0273-2289/00/84–86/0577/$14.25

Simulated Dynamics and Control of an Extractive Alcoholic Fermentation

ALINE C. COSTA,*,[1] EDUARDO C. DECHECHI,[1] FLÁVIO L. H. SILVA,[2] FRANCISCO MAUGERI,[3] AND RUBENS MACIEL[1]

[1]DPQ/FEQ/UNICAMP, Campinas, SP, Brasil-Cx., Postal 6066, 13081-970, E-mail: accosta@feq.unicamp.br; [2]DEQ/CCT/UFPB, Campina Grande, PB, Brasil Cx. Postal 10057, 59109-970; and [3]DEA/FEA/UNICAMP, Campinas, SP, Brasil Cx. Postal 6121, 13081-970

Abstract

In this study, we investigated the dynamics of a computer simulation of a continuous alcoholic fermentation process combined with a flash column under vacuum. The alcohol was partially extracted in order to maintain its concentration at about 40 kg/m^3 in the fermentor. The mathematical model of the fermentation was developed for industrial conditions and considers the effect of the temperature on the kinetic parameters. The performance of the dynamic matrix control algorithm, single input single output and multiple input multiple output, for the control of the extractive process was studied. The concepts of factorial design were used in a simulation study to determine the best control structures for the process.

Index Entries: Dynamic matrix control; extractive alcoholic fermentation.

Introduction

Despite many advantages of using ethanol produced from biomass as a fuel (it is a high-energy, clean-burning, and totally renewable liquid fuel), the costs of its production are higher than those of petroleum fuels. Thus, there is an increased interest in the optimization of all steps of the ethanol fermentation process.

The operation of the alcoholic fermentation process in a continuous mode is desirable, because this mode of operation reduces production costs. However, the industrial implementation of a continuous alcoholic fermentation process requires study of the kinetic behavior of the process and its use in the development of an efficient control strategy. The influence of the temperature in the kinetic parameters must be considered, because there is great difficulty in maintaining a constant temperature during industrial

*Author to whom all correspondence and reprint requests should be addressed.

alcoholic fermentation. This is an exothermic process and small deviations in temperature (2–4 K) can dislocate the process from the optimal operational conditions.

Because the conventional process is inhibited by ethanol, the selective extraction of this product during fermentation is essential to enhance process performance. Several schemes combining fermentation with a separation process have been developed, such as fermentation under vacuum *(1,2)*, pervaporation *(3)*, solvent extraction *(4)*, ultrafiltration *(5)*, fermentation combined with a flash vessel operating under atmospheric pressure *(6)*, fermentation combined with a flash vessel operating under vacuum *(7)*, and CO_2 gas stripping *(8)*.

In the present study, we investigated the dynamics of a continuous alcoholic fermentation process combined with a flash column under vacuum. The alcohol was partially extracted in order to maintain its concentration at about 40 kg/m^3 in the fermentor. The mathematical model of the fermentation was developed for industrial conditions and considers the effect of the temperature on the kinetic parameters *(9)*.

Another important aspect to be considered in the optimization of alcoholic fermentation is the development of an efficient control strategy, because it minimizes the costs by maintaining the process in its optimal conditions. We studied the performance of the dynamic matrix control (DMC) algorithm, single input single output (SISO) and multiple input multiple output (MIMO), for the control of the extractive process. The concepts of factorial design were used in a simulation study to determine the best control structures for the process.

Materials and Methods

Extractive Alcoholic Fermentation

Figure 1 presents a general scheme of the extractive alcoholic fermentation. The process consists of four interlinked units *(9)*:

1. Fermentor (ethanol production unit)
2. Centrifuge (cell separation unit)
3. Cell treatment unit
4. Flash vessel under vacuum (ethanol-water separation unit)

This scheme attempts to simulate industrial conditions *(10)*, with the difference that only one fermentor is used instead of a cascade system. The proposed scheme presents a better performance than the conventional process *(9)*.

At the beginning of the fermentation, substrate is fed into the fermentor, which contains an initial concentration of yeast cells. In the fermentor, substrate is consumed and ethanol is produced. The exit stream of the fermentor, containing substrate, biomass, and ethanol, is sent to the centrifuge, where it is separated into two phases: a heavy phase, containing the majority of the cells, and a light phase, almost without cells. The heavy

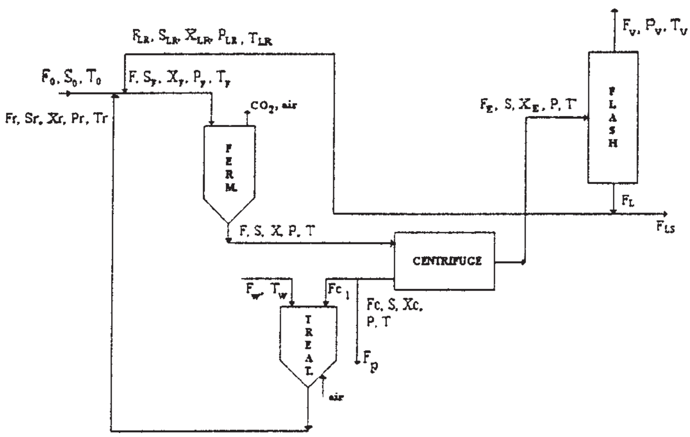


Fig. 1. Extractive alcoholic fermentation.

phase is sent to the cell treatment unit, after a purge is made to remove a small part of the cells. In this unit, the cell suspension is diluted with water and sulfuric acid is added until a pH between 2.0 and 2.5 is reached. The treated cell suspension is then returned to the fermentor.

