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On-Line Optimized Enzymatic Hydrolysis in a Continuous Stirred Tank Reactor by Extremum Seeking Control

Fernando López-Caamal*. Ixbalank Torres**
Héctor Hernández-Escoto ***

** Chemical Engineering Department, Guanajuato University, Guanajuato, México, (e-mail: fernando.lopez.caamal@gmail.com).*
*** Electronics Engineering Department, Guanajuato University, Salamanca, México (ORCID: 0000-0002-2047-1569)*
**** Chemical Engineering Department, Guanajuato University, Guanajuato, México, (e-mail: hhee@ugto.mx)}*

Abstract: Within a frame of optimized performance by Extremum Seeking Control, this work conceptualizes the enzymatic hydrolysis of cellulose carried out in an isothermal stirred tank reactor of continuous operation. This reactor operation is aimed at increasing the production rate of reducing sugars in biorefineries. The basis is a batch reactor model extended to describe continuous operation, resulting in a stable process for any process condition. Based on an objective function that ponders productivity with dilution rate, it is applied an Extremum Seeking Control algorithm driven by the on-line estimation of the gradient of the control input-objective function map, improving convergence rate and enabling practical implementation.

Keywords: Extremum seeking control, enzymatic hydrolysis, gradient-based optimization, CSTR.

1. INTRODUCTION

Enzymatic hydrolysis of cellulose to produce fermentable sugars is an essential process in the conversion chain of agro-industrial and forestry residues to high-value bioproducts. Currently, this process is carried out in a stirred tank reactor in batch or semi-batch operation at a certain temperature and pH, so its design lies in determining the load of biomass and enzyme, and the temperature and pH at which the process performs better. This task is mostly carried out in an experimental framework in which numerous batches are performed at diverse conditions (e.g., Hernández-Beltrán et al., 2018; Hernández-Beltrán and Hernández-Escoto, 2018). The production of reducing sugars depends on the biomass load and the time of the batch process, which evolves slowly; however, because of physical limitations, the concentration of raw materials in this bioprocess is low, as is the case in all other bioprocesses in biorefineries. As a result, the concentration of the product is also low, which in turn results in a high cost for the purification of the final bioproduct (Frolkova and Raeva, 2010). Therefore, obtaining a cellulose enzymatic hydrolysis process with a high production rate and a high concentration of reducing sugars is a challenge.

Although continuous operation of reactors enables a larger production rate in comparison with batch operation, it has not been explored for cellulose enzymatic hydrolysis, maybe because of its slow kinetics, and the assumed complex handling of cellulosic material (e.g., milled straw) in the input and output streams of the reactor. On the other hand, its process design, mainly meaning the determination of the flow rate of raw materials, provided the concentration of cellulose and enzyme in the input stream, and the temperature and pH of the reacting mixture, would be expensive if it were realized in an experimental framework as well, because of very long-time experiments for different input flow rates with different raw material concentrations.

In order to reduce the experimental work, an approach is to carry out the design task with model-based techniques. The mathematical models for this kind of process are scarce (e.g., Gusakov and Synitzin, 1998; Angarita et al., 2015), and when one is adopted for a certain biomass-enzyme-equipment system, parameter identification must be performed from time to time since the qualities of raw materials and enzymes vary throughout the process lifetime. Subsequently, related model-based adjustments and experimental ones, because of the inherent uncertainty enclosed in the kinetics models, would be necessary. To overcome the above-mentioned variations and kinetics uncertainty, inserting the process into a proper control system, not just to maintain effective performance but to take it to its best as much as possible, is an approach worthy of exploration.

In the last fifty years, different real-time optimization strategies have been developed to on-line optimize processes at steady state. Real-time optimization (RTO) encompasses a family of optimization methods that incorporate process measurements in the optimization framework to drive a real process to optimal performance, while guaranteeing constraint satisfaction. RTO has emerged to overcome the difficulties associated with process-model mismatch (Marchetti et al., 2016). Among such methods, Extremum Seeking Control (ESC) is an RTO technique that allows the system to be led towards the extreme of a measurable convex (or concave) function corresponding to the optimal conditions in an operating region. The input is directly updated in a control-inspired manner. The ESC is applicable in situations where there is a nonlinearity in the control problem, the nonlinearity

has a local minimum (or maximum), and the process model is uncertain as is the case of bioprocesses (Dewasme et al., 2020).

