A fuzzy multiobjective algorithm for multiproduct batch plant: Application to protein production

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Abstract

This paper addresses the problem of the optimal design of batch plants with imprecise demands and proposes an alternative treatment of the imprecision by using fuzzy concepts. For this purpose, we extended a multiobjective genetic algorithm (MOGA) developed in previous works, taking into account simultaneously maximization of the net present value (NPV) and two other performance criteria, i.e. the production delay/advance and a flexibility criterion. The former is computed by comparing the fuzzy computed production time to a given fuzzy production time horizon and the latter is based on the additional fuzzy demand that the plant is able to produce. The methodology provides a set of scenarios that are helpful to the decision's maker and constitutes a very promising framework for taken imprecision into account in new product development stage.

Keywords: Multiobjective optimization; Genetic algorithm; Fuzzy arithmetic; Batch plant design

1. Introduction

In recent years, there has been an increased interest in the design of batch processes due to the growth of specialty chemical, pharmaceutical, and related industries, because they are a preferred operating method for manufacturing small volumes of high-value products. The market demand for such products is usually changeable, and at the stage of conceptual design of a batch plant, it is almost impossible to obtain the precise information on the future product demand over the lifetime of the plant. However, decisions must be made on the plant capacity. This capacity should be able to balance the product demand satisfaction and extra plant capacity in order to reduce the loss on the excessive investment cost or that on market share due to the varying demands on products. The design of multiproduct batch plants has been an active area of research over the past decade (e.g. Pinto & Grossmann, 1998; Shah, 1998 for reviews). Most of the work has been yet limited to deterministic approaches, wherein the problem parameters are assumed to be known with certainty. However, in reality there can be uncertainty in a number of factors such as processing times, costs, demands, and not all the requirements placed by the technology of the process and the properties of the substances are defined. To cope with this, there has been a major interest in the development of different types of probabilistic models that explicitly take into account the various uncertainties (Sahinidis, 2003). It must be pointed out that in the context of engineering design, the term of imprecision is used to mean uncertainty in choosing among alternatives. For example, Wellons and Reklaitis (1989) proposed an MINLP model for the design of batch plants under uncertainty with staged capacity expansions. Based on the structure of multiproduct batch plants, Straub and Grossmann (1992) developed an efficient procedure to evaluate the expected stochastic flexibility, embedded within an optimization framework for selecting the design (size and number of parallel equipment). Two-stage stochastic programming approaches have also been applied for design under uncertainty (Cao & Yuan, 2002; Harding & Floudas, 1997; Ierapetritou & Pistikopolous, 1996; Petkov & Maranas, 1998).

It must be clearly said that the use of probabilistic models that describe the uncertain parameters in terms of probability distributions in an optimization framework may involve a large number of scenarios in the discrete representation of the uncertainty and use complex integration techniques when uncertainty

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Nomenclature

a	tax rate (0)
A_p	depreciation (M€/year)
B_{is}	batch size for product i in batch stage s (kg)
d_{ij}	power coefficient for processing time of product i in batch stage j
D_{ik}	duty factor for product i in semi-continuous stage k (L/kg)
D_p	operation cost (M€/year)
f	working capital (M€)
g_{ij}	coefficient for processing time of product i in batch stage j
H	due date (h)
H_i	production time of product i (h)
i	discount rate (0.1)
i	index for products
I	total number of products
Inv	investment cost (M€)
j	index for batch stages
J	total number of batch stages
J_s	total number of batch stages in sub-process s
k	index for semi-continuous stages
K	total number of semi-continuous stages
K_s	total number of semi-continuous stages in sub-process s
m_j	number of parallel out-of-phase items in batch stage j
M	number of stages
n	number of periods (5)
n_k	number of parallel out-of-phase items in semi-continuous stage k
p_{ij}	processing time of product i in batch stage j (h)
p_{ij}^0	constant for calculation of processing time of product i in batch stage j (h)
P	number of products to be produced
Prod_i	global productivity for product i (kg/h)
$\mathrm{Prodloc}_{is}$	local productivity for product i in sub-process s (kg/h)
Q_i	demand for product i
R_k	processing rate for semi-continuous stage k (L/h)
$R_{\max}$	maximum feasible processing rate for semi-continuous stage k (L/h)
$R_{\min}$	minimum feasible processing rate for semi-continuous stage k (L/h)
S	total number of sub-processes
S_{ij}	size factor of product i in batch stage j (L/kg)
S_{is}	size factor of product i in intermediate storage tanks (L/kg)
T_{ij}	cycling time of product i in batch stage j (h)
T_{is}^{L}	limiting cycling time of product i in sub-process s (h)
V_j	size of batch stage j (L)
$V_{\max}$	maximum feasible size of batch stage j (L)
$V_{\min}$	minimum feasible size of batch stage j (L)
V_p	revenue (M€/year)
V^{s}	size of intermediate storage tank (L)

Greek letters

α_j	cost factor for batch stage j
β_j	cost exponent for batch stage j
β_k	power cost coefficient for semi-continuous stage k
γ_{s}	power cost coefficient for intermediate storage
Θ_{ik}	operating time of product i in semi-continuous stage k

is modeled by continuous distributions. Besides, the use of probabilistic models is realistic only when a historic data set is available for uncertain parameters, which is rarely the case at the preliminary design stages in new product development.

In this work, fuzzy concepts and arithmetic constitute an alternative to describe the imprecise nature on product demands. For this purpose, we extended a multiobjective genetic algorithm, developed in previous works (Dietz, Azzaro-Pantel, Pibouleau, & Domenech, 2005, 2006), taking into account simultaneously the maximization of the net present value (NPV) and two other performance criteria, i.e. the production delay/advance and a flexibility criterion. The paper is organized as follows. Section 2 is devoted to a brief process description. Section 3 presents problem formulation and an overview of fuzzy set theory involved in the fuzzy framework within a multiobjective genetic algorithm. The presentation is then illustrated by some typical results in Section 4. Finally, the conclusions on this work are drawn.

2. Process description

The case study is a multiproduct batch plant for the production of proteins taken from the literature (Montagna, Vecchietti, Iribarren, Pinto, & Asenjo, 2000; Pinto, Montagna, Vecchietti, Iribarren, & Asenjo, 2001). This example is used as a test bench since short-cut models describing the unit operations involved in the process are available. The batch plant involves eight stages for producing four recombinant proteins, on one hand two therapeutic proteins, human insulin (I) and vaccine for hepatitis B (V) and, on the other hand, a food grade protein, chymosin (C) and a detergent enzyme, cryophilic protease (P).

Fig. 1 shows the flowsheet of the multiproduct batch plant considered in this study. All the proteins are produced as cells grow in the fermenter (Fer).

Vaccine and protease are considered as being *intracellular*: the first microfilter (Mf1) is used to concentrate the cell suspension, which is then sent to the homogenizer (Hom) for cell disruption to liberate the intracellular proteins. The second microfilter (Mf2) is used to remove the cell debris from the solution proteins.

The ultrafiltration (Uf1) step is designed to concentrate the solution in order to minimize the extractor volume. In the liquid–liquid extractor (Ext), salt concentration (NaCl) is used

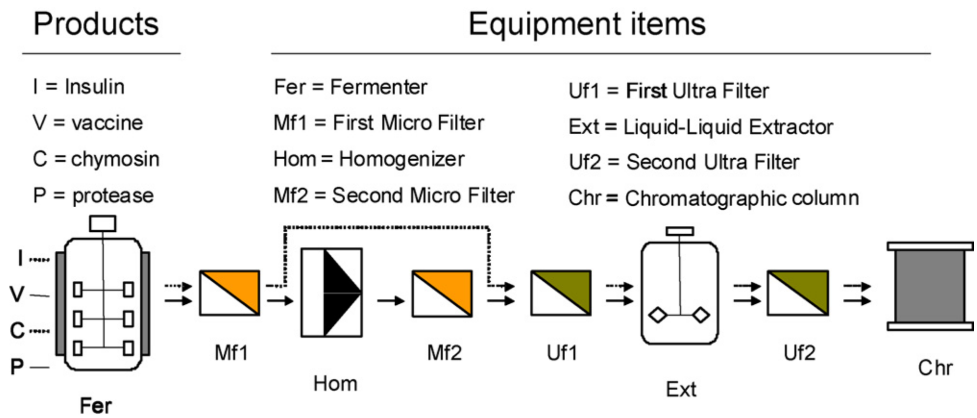


Fig. 1. Multiproduct batch plant for protein production.

to first drive the product to a poly-ethylene-glycol (PEG) phase and again into an aqueous saline solution in the back extraction. Ultrafiltration (Uf2) is used again to concentrate the solution. The last stage is finally chromatography (Chr), during which selective binding is used to better separate the product of interest from the other proteins.