Before steady state is reached, the operation of the extractive process is similar to that of the conventional process; that is, the light phase that leaves the centrifuge is sent to be distilled, for the separation of the water-ethanol mixture. When the steady state of the conventional process is attained, the vacuum separation system is activated. The light phase leaving the centrifuge is sent to the flash vessel, where part of the water-ethanol separation occurs. The flash vessel is operated at a temperature between 301 and 303 K. This temperature range is chosen in order to eliminate the necessity of a heat exchanger, which reduces drastically the fixed and maintenance costs of the process. The associated pressure range is between 4 and 5.33 kPa *(9)*. The process was shown to be able to maintain suitable conditions for the growth of *Saccharomyces cerevisiae*, by keeping a constant temperature, which is possible to control without heat exchangers *(9)*. The vaporized stream leaving the flash vessel is sent to a rectification column with a part of the liquid stream, and the other part of the liquid returns to the fermentor. This return is made to maintain the ethanol concentration in the fermentor at a value at which it can act as an antiseptic. According to practical knowledge in industrial units, this alcohol concentration is about 40 kg/m^3, which has low inhibitory effect for alcoholic yeast but is highly inhibitory for most contaminating microorganisms *(9)*.

To determine the feed rate and feed concentration of the fermentor, mass balances on the global process are necessary. Some approximations are made *(10)*:

1. The concentrations of substrate and product leaving the centrifuge in the light and heavy phases are equal to the concentrations leaving the fermentor.

2. The concentration of biomass in the cell recycle stream is fixed. To maintain this fixed concentration, the flow rate of the water that dilutes the ferment (F_W) is adjusted. The cell recycle stream flow rate (F_r) is maintained at the value fixed by the cell recycle rate (R) by varying the flow rate of the purge (F_p). The purge permits cell renovation and the withdrawal of secondary products accumulated into the fermentor.

Mathematical Model of the Fermentor and the Flash Vessel

The balance equations in the fermentor are as follows.

$$\frac{dX}{dt} = r_x - D(X - X_F) \tag{1}$$

$$\frac{dS}{dt} = D(S_F - S) - r_S \tag{2}$$

$$\frac{dP}{dt} = r_p - D(P - P_F) \tag{3}$$

$$\frac{dT}{dt} = D(T_F - T) + \frac{\Delta H r_S}{\rho C_p} \tag{4}$$

in which X, S, and P are the biomass, substrate, and product concentrations, respectively; T is the fermentor temperature; r_x, r_s, and r_p are the kinetic rates of growth, substrate consumption, and product formation, respectively, given by Eqs. 5–7; X_F, S_F, and P_F are the biomass, substrate, and product feed concentrations, respectively; T_F is the feed temperature; ΔH is the reaction heat; ρ is the medium density; C_p is the heat capacity; and D is the dilution rate.

The fermentor volume is assumed constant. In practice, it could be controlled by a conventional control level. This procedure appears to work well in industrial conditions for conventional cascade fermentors, as reported by Andrietta *(10)*.

The kinetic rates were obtained for *S. cerevisiae* and are given by Silva et al. *(9)*:

$$r_X = \mu_{\max}[S/(K_S + S)]\,[1 - (P/P_{\max})]^n X \tag{5}$$

$$r_S = (r_X / Y_{X/S}) \tag{6}$$

$$r_p = r_X(Y_{P/S} / Y_{X/S}) \tag{7}$$

Table 1 gives the kinetic parameters used.

The yield coefficients ($Y_{X/S}$ and $Y_{P/S}$) are not expressed as a function of the temperature but were obtained from industrial data *(11)* and are valid in the operational range considered.

Table 1
Kinetic Parameters for Eqs. 5–7

Parameter	Expressions or value	Reference
μ_{max}	$Z \exp[-E/(R_g T)]$	*11*
P_{max}	$638.1 \exp(-0.05741\ T)$	*12*
n	3	*11*
$Y_{X/S}$	0.033	*11*
$Y_{P/S}$	0.445	*11*
K_s	1.6	*11*
E	$1.54 \cdot 10^4$	*11*
Z	$4.5 \cdot 10^{10}$	*11*

The values of the constants in the energy balance equation (Eq. 4) are given by Silva et al. *(9)*:

$$\Delta H = 2.167 \cdot 10^5 \text{ J/kg};\ \rho = 1000 \text{ kg/m}^3;\ C_p = 4.183 \cdot 10^3 \text{ J/(kg} \cdot \text{K)}.$$

