also be useful for flexibility analysis of processes described by computationally expensive models. The proposed approach will be demonstrated for a series of test problems involving nonlinear, nonconvex and disjoint feasible regions. It will also be applied to evaluate the flexibility of a pharmaceutical roller compaction process with uncertainties described by both uniform and normal distributions.

1. Introduction

A variety of terms can be used to describe the concept of process robustness, including flexibility, resiliency and operability. The first two are more common in process systems engineering and operations research, while the latter tends to be used more often in the controls literature (Lima et al., 2010). This work will focus on process flexibility, which is useful in formulating problems of optimal process design under uncertainty. The concept of flexibility analysis is directly related to feasibility analysis, in that both evaluate the ability of a process to operate in the presence of potential variability. They are distinguished by the fact that feasibility refers to the limits within which a process is operable, while flexibility quantifies the ability of a process to maintain feasible operation in the presence of inherent variability or external disturbances (Biegler et al., 1997). Flexibility analysis can be applied to chemical process systems in order to evaluate robustness and has been employed extensively in the area of process design under uncertainty (Floudas et al., 2001; Halemane and Grossmann, 1983; Mohideen et al., 1996b; Pistikopoulos and Ierapetritou, 1995).

Algorithms for design under uncertainty are used in applications ranging from process synthesis (Mohideen et al., 1996a) and

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retrofit design (Bansal et al., 1998; Pistikopoulos and Ierapetritou, 1995) to supply-chain optimization (Guillén-Gosálbez and Grossmann, 2009; Tsiakis et al., 2001), and integrated design and scheduling (Subrahmanyam et al., 1994). However the use of these methods is limited to problems involving closed-form constraint expressions. This is due to the fact that algorithms for solving the flexibility index problem, which are described in Section 2, rely on deterministic optimization solvers. As a result, it is not straightforward to apply flexibility analysis to complex process models, or models involving black-box constraints.

Such models are often encountered in pharmaceutical applications, where data-based or black-box functions may be required to describe phenomena for which mechanistic understanding is limited (Boukouvala et al., 2011; Gernaey et al., 2012). As a result, the application of flexibility analysis and optimal design under uncertainty in the pharmaceutical industry has been relatively limited. While flexibility analysis has been applied to pharmaceutical supply-chain (Levis and Papageorgiou, 2004; Shah, 2004) and capacity planning (Linninger and Chakraborty, 2001) problems, it has not been extensively used in manufacturing process design. The concepts of feasibility and flexibility have the potential to aid in the development of robust and efficient pharmaceutical processes. Recent changes in the pharmaceutical regulatory framework, specifically the shift to a Quality by Design (QbD) approach (ICH, 2009), highlight the importance of developing robust processes. Therefore it would be advantageous to develop a method for evaluating process flexibility when closed form expressions for constraints are not available.

In this paper, a surrogate-based method for the evaluation of process flexibility will be introduced. This method combines concepts from surrogate-based feasibility analysis and flexibility analysis as well as stochastic flexibility analysis. The resulting algorithm is demonstrated for a series of test problems, including those with nonconvex and disjoint feasible regions and problems involving uncertain parameters sampled from non uniform distributions. A case study from the pharmaceutical industry involving a roller compaction process is also utilized to demonstrate the efficacy of the proposed approach. This article is organized as follows. Section 2 provides an overview of feasibility analysis, the flexibility index problem and the concept of stochastic flexibility. In Section 3, a method for surrogate-based flexibility analysis is presented. In Section 4, a number of case studies are used to demonstrate this approach, including a flexibility analysis of a pharmaceutical roller compaction process. Section 5 provides a discussion of the case study results. Finally, conclusions and directions for future research are described in Section 6.