Recently, Torres-Zúñiga et al. (2021) proposed an ESC strategy based on the super-twisting algorithm which profits the robust properties of sliding-modes to solve optimization problems on-line. The strategy consists of a gradient-based line search optimization algorithm proposed as a proportional–integral ESC. The integral term corresponds to the standard ESC action and is used to compute the steady-state optimum point. The proportional term corresponds to an adaptive term and is used to accelerate the convergence of the algorithm. Furthermore, the gradient is estimated by a super-twisting-based robust differentiator.

In this paper, the above-mentioned super-twisting-based ESC is considered to on-line maximize a performance function to take the continuous operation of the cellulose enzymatic hydrolysis reactor to optimal performance. In the next section, the process is described, and its design task is defined, so the ESC is justified as a technique to be resorted to. Third section describes the control system conformation and the specifics of the ESC controller. In the fourth section, the performance of the control system is discussed by considering practical scenarios related to the concentration of cellulose in the input stream. Finally, Conclusions remark the feasibility of the ESC application to the continuous operation of a stirred tank reactor in which cellulose enzymatic hydrolysis is carried out.

2. THE PROCESS AND ITS OPTIMIZATION PROBLEM

2.1 Process Description

It is considered the enzymatic hydrolysis of cellulose (CEH) carried out in a continuous stirred tank reactor (CSTR)(Fig. 1).

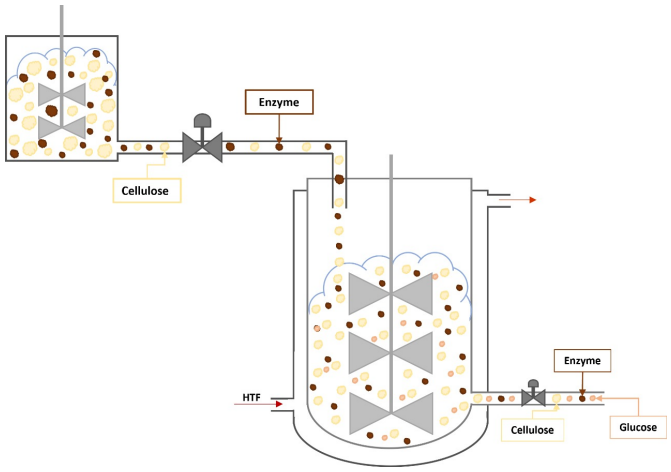

Fig. 1. Cellulose enzymatic hydrolysis in a continuous stirred tank reactor (CEH-CSTR).

It is assumed that the mixture is homogeneous since the cellulose concentration does not overpass a critical value that makes the mixture a slurry that is almost immovable, and that it is equipped with control devices that maintain the reactor mixture at required constant temperature and pH. A suspension of cellulose and enzyme, of certain composition, is continuously fed through an input stream at the reactor top, and the reactor mixture that contains the remaining cellulose, enzyme, and glucose is continuously withdrawn through a bottom output stream.

2.2 The Design Problem

It is started with a system cellulose-enzyme for which temperature, pH, and cellulose-enzyme ratio have been established in a design work of batch experiments. The cellulose enzymatic hydrolysis is being carried out in the continuous stirred tank reactor (Fig. 1), so the operation condition to be determined is the biomass feed flow that yields a high production rate of glucose. As mentioned above, due to physical constraints, the cellulose concentration is required to be below a certain critical value that makes the content a slurry.

2.3 The Mathematical Model

Cellulose enzymatic hydrolysis is a reaction in which, with the aid of enzymes, cellulose is depolymerized into glucose. The basic reaction mechanism is the following:

$$\mathrm{C} + \mathrm{E} \xrightarrow{v_{CB}} \mathrm{B} + \mathrm{E} \xrightarrow{v_{BG}} \mathrm{G} + \mathrm{E}, \qquad \mathrm{C} + \mathrm{E} \xrightarrow{v_{CG}} \mathrm{G} + \mathrm{E}$$

with a mass stoichiometric coefficient of 1. C represents cellulose, E is enzyme, G is glucose, and B is an intermediate sugar called cellobiose. v_{CB}, v_{BG}, and v_{CG} are the reaction rates of each mechanism step.