The mass balances over the flash tank are given by

$$F_E = F_V + F_L \tag{8}$$

$$F_E x_{Ei} = F_V y_i + F_L x_i \tag{9}$$

The vapor-liquid equilibrium of the ethanol-water mixture was calculated by Eq. 10, the value of p_i^{sat} was calculated by Antoine's equation (the assumption was made that the light phase was a binary mixture of ethanol-water), and the value of γ_i was calculated using the (nonrandom two-liquid model) *(9)*.

$$K_i = (y_i/x_i) = \gamma_i(p_i^{sat}/p) \tag{10}$$

A program written in Fortran was developed to solve the mathematical model equations. Equations 1–4 were integrated using an algorithm based on the fourth-order Runge-Kutta method.

Dynamic Behavior of the Extractive Alcoholic Fermentation Process

To choose a control structure that enables an efficient control of the alcoholic fermentation process, its open-loop dynamic behavior must be studied. The output variables of this process are as follows:

1. Biomass concentration in the fermentor (X)
2. Substrate concentration in the fermentor (S)
3. Product concentration in the fermentor (P)
4. Temperature in the fermentor (T)

It is important that these variables be controlled.

The input variables considered for manipulation are as follows:

1. Cell recycle rate (R)
2. Fermentor feed rate (F_0)
3. Flash recycle rate (r)

Table 2
Low and High Settings for Input Variables

	S_0 (kg/m^3)	R	F_0 (m^3/h)	r	T_0 (K)
–1	162	0.315	90	0.405	27
1	198	0.355	110	0.495	33

And these are the variables considered as possible load disturbances:

1. Feed substrate concentration (S_0)
2. Feed temperature (T_0)

The objective in a dynamic behavior study is to determine how the output variables of the process change with time influenced by changes in the inputs (manipulated variables and possible load disturbances). This can be done by changing the values of the various input variables (one by one) and observing the change of the output variables with time. Another approach is the use of the concepts of factorial design. In this case, it is also possible to have information about the effect of the interactions between the studied input variables in the outputs. A two-level factorial design can be used in a dynamic behavior study, because only a preliminary investigation is necessary to determine whether some factors (inputs) affect the outputs.

In a two-level factorial design, a high and a low level are defined (coded values of +1 and –1, respectively) in relation to a standard level (level 0 or central point) to each input variable (factor). Then, experiments are performed for each possible combination. Thus, to study the effects of n input variables, the number of experiments to be performed is 2^n.

In the present study, computer simulations were performed instead of experiments. The mathematical model was used to describe the process behavior. Table 2 gives the low and high settings (levels) for each input variable. They were calculated as variations of ±10% around the steady state, except for the cell recycle rate (R), whose higher value was restricted by operational requirements. The steady-state values are as follows: S_0 = 180 kg/m^3; R = 0.35; F_0 = 100 m^3/h; r = 0.45; and T_0 = 303 K.

Because the dynamic behavior of the process is being studied, the output variables must be calculated as a function of time. Thus, for each simulation, all the output variables were calculated from 0 to 10 h. This final time was chosen because after 10 h a new steady state had been reached in all simulations. The methodology for the calculation of the main effects as well as the interaction effects in a complete factorial design can be found in Box et al. *(13)*. The main effect can be interpreted as the difference (for the output variable) between the low and the high settings for the respective input variable. A program in Fortran was developed to calculate the main and interaction effects.

Figure 2 presents the main effects of the input variables on the biomass concentration as a function of time. The interaction effects between the input variables on this output variable are negligible.

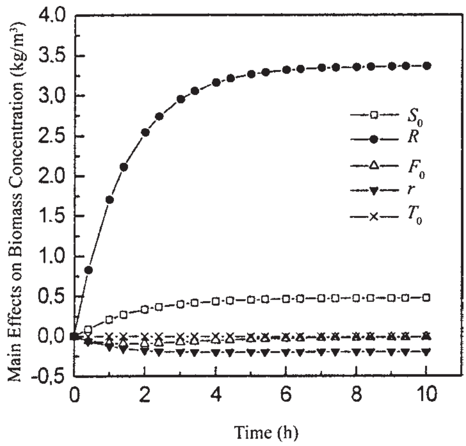


Fig. 2. Main effects of the input variables on biomass concentration.

Figure 3A presents the main effects of the input variables on the substrate concentration. In this case, the effects of interaction between some of the input variables have a significant effect on the output variable, as seen in Fig. 3B. This means that the main effect of the input variable (factor) on the output variable depends also on the values of the other factors. In this case, the main effects in Fig. 3A were used, but it should be clear that they are approximated mean values.

Figure 4 presents the main effects of the input variables on product concentration, and Fig. 5 presents the main effects of the input variables on temperature. The effects of interaction between the inputs on these output variables are negligible.