Insulin and chymosin are *extracellular products*. Proteins are separated from the cells in the first microfilter (Mf1), where cells and some of the supernatant liquid stay behind. To reduce the amount of valuable products lost in the retentate, extra water is added to the cell suspension. The homogenizer (Hom) and microfilter (Mf2) for cell debris removal are not used when the product is extracellular. Nevertheless, the ultrafilter (Uf1) is necessary to concentrate the dilute solution prior to extraction.

The final step of extraction (Ext), ultrafiltration (Uf2) and chromatography (Chr) are common to both the extracellular and intracellular products.

3. Problem formulation

3.1. Batch plant design and optimization criteria

In previous works (Dietz et al., 2005, 2006), batch plant design was carried out minimizing the investment cost and the production system was represented using discrete-event simulation techniques in order to take into account different production policies. Two strategies for campaign policies, either monoproduct or multiproduct, were tested. In this work, only the monoproduct campaign policy was considered, so that the computation of cycle time can be easily implemented using the classical formulation proposed in Montagna et al. (2000), involving size and time equations as well as constraints. The adaptations made are given in what follows.

Let us recall here that the methodology proposed by Montagna et al. (2000) was initially based on a mixed integer nonlinear programming approach solved within GAMS modeling environment (DICOPT module) (Brooke, Kendrick, Meeraus, & Raman, 1998). A similar formulation was adopted in this work but the optimization problem is solved by an extended version of the multiobjective genetic algorithm previously developed by Dietz et al. (2005, 2006). The model uses the formulation presented in Modi and Karimi (1989), then modified in Xu, Zheng, and Cheng (1993), for multiproduct batch plant design formulation. It considers not only treatment in batch stages, which usually appears in all kinds of formulation, but also represents semi-continuous units that are part of the whole process (pumps, heat exchangers, etc.). Let us recall that a semi-continuous unit is defined as a continuous unit working by alternating low-activity and normal activity periods. Besides, this formulation takes into account short-term or mid-term intermediate storage tanks. They are used to divide the whole process into sub-processes, in order to store materials corresponding to the difference of each sub-process productivity. This representation mode confers to the plant a major flexibility for numerical resolution, by preventing the whole process production from being paralysed by one bottleneck stage. So, a batch plant is finally represented by series of batch stages (B), semi-continuous stages (SC) and storage tanks (T).

The model considers the synthesis of I products treated in J batch stages and K semi-continuous stages. Each batch stage consists of m_j out-of-phase parallel items of same size V_j. Each semi-continuous stage consists of n_k out-of-phase parallel items of same processing rate R_k. The item size (continuous variables) and equipment number per stage (discrete variables) are bounded. The $S-1$ storage tanks, of size V_s^*, divide the whole process into S sub-processes.

The quantities which are considered as imprecise are denoted with a $\sim$-symbol and concern explicitly production requirements and a horizon time constraint for each product. The problem formulation is subjected to three kinds of constraints:

(i) Variable bounding:

$$V_{\min} \leq V_j \leq V_{\max} \quad \forall j \in \{1, \ldots, J\} \tag{1}$$

$$R_{\min} \leq R_k \leq R_{\max} \quad \forall k \in \{1, \ldots, K\} \tag{2}$$

(ii) Time constraint: the total production time for each product $\tilde{H}_i$ can be deduced from demands and productivities:

$$\sum_{i=1}^{I} \tilde{H}_i = \sum_{i=1}^{I} \frac{\tilde{Q}_i}{\text{Prod}_i} \tag{3}$$

where $\tilde{Q}_i$ is the demand for product I which is imprecise by nature.

(iii) Constraint on productivities: the global productivity for product i (of the whole process) is equal to the lowest local productivity (of each sub-process s):

$$\mathrm{Prod}_i = \min_{s \in S}[\mathrm{Prodloc}_{is}] \quad \forall i \in \{1, \ldots, I\} \tag{4}$$

These local productivities are calculated from the following equations:

(a) Local productivities for product i in sub-process s:

$$\mathrm{Prodloc}_{is} = \frac{B_{is}}{T_{is}^{\mathrm{L}}} \quad \forall i \in \{1, \ldots, I\};\ \forall s \in \{1, \ldots, S\} \tag{5}$$

(b) Limiting cycle time for product i in sub-process s:

$$T_{is}^{\mathrm{L}} = \max_{j \in J_s, k \in K_s} \left[T_{ij}, \Theta_{ik}\right]$$
$$\forall i \in \{1, \ldots, I\};\ \forall s \in \{1, \ldots, S\} \tag{6}$$

J_s and K_s are respectively the sets of batch and semi-continuous stages in sub-process s.

(c) Cycle time for product I in batch stage j:

$$T_{ij} = \frac{\Theta_{ik} + \Theta_{i(k+1)} + p_{ij}}{m_j}$$
$$\forall i \in \{1, \ldots, I\};\ \forall j \in \{1, \ldots, J\} \tag{7}$$

k and $k+1$ represent the semi-continuous stages before and after batch stage j.

(d) Processing time of product i in batch stage j:

A classical formula such as

$$p_{ij} = p_{ij}^0 + g_{ij} B_{is}^{d_{ij}}$$
$$\forall i \in \{1, \ldots, I\};\ \forall j \in \{1, \ldots, J_s\};\ \forall s \in \{1, \ldots, S\} \tag{8}$$

for the computation was used by Montagna et al. (2000) to obtain the processing time of product i in batch stage j. Instead, we used here the computation procedures developed by Dietz et al. (2005, 2006) to explicitly calculate the processing time as a function of the operating parameters at each processing step.

The general form of the involved model is proposed as follows:

$$(V_{\mathrm{batch}}^{\mathrm{s}}, C_i^{\mathrm{s}}, X_0^{\mathrm{s}}, X_1^{\mathrm{s}}, X_2^{\mathrm{s}}, \text{effluents})$$
$$= f_i(V_{\mathrm{batch}}^{\mathrm{e}}, C_i^{\mathrm{e}}, X_0^{\mathrm{e}}, X_1^{\mathrm{e}}, X_2^{\mathrm{e}}, \text{operating\_conditions}) \tag{9}$$

The objective is to compute batch size, concentration and composition at each processing step output, as well as the effluent as a function f_i of the input conditions.

More detail can be found in Dietz et al. (2005, 2006).

(e) Operating time for product i in semi-continuous stage k:

$$\Theta_{ik} = \frac{B_{is} D_{ik}}{R_k n_k} \quad \forall i \in \{1, \ldots, I\};\ \forall k \in \{1, \ldots, K_s\};$$
$$\forall s \in \{1, \ldots, S\} \tag{10}$$

(f) Batch size of product i in sub-process s:

Instead of using a classical formula involving size factors such as

$$B_{is} = \min_{j \in J_s} \left[\frac{V_j}{S_{ij}}\right] \quad \forall i \in \{1, \ldots, I\};\ \forall s \in \{1, \ldots, S\} \tag{11}$$

the batch size for each product is given by the maximal value that can be treated without splitting.