The mass balance in the CEH-CSTR (Fig. 1) results in the following mathematical model:

$$\dot{C} = r_C(C,B,G,E) + D * (C_{in} - C), \quad C(0) = C_0 \tag{1a}$$

$$\dot{B} = r_B(C,B,G,E) - D * B, \quad B(0) = 0 \tag{1b}$$

$$\dot{G} = r_G(C,B,G,E) - D * G, \quad G(0) = 0 \tag{1c}$$

$$\dot{E} = r_E(C,B,G,E) + D * (E_{in} - E), \quad E(0) = E_0 \tag{1d}$$

where C, B, G, and E are the concentrations in the reactor of C, B, G, and E, respectively. C_{in} is the concentration of C in the input stream, and E_{in} is the one of E. D is the dilution rate, which replaces the term F/V, in which V, the reactor volume, is considered constant; F is the volumetric flow of the input stream. r_m is the global reaction rate of the substance m (m = C, B, G or E),

$$r_C = -v_{CB} - v_{CG} \tag{2a}$$

$$r_B = +v_{CB} - v_{BG} \tag{2b}$$

$$r_G = +v_{BG} + v_{CG} \tag{2c}$$

$$r_E = 0 \tag{2d}$$

As it is noticeable in Eqn. (2d), it is assumed that the enzyme reincorporates into the broth once it breaks cellulose, and that it does not suffer any spoilage effect (e.g., denaturalization), so its reaction rate is assumed as quasi-stationary.

The reaction rates v_{CB}, v_{BG} and v_{CG} of each mechanism step are described by a Michaelis-Menten type kinetics form,

$$v_{CB} = \frac{V_{CB}(E)C}{K_{CB}\left(1+\frac{B}{K_{ICB}}\right)+C} \quad (3a)$$

$$v_{BG} = \frac{V_{BG}(E)B}{K_{BG}\left(1+\frac{G}{K_{IBG}}\right)+B} \quad (3b)$$

$$v_{CG} = \frac{V_{CG}(E)C}{K_{CG}\left(1+\frac{G}{K_{ICG}}\right)+C} \quad (3c)$$

Corresponding to each mechanism step, V_{CB}, V_{BG} and V_{CG} are the maximum reaction rates depending on E,

$$V_{CB} = a_{CB}E + b_{CB}E^2 + c_{CB}E^3 \quad (4a)$$

$$V_{BG} = a_{BG}E + b_{BG}E^2 + c_{BG}E^3 \quad (4b)$$

$$V_{CG} = a_{CG}E + b_{CG}E^2 + c_{CG}E^3 \quad (4c)$$

K_{CB}, K_{BG} and K_{CG} are Michaelis-Menten constants, and K_{ICB}, K_{IBG} and K_{ICG} are inhibition constants. The kinetics structures (3) are adopted from Gusakov and Sinitzyn (1985) since its comprehensive phenomenon addressing, which is encountered in recent works of modelling the enzymatic hydrolysis of lignocellulosic biomass (e.g., Angarita et al., 2015). Finally, the following Table 1 provides the values of the model parameters.

Table 1. Value of model parameters for enzymatic hydrolysis below 100 g/L of cellulose and between 5 and 60 g/L of enzyme (Gusakov and Sinitzyn, 1985)

Parameter	Value	Parameter	Value	Parameter	Value
K_{CB}	13	K_{BG}	0.6	K_{CG}	15
K_{ICB}	0.8	K_{IBG}	0.32	K_{ICG}	11
a_{CB}	0.294	a_{BG}	0.0054	a_{CG}	0.144
b_{CB}	-0.003	b_{BG}	-5.4×10^{-6}	b_{CG}	-4.8×10^{-5}
c_{CB}	1.8×10^{-5}	c_{BG}	6.0×10^{-7}	c_{CG}	-4.2×10^{-5}

2.4 The Design Problem as an Optimization Problem

Considering an optimization framework to design the process, the design problem means to maximize an objective function related to the production rate of glucose through dilution rate, with the constraints given by the process,

$$\max_{D(t)} J = \vartheta(G, D), \quad (5a)$$

s.t. Mathematical Model (1)-(4), (5b)

$$F(t) \geq 0, 0 < C(t) \leq C^*. \quad (5c)$$

Fig. 2 shows the steady states concentrations in the CEH-CSTR as the dilution rate varies for a case in which the input stream carries cellulose at a high concentration. These steady states are obtained by solving the algebraic equations resulting from equating to zero the change functions of the mathematical model (1).

