Trade-off-based multi-objective optimisation of a simultaneous saccharification and fermentation process

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Abstract: The demand for sustainable replacements for fossil-based products is steadily increasing, especially now that the effects of climate change are becoming more prominent. Lignocellulose, which is a sustainable and abundant carbon source, is dubbed to be the perfect replacement. Lignocellulose consists of lignin, hemicellulose, and cellulose. During the Simultaneous Saccharification and Fermentation (SSF) of cellulose, the hydrolysis and fermentation of the produced C6-sugars occurs simultaneously in the same vessel. The SSF process has mainly been developed to circumvent inhibitory effect and increase the overall product yield. Although the concept of the SSF process is promising, the applications are still limited. This contribution presents the trade-off-based multi-objective optimisation of an SSF process. Multi-objective optimisation allows for optimising (bio-)process with respect to multiple, and often conflicting, objectives. These optimisation problems do not render a unique optimal solution but instead an infinite set of so-called Pareto-optimal solutions, the Pareto front. From the Pareto front, the decision maker should select one working point. To aid decision makers in this selection process, the application of a novel genetic optimisation algorithm is presented in this contribution, i.e., tDOM, that is capable of filtering solutions using t-domination. This results in a less dense Pareto front that only contains solutions that are of interest for the decision maker. Additionally, by extending the t-domination concept to two subsequent solution populations, a novel problem-relevant stopping criterion is developed, resulting in a significant gain in the required computational time. A comparison to the well known NSGA-II is provided.

Keywords: Process modelling, Multi-objective optimisation, Simultaneous saccharification and fermentation, Bioprocesses, Trade-off, t-domination

1. INTRODUCTION

The past years have been characterised by increasingly harsh weather events. While the effects of climate change are becoming more tangible, the demand for sustainable replacements of fossil fuels is increasing. Lignocellulosic biomass, as it is the most abundant renewable carbon source on Earth, has been recognised as a sustainable replacement for fossil fuels (İsikgor and Becer, 2015). The raw biomass is converted into bio-fuels and other platform chemicals with the use of biorefinery processes. The processes can be subdivided based on the conversion platform they use: (i) Biological conversion platforms, (ii) Thermochemical conversion platforms, and (iii) Hybrid conversion platforms (De Buck et al., 2020b). Biological conversion platforms use enzymes and microorganisms to mediate the core processes needed to convert the raw biomass into usable products, whereas thermochemical conversion platforms use more general reactions. Biological conversion platform processes are mainly characterised by their high product selectivity but relatively low conversion rates. Contrarily, thermochemical conversion platform processes display high conversion rates but low product selectivity. Hybrid conversion platforms combine processes of the former two, displaying both high conversion rates and product selectivity (De Buck et al., 2020b). This contribution will focus on the multi-objective optimisation of a simultaneous saccharification and fermentation (SSF) process (Philippidis et al., 1992), which is associated with the biological conversion platform.

The structure of the SSF model that will be used in this contribution is developed by Shadabhr et al. (2017). In essence, the SSF model consists of a cellulose hydrolysis model (as developed by Kadam et al. (2004)), linked to an anaerobic fermentation model with the use of Saccharomyces cerevisiae. The SSF process, and used SSF model, are discussed more into detail in Section 2. Note, however, that despite the decades of research, the SSF process has not yet been applied on an industrial scale. The main reason for this is that the process itself is not optimal yet. Especially the conversion of cellulose into fermentable sugars, and the ethanol yield from the fermentation, are too limited to render an economically viable process (Shadabhr et al., 2018). Regarding this, a trade-off based multi-objective optimisation (MOO) of an SSF process will be presented in this contribution.