Finally, the size of intermediate storage tanks is estimated as the highest difference between the batch sizes treated by two successive sub-processes:

$$V^{\mathrm{s}} = \max_{i \in I}[\mathrm{Prod}_i S_{is}(T_{is}^{\mathrm{L}} + T_{i(s+1)}^{\mathrm{L}} - \Theta_{\mathrm{it}} - \Theta_{i(t+1)})]$$
$$\forall s \in \{1, \ldots, S-1\} \tag{12}$$

A key-point of the procedure is the computation of the so-called cycle time TL_i for each product, which corresponds to the limiting time, i.e. the time between two consecutive batches of the product. The objective is to determine the number and size of parallel equipment units/storage as well as some key process variables in order to satisfy one or several criteria (see Dietz et al., 2005), for a complete description of the problem. Although the minimizing investment is most often considered in the dedicated literature, it is not the most adequate objective for the optimal design problem. In real applications, designers preferentially not only consider to maximize the net present value (NPV), but also to satisfy a due date. The corresponding mathematical expressions of the objective functions are proposed as follows:

Maximize the net present value defined in (13):

$$\tilde{\mathrm{Max}}(\tilde{\mathrm{NPV}}) = \mathrm{Max}(\tilde{f}_1) =$$
$$-\mathrm{Inv} - f + \sum_{p=1}^{n} \frac{(\tilde{V}_p - \tilde{D}_p - A_p)(1-a) + A_p}{(1+i)^n} + \frac{f}{(1+i)^n} \tag{13}$$

where Inv is the investment cost given by (14):

$$\mathrm{Inv} = \sum_{j=1}^{M} N_j \alpha_j V_j^{\beta_j} \tag{14}$$

$$f = 0.15\,\mathrm{Inv} \tag{15}$$

$$\tilde{V}_p = \sum_{i=1}^{N} C_{\mathrm{P}_i} \tilde{Q}_i \tag{16}$$

$$\tilde{D}_P = \sum_{i=1}^{N} \sum_{j=1}^{M} C_{\mathrm{E}_j} \frac{\tilde{Q}_i}{B_{is}} + C_{\mathrm{O}_i} \tilde{Q}_i \tag{17}$$

$$A_p = \frac{I}{n} \tag{18}$$

and

$$\widetilde{\min}(\text{advance/delay}) = \tilde{\mathrm{Min}}(\tilde{f}_2) = \left|\tilde{H} - \sum_{p=1}^{P} \tilde{H}_i\right| \text{penalization} \tag{19}$$

$\tilde{H}$ represents the requirement on total time for production, which is part of customers' specifications. Nevertheless, a crisp value may be difficult to determine a priori and a more appropriate way is to consider tolerances on this quantity. This is why a $\sim$-symbol is also used at this level.

The definition of process and decision parameters is listed in Nomenclature.

The penalization term in (19) is equal to an arbitrary value of $1/\omega$ for an advance and ω for a delay in order to penalize more delays than advances. A sensitivity analysis leads to adopt a value of 4 for ω. Finally, an additional criterion was computed in case of an advance (respectively a delay), representing the additional production that the batch plant is able to produce. Without going further in the detailed presentation of the computation procedure, it can be simply said that a flexibility index (called criterion f_3) is computed by dividing the potential capacity of the plant by its actual value.

$$\max(\text{flexibility index}) = \max(f_3) \tag{20}$$

A key-point of the proposed approach which is presented in the following section is to consider all the criteria simultaneously rather than combine them into one hybrid criterion reflecting the different aspects. A thorough comparison of such an approach within a crisp framework was already performed (Dietz, 2004). A weighting sum, i.e. the function to optimize is the weighted sum of the set of objective function was computed. The main drawback is due to the different values to assign the weights to lead to the so-called Pareto front, for which the points may be not uniformly distributed and may require a great number of simulations to be constituted. This is why this technique was discarded.

3.2. *Overview of fuzzy multiobjective genetic algorithm approach*

In the context of engineering design, an imprecise variable is a variable that may potentially assume any value within a possible range because the designer does not know a priori the final value that will emerge from the design process. The fuzzy set theory was introduced (Zadeh, 1975) to deal with problems in which a source of vagueness is involved. It is well-recognized that fuzzy set theory offers a relevant framework to model imprecision.

3.2.1. *Representation of fuzzy demands and time horizon due date*

In this section, only the key concepts from the theory of fuzzy sets that will be used for batch plant design are presented; more detail can be found in Kaufmann and Gupta (1988). Different forms can be used for modeling the membership functions of fuzzy numbers. We have chosen to use normalized trapezoidal fuzzy numbers (TrFNs) for modeling product demand, which can be represented by a membership function $\mu(x)$.

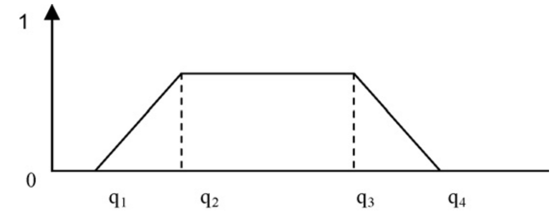


Fig. 2. Demand modeling by fuzzy numbers, $Q=(q_1, q_2, q_3, q_4)$.

Let us recall that the membership function values of a TrFN range from zero to one with the mode at one. The possibility distribution of TrFNs represented by a four-tuple $[q_1, q_2, q_3, q_4]$ with $q_1 \le q_2 \le q_3 \le q_4$ describes the more or less possible values for a demand. In other words, they can be interpreted as pessimistic or optimistic viewpoints of the designer. Fig. 2 describes the more or less possible values for the Q demand. Triangular fuzzy numbers, which need only two uncertain constants, i.e. for low and large values of demand could also be used, since they are special cases of TrFNs ($q_2 = q_3$). Nevertheless, the use of a TrFN is more intuitive to users: the interval (q_2, q_3) represents demands with a membership function at level $\mu = 1$, the intervals (q_1, q_2) and (q_3, q_4) represent the more and less possible values of demand, i.e. demand is guaranteed, its value may vary from q_1 to q_4 with conjuncture but may be expected to take values ranging from q_2 to q_3 (Kaufmann & Gupta, 1988) (see Fig. 2).

A fuzzy demand can thus be represented by a membership function $\mu_Q(x)$ at μ level by the following expression:

$$\forall \alpha \in [0, 1], \quad Q_\mu = [(q_2 - q_1)\alpha + q_1, -(q_4 - q_3)\alpha + q_4] \tag{21}$$

The membership function is defined by

$$\mu_Q(x) = \begin{cases} 0, & x < q_1, \\ \dfrac{x - q_1}{q_2 - q_1}, & q_1 \le x \le q_2, \\ 1, & q_2 \le x \le q_3, \\ \dfrac{q_4 - x}{q_4 - q_3}, & q_3 \le x \le q_4, \\ 0, & x > q_4. \end{cases} \tag{22}$$

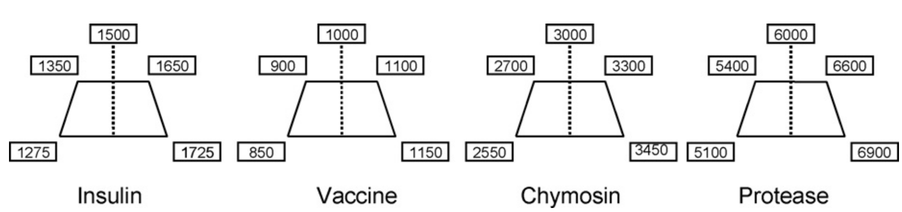


Fig. 3. Fuzzy representation of product demand (kg/year).

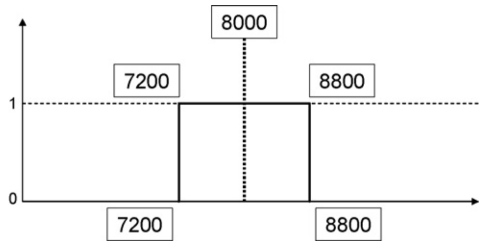


Fig. 4. Fuzzy representation of horizon time (h).

Fig. 3 presents the typical values adopted in this work which correspond respectively to an imprecision of 10% with mode at one (respectively 15% with mode at zero). We also introduced in the model a fuzzy horizon time with a "rectangular" representation which may be viewed as latest and earliest dates to satisfy, with an imprecision of 10% (see Fig. 4).

The fuzzy approach can also embed imprecision on a variable and tolerances on another one in a same formulation.

3.2.2. Fuzzy arithmetic operations

They involve addition, subtraction, taking the maximum of two fuzzy numbers (mainly at the selection stage and at the Pareto sort procedure), through the extension principle of (Zadeh, 1975).

The sum of two fuzzy numbers $\tilde{A}$ and $\tilde{B}$ given by $\tilde{A}(+)\tilde{B}$ is defined by

$$\mu_{\tilde{A}(+)\tilde{B}} = \sup \left\{\min(\mu_{\tilde{A}}(z-y), \mu_{\tilde{B}}(y)/y \in \Re, z \in \Re\right\} \quad (23)$$

The subtraction of two fuzzy numbers $\tilde{A}$ and $\tilde{B}$ given by $\tilde{A}(-)\tilde{B}$ is defined by

$$\mu_{\tilde{A}(-)\tilde{B}} = \sup \left\{\min(\mu_{\tilde{A}}(z+y), \mu_{\tilde{B}}(y)/y \in \Re, z \in \Re\right\} \quad (24)$$

Although the objective functions used in this problem are nonlinear and dependent on the uncertain variables, the computation can be made easily since the uncertain variables only involve addition and subtraction operations which are conservative.

