Dynamic modeling of the acrylic acid synthesis from renewable resources
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Dynamic modeling of the acrylic acid synthesis from renewable resources

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Abstract

The acrylic acid, know as propenoic acid, is one of the most important industrial chemical product. Usually it is obtained by oxidation of propylene that means using petrochemical feedstocks. A possible alternative way is proposed in this work through sugar cane fermentation by *Saccharomyces cerevisiae*, which is completely environmentally free aggressive process. The sugar cane sector figures among the most traditional old extractives, manipulation and processing industrials of biomass in Brazil as well as in others countries. In recent years new economical potentials alternative products from sugar cane fermentation arise as consequence of new research and discoveries making it possible to explore biological routes to produce molecules with high economic value. The full detailed model is a set of differential partial equations composed by the reactor equations together with the description of the microorganism metabolism aiming to follow the evolution of intracellular variable that are difficult to measure. In biotechnological processes, a great number of factors can influence the income productivity and conversion. Normally, it is not evident which of these factors are most important. In this work it is used the multivariate analysis techniques, as experimental design together with a detailed deterministic model. With such procedure is possible, beyond the determination of the important factors of the process, to identify the structures of control for differentiated strategies of operation. The mapping of the dynamics of the developed process is made using techniques of factorial design together with the methodology of Plackett-Burman. It is shown that it is possible to increase the process performance by choosing optimized conditions for the bioreactor operation. After identified the main kinetic and operational parameters of the process, was implemented an optimization strategy for search the optimal operational parameters through the Successive Quadratic Programming – SQP optimization algorithm. An improvement of 8% in acrylic acid end yield was observed for the optimized parameters.

Keywords: structured model, acrylic acid, biotechnological process, experimental design, successive quadratic programming

1. Introduction

The acrylic acid, known as propenoic acid, is one of the most important industrial chemical products. There are several chemical pathways to produce acrylic acid, but the most common is via the partial oxidation of propylene that means using petrochemical feedstocks. The process for production of acrylic acid occurs on two steps, where first the propylene is oxidized to acrolein and then acrolein is oxidized to acrylic acid. The reaction stoichiometric is shown below:

$$C_3H_6 + O_2 \longrightarrow C_3H_4O + H_2O \quad (1)$$

$$C_3H_4O + \frac{1}{2}O_2 \longrightarrow C_3H_4O_2 \quad (2)$$

From of the industrial point of view, the acrylic acid production by fermentative process is presented as an innovative process of great importance, due to the possibility of low cost for its production and due to be a renewable raw material. This is an important point to be considered, since acrylic acid is worldwide used and its production by fermentative via is environmental friend process.
Bearing this is mind, this work presents an alternative structured model, adapted from a structured growth model developed by Lei *et al*. (2001) and a structured model for ethanol production developed by Stremel (2001), and modified objectiving to simulate the intrinsic reactions taking place in the fermentation process to obtain acrylic acid.
The deterministic model includes the description of the microbiane metabolism aiming to follow the evolution of intracellular variable that are difficult to measure. With such model, it was investigated several operating strategies and evaluated the effect of process variables in order to achieve high performance operation.
An analysis of kinetic, design and operational parameters, used in a dynamic structured model for the acrylic acid production process was realized. Through this procedure, was possible to identify that the parameters with the most significant impact on the model to represent well the process of acrylic acid production. Finally, an optimization strategy was implemented where the aim was to maximize the end yield of acrylic acid.

2. Mathematical Modeling

A deterministic mathematical model for simulating the biotechnological synthesis of acrylic acid was developed in order to explore an alternative process. The proposed process makes possible to obtain acrylic acid continuously from the sugar cane fermentation.
A continuous bioreactor type plug flow reactor – PFR with immobilized cell of *Saccharomyces cerevisiae* was used in this work. The bioreactor behaviour is based on mass balances for the key chemical species of the fermentative process.
In *Saccharomyces cerevisiae*, the major flux of pyruvate metabolism is to ethanol, through *pyruvate decarboxylase* - PDC and *alcohol dehydrogenase* - ADH. By providing an alternative route for regenerating nicotinamide adenine dinucleotide -

NAD^+ through *lactate dehydrogenase* - LDH, which catalyses the reduction of pyruvate to lactate, it is theoretically possible to replace ethanolic fermentation (Skory, 2003).

The model of structured kinetic was based in Michaelis-Menten kinetic and the following assumptions were considered: glucose is metabolised for production of pyruvate (glycolysis process); pyruvate is converted to lactate; biomass is produced from glucose and lactate and converted into active cellular material; *lactate dehydrogenase* enzyme is produced from active cell material; acrylic acid is formed from dehydratation of the lactate. To simulate the dynamic model, orthogonal collocation was used to discretize the differential partial equations and it was used the method of lines.

Figure 1 shows the scheme of the metabolic pathway for obtaining the acrylic acid. Several parallel and consecutive reactions take place and are necessary to find out operating conditions, which allow the desired product to be obtained.