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Multi-objective optimisation allows for improving and optimising processes with respect to multiple, and often conflicting, objectives. These objectives can be of economic, societal, and environmental nature. The resulting optimisation problems are generally mathematically challenging and are tackled with the use of dedicated optimisation algorithms. While a multi-objective optimisation problem (MOOP) considers various objectives simultaneously, there is no longer one unique solution, but instead an infinitely large set of optimal trade-off solutions, called the Pareto front. The main goal when solving a MOOP is generating a close approximation of this Pareto front. Multi-objective optimisation algorithms can be subdivided into two main categories: (i) Deterministic algorithms, and (ii) Stochastic algorithms. Deterministic algorithms convert the multi-objective optimisation problem into a set of single-objective optimisation problems (SOOPs) with the use of parameters. The solutions of these SOOPs are also solutions of the original MOOP. Deterministic algorithms are, however, prone to converge to local optima and the eventually obtained Pareto front does not always display a satisfactory resolution. Additionally, they can only generate one solution per run. Stochastic algorithms on the other hand tackle the entire MOOP, rendering a global optimisation of the problem, and can generate multiple solutions per run. Moreover, while these algorithms do not require derivative information, they are excellent for the optimisation of black box problems (Logist et al., 2010). A subcategory of the stochastic algorithms are the genetic algorithms, whose functionality is based on the principles of biological reproduction and evolution. The optimisation algorithms used in this contribution, i.e., Non-dominated Sorting Algorithm II (NSGA-II), developed by Deb et al. (2002), and the novel t-Domination algorithm (tDOM), developed by De Buck et al. (2020a), belong to this category. Shadbahr et al. (2018) used a variant of NSGA-II in their contribution.

tDOM’s main functionalities are similar to those of NSGA-II but it employs t-domination, rather than non-domination, and features a problem-relevant stopping criterion. The former algorithm characteristic allows for generating Pareto-optimal solutions that are of interest to the decision maker (DM), resulting in a less cluttered and clearer Pareto front. The latter algorithm characteristic extends the concept of t-domination to two subsequent solution populations, enabling the algorithm to assess the overall difference between both. When the difference becomes negligible, the solutions have converged and the algorithm can stop. This leads to a significant gain in the required computational time (De Buck et al., 2020a). Both algorithms are explained more into detail in Section 3. The results of the MOOP and the comparison of these algorithms are discussed in Section 4. Conclusions are drawn in Section 5.

2. SIMULTANEOUS SACCHARIFICATION AND FERMENTATION

The SSF process considered in this contribution consists of the saccharification of cellulose into glucose, with the use of the enzymes cellulase and β-glucosidase. This hydrolysis process occurs simultaneously with the fermentation of the generated glucose into ethanol, with the use of Saccharomyces cerevisiae. Historically, the hydrolysis and fermentation processes have been conducted separately. The hydrolysis process, however, is hampered by product inhibition of the accumulating glucose on the used enzymes cellulase and β-glucosidase. This results in a poor cellulose conversion. Additionally, if conducted separately, the fermentation process is far from optimal while the high availability of substrate during the initial phase of the fermentation puts an increased stress on the used microorganisms. Again, this results in a poorer performance. The SSF process was developed to circumvent these disadvantages. Both the cellulose saccharification process, or hydrolysis, and the fermentation occur simultaneously in the same vessel. While the glucose is consumed immediately by the yeast, the accumulation of glucose, and thus product inhibition, is prohibited. Additionally, while the used microorganisms are exposed to a considerably lower substrate concentration, they are forced to use this limited available amount of substrate as efficiently as possible. Hence, when both processes are combined and occur simultaneously, a higher cellulose conversion and, thus, a higher product yield, are observed (Philippidis et al., 1992; Shadbahr et al., 2017).

During the hydrolysis step, cellulase initially reduces the dense cellulose strands into smaller pieces and, eventually, into its structural dimer cellulbiose. Cellulbiose consists of two D-glucose units that are connected with a β(1→4) glycosidic bond. Cellulbiose is subsequently hydrolysed into two β-D-glucose monomers with the use of β-glucosidase. The SSF process considered in this contribution uses S. cerevisiae to transform the formed glucose into ethanol.