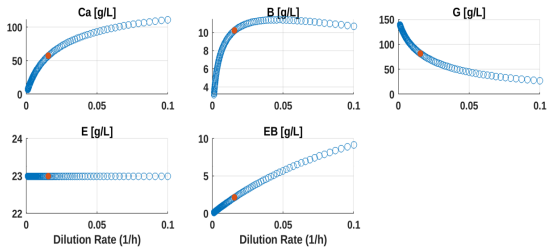

Fig. 2 Steady states concentrations in the CEH-CSTR with respect to D, with $C_{in} = 150\ g/L$.

Should we consider productivity ($J = G * D$) as an objective function, the optimal dilution rate is infinite since steady-state productivity grows monotonically as a function of the dilution rate. In other hand, should we consider only such glucose concentration as an objective function ($J = G$), the optimal dilution rate is zero since glucose grows up to the input cellulose concentration with the decrease of dilution rate, becoming a batch operation.

From a search for an appropriate objective function, the following objective function resulted:

$$J = G * D - f * D \quad (6)$$

which is productivity competing with a pondered dilution rate (f is the pondering factor), which in turn makes the objective function concave and then amenable for optimization. One may see from Fig. 3 that such a function is concave, and the maximum value is highlighted with a red marker.

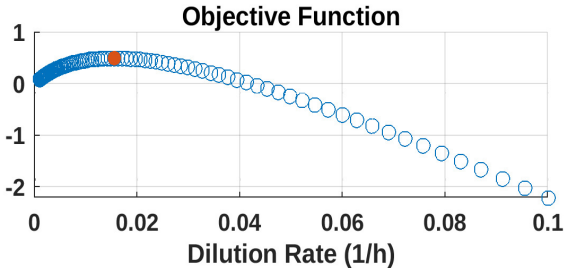

Fig. 3 Objective function $J = GD - fD$, with $C_{in} = 150\ g/L$ and $f = 50\ g/L$.

The following Table 2 shows the dilution rate that maximizes the objective function J (6) for different values of C_{in}, for which J is also concave. It is worthy to highlight that glucose concentrations reached at the corresponding steady states (C_{ss}) are pretty high, as encountered in any study of the enzymatic hydrolysis of cellulosic material carried out in a batch reactor.

Table 2. Optimal conditions for different glucose concentrations in the input stream ($f = 50\ g/L$)

$C_{in}\ (g/L)$	J_{max}	$D\text{x}10^3\ (1/h)$	$G_{ss}\ (g/L)$
100	0.205585	11.233	68.30
150	0.501057	15.557	82.20
170	0.609180	16.298	87.37
200	0.757273	17.074	94.35

Then, the optimization problem is the following:

$$\max_{D(t)} J = G * D - f * D \tag{5a}$$

s.t. Mathematical Model (1)-(4), (5b)

$$F(t) \geq 0,\ 0 < C(t) \leq C^*. \tag{5c}$$

3. THE EXTREMUM SEEKING CONTROL

Having an optimal control problem (5), in addition, it must be taken into account that the model process (1-4) has inherent uncertainties because of its biological nature and the potential operative deviations that appear along the process timeline. Therefore, it is resorted to an Extremum Seeking Control approach, in this case the one developed in Torres-Zúñiga et al. (2021).

Firstly, it is considered that there is a vector θ composed by the objective function J and the control input D, with an existing first time-derivative,

$$\theta := \begin{pmatrix} J \\ D \end{pmatrix}, \qquad \omega := \begin{pmatrix} \dot{J} \\ \dot{D} \end{pmatrix}. \tag{7a, b}$$