By using the data in Figs. 2–5, we constructed a table of the effects of the input variables on the output variables (*see* Table 3). In Table 3, the black area means that the input influences the output, the white area means that the influence is negligible, and the gray area means that the input has a weak influence in the output. Table 3 can be used to determine the best structures for an efficient control of the process. For example, it is easy to see that the only output variable affected by F_0 is the substrate concentration. Thus, a loop that manipulates F_0 and controls S can be considered decoupled from the other loops. If a disturbance deviates the substrate concentration from its set point, controlling this output through the manipulation of the feed rate F_0 does not affect the other output variables, which is a desirable characteristic. From Table 3 the following conclusions can be made:

1. The biomass concentration can be controlled by the manipulation of R, and disturbances in S_0 affect this output.
2. The substrate concentration can be controlled by the manipulation of R, F_0, or r, and disturbances in S_0 affect this output significantly.
3. The product concentration can be controlled by the manipulation of R or r, and disturbances in S_0 affect this output.

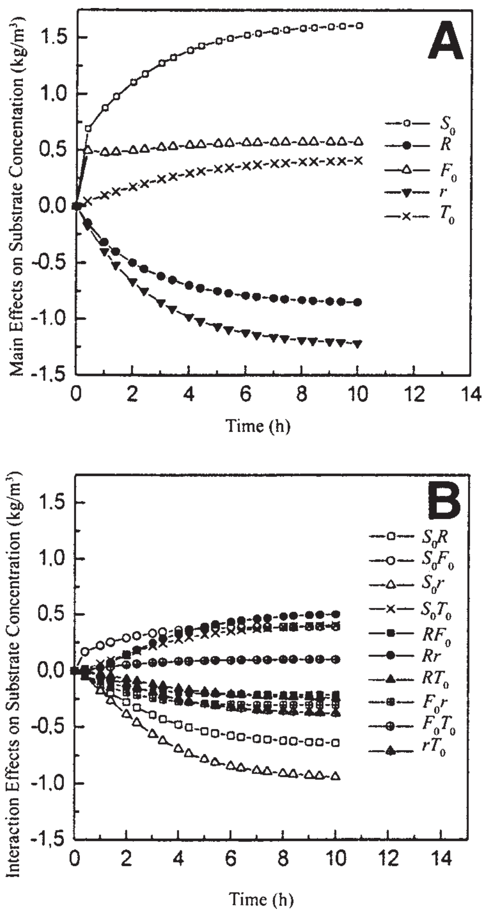


Fig. 3. **(A)** Main effects of the input variables on substrate concentration; **(B)** interaction effects between the input variables on substrate concentration.

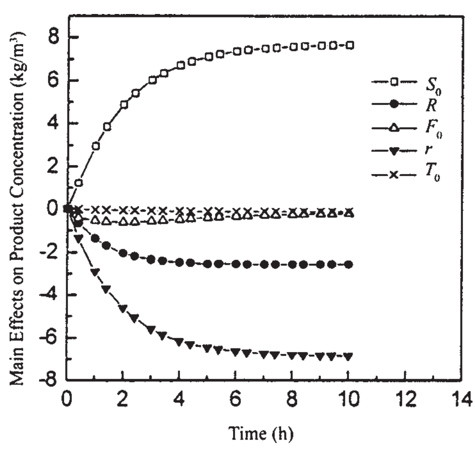


Fig. 4. Main effects of the input variables on product concentration.

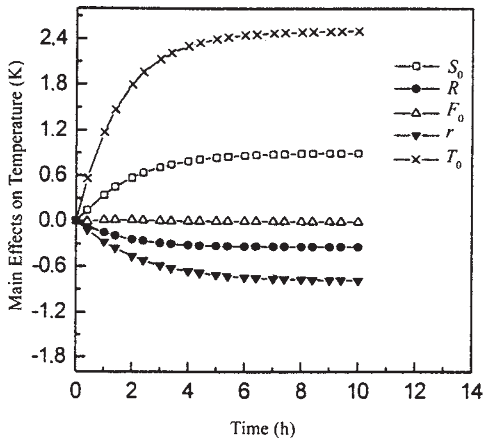


Fig. 5. Main effects of the input variables on temperature.

Table 3
Effects of Input Variables on Output Variables

	S_0 (kg m^{-3})	R	F_0 (m^{-3}h^{-1})	r	T_0 (K)
X (kg m^{-3})					
S (kg m^{-3})					
P (kg m^{-3})					
T (K)					

4. The control of temperature with the manipulations considered in this study is difficult, since only r has a weak influence in this output. However, this is not a problem, because the proposed scheme maintains the temperature constant without the necessity of a control system *(9)*. Disturbances in T_0 affect this output.

Dynamic Matrix Control

The basic concepts of the DMC algorithm were originally presented by Cutler and Ramaker *(14)* and can be found in Luyben *(15)* and Dechechi *(16)*. This control algorithm has great potential for industrial application. The basic idea is to use a time-domain step-response model of the process to calculate the future changes in the manipulated variables that will minimize some performance index. The DMC is discussed here for the SISO case. This procedure can be extended for the MIMO case with little conceptual effort.