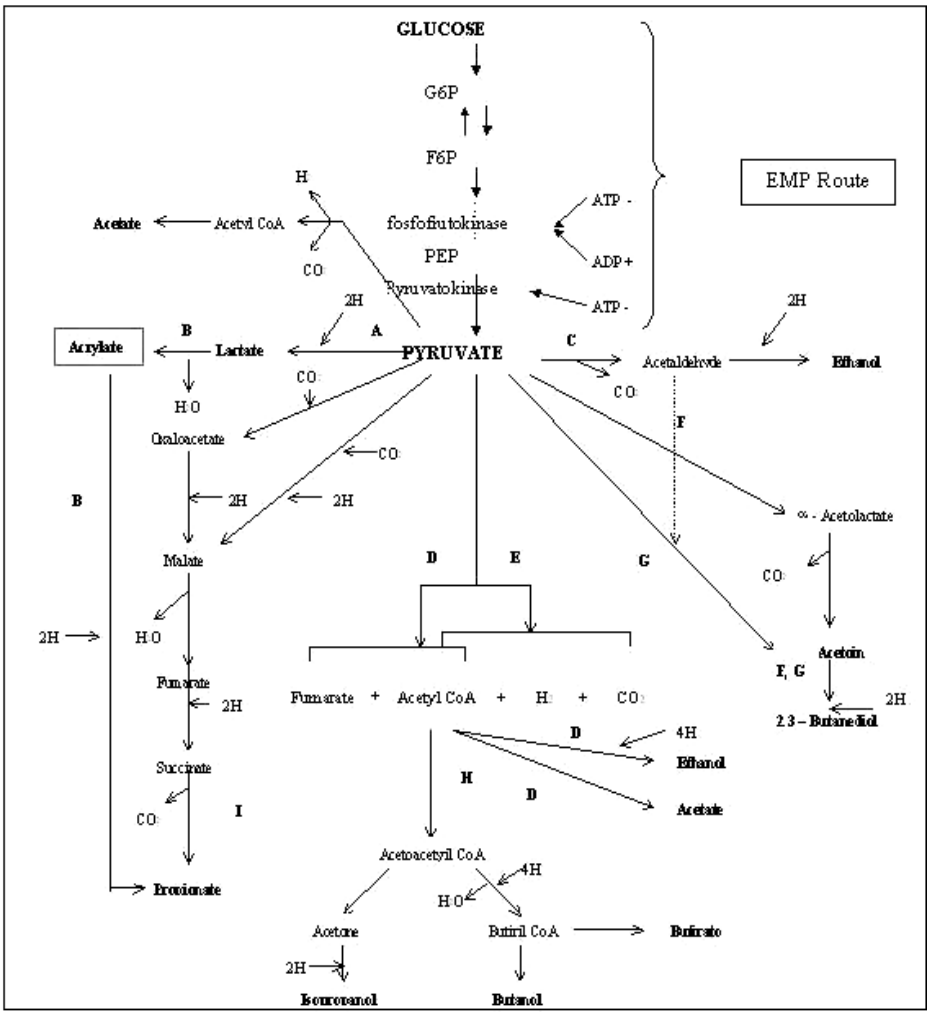

Figure 1: Glycolytic route. Pyruvate formed by catabolism of glucose is further metabolized by pathways which are characteristic of particular organism (Dawes and Large, 1982)

The Figure 2 shows a representative metabolic route involved in the process of acrylic acid production and also the reaction rates (see Table 1).