3.2.3. Fuzzy numbers comparison

A variety of methods for comparing or ranking fuzzy numbers has been reported in the literature (Baas & Kwakernaak, 1977; Bortolan & Degani, 1985; Chen, 1985; Delgado, Verdegay, & Villa, 1988; Dubois & Prade, 1983; Lee & Li, 1988; Liou & Wang, 1992; Yager, 1981; Yuan, 1991). According to Yuan (1991), different properties are desirable with a fuzzy ranking method: (1) fuzzy preference representation; (2) rationality of preference ordering; (3) distinguishability. However, most of the approaches based on the possibility theory that have been developed suffer from lack of discrimination (a consistent total ordering is not always guaranteed) and occasionally conflict with intuition. Some methods use probabilistic indexes (Lee & Li, 1988) and have defined generalized mean values of fuzzy numbers. In general, decisions makers having different degrees of optimism should give ranking outcomes under the same situation. Several authors have thus suggested methods of ranking fuzzy numbers with an index of optimism to reflect the decision maker's optimistic or pessimistic viewpoint. Among them, the approach proposed by Liou and Wang (1992) using an integral value is particularly attractive. It is independent of the type of the membership function and of the normality of the functions and can rank more than two fuzzy numbers simultaneously. It is particularly simple in computation, especially in ranking TrFNs and has proven its robustness to discriminate fuzzy numbers. Let us briefly recall here its principle: the membership function of a TrFN is decomposed into two functions:

$$\mu_A^{\mathrm{L}}(x) = \frac{x-a_1}{a_2-a_1} \quad (25)$$

$$\mu_A^{\mathrm{R}}(x) = \frac{x-a_4}{a_3-a_4} \quad (26)$$

They then resort to the inverse functions of $\mu_A^{\mathrm{L}}(x)$ and $\mu_A^{\mathrm{R}}(x)$, which are denoted in this study $\nu_A^{\mathrm{L}}(x)$ and $\nu_A^{\mathrm{R}}(x)$. They can be expressed as follows:

$$x \in [0,1], \quad \nu_A^{\mathrm{L}}(x) = a_1 + (a_2 - a_1)x \quad (27)$$

$$x \in [0,1] \quad \nu_A^{\mathrm{R}}(x) = a_4 + (a_3 - a_4)x \quad (28)$$

These functions are integrable, they are real numbers and the integral values of TrFn are given by

$$I_{\mathrm{L}}(A) = \int_0^1 \nu_A^{\mathrm{LG}}(x)\,\mathrm{d}x = \int_0^1 [a_1 + (a_2-a_1)x]\,\mathrm{d}x = 0.5(a_1+a_2) \quad (29)$$

$$I_{\mathrm{R}}(A) = \int_0^1 \nu_A^{\mathrm{RD}}(x)\,\mathrm{d}x = \int_0^1 [a_4 + (a_3-a_4)x]\,\mathrm{d}x = 0.5(a_3+a_4) \quad (30)$$

The left (respectively right) integral value is used to reflect the pessimistic (respectively optimistic) viewpoint of the decision maker. A combination of these integral values through an index of optimism denoted β is called the total integral value:

$$I_{\mathrm{T}}^{\beta} = \beta I_{\mathrm{R}}(A) + (1-\beta) I_{\mathrm{L}}(A) \quad (31)$$

A value of β equal to zero corresponds to the most pessimistic viewpoint of a decision's maker and, conversely, a value of β equal to 1 corresponds to his most optimistic viewpoint.

The computations were performed with an average value of β equal to 0.5.

3.2.4. Fuzzy extension of a multiobjective genetic algorithm

3.2.4.1. Brief literature survey on fuzzy multiobjective optimization. The literature on multiobjective optimization is abundant (Sawaragi, Nakayama, & Tanino, 1985) and will not be developed here exhaustively. Classically, a large number of methods imply the concept of Pareto-optimality. In that context, the big advantage of genetic algorithms over other methods, particularly over other stochastic procedures such as simulated annealing, is that a GA manipulates a population of individuals. It is therefore tempting to develop a strategy in which the population captures the whole Pareto front in one single optimization run. Literature surveys and comparative studies on multiobjective genetic algorithms are also given in Bhaskar, Gupta, and Ray (2000), Coello Coello (2000), Fonseca and Fleming (1995), and Holland (1975). They have divided multiobjective genetic algorithms in non-Pareto (Schaffer, 1985) and Pareto-based approaches (Goldberg, 1994). Yet unfortunately, multiobjective and fuzzy concepts are not very often taken into account simultaneously. A very interesting contribution is the work of Huang and Wang (2002) introducing a fuzzy decision-making approach to solve the fuzzy goal optimization problem. Three common aggregation functions have been used in fuzzy optimization problems discussed in the textbook of Sakawa (1993) and have adopted in their approach. A membership function is used to define the degree of satisfaction for each objective function so that the fuzzy goal optimization problem is then converted into an augmented minimax problem formulated as MINLP models. Such MINLP problems involving nonlinear real and integer variables are unable to be directly solved by some commercial algorithms, e.g. DICOPT++. In order to obtain a unique solution for the MINLP problem, the authors introduce a mixed coding evolutionary algorithm (EA) to solve the augmented minimax problem. In addition, an interactive algorithm is also proposed to obtain a satisfied solution for the fuzzy goal optimization problem.

3.2.4.2. Presentation of the proposed contribution. In our work, the multiobjective genetic algorithm presented elsewhere (Dietz et al., 2006), was extended to take into account the fuzzy nature of both demand and horizon time.

The originality of this proposed investigation is that fuzziness is maintained throughout the computation procedure and no defuzzification is operated so that fuzzy results are proposed to the decision's maker. In what follows, the typical features of the introduction of fuzzy concepts in the procedure are highlighted.

Let us mention that the same encoding procedure was adopted since no fuzzy parameter is involved at that stage. The optimization variables are structure variables (number of parallel equipment), equipment size and operating conditions. An individual which is generated at the initial population creation step will be entirely defined by a chromosome with three parts relative to these variable types. From production requirements, the initialization procedure for equipment unit values allows to compute (a crisp value is used for estimation purpose), the batch size for each product that can be treated in each equipment item without splitting. As abovementioned, the computation procedure replaces the traditional formulation in which batch size is computed from equipment volume and size factors. A call to the discrete-event simulator developed in Dietz et al. (2005) is thus carried out to compute the operating times of the involved processes from representation models. Then, limiting cycle time and productivities are computed classically. The fuzziness feature through the nonlinear model propagates mainly from the com-

