



Increasing the volumetric productivity of fermentative ethanol production using a fed-batch vacuform process

Vasiliki Kachrimanidou¹ · Anestis Vlysidis² · Nikolaos Kopsahelis¹ · Ioannis K. Kookos³

Received: 7 December 2019 / Revised: 11 February 2020 / Accepted: 5 March 2020 / Published online: 18 March 2020
© Springer-Verlag GmbH Germany, part of Springer Nature 2020

Abstract

This work presents theoretical evidence that the vacuform technology can confer several advantages even when the fermentor is operated in fed-batch mode with small cycle times aiming to avoid the accumulation of potentially inhibitory side products. More specifically, a mathematical model for a fed-batch fermentor coupled with a vacuum flash tank for in situ ethanol recovery is developed and the simplest possible operational strategy is optimized within the context of maximizing the volumetric productivity of the process. Using numerical values obtained from the literature, it is demonstrated that significant increase in the volumetric productivity of ethanol (up to 33.5 kg EtOH m⁻³ h⁻¹) can be achieved. Evidently, the results obtained indicate the potential to employ the proposed methodology to operate existing industrial facilities with minor modifications and equipment additions.

Keywords Bioethanol · Vacuform process · Fed-batch process · Optimization

1 Introduction

It is nowadays widely accepted that the gradual replacement of non-renewable raw materials with renewable ones can contribute to the protection of the environment and to the development of a sustainable society. Ethanol production in the USA, the largest bioethanol producer, was about 50.5 Mt in 2018 with more than 43 Mt of co-products output (distillers grain and distillers oil) and a gross value of US\$46 billion [1]. Besides an alternative to fossil fuels, ethanol constitutes an important platform chemical to formulate a wide spectrum of chemical

products. Ethanol can be produced by fermentation of various carbon sources such as starchy crops and lignocellulosic materials with a maximum (theoretical) glucose to ethanol yield of 0.51 g g⁻¹. *Saccharomyces cerevisiae* and *Zymomonas mobilis* have been identified among the most promising microorganisms capable of producing ethanol from sugars [2, 3]. Although *Z. mobilis* shows better ethanol yield (up to 97% of theoretical) than that of *S. cerevisiae* (90–93% of theoretical) and higher productivity (three to five times) compared to *S. cerevisiae*, it is not the predominant microorganism used. This is attributed to its specific substrate spectrum and extracellular formation of fructose oligomers (e.g. levans) and sorbitol making it only suitable to produce ethanol from pure glucose [4]. It should be also stressed out that *Z. mobilis* catabolizes the sugar substrate through the Entner-Doudoroff glycolysis pathway. Hence, in fermentations carried out by *Z. mobilis*, biomass production is almost twofold lower, compared to the alcoholic fermentation performed by *S. cerevisiae*. Research on ethanol production is focussed on the development of new processes and new strains to deploy the utilization of C5 and C6 sugars from lignocellulosic biomass. For instance, engineered *E. coli* and *S. cerevisiae* strains have been developed for the production of ethanol from xylose with conversion yields of 0.48 g g⁻¹ and 0.46 g g⁻¹ [5], respectively.

Pretreatment of lignocellulosic resources is necessary in order to break down its recalcitrant structure, facilitate

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s13399-020-00673-6>) contains supplementary material, which is available to authorized users.

✉ Nikolaos Kopsahelis
kopsahelis@upatras.gr

✉ Ioannis K. Kookos
i.kookos@chemeng.upatras.gr

¹ Department of Food Science and Technology, Ionian University, Argostoli, 28100 Kefalonia, Greece

² Department of Food Science and Human Nutrition, Agricultural University of Athens, Iera Odos 75, 118 55 Athens, Greece

³ Department of Chemical Engineering, University of Patras, Rio, 26504 Patras, Greece

enzymatic hydrolysis and increase the yield of C5 and C6 sugars production [6, 7]. Pretreatment involves the application of physical processes (e.g. chipping, grinding and milling), physico-chemical processes (e.g. autohydrolysis, steam explosion) and chemical processes such as acid or alkaline hydrolysis [8, 9]. Application of pretreatment processes to render cellulose and hemicellulose susceptible to the action of hydrolytic enzymes associates with the structure of lignocellulosic material and varies with respect to the economic feasibility and the environmental footprint. Evidently, C5 and C6 sugar formations from lignocellulose exhibit several complexities as opposed to starch conversion. The non-cook concept for starch processing, although firstly reported in the 1940s, has been considered at large scale only during the last decade. The process comprises the use of raw starch degrading amylases, implemented after feedstock milling, without previous high-temperature cooking and liquefaction. As a consequence, capital and operational costs are significantly lower and overall yields are higher due to the absence or almost absence of cross reactions (e.g. Maillard reaction). This process concept is being considered as a major breakthrough in the starch-to-ethanol industry and is known as granular starch hydrolysis, raw starch hydrolysis, cold hydrolysis, native starch hydrolysis or sub-gelatinization temperature starch hydrolysis [10].