Then, the control system takes the following form:

$$\dot{x} = f(x, D, d), \quad x(0) = x_0, \quad x = [C, B, G, E]', \tag{8}$$

$$D(t) = -\lambda * \sqrt{|\hat{\sigma}|} * \text{sign}(\hat{\sigma}) + D_1(t), \quad \hat{\sigma} = -\frac{d\hat{J}}{dD} \tag{9a}$$

$$\dot{D}_1(t) = -\alpha * \text{sign}(\hat{\sigma}), \quad D_1(0) = D_{10}; \quad \lambda, \alpha > 0. \tag{9b}$$

$$\hat{\sigma} = -\frac{\hat{\omega}_1}{\hat{\omega}_2}, \quad \hat{\omega}_2 \neq 0. \tag{10}$$

$$\dot{\hat{\theta}}(t) = -\kappa_1 * \phi_1(e_\theta) + \hat{\omega}(t), \quad e_\theta = \hat{\theta} - \theta, \tag{11b}$$

$$\dot{\hat{\omega}}(t) = -\kappa_2 * \phi_2(e_\theta), \quad \kappa_1, \kappa_2 > 0, \tag{11c}$$

$$\phi_1(e_\theta) := \left(\eta \|e_\theta\|_2^{-p} + \beta + \gamma \|e_\theta\|_2^{q}\right) e_\theta, \quad \phi_1(0) := 0, \tag{11d}$$

$$\phi_2(e_\theta) := \left(\eta(1-p)\|e_\theta\|_2^{-p} + \beta + \gamma(1+q)\|e_\theta\|_2^{q}\right) \phi_1(e_\theta). \tag{11e}$$

$$\|e_\theta\|_2 := \sqrt{e_\theta{}^T e_\theta}, \quad \eta, \beta, \gamma > 0, \quad \tfrac{1}{2} \geq p > 0, \quad q > 0. \tag{11f}$$

Eqn. (8) represents the process (1-4). Eqns. (9) form a controller, that is intended to be driven by the gradient of the objective function with respect to the dilution rate ($\sigma = dJ/dD$), where λ and α are constant gains. This gradient cannot be on-line measured, so its estimate $\hat{\sigma}$ (10) is calculated on the basis of the time-derivative of the objective function ($\omega_1 = \dot{J}$) and the one of the dilution rate ($\omega_2 = \dot{D}$) (7b). The super-twisting-based ESC generates the control input $D(t)$ that maximizes the concave objective function $J(D(t))$ at steady state.

Since σ is unknown but J is measured online, it is estimated together to the known control input $D(t)$ by the super-twisting-based differentiator (11). By assuming that the absolute value of $\dot{\omega}$ is element-wise bounded, the differentiator (11b, c) provides, in finite-time, an estimate of both $\dot{\theta}$ and $\dot{\omega}$.

4. CONTROL SYSTEM PERFORMANCE

In this section, the super twisting-based control system of the CEH-CSTR (8–11) is tested by considering scenarios in which the process is started up and the control system must take the process to its optimal performance. Later, the control system is faced with changes in the cellulose concentration of the input stream. The first scenario means that process is initiated with the following conditions:

$$C(0) = B(0) = G(0) = 0, \quad E(0) = 23\ g/L,$$

$$C_{in} = 150\ g/L, \quad D(0) = 0\ h^{-1}.$$

Next, once the process reaches its first optimal steady-state, a piece-wise trajectory of C_{in} with subsequent constant levels of $150\ g/L$, $170\ g/L$, $200\ g/L$, and $100\ g/L$ is applied. Such a variation of C_{in} tries to mimic the variability of the raw material preparation throughout the process lifetime.

The following values for parameters of the controller and differentiator were considered:

$$\alpha = 2 \text{ x } 10^{-6},\ \lambda = 1 \text{ x } 10^{-3},\ \kappa_1 = 3 \text{ x } 10^{-3},\ \kappa_2 = 3 \text{ x } 10^{-3},\ \eta = 2,\ \beta = 4,\ \gamma = 10,\ p = 0.25,\ q = 0.5.$$

Fig. 3 shows the dilution rate, objective function, and estimated gradient as a function of time for the control system when the above-mentioned conditions are applied, whereas Fig. 4 depicts the evolution of the CEH-CSTR state variables.

