Pharmaceutical Waste Management Under Uncertainty

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Abstract

Due to seasonal differences in production demands, effluent streams from batch manufacturing sites may exhibit considerable variations in number, amount as well as composition. Pharmaceutical and fine chemical production distinguishes itself also in recycling practices since stringent purity requirement often prohibit direct reuse of raw materials in the next batch. Further complications stem from ever changing production campaigns, where each may last only for a few months. In such a dynamic environment, selection of recovery and treatment options as well as assessments of their benefits and costs constitutes a formidable task. Designing plant-wide waste management policies assuming perfect information may not be satisfactory given the variability of the production campaigns. Therefore this article addresses the problem of finding optimal waste management policies for entire manufacturing sites in the presence of uncertainty. It will offer a mathematical programming framework for implementing three contrasting strategies. Small case studies exemplify the impact of different perspectives on the structural design decisions in the overall plant design.

Keywords
Waste Scenario, Monte Carlo Simulation, Cost Effective Policy, Flexibility Index

1. Introduction

Automatic waste management is concerned with the search for effective recovery and treatment policies for entire manufacturing sites. A deterministic two-phase methodology for the computer-aided synthesis of waste management policies for batch processes has been presented earlier [Linninger and Chakraborty, 1999]. In step one of that methodology, a knowledge-based monotonic planning algorithm evaluates the waste properties against regulatory limits and a relaxed set of technology selection criteria. For each violation of a recovery or treatment target, a feasible treatment process is selected from among the database of available treatment options. Shortcut models are employed for computing the residues emanating from different treatment steps and the associated treatment costs [Linninger et al, 2000]. Repeated application of the reasoning mechanism leads to a tree of feasible treatment options for each waste stream. The union of all treatment trees is entitled the superstructure which implicitly contains all feasible treatment policies on a plant-wide level. A schematic representation of the superstructure as obtained in phase one is depicted in Fig. 1. It shows the state task network representation of the superstructure, where each node represents an effluent stream, wk, and the arcs, xk,i stand for the treatment alternatives for node k.

Phase two of the methodology optimizes a desired performance function subject to plant-wide capacity, environmental, emission and logical constraints. The objective (1), may also contain environmental cost terms, ψ, measuring the burden of final emissions on the environment. X is the vector of all binary decision variables within the superstructure, SS, and is denoted by

\[ X = \begin{bmatrix} x_{1,1} & x_{1,2} & \cdots & x_{k,1} & x_{k,2} & \cdots \end{bmatrix}^T \]

For any given treatment step, xk,i each element of the vectors, Cost, denotes its expected operating cost. A multi-
objective cost function accounting for the environmental impact, e.g. CO2, wastewater, heavy metals, BOD, emission etc, is described in Chakraborty and Linninger [1999]. Inequality (2) safeguards that each treatment process is used only up to its available limit. Inequality (3) enforces site-specific emission limits. Even though all terminal streams of the superstructure are compliant, the total emission at a specific site must not exceed local permits or voluntary corporate emission standards [Linninger and Chakraborty, 1999]. Equ. (4) are path constraints that ensure the logical connectivity of the superstructure found in phase one. In the inequalities (3) and (4), \( D \) is the matrix of capacity demands for treatment technologies, in all steps, \( x_{k,i} \), denoted as follows:

\[
D = \begin{bmatrix}
  d_{1,1}^1 & d_{1,2}^1 & \cdots & d_{k,1}^1 & \cdots \\
  d_{1,1}^2 & d_{1,2}^2 & \cdots & d_{k,1}^2 & \cdots \\
  \vdots & \vdots & \ddots & \vdots & \ddots \\
  d_{1,1}^\alpha & d_{1,2}^\alpha & \cdots & d_{k,1}^\alpha & \cdots 
\end{bmatrix}
\]

Similarly, \( E \) is the matrix of emissions of type \( \beta \) stemming from treatment steps, \( x_{k,i} \).

\[
E = \begin{bmatrix}
  e_{1,1}^1 & e_{1,2}^1 & \cdots & e_{k,1}^1 & \cdots \\
  e_{1,1}^2 & e_{1,2}^2 & \cdots & e_{k,1}^2 & \cdots \\
  \vdots & \vdots & \ddots & \vdots & \ddots \\
  e_{1,1}^\alpha & e_{1,2}^\alpha & \cdots & e_{k,1}^\alpha & \cdots 
\end{bmatrix}
\]

Solutions to the combinatorial optimization problem of (1) - (4) describe optimal waste treatment policies on a plant wide level. Each policy is composed of exactly one treatment path per waste stream. It is worth noting that treatment selection typically does not allow a change of the operating conditions in treatment and recovery facilities. The operating parameters of destructive treatment facilities such as the combustion temperature of a furnace is not subject to optimization since the operation parameters cannot be adjusted for any new campaign in a multi-purpose plant. Similar restrictions apply to the solvent recovery plants that typically entail dedicated standardized equipment, such as extraction towers, distillation columns, at a fixed operating mode. Direct recycle options in batch pharmaceutical plants are often limited, since stringent purity requirements do not allow direct recycle into the original recipe.