Apart from the aforementioned strategies to improve bioethanol production economics, a large number of ingenious engineering ideas have also been presented in the open literature. Most of them encompass the intensification of the fermentor operation by performing partial in situ removal of the produced ethanol from the fermentation broth. The aim is to enhance the volumetric productivity by mitigating the product inhibition which may otherwise become dominant in alcoholic fermentations. Some of these technologies are illustrated in Fig. 1, comprising a small part of the technologies reviewed by Cardona and Sanchez [11]. In the vacuform process [12, 13], shown in Fig. 1a, ethanol inhibition is eliminated by operating the continuous fermentor under vacuum so as to boil away the ethanol produced. The volumetric productivities achieved with the vacuform technology are an order of magnitude greater than that of a simple continuous fermentor whereas Cysewski and Wilke [13] report volumetric productivities greater than $80 \text{ kg EtOH m}^{-3} \text{ h}^{-1}$. However, the classical vacuform technology exhibits several drawbacks: continuous operation, operation of a potentially large fermentor under vacuum (50 mmHg) and the need to compress the large amounts of the produced CO_2 . In an effort to remove the need to operate the fermentor under vacuum, a flash tank operated under vacuum (Fig. 1b) or an external solvent extraction process (Fig. 1c) can be used [14–16]. The fermentor is again operated in continuous mode under atmospheric pressure and the need to operate, a potentially large fermentor, under vacuum is circumvented (note that CO_2 is also removed directly from the fermentor in a separate stream). The use of

membranes in the external loop has been also extensively studied [11, 17].

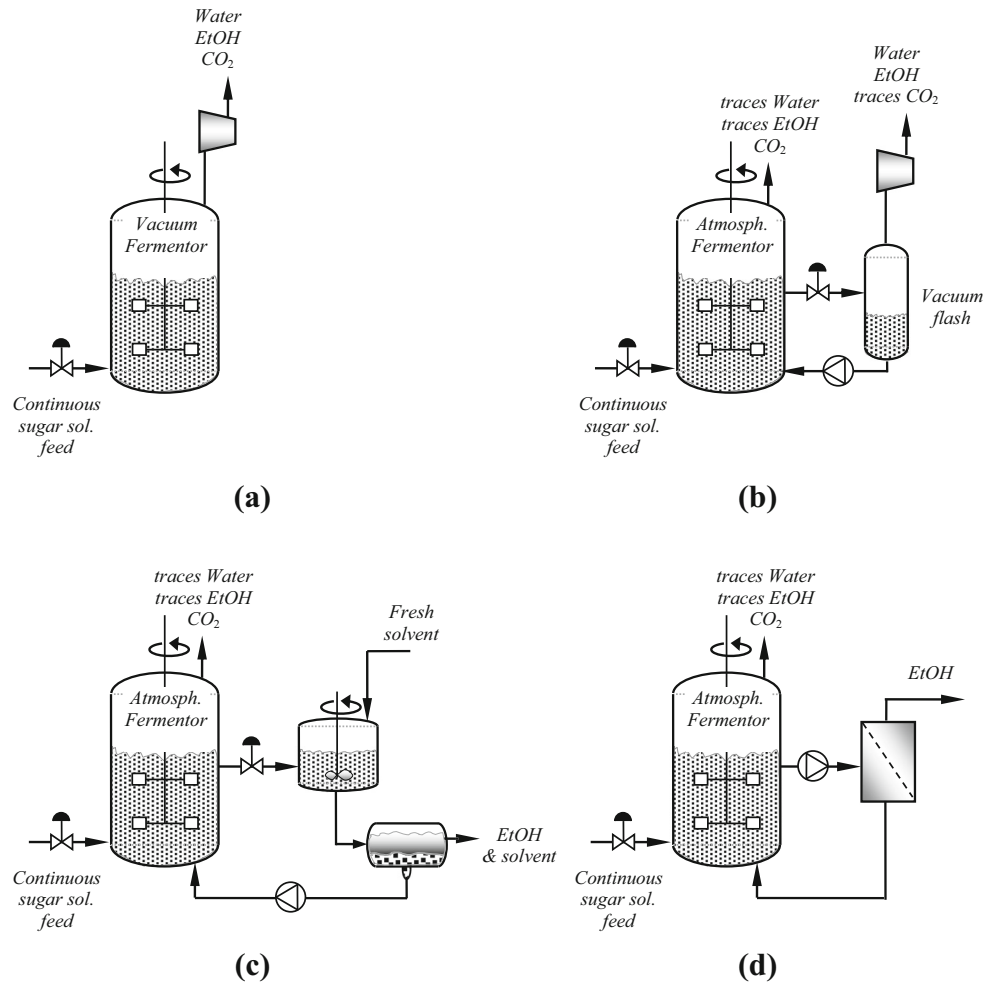
To summarize, despite the impressive volumetric productivities that can be achieved in fermentative ethanol production using the concept of in situ ethanol removal, the technology has not been adopted by the industry. In our opinion, this is correlated to the fact that all experimental and theoretical research has been concentrated on the continuous operation of the fermentor. Risk attributed to genetic instability, cell accumulation and lack of homogeneity along with problems associated with the maintenance of sterility entail only few of the reasons why the penetration of continuous bioprocesses has been very limited in industry. Additional operational problems associated with the use of membrane processes or the use of expensive and toxic solvents make things even worse. In this work, we demonstrate theoretical evidence that the vacuform technology can offer advantages even when the fermentor is operated in fed-batch mode with small cycle times to ultimately avoid the accumulation of potentially inhibitory side products. More specifically, we develop a mathematical model for a fed-batch fermentor coupled with a vacuum flash tank for in situ ethanol recovery. On top of that, we develop and optimize the simplest possible operational strategy targeting to maximize the volumetric productivity of the process. Remarkably, the proposed methodology of this work elicits the potential implementation to operate existing industrial facilities with minor modifications and equipment additions. Evidently, it can be speculated that the optimized operating regime will also apply in ethanol conversion processes that implement the utilization of C5 and C6 sugars deriving from the hydrolysis of lignocellulosic resources.