The output of an SISO system can be computed from its step-response model (b_i) as follows:

$$\hat{y}_{ol,i} = y_0^{\text{meas}} + \sum_{k=0}^{-NP+1} (b_{i+1-k} - b_{1-k})\,(\Delta m_k)^{\text{old}} \qquad (11)$$

in which y_i is the value of the output y at sampling time i (in the future); m_k is the value of the manipulated variable at sampling time k (in the past); and y_0^{meas} is the measured value of y at the actual sampling time.

The DMC algorithm minimizes the square of the deviation between the predicted output in closed loop and the set-point values at NC future sampling periods by solving the constrained least squares minimization problem:

$$J = \sum_{i=1}^{NP} (y^{\text{set point}} - y_{cl,i})^2 + f^2 \sum_{k=1}^{NC} [(\Delta m_k)^{\text{new}}]^2 \tag{12}$$

in which J is the performance index to be minimized; Δm is the vector of the NC future changes in the manipulated variable to be calculated; f is the suppression factor or tuning parameter that penalizes the objective function for changes in the inputs Δm; NP is the prediction horizon; and NC is the control horizon.

The minimization of Eq. 12 using the least squares method results in Eq. 13:

$$(\underline{\Delta \boldsymbol{m}}) = [\underline{\boldsymbol{A}}^T \underline{\boldsymbol{A}} + f^2 \underline{\boldsymbol{I}}]^{-1} \, \underline{\boldsymbol{A}}^T \underline{\boldsymbol{y}} \tag{13}$$

in which

$$\underline{y} = \underline{y}^{\text{set point}} - \underline{y}_{\underline{ol}} \tag{14}$$

The matrix A in Eq. 13 is the dynamic matrix and is composed by the step-response coefficients.

The DMC controller has three parameters that can be adjusted to a good performance of the controller: NP, NC, and f. In this study, the DMC algorithm was implemented in a Fortran program.

Results

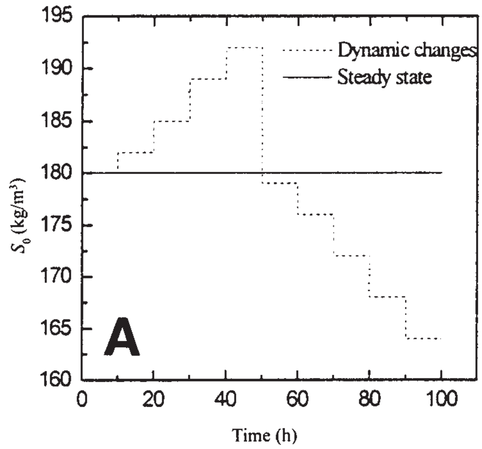
Dynamic Matrix Control SISO

The first case studied is the DMC SISO, used to control the substrate concentration in the fermentor (S). The manipulated variable is the feed rate of the fermentor (F_0). This control structure was chosen based on the study results of dynamic behavior. Since the feed rate (F_0) influences only the substrate concentration, it is a good variable to be manipulated to control that output variable.

In all the tests with the DMC control, the steady-state conditions were as follows: $X = 34.5$ kg/m^3; $S = 1.5$ kg/m^3; $P = 39.2$ kg/m^3; $T = 306$ K. The volume of the fermentor was 383 m^3.

In the first test of the performance of the controller, dynamic changes were made in the feed substrate concentration (S_0); Figure 6A shows these changes. Figure 6B shows the open-loop response and the result when the DMC controller was used. It can also be seen from Fig. 6b that the controller maintained the controlled variable near to the set-point value in the presence of the load disturbances considered.

The performance of the DMC controller for the servo problem was tested by making a step change of ±50% in the set-point value. Figure 7



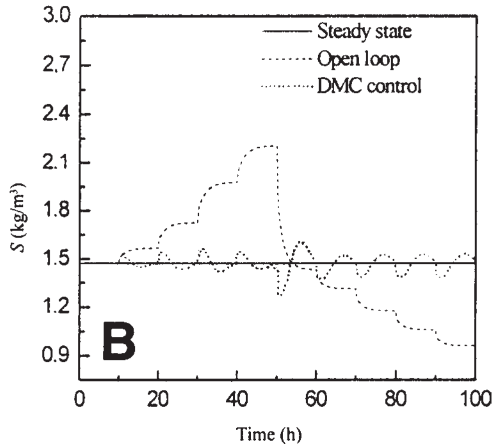


Fig. 6. **(A)** Dynamic changes in the feed substrate concentration; **(B)** output substrate concentration vs time in the presence of the changes shown in (A).

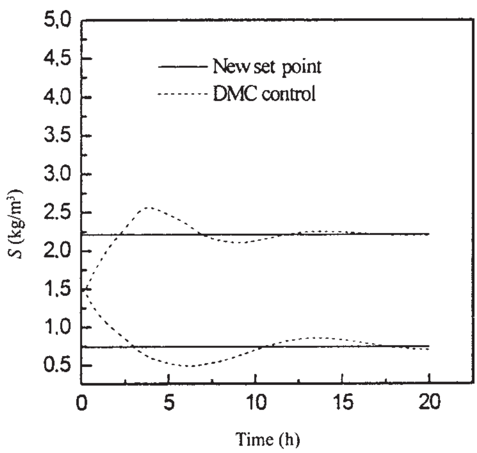


Fig. 7. Output substrate concentration vs time for step change of ±50% in the set-point value.