2.1 Model description

The simultaneous saccharification and fermentation model employed in this paper follows the structure proposed by Shadbahr et al. (2017) and is based on the following reaction network:

\[
\text{Cellulose}(C) \xrightarrow{\beta} \text{Cellulbiose}(B)
\]

\[
\text{Cellulbiose}(B) \xrightarrow{\beta} \text{Glucose}(G)
\]

\[
\text{Glucose}(G) \xrightarrow{rG} \text{Ethanol}(E) + \text{Biomass}(X)
\]

\[
\text{Mannose}(M) \xrightarrow{rX} \text{Ethanol}(E) + \text{Biomass}(X)
\]

Cellulose is broken down into cellulbiose (with the use of cellulase), which is subsequently broken down into two β-D-glucose monomers. Although only β-D-glucose is produced during the hydrolysis reactions, mannose is also considered as a substrate for S. cerevisiae. Mannose is a C-2 glucose epimer which can be formed during the (acid) pretreatment of the lignocellulosic feedstock, especially in the case of softwood (Shadbahr et al., 2017). The SSF process is described by a collection of mass balance equations for its states, respectively cellulose, cellulbiose, glucose, mannose, biomass and ethanol where the reaction rates are given by (for the mass balances, see Table 1):

\[
r_1 = \frac{k_1 C \exp(-\lambda \cdot t)}{1 + B/K_1B + G/K_1G} - \frac{K_{1E}}{K_{1E} + E}
\]

\[
k'_1 = \frac{k_1 \cdot \text{enzc}}{K_{eq} + \text{enzc}}
\]

\[
r_2 = \frac{k_2 \cdot \text{enzg} \cdot B}{K_M(1 + G/K_2G) + B}
\]

\[
x = \mu_m X \left( \frac{G + M}{K_G + G + M} \right) \left( \frac{K_E}{K_E + E} \right)
\]

\[
r_G = \frac{G + M}{Y_{XG} + m_s X} \left( \frac{r_X}{r_X} \right)
\]

\[
r_M = \frac{M}{Y_{XG} + m_s X} \left( \frac{r_X}{r_X} \right)
\]
with enzc and enzg respectively the cellulase activity concentration and β-glucosidase activity concentration. The exponential time-dependency of \( r_1 \) represents the decrease in cellulose surface due to the hydrolysis process. The numerical values of the parameters are given in Table 1. The hydrolysis reactions are characterised by product inhibition, with \( K_{iB} \) and \( K_{iG} \) the inhibition constants of cellobiose and glucose, respectively, on reaction rate \( r_i \) (with \( i = 1, 2 \)). Additionally, the inhibitory effect of the eventually produced ethanol is taken into account with \( K_E \) the inhibition constant of ethanol on the cellulase activity. Figure 1 displays the cellulose concentration time evolution for the entire length of the SSF-process (\( t_{SSF} = 96 \) h).

![Cellulose concentration in function of time.](image)

**Figure 1.** Cellulose concentration in function of time.

Figure 2 displays the time evolutions of cellobiose, glucose, mannose, biomass, and ethanol during the first 50 hours of the process, for the sake of clarity.

![Cellobiose, glucose, mannose, biomass, and ethanol concentration in function of time.](image)

**Figure 2.** Cellobiose, glucose, mannose, biomass, and ethanol concentration in function of time.

### 2.2 Case studies

For the multi-objective optimisation of the SSF-process, two case studies are considered. Both aim to decrease the total enzyme usage per 1 gram of ethanol produced. The first case study simultaneously aims at increasing the cellulose conversion, while the second case study aims at increasing the ethanol yield. The objective functions of case study I are given by (Shadbahr et al., 2018):

\[
J_{1.1}(x) = \frac{C_0 - C_f}{C_0} \cdot 100 \% \tag{10}
\]

\[
J_{1.2}(x) = \frac{enzc + enzg}{E_f}[g] \tag{11}
\]

with \( Y_0 \) and \( Y_f \) the respective initial and final concentration of component \( Y \). \( x \) is the \((1 \times 6)\) vector containing the 6 process variables that are considered for optimisation (in this particular order): \( C_0, G_0, M_0, X_0, enz_c, \) and \( enz_g \).