2 The fed-batch vacuform process

2.1 Fed-batch vacuform process—process description

The proposed fed-batch vacuform process is presented in Fig. 2. The bioreactor is operated at fed-batch mode where a feed stream with carbon source and nutrients is continuously fed to the bioreactor using the simplest possible feeding strategy, i.e. constant feed with constant carbon source concentration. A liquid stream is constantly removed from the fermentor and fed to the flash tank, which is operated at such a pressure (vacuum) so as the temperature in the flash distillation to be as close as possible to the temperature of the fermentor. This pressure is determined by the composition of the incoming liquid stream and the amount of vapour stream removed from the flash unit. The vapour stream is enriched in ethanol since, for compositions below the azeotropic point, ethanol is the volatile component. The liquid holdup into the flash unit exhibits an ethanol composition that can be significantly lower than the composition of ethanol in the fermentor. A liquid

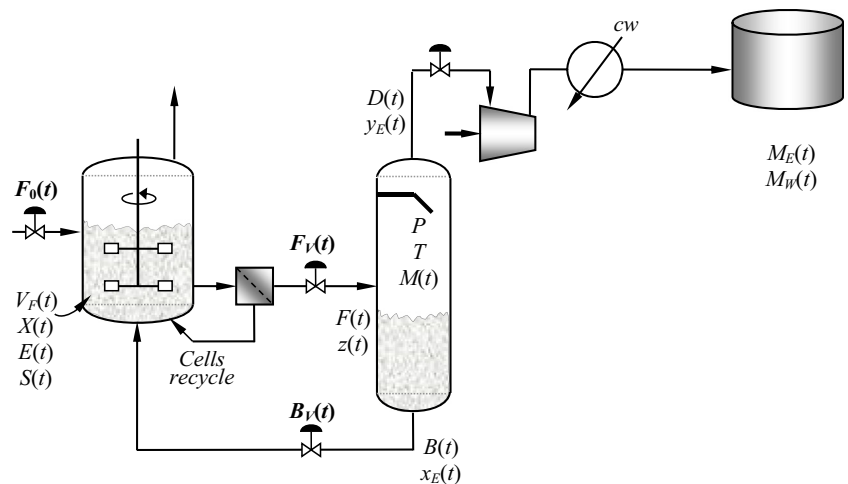
Fig. 1 Alternative technologies for in-situ removal of inhibitory products. **a** The vacuform process. **b** Modified vacuform process with external vacuum flash tank. **c** Product removal using external solvent extraction. **d** Product removal using a membrane process



stream is withdrawn from the flash unit and is then returned to the fermentor. The possibility of using a bleed liquid stream has been examined, but despite the increased complexity, no tangible advantage was detected. The liquid stream flowrate that returns to the fermentor is under ratio control with the

liquid stream that is fed to the flash unit while the vapour stream flowrate is used in order to achieve a constant holdup into the flash distillation unit. The vapour stream is compressed to atmospheric pressure and condensed using a heat exchanger before stored in a liquid storage tank.