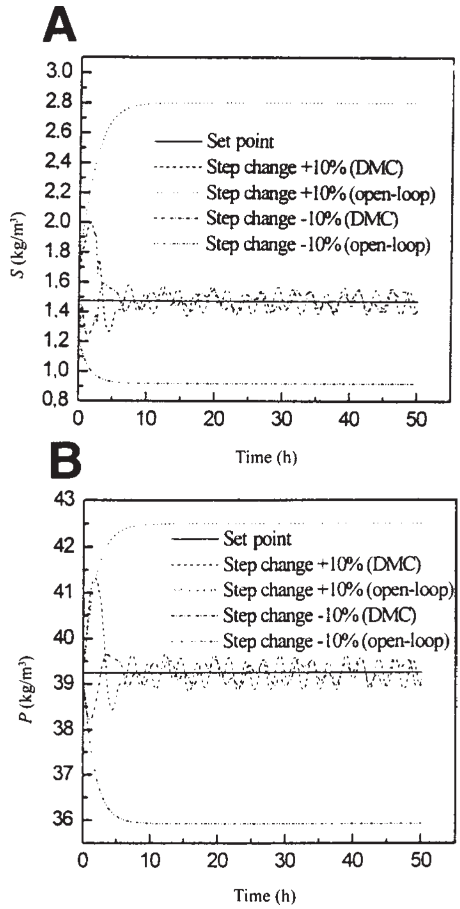


Fig. 8. **(A)** Output substrate concentration vs time for step change of ±10% in feed substrate concentration; **(B)** output ethanol concentration vs time for step change of ±10% in feed substrate concentration.

presents the results for the controlled variable when the process was operated with the DMC controller. It can be seen that the DMC controller presented good performance for the servo problem.

Dynamic Matrix Control MIMO

Based on the study results of dynamic behavior, the control structure chosen for the DMC MIMO control of the process was as follows:

1. Controlled variables: substrate and product concentrations in the fermentor (S and P)
2. Manipulated variables: feed rate (F_0) and flash recycle rate (r)

The choice of the controlled variables was made based not only on the importance of these variables for the performance of the process but also on the possibility of controlling these variables with the available manipula-

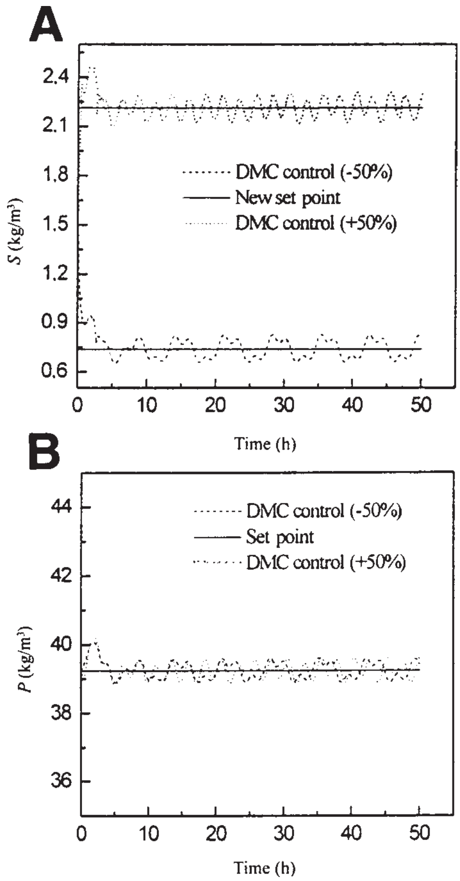


Fig. 9. **(A)** Output substrate concentration vs time for step changes of ±50% in substrate concentration set point; **(B)** output ethanol concentration vs time for step changes of ±50% in substrate concentration set point.

tions. Table 3 shows that the control of the biomass concentration can adequately be made by manipulating the cell recycle rate (R). Because this manipulation is restricted by process requirements (the maximum value this variable can reach is 0.355, for the considered operational conditions), controlling the biomass is quite difficult for this process. Control of the fermentor temperature is also quite difficult with the manipulations available, because the flash recycle rate (r) has only a weak influence in this output variable.

There are three possible manipulated variables. The feed rate and flash recycle rate were chosen, because the restriction in the cell recycle rate makes its use for manipulation difficult. In the first test of the performance of the DMC MIMO controller, step changes of ±10% were made in the feed substrate concentration (S_0). Figure 8A,B presents the open-loop responses and the results when the DMC controller was used for the two output variables.

