Optimization of Operating Temperature for an Continuous Immobilized Glucose Isomerase Reactor with Pseudo Linear Kinetics

By *Naim M. Faqir**

In this work, the optimal operating temperature for the enzymatic isomerization of glucose to fructose using a continuous immobilized glucose isomerase packed bed reactor is studied. This optimization problem describing the performance of such reactor is based on reversible pseudo linear kinetics and is expressed in terms of a recycle ratio. The thermal deactivation of the enzyme as well as the substrate protection during the reactor operation is considered. The formulation of the problem is expressed in terms of maximization of the productivity of fructose. This constrained nonlinear optimization problem is solved using the disjoint policy of the calculus of variations. Accordingly, this method of solution transforms the nonlinear optimization problem into a system of two coupled nonlinear ordinary differential equations (ODEs) of the initial value type, one equation for the operating temperature profile and the other one for the enzyme activity. The ODE for the operating temperature profile is dependent on the recycle ratio, operating time period, and the reactor residence time as well as the kinetics of the reaction and enzyme deactivation. The optimal initial operating temperature is selected by solving the ODEs system by maximizing the fructose productivity. This results into an unconstrained one-dimensional optimization problem with simple bounds on the operating temperature. Depending on the limits of the recycle ratio, which represents either a plug flow or a mixed flow reactor, it is found that the optimal temperature of operation is characterized by an increasing temperature profile. For higher residence time and low operating periods the residual enzyme activity in the mixed flow reactor is higher than that for the plug flow reactor, which in turn allows the mixed flow reactor to operate at lower temperature than that of the plug flow reactor. At long operating times and short residence time, the operating temperature profiles are almost the same for both reactors. This could be attributed to the effect of substrate protection on the enzyme stability, which is almost the same for both reactors. Improvement in the fructose productivity for both types of reactors is achieved when compared to the constant optimum temperature of operation. The improvement in the fructose productivity for the plug flow reactor is significant in comparison with the mixed flow reactor.

1 Introduction

The enzymatic conversion of glucose to fructose is an important industrial process, especially in the production of high fructose corn syrup (HFCS) using immobilized glucose isomerase (IGI) [1,2]. HFCS is a mixture of glucose and fructose, and it is produced by the isomerization of glucose syrup into its isomer fructose by the action of enzyme glucose isomerase. Glucose syrup, which is produced from cornstarch, is used as a source of raw material. Fructose is nearly 1.7 times sweeter than glucose and HFCS with a fructose content of 42% is mainly used as a sweetener in soft drinks. Different organisms produce the enzyme glucose isomerase, such as Flavobacterium, Bacillus and some Streptomyces and Arthrobacter species [3].

The literature on the isomerization of glucose to fructose with immobilized glucose isomerase is quite comprehensive [1, 2, 4–13]. Actually, Chamacho-Rubio *et al.* [2] reviewed the vast literature concerning this reaction. In general, the isomerization reaction of glucose to fructose is described by a reversible Michaelis-Menten kinetics. However, several researchers stated that the isomerization reaction of glucose could be described by a pseudo-first order reversible reaction [2, 5–7, 9, 11–14]. Actually, Palazzi and Converti [11] verified experimentally the validity of assuming linear kinetics for the isomerization of glucose to fructose within the temperature range (60 to 80 °C) and glucose concentration (500 to 3000 mol/m^3) of practical interest.

For continuous operation with immobilized enzymes, different types of reactors operating as plug or mixed tank reactors are used. Moreover, these reactor operations should be carried out in such a way that consistent product composition is assured. Since the enzyme activity is progressively decreasing with time, which is mainly thermal deactivation, constant product quality and conversion cannot be achieved. Thus, the operating temperature could be considered as one of the most important factors affecting the reactor performance. The operating temperature affects the isomerization process in many important ways. It affects the kinetic parameters of the isomerization reaction, enzyme deactivation, and the enzyme substrate protection factor as well. Accordingly, the reaction rate and the deactivation rate of the en-

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zyme increase with increasing temperature, which in turn affects the reactor performance. Thus, high reactor productivity requires a varying temperature operation profile instead of one constant temperature. To achieve high fructose yield, the optimal temperature profiles should be known, which requires that the reactor performance should be formulated as an optimization problem.