Fig. 2 The proposed fed-batch vacuform process



2.2 Fed-batch vacuform process—mathematical modelling

All the variables employed in the development of the mathematical model are listed in Table 1. The mathematical model of the fed-batch vacuform process consists of the total material balance under the assumption of constant thermophysical properties

$$\frac{dV_F(t)}{dt} = F_0(t) + B_V(t) - F_V(t) \quad (1)$$

Table 1 List of symbols used in this study

Symbols	Definition
B	Molar flowrate of the outgoing liquid stream
B_V	Volumetric flowrate of the liquid stream coming out of the flash unit
D	Molar flowrate of the outgoing vapour stream
E	Ethanol concentration
E_B	Concentration of ethanol in the liquid stream from the flash unit
F	Molar flowrate of the feed stream
F_0	Volumetric flowrate of the fresh feed
F_V	Volumetric flowrate of the liquid stream coming out of the fermentor
K_E	Equilibrium ratio of ethanol
M	Molar holdup of the liquid in the flash unit
$M_E (M_W)$	Mass of ethanol (water)
$MW_E (MW_W)$	Molecular weight of ethanol (water)
P	Pressure
$P_i^s(T)$	Saturation pressure of component i
R	Ideal gas constant
S	Substrate concentration
S_0	Substrate concentration in the fresh feed
T	Temperature
t_f	Fermentation time
ν	Specific rate of ethanol production
V_F	Volume of the broth
V_j	Molar volume of component j
X	Concentration of biomass
x_E	Mole fraction of ethanol in the liquid
$Y_{E/S}$	Yield coefficient
z	Mole fraction of ethanol in the feed stream
α_{ij}	Constants from the literature
γ_i	Activity coefficient of component i
Λ_{ij}	Temperature dependence of the parameters
μ	Biomass specific growth rate
$\mu_m, \nu_m, K_S, E'_m, K'_S, K'_I, K_I$	Constants

where V_F is the volume of the broth, F_0 is the volumetric flowrate of the fresh feed, B_V is the volumetric flowrate of the liquid stream coming out of the flash unit and fed to the fermentor and F_V is the volumetric flowrate of the liquid stream coming out of the fermentor and fed to the flash unit. The material balance for the biomass is as follows

$$\frac{dV_F(t)X(t)}{dt} = \mu(S, E)X(t) V_F(t) \quad (2)$$

where X is the concentration of biomass and μ the biomass specific growth rate. The material balance of the product can be written as

$$\frac{dV_F(t)E(t)}{dt} = \nu(S, E)X(t)V_F(t) - F_V(t)E(t) + B_V(t)E_B(t) \quad (3)$$

where E is the ethanol concentration, ν is the specific rate of ethanol production and E_B is the concentration of ethanol in the liquid stream coming out from the flash unit and fed to the fermentor. Finally, the fermentor model is completed by adding the material balance of the substrate

$$\frac{dV_F(t)S(t)}{dt} = -\frac{\nu(S, E)X(t)V_F(t)}{Y_{E/S}} + F_0(t)S_0 \quad (4)$$

where S is the substrate concentration, S_0 is the substrate concentration in the fresh feed and $Y_{E/S}$ is the yield coefficient. With respect to the biomass specific growth rate and the ethanol specific production rate, they can be described by the following equations that involve product and substrate inhibition [18].

$$\mu(S, E) = \mu_m \cdot \left(1 - \frac{E(t)}{E_m}\right) \cdot \frac{S(t)}{K_S + S(t) + \frac{S(t)^2}{K_I}} \quad (5)$$

$$\nu(S, E) = \nu_m \cdot \left(1 - \frac{E(t)}{E'_m}\right) \cdot \frac{S(t)}{K'_S + S(t) + \frac{S(t)^2}{K'_I}} \quad (6)$$

where $\mu_m, \nu_m, E_m, K_S, K_I, E'_m, K'_S,$ and K'_I are constants.

The flash distillation unit is modelled by the total material balance

$$\frac{dM(t)}{dt} = F(t) - B(t) - D(t) \quad (7)$$

where M is the molar holdup of the liquid in the flash unit, F is the molar flowrate of the feed stream, B is the molar flowrate of the outgoing liquid stream and D is the molar flowrate of the outgoing vapour stream. The material balance of ethanol in the flash distillation unit can be written as

$$\frac{dM(t)x_E(t)}{dt} = Fz - (B + DK(x_E, T, P))x_E \tag{8}$$

where x_E is the mole fraction of ethanol in the liquid, z is the mole fraction of ethanol in the feed stream and K_E is the equilibrium ratio of ethanol calculated in the conditions of the flash distillation unit. The equilibrium ratios as well as the temperature in the flash are calculated using vapour-liquid equilibrium calculations

$$\sum_{i \in \{E, W\}} K_i(x_E, T, P) x_i - 1 = \sum_{i \in \{E, W\}} \gamma_i(x_i, T) \frac{P_i^s(T)}{P} x_i - 1 = 0 \tag{9}$$

where the subscript W denotes water, $P_i^s(T)$ is the saturation pressure of component i that is calculated using Antoine’s equation [19] and is a function of temperature T only, P is the pressure in the flash unit and γ_i is the activity coefficient of component i which is calculated using Wilson’s equation [19].

$$\gamma_i(x_i, T) = 1 - \ln \left(\sum_j x_j \Lambda_{ij} \right) - \sum_k \frac{x_k \Lambda_{ki}}{\sum_j x_j \Lambda_{ij}} \tag{10}$$

The temperature dependence of the parameters Λ_{ij} is given by

$$\Lambda_{ij} = \frac{V_j}{V_i} \exp \left(-\frac{\alpha_{ij}}{RT} \right), \quad i \neq j \tag{11}$$

where R is the ideal gas constant, V_j the molar volume of component j and α_{ij} constants that are available in the literature.