The objective functions of case study II are given by (Shadbahr et al., 2018):

\[
J_{2.1}(x) = \frac{E_f - E_0}{0.511 \cdot (G_0 + M_0 + 1.111 \cdot C_0)} \cdot 100 \% \tag{12}
\]

\[
J_{2.2}(x) = \frac{enzc + enzg}{E_f}[g] \tag{13}
\]

### 3. MULTI-OBJECTIVE OPTIMISATION

Multi-objective optimisation (MOO) allows process operators and designers to optimise processes relative to multiple, and often conflicting, objectives. These process objectives can be of economical, societal, and environmental nature. Contrary to single-objective optimisation problems (SOOPs), multi-objective optimisation problems (MOOPs) do not render a single optimal solution, but instead an infinite set of equally optimal solution, i.e., the Pareto front, from which the decision maker (DM) should select one.

#### 3.1 Mathematical background

The mathematical formulation of a MOOP used throughout this contribution is presented in (14) (Das and Dennis, 1997).

\[
\min_{x \in C} F(x) = \{ J_1(x), \ldots, J_M(x) \} \tag{14}
\]

with \( C = \{ x : h(x) = 0, g(x) \leq 0, a \leq x \leq b \} \tag{15} \)

The feasible space \( C \) of variables \( x \in \mathbb{R}^N \) is defined by the (non-)linear equality constraints \( h : \mathbb{R}^N \mapsto \mathbb{R}^b \), the (non-)linear inequality constraints \( g : \mathbb{R}^N \mapsto \mathbb{R}^a \), and the lower and upper variables bounds \( a \) and \( b \), respectively. \( J_i \) represents the \( i \)-th objective function, with \( i \in \{1, \ldots, M\} \).

#### 3.2 Genetic algorithms

Genetic algorithms are global optimisation algorithms that mimic the evolution of species as seen in nature. The individuals that are best adapted to their environment, i.e., the most optimal ones, are more prone to prosper and reproduce than other individuals. One of the most commonly used genetic algorithms is NSGA-II, developed by Deb et al. (2002). The first iteration of NSGA-II consists of generating a random set \( P_0 \) of parent solutions in the feasible space. With the use of parent solution crossovers and mutations, \( N \) offspring solutions
are generated. A crossover of two parent solutions consists of a random linear recombination of both solutions, mirroring sexual reproduction. Mutations generate a new offspring solution by randomly altering several variables of a parent solution. The offspring set \( Q_t \) and parent set \( P_{t-1} \) of iteration \( t \) are merged into a combined population \( R_t = P_{t-1} \cup Q_t \). The overall fitness of the \( 2N \) solutions of the combined population set \( R_t \) is subsequently assessed. A fit solution is defined by a high convergence to the optimal Pareto front and contributes to the overall solution diversity. Merging the offspring and parent populations into a combined population allows for assessing the fitness of offspring solutions mutually, but also in regard to their parents. If some parent solutions display a higher fitness than their parents. If some parent solutions display a higher fitness compared to the Pareto front, the newly developed tDOM algorithm circumvents these major disadvantages.