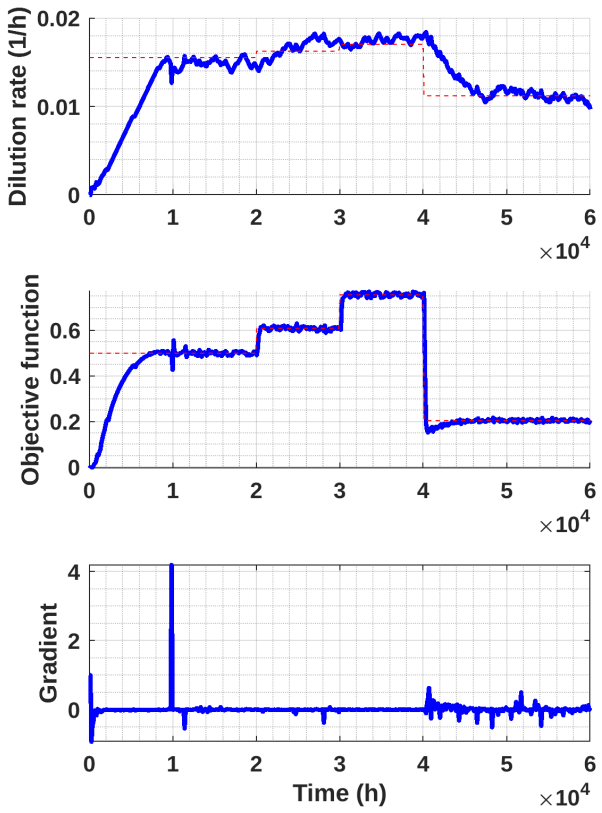

Fig. 3 Closed-loop dilution rate and objective function towards the optimal performance of the CEH-CSTR. The dotted line represents the optimal values, whereas the continuous line shows the actual values.

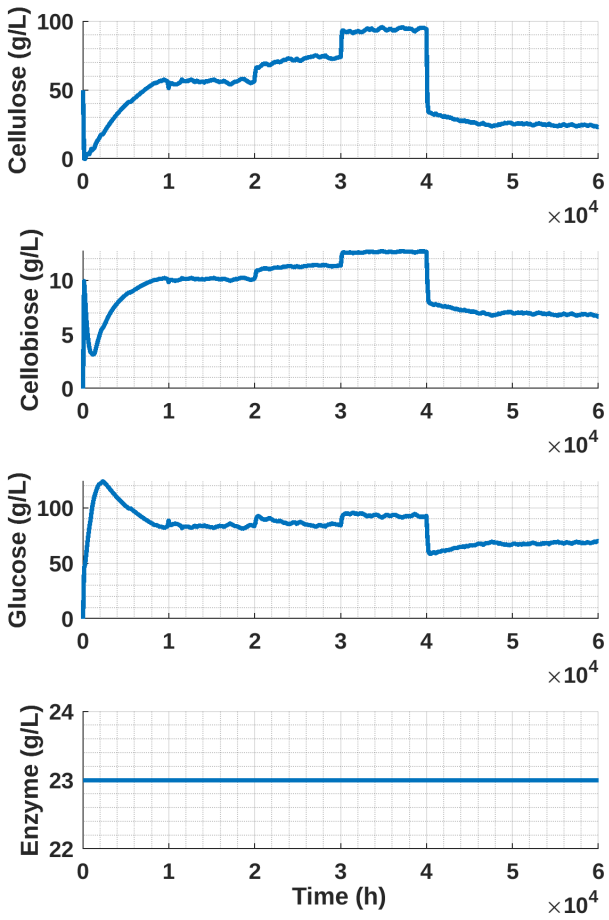

Fig. 4. Evolution of the CEH-CSTR state variables towards optimal steady states.

The numerical implementation of the ESC controller considers an update of the dilution rate every 5 days, thus allowing the plant to reach its steady state before computing a new value for the dilution rate. The gradient estimate (10), however, is continuously computed throughout the simulation span.

It can be observed that the optimal values of the objective function, dilution rate, and glucose concentration, given in Table 1, are reached for every level of C_{in}. The search for the first optimal steady state, starting from zero initial concentrations of bio-substances, takes a very long time. Although expected to be shorter, this long time is a typical characteristic of the ESC controllers. Next, the search for the optimal conditions for the following changes in C_{in} takes a much shorter time; for the scale-time set by the first search, the convergence times seem almost instantaneous.

In other hand, it is worthy to highlight that cellulose concentration is below 100 g/L, which is a value that enables mixing.

6. CONCLUSIONS

In this work, the enzymatic hydrolysis of cellulose carried out in a continuous stirred tank reactor was conceptualized and designed through an ESC controller. Based on an objective function, it was determined that the process is feasible to perform since the cellulose concentration is sufficiently low and the glucose concentration is like the one obtained in a batch process. Although the ESC controller takes the process to its optimal condition for a long time, it motivates future work aimed at improving convergence velocity.

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