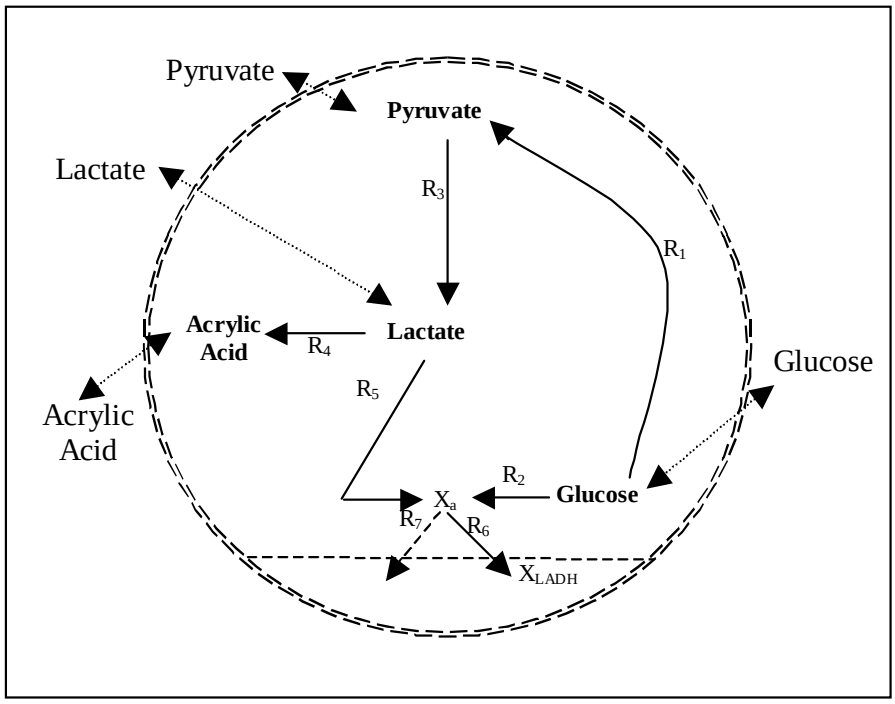

Figure 2: Representative route

The reaction rate (R_1) describes the glucose uptake and glycolytic pathway and it is represented by two Michaelis-Menten equations.
R_2 represent the cell growth (biomass formation) from glucose with inhibition by lactate. The biomass formed is converted into active cellular material.
The reaction rates (R_3) and (R_4), describes the lactate and acrylic acid formation, respectively.
Equation (R_5) correspond the biomass formation from lactate, where a glucose inhibition term is included in the equation. The Equation (R_6) describes the formation of lactate dehydrogenase from active component in the cellular material (X_a). An acrylic acid inhibition term was added in this equation. Equation (R_7) shows the degradation rate of the active compartment and depends of the glucose and acrylic acid present in the medium.
These reaction rates as well as the kinetic parameters values were obtained of Lei *et al.* (2001) and modified to describe the acrylic acid production process.
The reaction rates are shown in Table 1. Table 2 and 3 show the mass balance equations for fluid and solid phases, respectively. The study is theoretical (predictive) and all data were simulated.

$R_1 = k_1 \frac{S_{glucose}}{S_{glucose} + K_1} X_a + k_{1a} \frac{S_{glucose}}{S_{glucose} + K_{1a}} X_a$	(3)
$R_2 = k_2 \frac{S_{glucose}}{S_{glucose} + K_2} \frac{1}{1 + \left(\frac{S_{lactate}}{K_{2i}} \right)} X_a$	(4)
$R_3 = k_3 \frac{S_{pyruvate}}{S_{pyruvate} + K_3} X_a$	(5)
$R_4 = k_4 \frac{S_{lactate}}{S_{lactate} + K_4} X_a$	(6)
$R_5 = k_5 \frac{S_{lactate}}{S_{lactate} + K_5} \left(\frac{1}{1 + K_{5i} S_{glucose}} \right) X_a$	(7)
$R_6 = k_6 \left(\frac{S_{glucose.}}{S_{glucose} + K_6} + \frac{S_{lactate}}{S_{lactate} + K_{6a}} \right) \left(\frac{1}{K_{6i} S_{acrylicac} + 1} \right) X_a$	(8)
$R_7 = \left(k_7 \frac{S_{glucose}}{S_{glucose} + K_7} \right) X_a + \left(k_{7acrylicac.} \frac{S_{acrylicac}}{S_{acrylicac.} + K_{7acrylicac.}} \right) X_a$	(9)

Table 1: Reaction rates

$\frac{\partial S_{glucose}}{dt} = D_{az} \left(\frac{\partial^2 S_{glucose}}{\partial z^2} \right) - u \left(\frac{\partial S_{glucose}}{\partial z} \right) - \frac{1-\varepsilon}{\varepsilon} \eta \left[(R_1 + R_2) e^{-K_A S_{acrylicac}} X \right]$	(10)
$\frac{\partial S_{pyruvate}}{dt} = D_{az} \left(\frac{\partial^2 S_{pyruvate}}{\partial z^2} \right) - u \left(\frac{\partial S_{pyruvate}}{\partial z} \right) + \frac{1-\varepsilon}{\varepsilon} \eta \left[(0.978 R_1 - R_3) e^{-K_A S_{acrylicac}} X \right]$	(11)
$\frac{\partial S_{lactate}}{dt} = D_{az} \left(\frac{\partial^2 S_{lactate}}{\partial z^2} \right) - u \left(\frac{\partial S_{lactate}}{\partial z} \right) + \frac{1-\varepsilon}{\varepsilon} \eta \left[(1.023 R_3 - R_4 - R_5) e^{-K_A S_{acrylicac}} X \right]$	(12)
$\frac{\partial S_{acrylicac}}{dt} = D_{az} \left(\frac{\partial^2 S_{acrylicac}}{\partial z^2} \right) - u \left(\frac{\partial S_{acrylicac}}{\partial z} \right) + \frac{1-\varepsilon}{\varepsilon} \eta \left[(0.8 R_4 - R_7) e^{-K A S_{acrylicac}} X \right]$	(13)