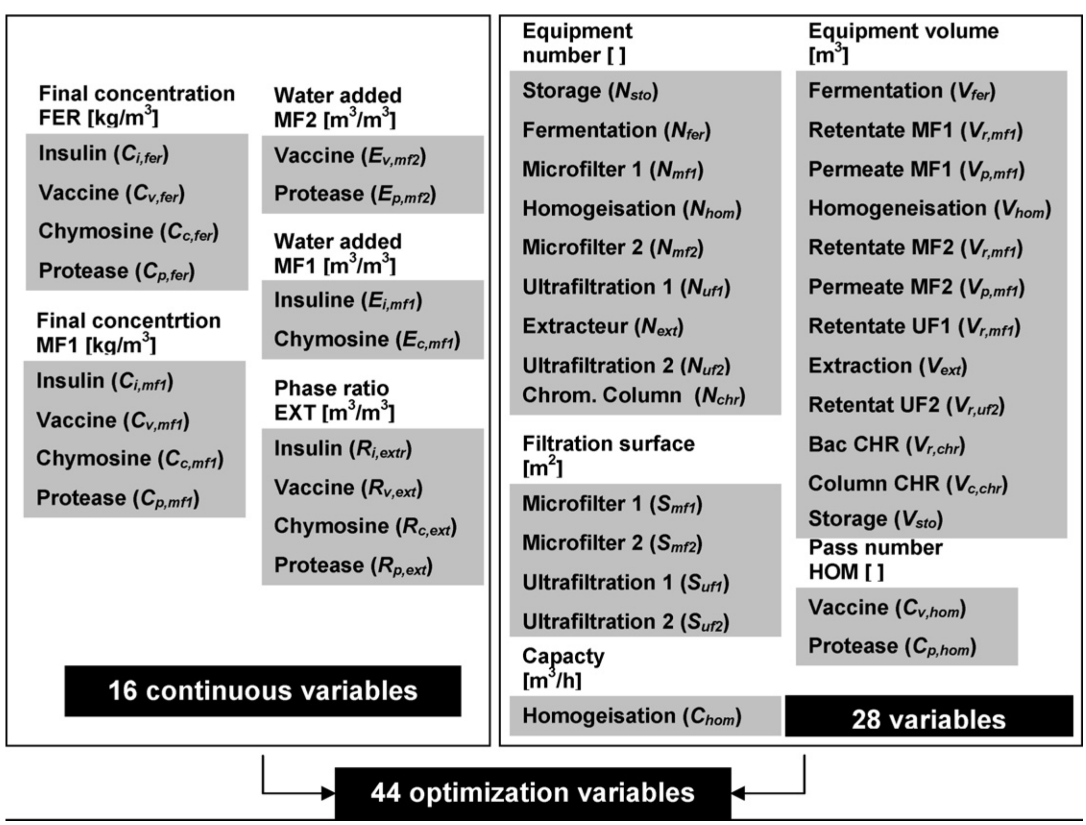


Fig. 5. List of optimization variables.

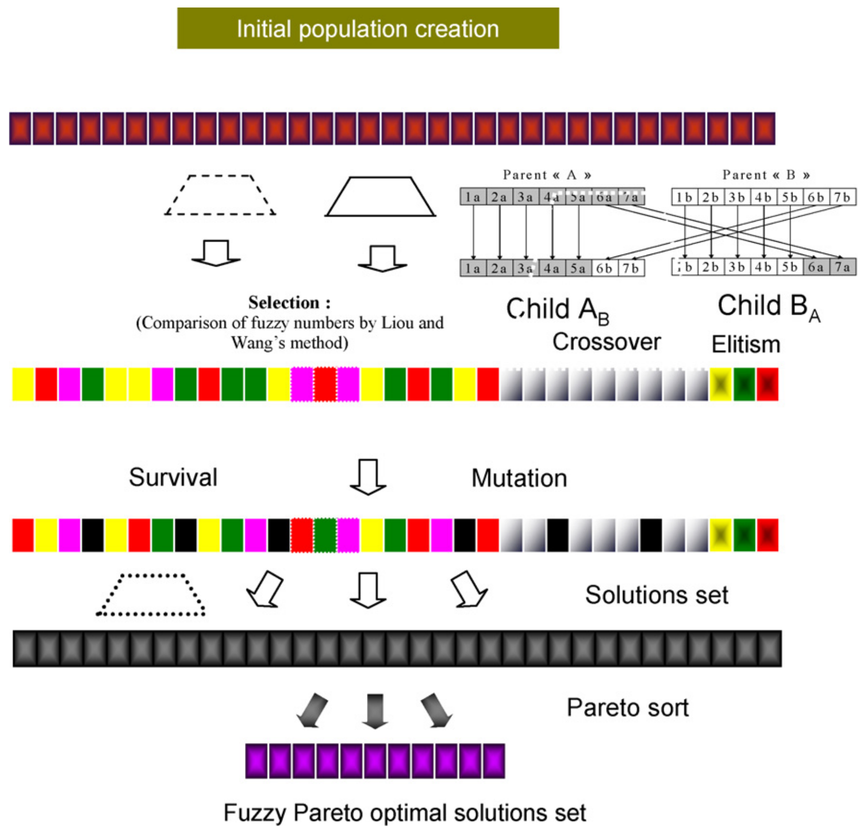


Fig. 6. Fuzzy genetic algorithm flowchart.

putation of the total production time for each product $\tilde{H}_i$ which is calculated from fuzzy demands and productivities (these are deduced from the following equations of the model, see Eq. (3)). The interest of the upper optimization procedure is that the time horizon constraint prevents from obtaining too relaxed values for total production times, for which the membership function will be too dispersed so that no valuable decision can be deduced.

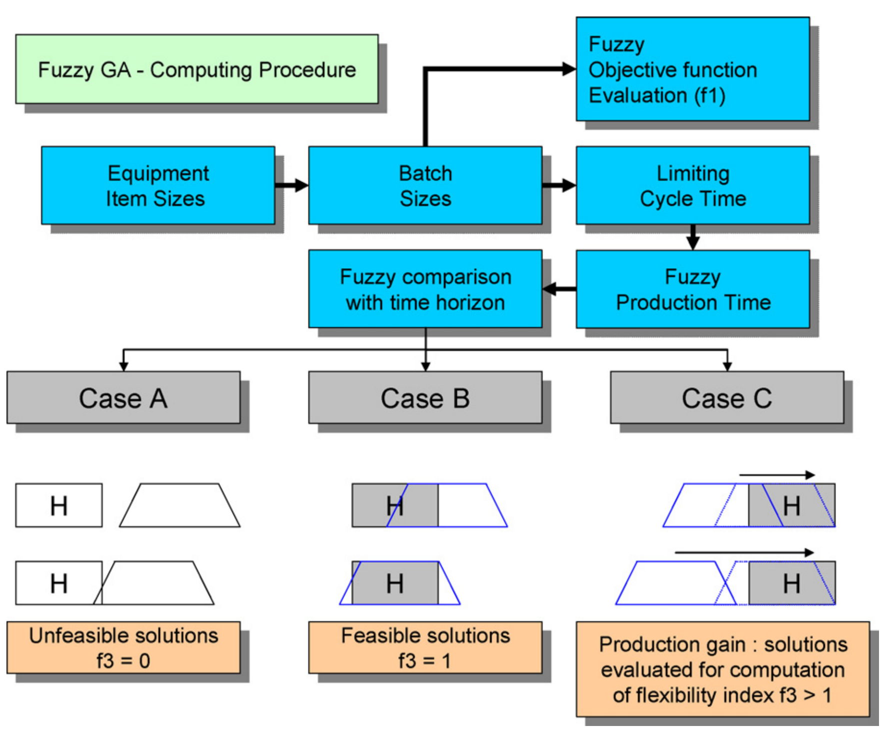


Fig. 7. Fuzzy evaluation procedure in the GA.

From Montagna et al. (2000), the optimization variables adopted in this study are presented in Fig. 5. More detail can be found in Dietz et al. (2005).

The tunable parameters of the GA will also not be discussed here. Although the GA basic principles will not be recalled, it must be said that arithmetic operations on fuzzy numbers that will be used concern exclusively the objective functions and the constraints.

Only the main steps of the MOGA are presented here (see Fig. 6):

- *Initial population creation*: it is generated randomly but, only the individuals that do not violate the horizon time constraint are selected to follow the remaining algorithmic process, i.e.

$$\sum_{i=1}^{I} \tilde{H}_i = \sum_{i=1}^{I} \frac{\tilde{Q}_i}{\text{Prod}_i} \leq \tilde{H} \tag{32}$$

- *Crossover and mutation procedures*: they are identical to the crisp version of the algorithm (see Dietz et al., 2005).
- *Selection*: the selection procedure is identical to the one proposed by Dietz (2004), in which the multicriteria aspects are taken into account at the selection step whereas the search for compromise solutions occurs at the crossover step. The same number of surviving individuals is chosen for each criterion. The selection procedure is carried out by a classical Goldberg's wheel. At this level, a distinction must be made between the randomly sort procedure involved in the roulette wheel and the computation of the fitness function. Although fitness computations are performed with fuzzy numbers, the wheel partitioning occurs by defuzzifying the fitness values to avoid overlapping of sectors, which can be detrimental to results interpretation.
- The fuzzy numbers comparison is performed by means of Liou and Wang's method (1992), as already discussed.

Looking more closely at the selection stage, three cases were considered, as qualitatively shown in Fig. 7, corresponding to either unfeasible solutions leading to unacceptable violations of a time horizon constraint ($f_3 = 0$), or to acceptable solutions sharing a time domain with an horizon constraint ($f_3 = 1$), or, finally, to solutions for which the computation of the additional demand that the batch plant is able to satisfy is interesting from a flexibility viewpoint ($f_3 > 1$).