The model is complete if we add the material balances for the storage tank

$$\frac{dM_E(t)}{dt} = MW_E DK_E(x_E, T, P)x_E \tag{12}$$

$$\frac{dM_W(t)}{dt} = MW_W DK_W(x_E, T, P)(1 - x_E) \tag{13}$$

where M_E (M_W) is the mass of ethanol (water) in the storage tank and MW_E (MW_W) the molecular weight of ethanol (water).

2.3 Fed-batch vacuform process—operating policy

As the process is a dynamic process, an operating policy needs to be devised so as to achieve the desired objective, i.e. to maximize the volumetric productivity of ethanol. The process has four manipulated variables denoted by control valves in Fig. 2 which are the following

- The fresh feed flowrate F_0
- The flowrate of the liquid withdrawn from the fermentor F_V
- The flowrate of the liquid returned to the fermentor B_V
- The molar flowrate of the vapour stream withdrawn from the flash unit D

It is important to note that the molar flowrate of the vapour stream is used to control the liquid level in the flash distillation unit and is not available for optimization. In addition, the initial concentration of the carbon source in the fermentor ($S(0)$) is considered as an optimization variable. As it is stated in the introduction, our aim is to determine the simplest possible operating policy to increase the potential of industrial application. It is decided to use an operating policy that is characterized by constant (time invariant) manipulated inputs. In order to determine the optimal values of the three dynamic degrees of freedom as well as the initial concentration of the substrate in the fed-batch reactor, we propose solving the following optimization problem

$$\max_{S(0), F_0, F_V, B_V} \frac{V_F(t_f)E(t_f) + M_E(t_f)}{t_f \max_t [V_F(t)]} \tag{14}$$

s.t. Eqs. (1)–(13) and bound constraint on optimization variables, where t_f is the fermentation time. This is a highly non-linear and non-convex dynamic optimization problem that features a multitude of local solutions. To avoid local solutions and also convergence problems, we use a stochastic optimization methodology known as simulated annealing [20]. Simulated annealing has been proved an efficient stochastic optimization methodology that can be used to solve practical problems avoiding local solutions through an ingenious search algorithm. The final optimization problem was solved in MATLAB (www.mathworks.com).

3 Results

In order to demonstrate the potential of achieving increased values of ethanol volumetric productivity, using a fed-batch vacuform process, the numerical values for parameters appearing in the mathematical model are selected from the literature and are shown in Table 2 [13, 18]. Operation under

Table 2 Model parameters

Parameter	Value	Units
$V_F(0)$	100	m^3
$X(0)$	1	kg m^{-3}
S_0	300	kg m^{-3}
$Y_{E/S}$	0.47	kg kg^{-1}
μ_m	0.4	h^{-1}
E_m	87	kg m^{-3}
K_S	0.476	kg m^{-3}
K_I	203.5	kg m^{-3}
ν_m	1.4	h^{-1}
E'_m	114	kg m^{-3}
K'_S	0.666	kg m^{-3}
K'_I	303	kg m^{-3}
V_E	58.68	L m^{-3}
V_W	18.07	L m^{-3}
$\alpha_{EW/R}$	165.111	K
$\alpha_{EW/R}$	479.758	K
$M(0)$	1	kmol
t_f	20	h

lower temperature to alleviate ethanol inhibition can also be considered [21]. A fermentor with active volume of 100 m^3 is selected. In order to determine the relative advantages of the fed-batch vacuform process, when compared to simple batch/fed-batch operation, the optimization problem given by Eq. (14) is first solved by setting the volumetric flowrate to the flash unit equal to 0 (and thus effectively eliminating the flash distillation unit). The remaining optimization variables ($S(0)$, F_0) are then optimized, and the maximum volumetric productivity is $4.6975 \text{ kg EtOH m}^{-3} \text{ h}^{-1}$, achieved when $S(0) = 149 \text{ kg m}^{-3}$ and $F_0 = 0$ (batch operation). It should be noted that the initial biomass concentration considered is $X(0) = 1 \text{ kg m}^{-3}$ (the optimization with respect to $X(0)$ will be discussed shortly).