Table 2: Mass balance for fluid phase

$\frac{\partial S_{glu\cos e}}{\partial t} = \frac{D_{Ag}}{R^2}\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial S_{glu\cos e}}{\partial r}\right) - \left(R_1 + R_2\right)e^{-K_A S_{acrylicac}} X$	(14)
$\frac{\partial S_{pyruvate}}{\partial t} = \frac{D_{Ap}}{R^2}\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial S_{pyruvate}}{\partial r}\right) + \left(0.978R_1 - R_3\right)e^{-K_A S_{acrylicac}} X$	(15)
$\frac{\partial S_{lactate}}{\partial t} = \frac{D_{Al}}{R^2}\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial S_{lactate}}{\partial r}\right) + \left(1.023R_3 - R_4 - R_5\right)e^{-K_A S_{acrylicac}} X$	(16)
$\frac{\partial S_{acrylicac}}{\partial t} = \frac{D_{Aaa}}{R^2}\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial S_{acrylicac}}{\partial r}\right) + \left(0.8R_4 - R_7\right)e^{-K_A S_{acrylicac}} X$	(17)
$\frac{\partial X}{\partial t} = \left(0.732R_2 - 0.821R_5\right)X\left(1 - \frac{X}{X_{sat}}\right)e^{-K_A{}'' S_{acrylicac}} - k_d X$	(18)
$\frac{\partial X_a}{\partial t} = \left(0.732R_2 - 0.821R_5 - R_6 - R_7\right) - \left(0.732R_2 + 0.821R_5\right)X_a$	(19)
$\frac{\partial X_{LADH}}{\partial t} = R_6 - \left(0.732R_2 + 0.821R_5\right)X_{LADH}$	(20)

Table 3: Mass balance for solid phase

3. Experimental Design

Design of experiments is a powerful technique used for discovering a set of process factors that are most important to the process and then determine at what levels these factors must be kept to optimize the process performance (Antony and Kaye, 1999).
In the development of new process and product, the number of potential factor or variables is often excessively large. Experimental design are useful to reduce the number of variable to a manageable size so that further experiments can be performed using these key variables for a better understanding of the process/product (Antony and Kaye, 1999).
A large number of kinetics parameters are evolved in the definition of the best operating conditions to achieve the acrylic acid, taking into account all others possible products. Bearing this in mind, 24 parameters are chosen as the necessary to be investigated in order to produce acrylic acid.
For studying such 24 kinetic parameters, it was selected a Plackett-Burman design with 32 runs and 31 degrees of freedom.
Plackett-Burman is a tool for this initial screening, since it makes it possible to determine the influence of various factors with only a small of number of trials, instead of using more extensive factorial design, which would furnish more complete information, but which involves unfeasible complexity (Plackett and Burman, 1946).
The different parameters were prepared in two levels, (-1) for low level and (+1) for high level. Seven dummy variables are used to estimate the standard error during

analysis of data. The kinetic parameters analyzed in this study and their levels (low and high) are shown in Table 4. These values were obtained through simulations realized in the process model of acrylic acid production.
STATISTICA software was used to generate the matrix of the parameters values and a simulation program based on a detailed model described in section 2, written in FORTRAN language, was used to generate the desired process response. The simulations were conducted according to the 32-runs Plackett-Burman design for the twenty-four kinetic variables. Each simulation (test) generates a result of acrylic acid concentration in the steady state (desired response).

Parameters	Values	
	Low level (-1)	High level (+1)
k_1	1.92	2.88
k_{1a}	0.4672	0.7008
k_2	2.64	3.96
k_3	4.16	6.24
k_4	3.40	5.10
k_5	0.96	1.44
k_6	0.024	0.036
k_7	0.032	0.048
k_{7a}	0.0032	0.0048
K_1	0.0008	0.0012
K_{1a}	0.00928	0.01392
K_2	2.32	3.48
K_3	2.56	3.84
K_4	1.68	2.52
K_5	1.88	2.82
K_6	1.56	2.34
K_{6a}	10.40	15.60
K_7	0.016	0.024
K_{7a}	0.00072	0.00108
K_{2i}	0.072	0.108
K_{5i}	1.584	2.376
K_{6i}	2.0	3.0
K_A	0.072	0.108
$K_{A"}$	0.152	0.228

Table 4: Kinetic parameters used in the experimental design and their levels

In order to analyze the operational and design parameters used in the acrylic acid production process, a fractional factorial design of two-level (2^{k-p}) with two level of fractionation was used. In this experimental design were investigated six variables (S_{in}, F_{in}, X_{in}, D_p, D_r, and L) in 16 runs. The parameters values are shown in Table 5.