Let us illustrate how the criteria are determined in this case.

It was arbitrarily selected to share equitably the available time among the products to manufacture.

$$\text{Available production time for each product(APT)} = \frac{\tilde{H}^*}{\text{number of products}} \tag{33}$$

To compute the additional demand for each product, the following formulation was adopted involving the available time and the productivity of each product:

$$\tilde{Q}_i^* = \text{Productivity}_i(\text{available time for each product}) \tag{34}$$

From this new global demand, the demand of each product is computed by:

$$\tilde{Q}_{\text{new}} = \sum_{i=1}^{I} \tilde{Q}_i^* \tag{35}$$

The new total demand is then computed:

$$\tilde{Q}_{\text{total}} = \tilde{Q}_{\text{new}} + \tilde{Q}_{\text{initial}} \tag{36}$$

The flexibility index is computed by the following relation in a defuzzifying way:

$$\text{Flexibility index} = \frac{Q_{\text{total}}}{Q_{\text{new}}} \tag{37}$$

The procedure is similar in the other cases.

In case C, the computed value of the total time necessary to manufacture all the products is shifted to the right so that the highest (respectively lowest) value of the four-tuple of the TrFN corresponds to that of the due date for time horizon.

The computation procedure for flexibility criterion evaluation is illustrated in Fig. 8. When production is in advance with respect to horizon due date (case C), the discrepancy between these two fuzzy values is then computed and considered as an additional potential production time. Considering once more the batch plant productivity for the different products and product mix and ratio, this time is assigned for an additional product manufacture. The new production is then compared to the expected value and two cases are exhibited. In the former, the main cores of the two fuzzy numbers are overlapping, so the new production is then accepted and the new NPV criterion is computed for this new production value as well as the flexibility criterion. When the two main cores are not overlapping, the production capacity of the plant is considered superior to the desired one. This capacity is used to compute the flexibility criterion and then a production correction is carried out as shown in Fig. 8 in order to compute the NPV criterion. It must be noted that the delay–advance criterion is not modified, which in turn penalizes this solution when the multicriteria batch plant design framework is applied.

4. Typical results

4.1. Monocriterion case

A monocriterion study was first performed with NPV as the only criterion to serve as a reference for the multicriteria study. The data used are proposed in Fig. 9.

The GA parameters used in the example are displayed in Table 1 and GA typical results are presented in Table 2. Ten runs were performed to guarantee the stochastic nature of the GA.

It must be pointed out that a thorough study on how the computational demand is expected to increase with problem sizes was already performed in Ponsich, Azzaro-Pantel, Domenech, and Pibouleau (2007) for a crisp study in a monocriterion case. It could be expected here that computational time would practically increase by a factor 4 (superior bound) from the results of

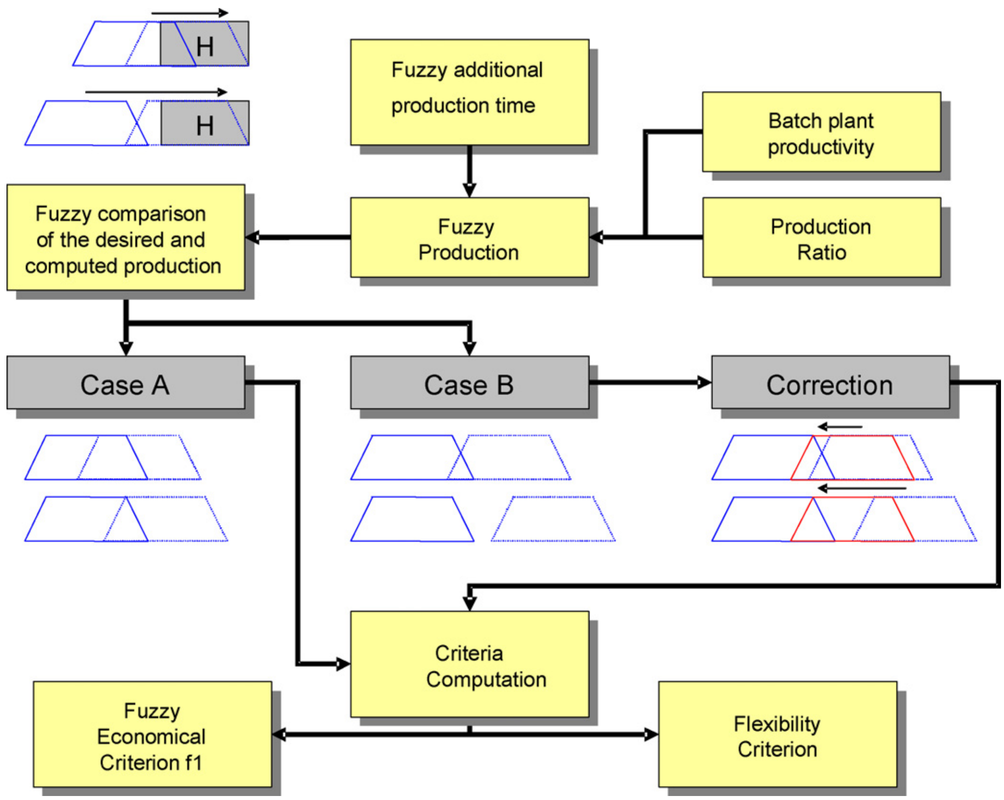
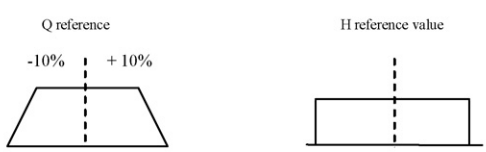


Fig. 8. Computing procedure for solution evaluation: correcting procedure.



Q reference values

Production (kg/an):

Insulin = 1500 Vaccine = 1000

Chymosin= 3000 Protease= 6000

Insulin= [1275, 1350, 1650, 1725]

Chymosin= [2550, 2700, 3300, 3450]
Vaccine=[850, 900, 1100, 1150]
Protease=[5100, 5400, 6600, 6900]

H reference values (h)

H=8000

H=[7200, 7200, 8800, 8800]

Economical data

Unit price for product *i*, C_{Pi} ($/Kg):

Insulin= 850
Vaccine= 750
Chymosin= 100
Protease=50

Operating cost for product *i* C_{Oi}

C_O= 5 ($/Kg) for the 4 proteins

C_E= 2 ($) for the 4 proteins

Fig. 9. Data used in the example.

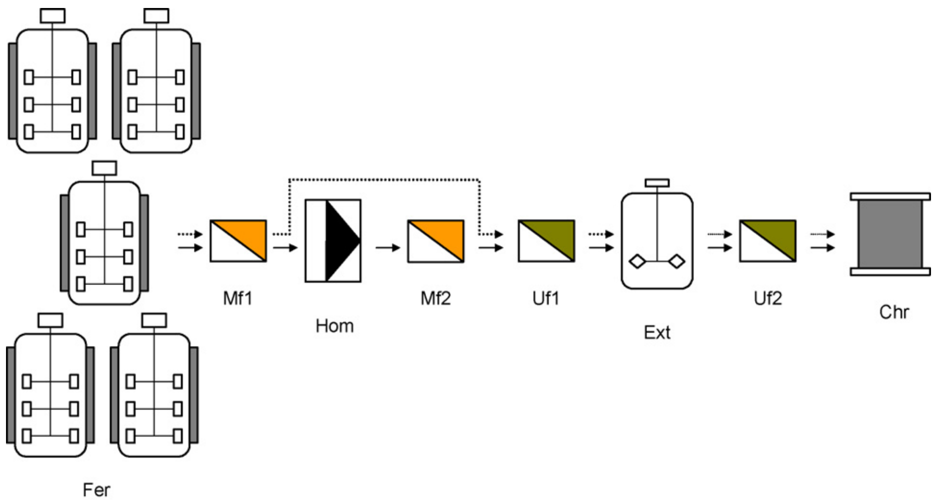


Fig. 10. Best solution for the monocriterion case.

Table 1
Parameter setting for GA

Population size	200
Generation number	1000
Survival rate	0.5
Mutation rate	0.4
Elitism	1

the cited reference, since a four-tuple is used here to represent the demand and the horizon time.