The controller performance for the servo problem was tested by making step changes in the set points of the two controlled variables. Figure 9A shows the results for step changes of ±50% in the substrate concentration

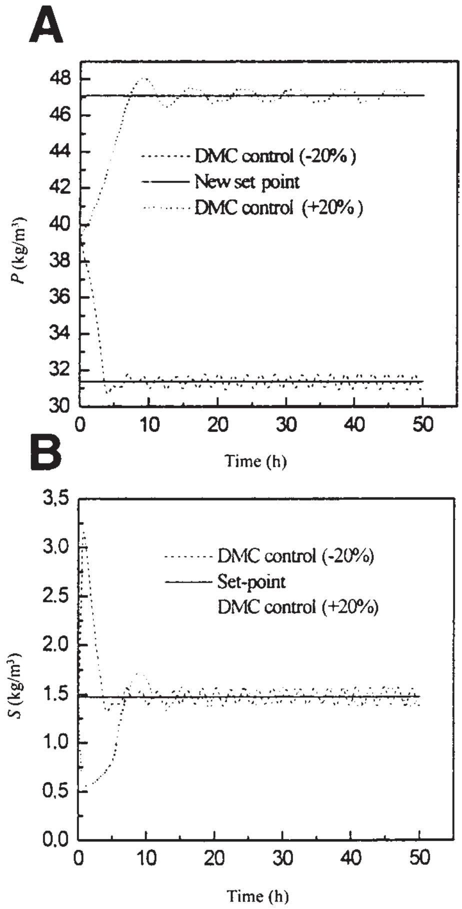


Fig. 10. **(A)** Output product concentration vs time for step changes of ±20% in product concentration set point; **(B)** output substrate concentration vs time for step changes of ±20% in product concentration set point.

set point. Figure 9B depicts the behavior of the product concentration for the same set-point change. It can be seen that the controller presents good performance for the servo problem. Figure 9B shows that changes made in the manipulated variables leading the substrate concentration to its new set-point value affect the product concentration, but that the MIMO controller is able to maintain this controlled variable at its set point.

Figure 10A presents the results for step changes of ±20% in the product concentration set point. Figure 10B shows the behavior of the substrate concentration for the same change. It can be seen that the DMC MIMO controller presents good performance for this test.

Discussion

The industrial operation of the alcoholic fermentation process in a continuous mode requires the development and implementation of an efficient control strategy, able to keep the main process variables in its set points in spite of load disturbances and/or set-point changes. The DMC controller has great potential for industrial application, because this algorithm is considered robust and easily implemented.

To choose the best structures for an efficient control of the alcoholic fermentation process, its dynamic behavior must be studied. The concepts of factorial design were successfully used to achieve this goal. The DMC algorithm, SISO and MIMO, with the control structures chosen, was shown to have great potential for controlling the process in the presence of all the disturbances tested. However, an oscillatory behavior on the manipulated variables (not shown) was observed, mainly for the MIMO case. This means that a best set for the controller parameters should be found (specifically changes in the suppression factor). But, this was not extensively studied in this study, because the main objective was to present a suitable control strategy for an industrial ethanol fermentation.

In this simulation study, the measurements were assumed to be perfect, with high accuracy. A high accuracy in concentration (e.g., better than 0.1 kg/m^3) was difficult to obtain with the equipment available. However, some analytical techniques have shown a significant evolution in the past few years (e.g., near infrared technique), which create expectancy that this high accuracy will be available in reasonable costs and not require highly trained personnel. Additionally, this is a case study from simulation, and the global results obtained by the control system would not be changed much if a lower accuracy were admitted, only the range of variation around the steady state could be wider.

The control strategy proposed in this study could be substituted by a feedforward scheme. However, the use of a feedback strategy is adequate, because it takes actions at the inputs after all possible variations occur in the fermentation medium (this includes changes in other parameters, e.g., the viability of the yeast, although it was not considered in this work). Besides, a feedforward scheme may add problems related to the need to measure a larger number of input variables, which would be reflected in the entire cost of the control system.

Acknowledgment

We acknowledge Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) for financial support.

Nomenclature

A = Dynamic matrix in the DMC algorithm
b = Coefficients in the step-response model
C_p = Heat capacity (J/[kg · K])
$D = F/V$ = Dilution rate (h^{-1})
E = Activation energy (J/mol)
f = Weighting factor in the DMC algorithm
F = Feed stream flow rate (m^3/h)