Parameters	Values	
	Low level (-)	High level (+)
S_{in}	80	120
F_{in}	0.032	0.048
X_{in}	16	24
D_p	0.024	0.036
D_r	0.4	0.6
L	1.6	2.4

Table 5: Operational and design parameters used in the experimental design and their levels

4. Successive Quadratic Programming

Successive Quadratic Programming is used in this work to optimize a given objective function over a given search space. The formulation of objective functions $f(\vec{x})$ is one of the crucial steps in the application of optimization to a practical problem. A general non-linear optimization problem (Biegler and Grossmann, 2004) subjected to the equality and inequality constraints $g_i(\vec{x})$ and $h_j(\vec{x})$, respectively, may be defined as:

Optimize $f(\vec{x})$

Subject to $g_i(\vec{x}) \leq 0 \qquad i = 1,\ldots,p$

$h_j(\vec{x}) = 0 \qquad j = p+1,\ldots,m$ (21)

$l_k \leq x_k \leq u_k,\ k = 1,\ldots,n$

Where $\vec{x}$ is a vector of n decision variables ($x_1,\ldots,x_n$). The l_k and u_k are specified lower and upper bounds on the variables with $l_k \leq u_k$.

It is important to properly define constraints on the possible parameter values. First, constraints limit the search space and thus speed up the optimization. Second, physically impossible values for the parameters are avoided, which improves the reliability of the approach. Additional constraints depend on the type of model that is used.

The optimization problem is to maximize the acrylic acid yield. Thus, the objective function can be formulated as follows:

Maximize *yield* (22)

The equation that describes the yield is:

$$Y_{A/s} = \frac{A}{S_{in} - S} \tag{23}$$

The optimization was conducted with the deterministic steady state model of the process. The optimization operational parameters are: feed substrate concentration (S_{in}), feed biomass concentration (X_{in}) and feed rate (F_{in}).

5. Results and Discussion

In this work, a structured deterministic model for producing acrylic acid is proposed. Structured models describing culture kinetics are powerful tools in the control of bioreactors, as they are able to provide a mathematical description of the cellular fermentation mechanism of the process, i.e. to predict the concentrations of intermediate products, desired product, substrate and cell concentrations.

The acrylic acid synthesis from fermentative process is a recent subject, with very few works published in the literature without conclusive kinetic data of the process. Thus, this study makes use of theoretical information including the kinetic and parameters values. These values can also be changed by the users together with the operating as well as design conditions and the physiological properties of the microorganism, so that the process can be extensively investigated.

Figure 3 shows the concentration profiles of glucose, acrylic acid (Fig. 3.a), pyruvate and lactate (Fig. 3.b) and biomass (Fig. 3.c) as well the amount of active cell for biomass produced (Fig. 3.d) obtained in dynamic behaviour of the continuous bioreactor used in the process simulation of acrylic acid production.

Figure 4 shows the concentration profiles of acrylic acid, biomass and glucose obtained when the steady state is reached

The Pareto chart (Figure 5 and Figure 6) was used for identifying which estimated effects are the most important in the rote to obtain acrylic acid, as well as to identify possible interaction effects showed later on.

The Figure 5 depicts that of the twenty-four parameters analysed, ten parameters, K_A (inhibition constant by product), $K_{A'}$ (inhibition constant by product related with cell), $k_{1,}$ k_{1a}, k_2, $k_{4,}$ (specifics reaction rates), K_3, K_4, K_5 (affinity constants) and K_{5i} (inhibition constant) were statistically significant for acrylic acid concentration at 99% of confidence level (the dot line is the reference).

As can be seen through the analyses of Figure 6, it is possible to observe that the parameters, F_{in} (feed rate), X_{in} (feed biomass concentration), D_r (reactor diameter), and L (reactor length) are statistically significant at 99% confidence level. Two first variables are possible to be used as operating variables, but the last two (reactor diameter and length) are design parameters that have to be chosen in a early design stage. If this investigation is not carried out it is possible to have a process with lower operational performance since changes in the operational may not enough to drive the process to high operational performance. At this point is worthwhile mentioning that the economical success of the this alternative acrylic acid production process is depending upon to achieve high concentrations since the downstream operations are complex and expensive and the conventional process, even environmentally aggressive, are well established nowadays.

With the operational parameters (S_{in}, X_{in} and F_{in}) optimization an improvement of 8% in acrylic acid yield was observed.