### 3.3 tDOM-algorithm

The tDOM-algorithm use the same structural backbone as NSGA-II but uses t-domination instead of non-domination. This allows the generation of Pareto front only containing solutions that are relevant to the DM. The required relevance can be translated into a minimally required trade-off between two solutions. A trade-off occurs when it is impossible to improve with respect to one objective without worsening with respect to at least one other objective, which is the case when the DM switches between the non-dominated solutions of the Pareto front. The solutions of interest for the DM are located in the steep regions of the Pareto front, i.e., the knees of the Pareto front. The tDOM-algorithm is capable of mainly generating solutions located within these high trade-off regions by using the concept of t-domination. This is done by considering the density of the region of Practical Insignificant Trade-off (PIT-region) around a solution \( x \). The PIT-region was introduced by Mattson et al. (2004) (see Fig. 3) as a smart Pareto filter that can be used to filter relevant solutions from a large population. The shape and size of the PIT-region are defined by the minimum required trade-off \( \Delta t \) and distribution \( \Delta r \) required by the DM. The smart Pareto filter proposed by Mattson et al. (2004), however, introduces a waste in computational time as discarding solutions inherently also implies wasting computational time. The genetic nature of the tDOM-algorithm allows to introduce the density of the PIT-region of solutions as an additional inherent solution property, just like their non-dominated rank and crowding distance, based on which they can be selected. This results in the generation of high trade-off solutions without having to discard a large portion of the population at the end of the optimisation process. The general idea of the PIT-region is that if a solution is located within the PIT-region of another solution, the difference between the two solutions is deemed to be insignificant and they do not contribute to the overall diversity of the solution population. As a result, both solutions are downgraded, rendering both less prone to be selected as parent solutions for the next iteration or solution generation. By iteratively repeating this downgrading process, the final Pareto front mainly consists of high trade-off solutions (De Buck et al., 2020a).

**Fig. 3.** PIT-region of a solution \( p \). Red solutions are discarded, green ones are kept (adapted from Mattson et al. (2004)).

The tDOM-algorithm additionally employs t-domination as a problem-relevant stopping criterion by extrapolating the concept to two subsequent solution populations. If two subsequent
solution populations are located within each others PIT-region, there is no significant difference between them. This scenario only occurs when the solutions have converged to the Pareto front and, consequently, the algorithm can stop. While the stopping criterion of NSGA-II is generally overestimated, this novel t-domination-based stopping criterion results in a significant gain in computational time. On the other hand, it also ensures the DM that the final solution population has converged to the Pareto front while the stopping criterion is only triggered if the difference between two subsequent solutions is insignificant. The use of elitism ensures that this scenario can only occur when the solution population has converged to the Pareto front (De Buck et al., 2020a).

4. RESULTS & DISCUSSION

The used optimisation parameters for both case studies are summarised in Table 2.

Table 2. Numerical values of the optimisation parameters

| NSGA-II & tDOM | tDOM | NSGA-II |
|---------------|------|---------|
| N             | 75   | 50      |
| $p_m$         | 0.1  | 0.2     |
| $p_c$         | 0.9  | 0.8     |
| Lower bound   | [40, 0, 0, 1, 5, 20] | [75, 15, 15, 8, 30, 20] |
| Upper bound   | [85, 15, 15, 8, 30, 40] | [85, 15, 15, 8, 30, 40] |
| Maximum iterations | 100 | 100 |

with $N$ the required population size and $p_m$ and $p_c$ the respective mutation and crossover probability. The simulations and optimisation are run in Matlab R2018b on a 64-bit Windows 10 system with an Intel Core i5-8500 CPU @ 3.00 GHz processor and 16 GB of RAM installed.

4.1 Case study I

The first case study is a MOOP with two objectives: increasing the cellulose conversion whilst decreasing the enzyme consumption per gram of ethanol that is produced.

![Fig. 4. Pareto front of case study I.](image)

Figure 4 displays the Pareto front of case study I, generated with tDOM and NSGA-II. The high trade-off solutions, which are of interest for the DM, are located in the knee of the Pareto front. These solutions correspond roughly to a cellulose conversion of 22 to 24 % and an enzyme consumption of 2.2 to 2.5 g/g. Between a cellulose conversion of roughly 9 to 21 %, the cellulose conversion rapidly increases while the enzyme consumption per gram of ethanol produced stays reasonably the same. This plateau corresponds with an increase in $enzc$ while the $enzg$ does not increase. The former enzyme loading, i.e., the cellulase loading, has a direct effect on the breakdown of cellulose into cellobiose. The $enzg$, or $\beta$-glucosidase loading has a minor effect on the conversion of cellulose while an increased $\beta$-glucosidase will only decrease the inhibitory effect of the accumulating cellobiose on the cellulase, and thus the cellulose breakdown.