The optimization of the vacuform process is then performed and the maximum volumetric productivity is $11.059 \text{ kg EtOH m}^{-3} \text{ h}^{-1}$, achieved when $S(0) \approx 0 \text{ kg m}^{-3}$ and $F_0 = 7.872 \text{ m}^3 \text{ h}^{-1}$, $F_V = 33.733 \text{ m}^3 \text{ h}^{-1}$ and $B_V = 26.413 \text{ m}^3 \text{ h}^{-1}$. The time evolution of the substrate, biomass and product concentration in the fermentor as well as the fermentor volume are presented in Fig. 3. No substrate is charged initially into the fermentor and the substrate concentration response is similar to a semicircle with a maximum concentration close to the value that is optimal for the batch operation. The storage tank contains $177,636.5 \text{ kg}$ of EtOH and water mixture that is 9.72% w/w in EtOH at the end of the production cycle. The total ethanol produced is $22,128.45 \text{ kg EtOH}$ in 20 h of operation resulting in a volumetric productivity of $11.059 \text{ kg EtOH m}^{-3} \text{ h}^{-1}$. We observe that the

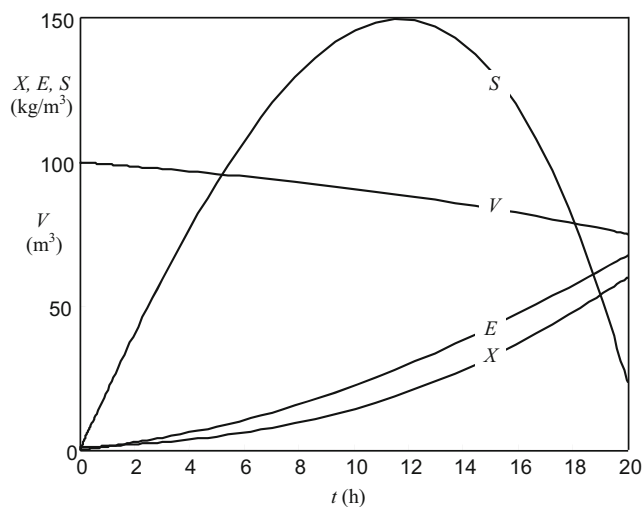


Fig. 3 Concentration of the substrate, biomass and product and broth volume in the optimized fed-batch vacuform achieving volumetric productivity of $11.059 \text{ kg EtOH m}^{-3} \text{ h}^{-1}$ ($X(0) = 1 \text{ kg m}^{-3}$)

volumetric productivity achieved by the fed-batch vacuform process is 2.35 times (135% increase) the volumetric productivity that can be realized by the batch process. This is evidently an impressive increase of the productivity of the process, and further analysis is clearly justified.

Further on, the next step entails the inclusion of the initial biomass concentration $X(0)$ in the set of optimization variables (or dynamic degrees of freedom). The optimization is subjected to the following bound constraint on $X(0)$

$$1 \leq X(0) \leq X_0^U \quad (15)$$

where X_0^U is an upper bound on the initial biomass concentration. The result of the optimization shows that, at the optimal solution, the initial biomass concentration is always equal to the upper bound. Figure 4 summarizes the results. As

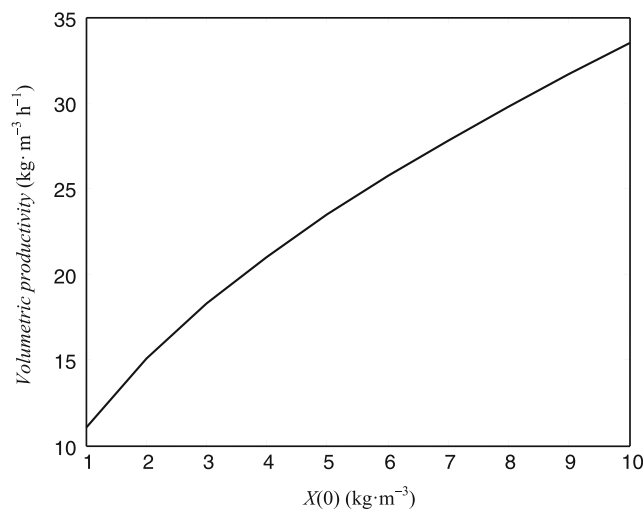


Fig. 4 Maximum volumetric productivity that can be achieved as a function of the initial biomass concentration ($X(0) = 1\text{--}10 \text{ kg m}^{-3}$)

it is seen from Fig. 4, the volumetric productivity is increased significantly, as the initial biomass concentration is increased, and becomes 7.133 times the productivity of the optimal batch process. In a similar manner, this is again a rather impressive result with respect to the simplicity of the process. The storage tank contains 483,588.2 kg of EtOH and water mixture that is 12.8% w/w in EtOH at the end of the production cycle. The total ethanol produced is 67,491.9 kg EtOH in 20 h of operation, resulting in a volumetric productivity of 33.76 kg EtOH m⁻³ h⁻¹. The time evolution of the substrate, biomass and product concentration in the fermentor, as well as the fermentor volume are shown in Fig. 5.

There are two points of concern. The first one is related to the fact that all optimized operating policies require that $S(0) \approx 0$ kg m⁻³, i.e. no substrate is loaded initially into the fermentor. This is due to the inhibitory effect of substrate and the fact that the model used does not account for the adaptation of the microorganism to the substrate. In an effort to perform a more realistic simulation, we add a lower bound constraint to the initial substrate concentration

$$S(0) \geq S_L(0) \tag{16}$$

where $S_L(0)$ is a lower bound on initial substrate concentration, assumed 5 kg m⁻³.