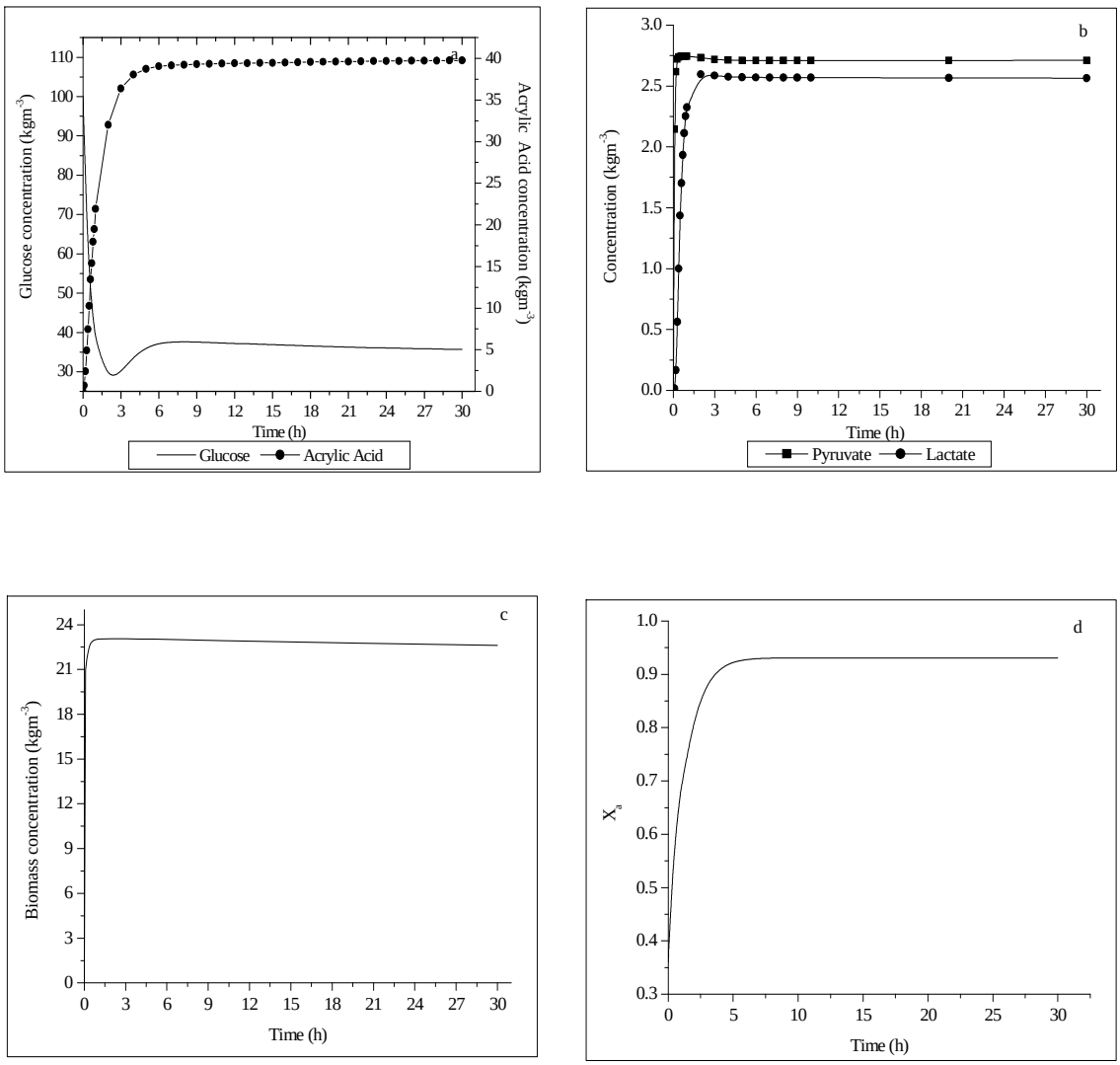

Figure 3: Concentration profiles (a – glucose and acrylic acid; b – pyruvate and lactate; c – biomass) and d - active cell material (X_a)