Table 2 presents the mean value of the NPV as well as the right core and support deviation from the mean value. Symmetrical values are obtained since symmetrical data were considered for both product demand and horizon due date. It must be pointed out that the order of magnitude of the results is of interest at the design preliminary stages.

The batch plant configuration with the highest value for NPV is presented in Fig. 10. The results of the optimization variables are presented in Table 3.

The results of the 10 runs exhibit symmetrical values for NPV since demands were also symmetrical but with different opening range. These results cannot be yet compared directly with the ones obtained in the previous works (Dietz et al., 2005, 2006) since only the investment cost was considered. It is yet interesting to point out that the same batch plant structure was obtained containing five fermentation units and one equipment item for each separation and purification treatment stage.

Table 2
Monocriterion (NPV) batch plant design

Run	Mean value (M€)	Right core deviation (%)	Right support deviation (%)
AG01	4.64	12.5	18.8
AG02	4.65	12.5	18.7
AG03	4.59	12.6	19.0
AG04	4.61	12.6	18.9
AG05	4.29	13.5	20.3
AG06	4.60	12.6	12.6
AG07	4.77	12.9	12.9
AG08	4.61	12.6	12.6
AG09	4.65	12.5	12.5
AG10	4.63	12.5	12.5

4.2. Bicriteria case

The optimization criteria were then considered by pairs in order to visualize the compromise existing between them.

The NPV criterion and the production delay–advance criterion (Fig. 11) are first examined and the non-dominated Pareto solutions of each GA implementation are presented in Fig. 11 for three optimization runs. It can be observed that the solution proposed at each implementation is qualitatively similar. From this set of solution, a final Pareto sort procedure is carried out in order to obtain the final solution to the optimization problem. It can be observed that the optimal solution for each criterion is obtained as well as a complete set of compromise solutions. Considering the best solutions for the delay–advance criterion, it can be observed that both figures are completely overlapping while maximizing the surface and, consequently, the just-in-time case.

Fig. 12 presents the results obtained when the NPV and the flexibility criterion were considered after the final Pareto procedure. In this case, the best solution for the NPV is obtained again and the production advance is used to compute the flexibility criterion. It can be shown that the interest region corresponds to a low advance, thus reducing the risk of a high storage cost. This solution yet confers some flexibility to the batch plant with respect to the production capacity.

Finally, the bicriteria {production delay/advance – flexibility} case was considered (Fig. 13). From a practical point of view, there is not interest in carrying out this design but helps understand the results obtained when the three criteria will be considered simultaneously.

As the economical criterion was not considered, it is not surprising that a large number of solutions are obtained. For instance, the optimal solution for the delay–advance criterion leads to a batch plant having a production time that overlaps

Table 3
Optimization variables for the best solution

Discrete variables	
Fermentation unit number	5
Fermentation size (m^3)	M
Number of Mf1 units	1
Retentate size	M
Filtration surface size	G
Permeate size	***G***
Homogenization unit number	1
Homogenization storage size	P
Homogenization unit capacity	***M***
Number of Mf2 units	1
Retentate size	P
Filtration surface size	***M***
Permeate size	***P***
Number of Uf1 units	1
Retentate size	***G***
Filtration surface size	M
Liquid–liquid extraction unit number	1
Liquid–liquid extraction unit size	P
Number of Uf2 units	1
Retentate size	P
Filtration surface size	P
Chromatographic column number	1
Storage size	P
Column size	G
Storage tank number	0
Continuous variables	
Final concentration, Fer (kg/m^3)	
Insulin, $C_{i,Fer}$	53.9
Vaccine, $C_{v,Fer}$	34.6
Chymosie, $C_{c,Fer}$	43.7
Protease, $C_{p,Fer}$	38.4
Final concentration, Mf1 (kg/m^3)	
Insulin, $C_{i,Mf1}$	209.2
Vaccine, $C_{v,Mf1}$	224.1
Chymosin, $C_{c,Mf1}$	150.3
Protease, $C_{p,Mf1}$	221.7
Pass number, HOM	
Vaccine, $C_{v,Hom}$	2.2
Protease, $C_{p,Hom}$	1.2
Eau de lavage, Mf2 (m^3/m^3)	
Vaccine, $E_{v,Mf2}$	1.9
Protease, $E_{p,Mf2}$	2.5
Water, Mf1 (m^3/m^3)	
Insulin, $E_{i,Mf1}$	1.5
Chymosin, $E_{c,Mf1}$	2.5
Phase ratio, Ext (m^3/m^3)	
Insulin, $R_{i,Ext}$	0.7
Vaccine, $R_{v,Ext}$	0.6
Chymosin, $R_{c,Ext}$	0.4
Protease, $R_{p,Ext}$	0.7

completely the horizon time. For the flexibility criterion, the best solution corresponds to the biggest batch plant size that maximizes the production and the other ones are compromise solutions.

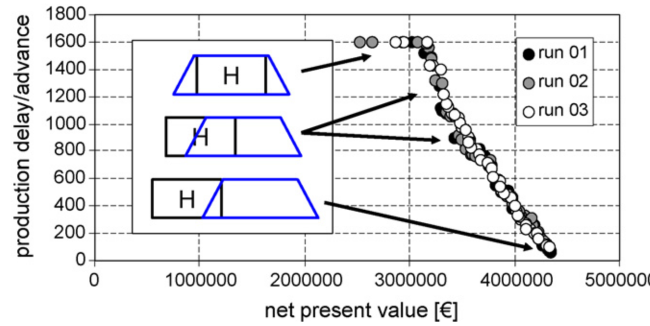


Fig. 11. Bicriteria NPV–PDA results: three optimization runs.

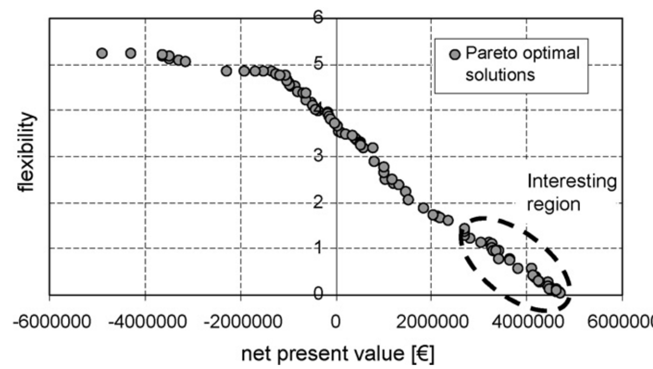


Fig. 12. Bicriteria NPV–flexibility results: final Pareto sort procedure.

4.3. Tricriteria case

Table 4 presents the results obtained at each optimization run when the three criteria are considered simultaneously. For the net present value criterion, a similar behaviour to the mono- and bicriteria cases can be observed; the best solution is obtained once and the other are around 2–3% from it. Concerning the flexibility index, the best value has no practical interest because it treats five times the initial demand. This criterion was considered in order to screen compromises near the optimal value for the net present value criterion.

We do not pretend that the optimizations have converged from a mathematical rigorous viewpoint. This is a criticism which is often used against stochastic algorithms. The difficulty is all the

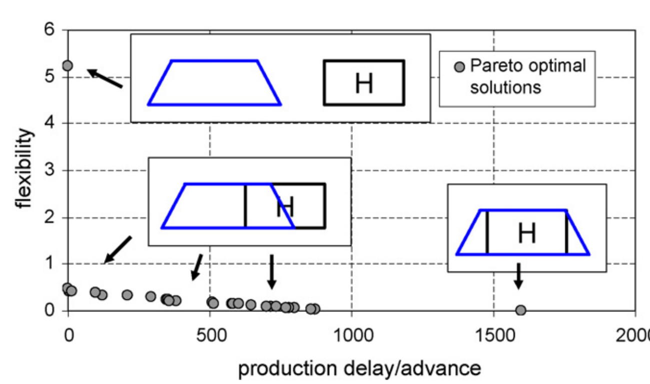


Fig. 13. Bicriteria PDA–flexibility results: final Pareto sort procedure.