The second point of concern associates to the high concentration of biomass (177.12 kg m⁻³) at the end of fermentation in the fermentation broth. Cysewski and Wilke [13] have also reported very high biomass concentrations (approximately 125 kg m⁻³) in their experimental continuous vacuform process. Therefore, it is reasonable to assume that the biomass concentrations calculated for the fed-batch vacuform process can be achievable in practice without serious operational problems. However, we perform a final optimization where the optimization problem (Eq. (14)) is augmented by the bound

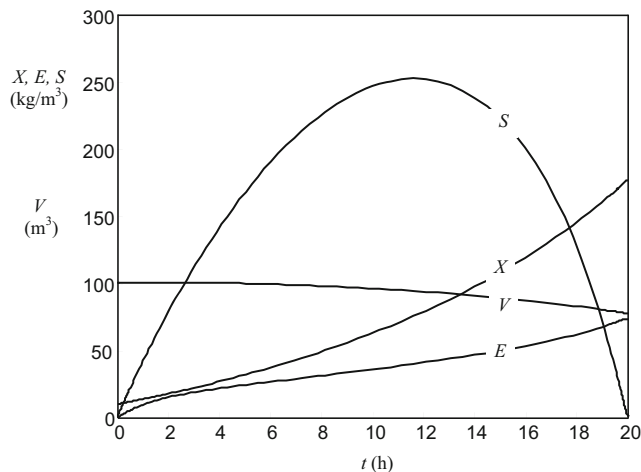


Fig. 5 Concentration of the substrate, biomass and product and broth volume in the optimized fed-batch vacuform achieving volumetric productivity of 33.76 kg EtOH m⁻³ h⁻¹ ($X(0) = 10$ kg m⁻³)

constraints (Eqs. (15) and (16)) and the following terminal inequality constraints (observe that from the biomass material balance, Eq. (2), it follows that the biomass concentration is, under assumption that are satisfied easily, a monotonically increasing function of time)

$$X(t_f) \leq 125 \text{ kg m}^{-3} \tag{17}$$

Simultaneous satisfaction of the constraints (Eqs. (15), (16) and (17)) causes the maximum volumetric productivity to be decreased to 30.2 kg EtOH m⁻³ h⁻¹ which is obtained using an initial biomass concentration of 9.97 kg m⁻³ (the final biomass concentration is exactly 125 kg m⁻³) and an initial substrate concentration of 5 kg m⁻³ (equal to the lower bound). The volumetric productivity achieved under these practical constraints is 6.43 times the maximum volumetric productivity that a batch or fed-batch system can accomplish.

A final issue that needs to be addressed is the robustness of the volumetric productivity achieved, against inaccuracies in implementing the optimal operating policy in practice. To this end, it is assumed that the three operating variables (F_0 , F_V and $X(0)$) follow normal probability distribution functions (pdf), when implemented in practice, with mean values ($F_V = 94.07$ m³ h⁻¹, $F_0 = 24.19$ m³ h⁻¹ and $X_0 = 9.66$ kg m⁻³) equal to the optimal values and standard deviations that are 1% of the mean values (detailed distributions are supplied in the supplementary information). Then, Monte Carlo (MC) simulations are performed and the volumetric productivities achieved are recorded and analysed. The results of the MC analysis are summarized in Fig. 6, where the empirical cumulative distribution function (cdf) of the volumetric productivity is shown. From this figure, it can be observed that the process can achieve volumetric productivities greater than 28 kg EtOH m⁻³ h⁻¹ with approximate probability 95%.

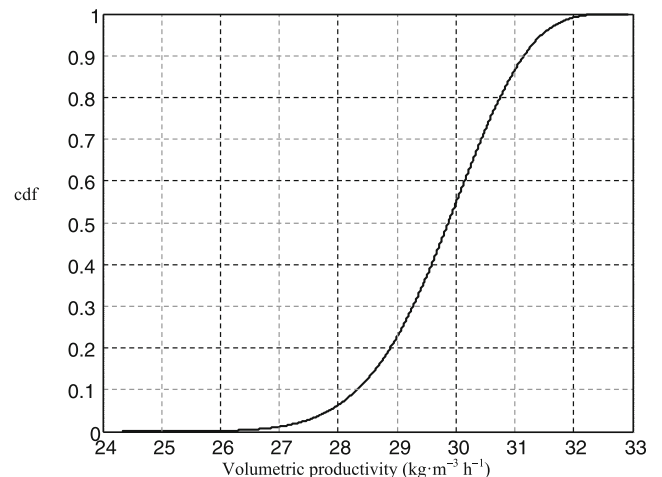


Fig. 6 Empirical cdf of the volumetric productivity

4 Conclusions

Continuous vacuform processes have been discussed in great detail in the open literature, and their potential for increasing ethanol productivity has been demonstrated. However, continuous operation exhibits several drawbacks that render the process unfavourable, from the industrial implementation point of view. To this end, a novel fed-batch vacuform process is described and the simplest possible operating policy is developed and subsequently optimized in this work. Significant improvement can be also achieved by deploying the proposed fed-batch vacuform technology, thus conferring a higher potential to be accepted by the industry. It is of paramount importance to also note that existing batch ethanolic fermentation units can be modified to incorporate the proposed in situ ethanol removal process and thus to significantly enhance their volumetric productivity. The proposed scheme is expected to substantially reduce the cost of manufacture, thereby entailing a proportional reduction in the unitary production cost of bioethanol. On top of that, it is expected that the proposed operating strategy could be also applied in ethanolic bioconversions implementing renewable resources as onset material and further enhance the feasibility of the process.