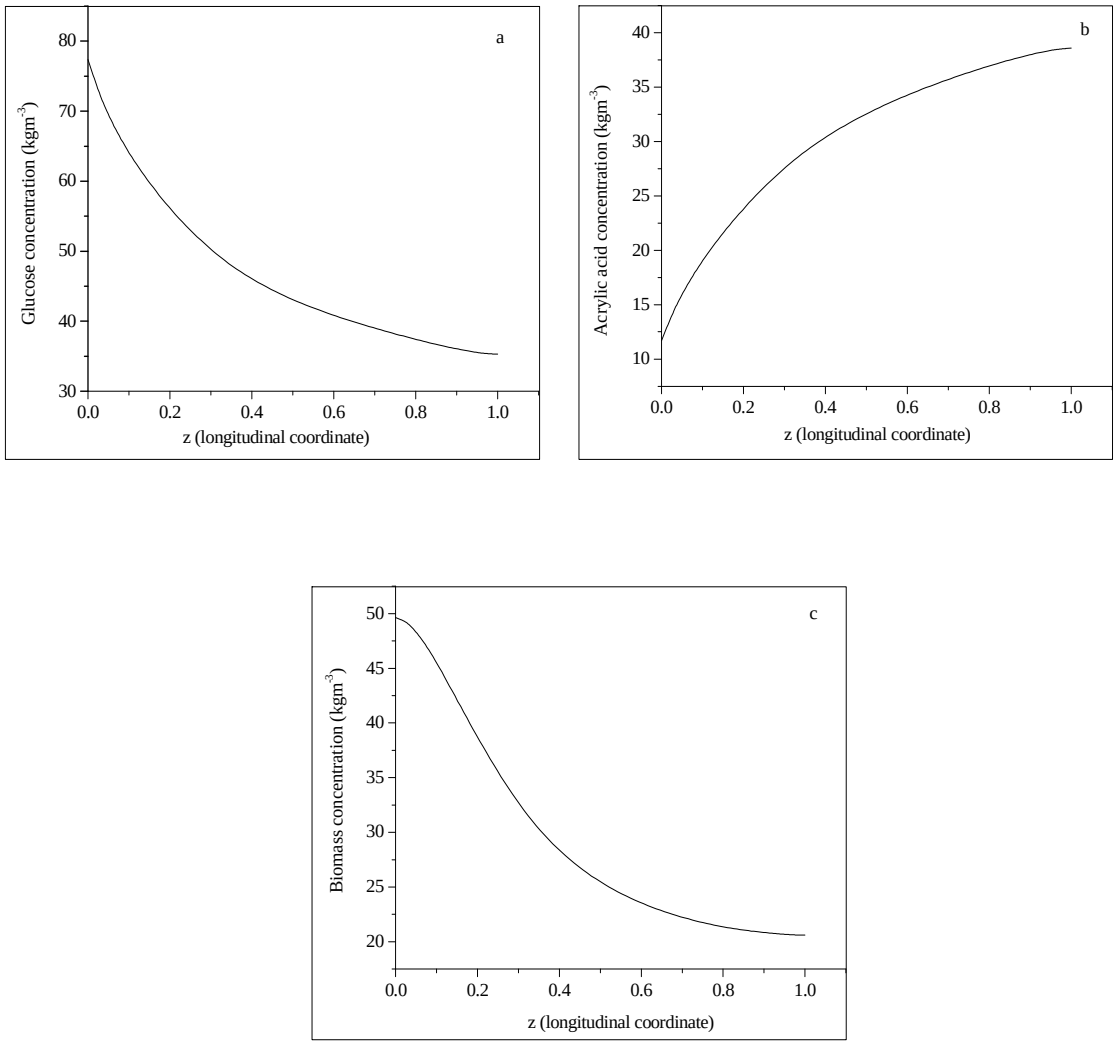

Figure 4: Steady-state model simulations (a – glucose; b – acrylic acid; c – biomass)

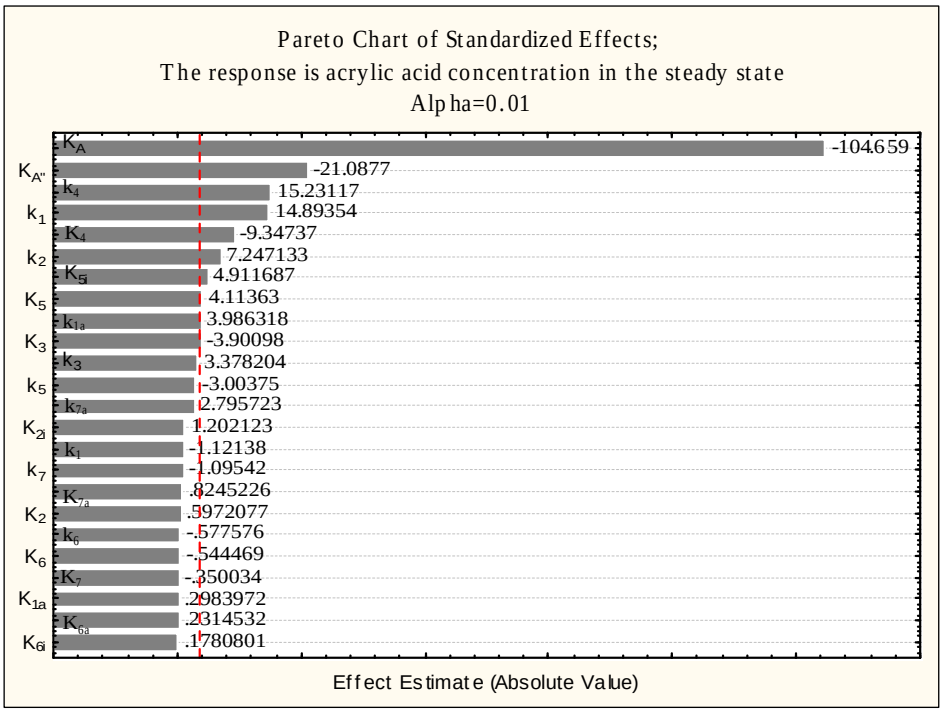

Figure 5: Pareto chart of effects of the kinetics parameters on the acrylic acid concentration from 32-run Plackett-Burman design