Outline. In this paper we will derive a mathematical framework for quantifying the impact of uncertainty on waste management at batch manufacturing sites. In a first approach to this problem, we would like to address how variable waste loads affect the decision-making process on a plant wide level. This will be done under the assumption of varying waste amounts but at fixed composition. Section 2 of the presentation discusses the methodology adopted for discrete representation of the uncertain parameters. In section 3, individual waste treatment policies are assessed for their adaptability to waste load variation by means of a flexibility test. Section 4 discusses in details three different solution strategies for finding waste treatment policies for changing waste loads. In section 5, the different solution strategies are illustrated by two simple case studies from a batch pharmaceutical plant.

2 Methodology

2.1 Discrete Representation of Waste Loads

First, we assume that the variations of each effluent, \( w_k \), can be specified by a finite number of possible states, \( w_k^a, w_k^b, w_k^c, \ldots w_k^n \). Each outcome occurs with the likelihood, \( P(w_k^j) \). Here, \( w_k^j \) is the load of state \( j (j \in M) \) for the \( k \)th waste stream \( (k \in N) \). A waste scenario, \( W^S \), is the combination of individual state for each waste stream, \( w_k^j \), cf. Equ. (5). The probability of a scenario, \( P(W^S) \), is given by the compound probability of the individual states. When the waste loads variations are independent events [Bard, 1974], this compound probability is the product of the likelihood as formulated below, cf. Equ. (6). A rigorous treatment for correlated effluent streams based on
principal component analysis (PCA) is described elsewhere [Chakraborty and Linninger, 2000].

$$W^S = \bigcup_{k \in N} w^k_j$$  \hspace{1cm} (5)

$$P(W^S) = \prod_{j,k} P(w^k_j)$$  \hspace{1cm} (6)

Obviously the sum of the compound probabilities of all distinct waste scenarios should add up to unity. In our discrete probability model, N waste streams in M discrete states need to be considered. Then, the size of the uncertain space is given by $M^N$. Thus, for a set of 6 discrete waste streams each incurring 5 states, a total of $5^6 = 15625$ different waste scenarios exist. Explicit enumeration of all possible scenarios for numerous waste streams would lead to a massive amount of uncertain parameters. Hence, Monte-Carlo simulation was used to reduce the volume of the uncertain space. A large randomly selected sample can statistically represent the entire uncertain space. More sophisticated sampling techniques [e.g. Diwekar and Kalagnanam, 1997; Diwekar and Wang, 2000, Morgan and Henrion, 1990] could further reduce the quality of the sample with smaller computational effort.

2.2. Dynamic Linearization

The variability of the waste loads introduce continuous variables into the optimization problem. The mathematical solution of the problem, i.e. stochastic MINLP, may be hard or even intractable given the size of the uncertain space combined with the inherent non-linearities in residual computations, e.g. vapor-liquid equilibrium in condense operation, or cost functions. Hence, dynamic linearization of the non-linear terms is proposed.

Although the cost and residual calculations models are in general non-linear, they can be linearized for moderate perturbations from the nominal value. The sensitivity of treatment cost and residual amount is computed as a linear deviation from the value corresponding to the nominal value, $w_k^*$ as illustrated in Fig. 2. The specific cost $c_{k,i}$ are computed by symbolic or numerical differentiation at the nominal value with respect to the amount of effluent. The specific cost reflects the gradient of the non-linear cost models at a specific level of the nominal value. Clearly, these gradients may vary depending on the magnitude of the nominal value as depicted in Fig. 2. Hence the overall non-linear behavior is still captured. The treatment cost of a particular scenario are expressed as the nominal cost plus the product of specific cost, $c_{k,i}$, times waste load variation, $\Delta w_k$, cf. Equ. (7).

$$\Delta \text{cost}_{k,i} = c_{k,i} \times \Delta w_k$$  \hspace{1cm} (7)

$$\Delta d_{k,i} = \rho_{k,i}^T \times \Delta w_k$$  \hspace{1cm} (8)

$$\Delta e_{k,i}^E = \xi_{k,i}^E \times \Delta w_k$$  \hspace{1cm} (9)

Together with the assumption of invariant compositions, the selections and computations for the nominal case apply also for varying waste load scenarios. In effect, the recovery and treatment options embedded in the superstructure remains constant for all scenarios. This is due to the fact that regulatory limits and technology selection criteria of phase one are functions of the compositions, but are independent of the waste amounts.

3. Measure of Flexibility of a Treatment Policy

Waste load variations impact the treatment cost, but may even render the entire design infeasible due to constraint violations. Hence, economic optimality at nominal conditions is insufficient as a performance criterion. Practical and implementable policies must also exhibit sufficient flexibility to variations of uncertain parameters. A quantitative measure of the process flexibility is necessary in order to select among alternative designs. The Flexibility Index, F, measures the elasticity of a waste treatment policy to changing waste loads. The definition of F is depicted by Equ. (10):

$$F = (w_k - w_k^*) / \Delta w_k.$$  \hspace{1cm} (10)

The concept of flexibility index has been studied intensively by Grossman and coworkers [e.g. Swaney and Grossmann, 1985; Pistikopoulos and Grossmann, 1988].

![Slope = Specific Cost](image)

Fig. 2. Dynamic Linearization of treatment cost at different levels of nominal waste loads $W_1^*$, $W_2^*$.