Table 4
Tricriteria results

Run	Criterion 1	Criterion 2	Criterion 3
AG01	€4,415,720	1600	519,192
AG02	€4,551,110	1600	520,444
AG03	€4,444,000	1600	519,749
AG04	€4,495,280	1600	523,219
AG05	€3,935,540	1600	522,881
AG06	€4,555,870	1600	523,356
AG07	€4,628,410	1600	516,386
AG08	€4,261,440	1600	522,571
AG09	€4,018,120	1600	519,471
AG10	€4,279,590	1600	523,328
Best	€4,628,410	1600	523,356
Average	€4,358,508	1600	521,060
Std. Dev.	€232,999	0	002,371

more important here as trapezoidal fuzzy numbers are involved and as a multiobjective optimization is performed. In the computations performed, we use a maximum number of generations (1000), which is high enough to guarantee a non-evolution of the criteria.

From the results in Table 4, the standard deviation represents 5% of the average value, which is an acceptable order of magnitude at the earlier stages of process design.

Fig. 14 displays the results when the three criteria are considered simultaneously after the final Pareto sort procedure over the solutions corresponding to each optimization run. Only the average value of the involved criteria is reported here. Although a thorough analysis was performed, only the guidelines that may be useful for the practitioner are given. For instance, this curve may be useful to detect unfeasible regions and to identify the promising regions from the viewpoints of NPV and flexibility index. We also indicate some regions which may be interesting to explore since they involve high values for the net present value and exhibit a flexibility index greater than 1, corresponding to an acceptable advance in production: a front of solutions where the NPV criterion is comprised between 1000 and 45,000 k€, the delay–advance criterion is around 500 and the flexibility of around 10% is thus exhibited.

It must be pointed out that not only interesting isolated solutions can be obtained, but also a compromise pattern region is shown, from which the decision's maker can select a strategy.

We are aware that the proposed method is not strictly speaking a decision-making one, in the sense that it does not lead to a set of solutions, ranked by preferential order. From our viewpoint, it is important to give the decision's maker a zone of compromise solutions among them he has to choose the most appropriate one from considerations which may be difficult to formulate mathematically. The illustration which has just been presented through several optimization runs (mono-, bi- and tricriteria) serves as a kind of guidance for the treatment of similar examples.

4.4. *Fuzzy MOGA performance*

The best solutions obtained for the net present value criterion at the different optimization steps, monocriterion, bicriteria and

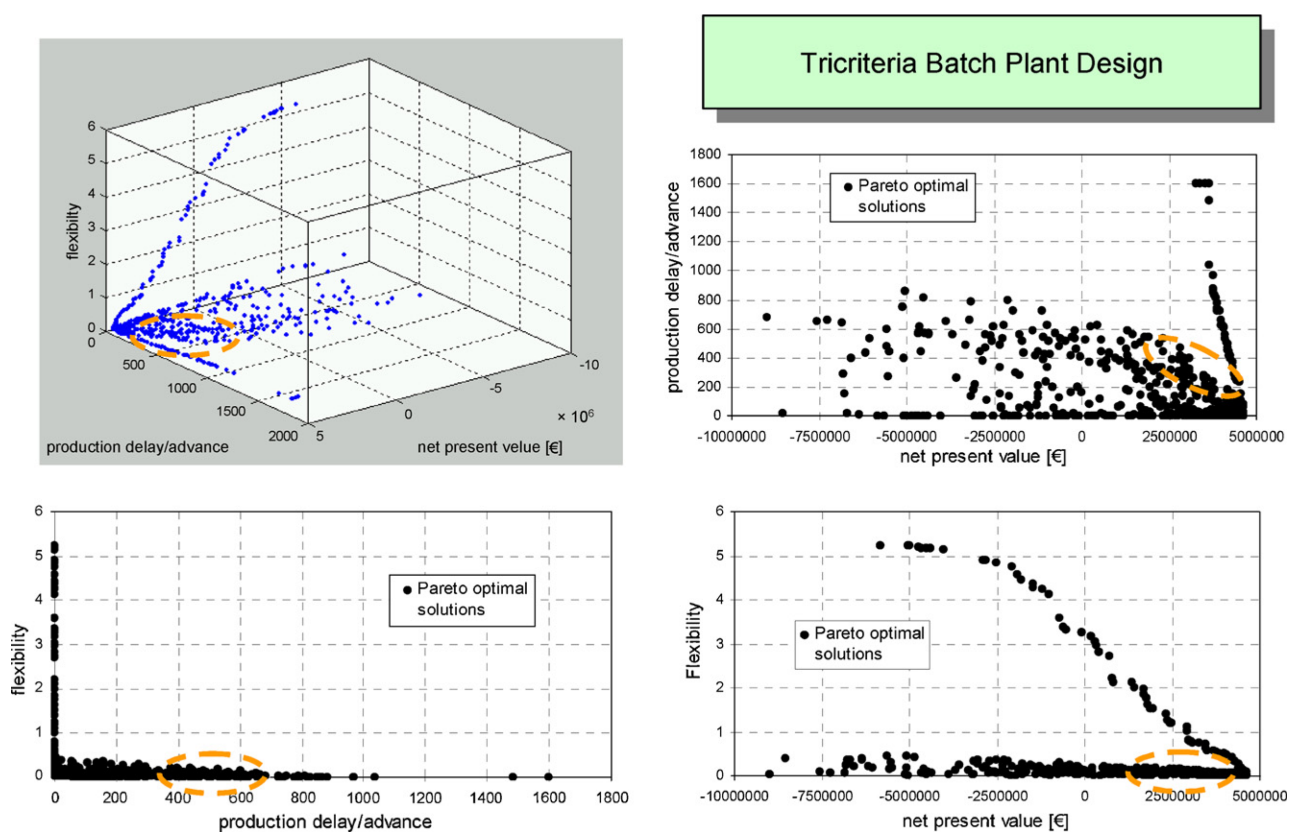


Fig. 14. Tricriteria results.

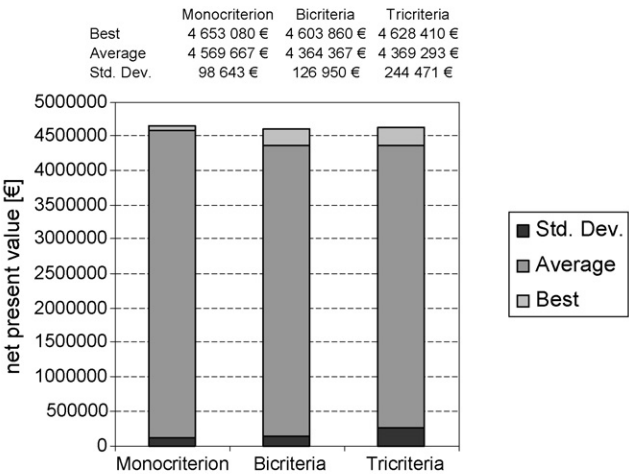


Fig. 15. GA search performances.

tricriteria, respectively, are presented in Fig. 15. The best result was not surprisingly obtained for the monocriterion case, however when the other criteria are considered, the best solution is near to the global best solution. Note that a better solution was obtained in the tricriteria case than in the bicriteria one, which may come from the stochastic aspects of GA.

The best solution for the NPV criterion was obtained in the bicriteria optimization case. It can be explained by the fact that when considering several criteria simultaneously, the GA search is diversified, extracting the algorithm from the local optimal solution, which is also confirmed in the tricriteria case.

Concerning the average value of the best solution obtained at each GA implementation, it can be observed that almost identical values are obtained for the multicriteria optimization.

5. Conclusions

In this paper, we have proposed a fuzzy approach to the treatment of imprecise demands in the batch design problem. Its benefits can be summarized as follows:

- Fuzzy concepts allow us to model imprecision in cases where historical data are not readily available, i.e. for demand representation.
- The models do not suffer from the combinatorial explosion of scenarios that discrete probabilistic uncertainty representation exhibit.
- Another significant advantage is that heuristic search algorithms, namely genetic algorithms for combinatorial optimization can be easily extended to the fuzzy case.
- Multiobjective concepts can also be taken into account.
- The preferences of customers can also be captured by fuzzy sets via acceptable values for due dates.

An example was used to illustrate the proposed approach. The results show that a set of compromise solutions is generated to the decision's maker, with an acceptable degree of imprecision affecting the defined criteria, which seems more realistic than a classical crisp approach. This will reduce the risk of making design decisions incorrectly. Providing (fuzzy) set based information can thus facilitate design.

Finally, this framework provides an interesting decision-making approach to design multiproduct batch plants under conflicting goals.

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