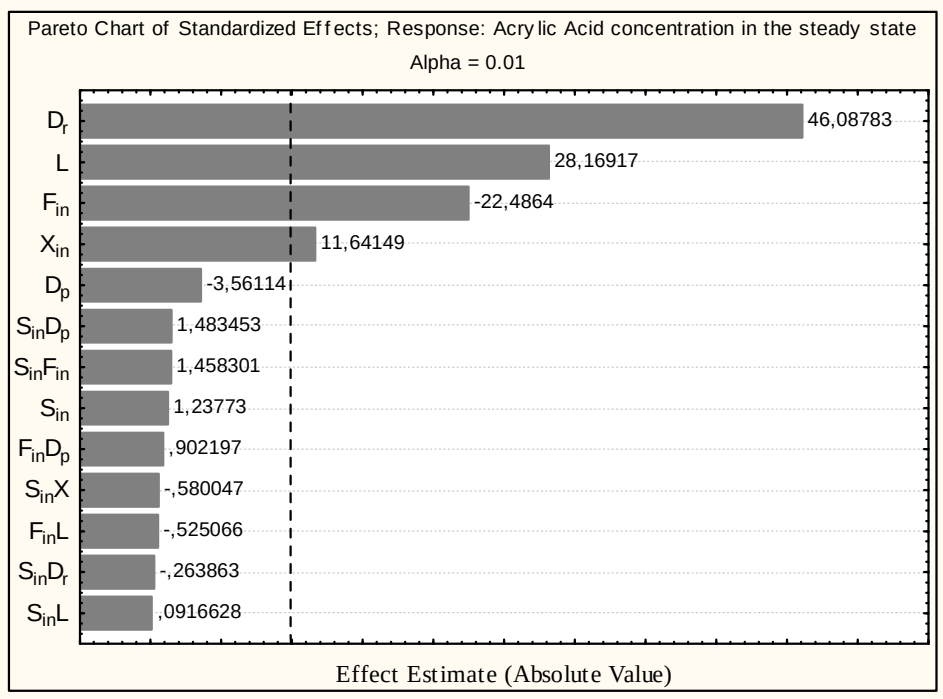

Figure 6: Pareto chart of effects of the operational parameters on the acrylic acid concentration from fractional factorial design (2^{6-2})

6. Conclusion

The acrylic acid synthesis from fermentative process is a recent subject with very few works published in the literature without conclusive kinetic data of the process. Therefore, it is valuable to identify the effect of the kinetic parameters values in order to trace guidelines to process design and operation as well as to gain some insights on how genetic medications should be made in the microorganism in order to met specific objectives, in this case to enhance the acrylic acid conversion. Besides that, extensive simulation can be made allowing an understanding of the process features, which is useful to take decisions at an early design stage.

In this work was analyzed the kinetic, design and operational parameters used in the acrylic acid production from biotechnological process, bearing in mind that high operational performance are required to become this alternative process competitive with the well established conventional ones. The appeal environmental less aggressive and renewable feedstock based process is nowadays a target to be met however economical considerations have to be made. This is an issue that can be suitably dealt with through simulation tools as has been extensively made in others industry (as car makers using computational fluid dynamics to find out the best vehicle design).

In this work is proposed and used a procedure based on the experimental design that allows to design and operate the alternative process to obtain acrylic acid. This was made in two stages. First, using the methodology of Plackett-Burman design, was possible evaluate of the kinetic parameters and identify the parameters that have significant impact in the acrylic acid production process.

Later on, through fractional factorial design was identified the operational and design parameters with a significant impact in the process. Also it was possible to identify the optimal values for kinetic, design and operational parameters. The optimal values such parameters, identified in these experimental designs, are able to drive the process to maximize the acrylic acid yield.

Nomenclature

A	acrylic acid concentration (kgm^{-3})
D_{Ai}	effective diffusivity coefficient (m^2h^{-1})
D_{az}	axial dispersion coefficient (m^2h^{-1})
D_p	particle diameter (m)
D_r	reactor diameter (m)
F_{in}	feed rate (m^3s^{-1})
k	factors number
K_A, $K_{A''}$	inhibition constant related with the product (m^3kg^{-1})
k_d	cell dead constant (h^{-1})
k_i	rate constant for reaction (h^{-1})
K_i	affinity constant (kgm^{-3})
K_{ji}	inhibition constant (m^3kg^{-1})
L	reactor length (m)
p	level of fractionation

R_i	reaction rate (h^{-1})
S	substrate concentration (kgm^{-3})
S_i	extracellular concentration (kgm^{-3})
S_{in}	feed substrate concentration (kgm^{-3})
u	superficial velocity (ms^{-1})
X_a	active cell material ($kgkg^{-1}$)
X_{in}	feed biomass concentration (kgm^{-3})
X_{LADH}	lactate dehydrogenase enzyme ($kgkg^{-1}$)
X_{sat}	cell saturated concentration (kgm^{-3})
$Y_{A/s}$	yield coefficient ($kgkg^{-1}$)

Greek Letters

η	effectiveness factor
ε	porosity

Acknowledgements

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