References

- Renewable Fuels Association, <http://www.ethanolrfa.org/> (accessed 30 November, 2019)
- Jang YS, Kim B, Shin JH, Choi YJ, Choi S, Song CW, Lee J, Park HG, Lee SY (2012) Bio-based production of C2-C6 platform chemicals. *Biotechnol Bioeng* 109:2437–2459
- Xia J, Yang Y, Liu CG, Yang S, Bai FW (2019) Engineering *Zymomonas mobilis* for robust cellulosic ethanol production. *Trends Biotechnol* 37(9):960–972
- Sprenger GA (1996) Carbohydrate metabolism in *Zymomonas mobilis*: a catabolic highway with some scenic routes. *FEMS Microbiol Lett* 145:301–307
- Koutinas AA, Vlysidis A, Pleissner D, Kopsahelis N, Garcia L, Kookos IK, Papanikolaou S, Kwan TH, Sze Ki Lin C (2014) Valorization of industrial waste and by-product streams via fermentation for the production of chemicals and biopolymers. *Chem Soc Rev* 43:2587–2627
- Hassan SS, Williams GA, Jaiswal AK (2018) Emerging technologies for the pretreatment of lignocellulosic biomass. *Bioresour Technol* 262:310–318
- Guo GN, Cai B, Li R, Pan X, Wei M, Zhang C (2019) Enhancement of saccharification and ethanol conversion from tobacco stalks by chemical pretreatment. *Biomass Conversion Bioref*:1–8. <https://doi.org/10.1007/s13399-019-00478-2>
- Chiaromonti D, Prussi M, Ferrero S, Oriani L, Ottonello P, Torre P, Cherchi F (2012) Review of pretreatment processes for lignocellulosic ethanol production, and development of an innovative method. *Biomass Bioenergy* 46:25–35
- Rajendran K, Drielak E, Sudarshan Varma V, Muthusamy S, Kumar G (2018) Updates on the pretreatment of lignocellulosic feedstocks for bioenergy production—a review. *Biomass Conversion Bioref* 8(2):471–483. <https://doi.org/10.1007/s13399-017-0269-3>
- Cinelli BA, Castilho LR, Freire DMG, Castro AM (2015) A brief review on the emerging technology of ethanol production by cold hydrolysis of raw starch. *Fuel* 150:721–729
- Cardona CA, Sánchez ÓJ (2007) Fuel ethanol production: process design trends and integration opportunities. *Bioresour Technol* 98:2415–2457
- Ramalingham A, Finn RK (1977) The vacuform process: a new approach to fermentation alcohol. *Biotechnol Bioeng* 19:583–589
- Cysewski GR, Wilke CR (1977) Rapid ethanol fermentations using vacuum and cell recycle. *Biotechnol Bioeng* 19:1125–1143
- Maiorella BL, Blanch HW, Wilke CR (1983) By-product inhibition effects on ethanolic fermentation by *Saccharomyces cerevisiae*. *Biotechnol Bioeng* 25:103–121
- Maiorella BL, Blanch HW, Wilke CR (1983) Economic evaluation of alternative ethanol fermentation processes. *Biotechnol Bioeng* 26:1003–1025
- Roffler SR, Blanch HW, Wilke CR (1984) In situ recovery of fermentation products. *Trends Biotechnol* 2:129–136
- Fan S, Xiao Z, Zhang Y, Tang X, Chen C, Weijia L, Qing DQ, Yao P (2014) Enhanced ethanol fermentation in a pervaporation membrane bioreactor with the convenient permeate vapor recovery. *Bioresour Technol* 155:229–234
- Ghose TK, Tyagi RD (1979) Rapid ethanol fermentation of cellulose Hydrolysate. *Biotechnol Bioeng* 21:1401–1420
- Smith JM, Van Ness HC, Abbott MM (2001) Chemical engineering thermodynamics, 6th edn. McGraw Hill, New York
- Kookos IK (2004) Optimization of batch and fed-batch bioreactors using simulated annealing. *Biotechnol Prog* 20:1285–1288
- Palacios-Bereche R, Ensinas A, Modesto M, Nebra SA (2014) New alternatives for the fermentation process in the ethanol production from sugarcane: extractive and low temperature fermentation. *Energy* 70:595–604

Publisher's note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.