Two observations that can be made based on Fig. 4 are that the overall diversity of solutions generated by tDOM is higher than of those generated by NSGA-II, but they display a lower convergence to the Pareto front than the solutions generated by NSGA-II. The higher solution diversity in case of tDOM can be attributed to the fact that, during the successive solution generations, solutions with a less dense PIT-region are favoured. This results in a sparser solution density on the plateaus of the Pareto front, as can be seen between a cellulose conversion of 9 to 21 %, but also effectively pushes all solutions further apart, resulting in an increased exploration of the Pareto front. The implementation of the PIT-regions on the other hand also introduces a so-called zone of insignificance in the circumference of the actual Pareto front (see Fig. 5), which may lead to a poorer convergence.

![Fig. 5. Zone of insignificance in the close circumference of the Pareto front.](image)

Solutions that are located within the zone of insignificance are also located in the PIT-region of at least one solution found on the Pareto front. The definition of the PIT-region stipulates that in that scenario, the DM does not consider both solutions to be significantly different from each other and considers them as equal. The tDOM-algorithm’s new stopping criterion causes the optimisation to terminate when all solutions of a certain generation $f$ are located in that zone of insignificance. Comparing this with the solutions generated by NSGA-II, whose stopping criterion is usually overestimated, it might seem that the convergence of the solution generated by tDOM is poor. However, as stated above, once all solutions have converged into the zone of insignificance, the DM will no longer consider them to be different from the solutions on the actual Pareto front, and thus
the algorithm can be stopped. The tDOM algorithm required 104 s of computational time, while NSGA-II required 603 s.

4.2 Case study II

The optimisation problem of case study II aims at increasing the ethanol production whilst decreasing the enzyme consumption. The Pareto fronts, generated with tDOM and NSGA-II respectively, are represented in Fig. 6.

Fig. 6. Pareto front of case study II.

The Pareto front of case study II does not display a plateau as large as the plateau of the Pareto front of case study I. This is a result of the fact that in this case study, both enzymes used during the hydrolysis process have a direct influence on the amount of ethanol that is produced. Namely, in order to increase the ethanol production, more fermentable sugars should be produced during the hydrolysis phase, and for this both cellulase and β-glucosidase are required. An additional observation that can be made, when comparing the quality of the Pareto front of both case studies, is that the tDOM solutions have fully converged in case study II whereas this was not the case for case study I. This is mainly the result of the longer and moderate slope of the high trade-off area of the Pareto front of case study II. This particular Pareto front shape gives rise to, on average, less dense PIT-regions than a Pareto front with a higher (or lower) slope. Because of this, the stopping criterion was delayed, allowing the solutions to converge fully to the Pareto front. The tDOM algorithm required 577 s of computational time, whereas NSGA-II required 1153 s.

5. CONCLUSION

In this contribution, a simultaneous saccharification and fermentation (SSF) process was optimised with regard to multiple objectives. The modelled SSF process consisted of a hydrolysis and fermentation step, both occurring simultaneously in the same vessel. During the hydrolysis step, cellulose is broken down into cellobiose and β-D-glucose by cellulase and β-glucosidase. The produced β-D-glucose is subsequently transformed into ethanol with the use of S. cerevisiae. A first case study focussed on increasing the cellulose conversion whilst decreasing the enzyme consumption. A second case study focussed on increasing the ethanol yield whilst decreasing the enzyme consumption. When multiple objectives are considered simultaneously, there is no longer one unique solution available for the problem at hand. Instead, the goal of the optimisation process is to generate an approximation of the (infinite) set of equally optimal non-dominated, or trade-off, solutions, called the Pareto front. To ensure that the Pareto front is not cluttered with insignificant solutions, the application of a novel trade-off-based optimisation algorithm is presented in this contribution. It features a trade-off-based solution selection process and a novel problem-related stopping criterion, resulting in a less dense and clearer Pareto front combined with a significant gain in the required computational time. Its effectiveness is proven by comparison to the well known NSGA-II algorithm.

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