F_c = Cell suspension flow from centrifuge (m^3/h)
F_{c1} = Cell suspension flow to treatment tank (m^3/h)
F_E = Light phase flow rate to flash tank (m^3/h)
F_L = Liquid outflow from the vacuum flash tank (m^3/h)
F_{LR} = Liquid phase recycling flow rate (m^3/h)
F_{LS} = Liquid phase flow to rectification column (m^3/h)
F_p = Purge flow rate (m^3/h)
F_r = Cell recycling flow rate (m^3/h)
F_V = Vapor outflow from the vacuum flash tank (m^3/h)
F_w = Water flow rate (m^3/h)
F_0 = Fresh medium flow rate (m^3/h)
I = Identity matrix
J = Performance index
K_i = Equilibrium constant
K_s = Substrate saturation constant (kg/m^3)
n = Product inhibition power
NC = Control horizon in the DMC algorithm
NP = Prediction horizon in the DMC algorithm
p = Pressure (Pa)
p_i^{sat} = Vapor pressure (Pa)
P = Product concentration in the fermentor (kg/m^3)
P_F = Product concentration in the feed stream (kg/m^3)
P_{LR} = Product concentration in the light phase from centrifuge (kg/m^3)
P_{max} = Product concentration when cell growth ceases (kg/m^3)
P_r = Product concentration in the recycle (kg/m^3)
P_V = Product concentration in the vapor phase from flash tank (kg/m^3)
$r = F_{LR}/F_L$ = Flash recycle rate
r_p = Kinetic rate of product formation (h^{-1})
r_s = Kinetic rate of substrate consumption (h^{-1})
r_x = Kinetic rate of growth (h^{-1})
$R = F_r/F$ = Cell recycle rate
R_G = Gas constant (8.314 J/[mol · K])
S = Substrate concentration in the fermentor (kg/m^3)
S_F = Substrate concentration in the feed stream (kg/m^3)
S_{LR} = Substrate concentration in the light phase from centrifuge (kg/m^3)
S_r = Substrate concentration in the recycle (kg/m^3)
S_0 = Inlet substrate concentration (kg/m^3)
T = Temperature in the fermentor (K)
T_F = Feed stream temperature (K)
T_{LR} = Light phase temperature (K)
T_r = Recycle temperature (K)
T_w = Water temperature (K)
T_0 = Inlet temperature of the fresh medium (K)
x_{Ei} = Component *i* concentration in the light phase (mol %)
x_i = Component *i* concentration in the liquid (mol %)
X = Biomass concentration in the fermentor (kg/m^3)

X_c = Cell concentration in the heavy phase from centrifuge (kg/m^3)
X_E = Cell concentration in the light phase flow rate to flash tank (kg/m^3)
X_F = Cell concentration in the feed stream (kg/m^3)
X_{LR} = Cell concentration in the light phase from centrifuge (kg/m^3)
X_r = Cell recycling concentration (kg/m^3)
y = Controlled variable
y_i = Component *i* concentration in the vapor (mol %)
$Y_{P/S}$ = Yield constant (kg product/kg substrate)
$Y_{X/S}$ = Yield constant (kg cell/kg substrate)
Z = Constant (s^{-1})
γ_i = Activity coefficient of component *i*
ΔH = Reaction heat (J/kg)
Δm = Variation in the manipulated variable
μ_{max} = Maximum specific growth rate (h^{-1})
ρ = Density (kg/m^3)

References

1. Ramalingham, A. and Finn, R. K. (1977), *Biotechnol. Bioeng.* **19,** 583–589.
2. Cysewski, G. R. and Wilke, C. R. (1977), *Biotechnol. Bioeng.* **19,** 1125–1143.
3. Christen, M., Minier, M., and Renon, H. (1990), *Biotechnol. Bioeng.* **36,** 116–123.
4. Minier, M. and Goma, G. (1982), *Biotechnol. Bioeng.* **24,** 1565–1579.
5. Sourirajan, S. (1987), *Membrane* **12,** 367–369.
6. Ishida, K. and Shimizu, K. (1996), *J. Chem. Technol. Biotechnol.* **66,** 340–346.
7. Maiorella, B. L., Blanch, H. W., and Wilke, C. R. (1984), *Biotechnol. Bioeng.* **26,** 1003–1025.
8. Taylor, F., Kurantz, M. J., Goldberg, N., and Craig, J. C. (1998), *Biotechnol. Lett.* **20,** 67–72.
9. Silva, F. L. H., Rodrigues, M. I., and Maugeri Filho, F. (1999), *J. Chem. Technol. Biotechnol.* **74,** 176–182.
10. Andrietta, S. R. (1994), DSc thesis, Faculdade de Engenharia de Alimentos, UNICAMP, Campinas, SP, Brazil.
11. Andrietta, S. R. and Maugeri, F. (1996), in *Advances in Bioprocess Engineering*, vol. 1, Galindo, E. and Ramirez, O. T., eds., Kluwer Academic, The Netherlands, pp. 47–52.
12. Alves, J. G. L. F. (1996), DSc thesis, Faculdade de Engenharia de Alimentos, UNICAMP, Campinas, SP, Brazil.
13. Box, G. E. P., Hunter, W. G., and Hunter, J. S. (1978), *Statistics for Experimenters*, John Wiley & Sons, New York.
14. Cutler, C. R. and Ramaker, B. L. (1980), Proc. Joint Auto Control Conf., Paper WP5-B, San Francisco.
15. Luyben, W. L. (1989), *Process Modeling, Simulation and Control for Chemical Engineers*, 2nd ed., McGraw-Hill, New York.
16. Dechechi, E. C. (1998), DSc thesis, Faculdade de Engenharia Química, UNICAMP, Campinas, SP, Brazil.