2. Background

Mathematical descriptions of process feasibility and flexibility were introduced in the 1980s, with the goal of facilitating robust and flexible process design (Grossmann and Floudas, 1987; Morari, 1983; Swaney and Grossmann, 1985a, 1985b). Feasibility analysis can be used to determine if all relevant constraints for a process can be satisfied in the presence of uncertainty. Flexibility analysis can be used to quantify the extent to which uncertainty is tolerated by a particular process design (Biegler et al., 1997). Sources of uncertainty can include variability in operating conditions, changes in process inputs and plant-model mismatch (Lima et al., 2010). Constraints on the process may be related to safety, capacity, quality or production rate. Throughout this article, sources of uncertainty in the process will be denoted as θ. Control variables that can be manipulated to maintain feasible operation in the presence of uncertainty will be denoted as z. Design alternatives will be indicated as d.

2.1. Feasibility analysis

Feasibility can be described by the feasibility function $\Psi(d,\theta)$ shown in Eq. (1). In Eq. (1), the uncertain parameters that vary on the interval $T=\left\{\theta|\theta^L\le\theta\le\theta^U\right\}$ where θ^L and θ^U are lower and upper bounds respectively. Note that in formulation (1), the state variables for the process (x) have been eliminated, as they can be expressed in terms of the other variables d, z and θ (Biegler et al., 1997). The constraints g_j are expressed in the form $g_j(d,z,\theta)\le 0$ (Biegler et al., 1997; Swaney and Grossmann, 1985a, 1985b).

$$\Psi(d,\theta)=\min_{z}\max_{j\in J}\left\{g_j(d,z,\theta)\right\}$$
$$s.t.\,\theta\in T=\left\{\theta|\theta^L\le\theta\le\theta^U\right\} \tag{1}$$

The feasibility function $\Psi(d,\theta)$ will be less than or equal to 0 for a given design d and realization of the uncertain parameters θ if it is possible to satisfy all constraints g_j by adjusting the control variables z accordingly. If $\Psi(d,\theta)\le 0$ then the process is feasible for the given design and realization of the uncertain variables. If $\Psi(d,\theta)\le 0$ for all $\theta\epsilon T$ then the design d is feasible.

2.2. Surrogate-based feasibility analysis

Solving the feasibility test problem (1) for process models with closed-form expressions for all constraints g_j can be accomplished using commercially available LP or NLP algorithms. For processes involving black-box constraints or in cases where the process is described by a complex or computationally expensive model, surrogate-based feasibility analysis may be preferred (Banerjee et al., 2010). This approach has the benefit of being applicable to processes with black-box constraints, and also does not require assumptions regarding the convexity of the feasible region (Banarjee and Ierapetritou, 2005). Surrogate-based feasibility analysis involves the use of a surrogate approximation of the feasibility function, which may be developed using an iterative algorithm based on adaptive sampling (Banerjee et al., 2010; Boukouvala and Ierapetritou, 2012). The surrogate feasibility function can be used to evaluate process feasibility over the range of conditions $\theta\epsilon T$. In this work, a surrogate-based feasibility algorithm based on kriging is implemented, the details of which are described in Part 1 of this series.

2.3. Flexibility analysis

2.3.1. The flexibility index problem

A rigorous mathematical formulation for process flexibility was first introduced by Halemane and Grossmann (1983). In this formulation, process robustness is quantified using the flexibility index. The flexibility index describes the extent to which a process remains feasible over a range of potential deviations in process inputs, operating conditions and model parameters. The formulation of the flexibility index problem follows directly from the feasibility test problem (1). The flexibility test problem (2) can be used to determine if a particular process design d is feasible over a range of potential deviations in the uncertain parameters $\theta\epsilon T$. If $\chi(d)\le 0$ in problem (2), then there exists a set of control actions that result in feasible process operation over the full range of deviations $\theta\epsilon T$. If not, the process is infeasible for some realizations of the uncertain parameters $\theta\epsilon T$ (Biegler et al., 1997; Grossmann and Floudas, 1987; Swaney and Grossmann, 1985a, 1985b).

$$\chi(d)=\max_{\theta\in T}\min_{z}\max_{j\in J}\left\{g_j(d,z,\theta)\right\}=\max_{\theta\in T}\Psi(d,\theta) \tag{2}$$

The flexibility index problem (3) follows directly from the flexibility test problem and can be used to quantify how robust a particular process design is with respect to variability in the