For immobilized enzyme packed bed reactors, Faqir and Attarakih [13] solved this optimization problem for the general case of enzymatic reactions, which can be described by a reversible Michaelis-Menten kinetics, using the disjoint policy, which makes use of the calculus of variations. By applying the disjoint policy, they reduced the optimization problem into a differential-algebraic system, DAE. An efficient solution algorithm is developed to solve this DAE system, which results in an unconstrained one-dimensional optimization problem [13]. They showed that the computed conversion profiles are almost constant over most of the operating time, and thus producing a product with consistent quality.

In the present work, the optimization of the reactor performance of an immobilized glucose isomerase (IGI) reactor with pseudo linear kinetics is studied. Modeling of the continuous immobilized enzyme packed bed reactor is expressed in terms of the recycle ratio, Rc [15]. This recycle ratio varies from zero to infinity, when ($Rc = 0$), the reactor corresponds to a plug flow reactor, while ($Rc \to \infty$), the reactor approaches a mixed flow reactor. Hence, in this general modeling, the performance of both types of reactors will be investigated. The reactor performance is expressed in terms of maximization of fructose productivity, where pseudo linear kinetics, first order enzyme deactivation as well as substrate protection for glucose isomerization were assumed. This optimization problem is solved using the disjoint policy, which transforms the nonlinear optimization problem into a system of two coupled nonlinear ordinary differential equations (ODEs) of the initial value type. One equation represents the operating temperature profile and the other one the enzyme activity. This system of ODEs defines completely the optimal temperature operation profile. The optimal initial operating temperature is selected by solving the ODEs system by maximizing the fructose productivity. This results into an unconstrained one-dimensional optimization problem with simple bounds on the reactor operating temperature. The solution algorithm developed by Faqir and Attarakih [13] is used to solve this ODEs system, which requires no nonlinear algebraic equation solver for this special case of pseudo linear kinetics.

2 Problem Formulation Using the Disjoint Policy

2.1 Glucose Isomerization Kinetics

The isomerization of glucose to fructose by the action of enzyme glucose isomerase is described by reversible Michaelis-Menten mechanism, and can be represented by [16][1]:

$$E + S \underset{k_{-1}}{\overset{k_1}{\Leftrightarrow}} ES \underset{k_{-2}}{\overset{k_2}{\Leftrightarrow}} E + P \tag{1}$$

Applying the quasi-steady state approach for the enzyme-substrate complex, ES, and assuming no initial product in the feed, the reaction rate is described by [9, 17]:

$$r(C_s(x)) = \frac{V_m(C_s - C_{se})}{k_m + C_s - C_{se}} = \frac{V_m C_{s0}(x_e - x)}{k_m + C_{s0}(x_e - x)} \tag{2}$$

where

$$k_m = \frac{k_s k_p}{k_p - k_s}\left[1 + \left(\frac{k_e}{k_p} + \frac{1}{k_s}\right)\frac{C_{s0}}{1 + k_e}\right]$$

$$V_m = \frac{k_P V_s (1 + k_e)}{\left(k_p - k_s\right) k_e}$$

$$k_p = k_{p0} e^{-E_p/RT}; \qquad k_s = k_{s0} e^{-E_s/RT};$$

$$V_p = V_{p0} e^{-E_{Vp}/RT}; \qquad V_s = V_{s0} e^{-E_{Vs}/RT};$$

$$k_e = k_{e0} e^{-E_e/RT}; \qquad V_s = C_{E0} k_2; \qquad V_p = C_{E0} k_{-1};$$

$$k_s = \frac{k_{-1} + k_2}{k_1}; \qquad k_p = \frac{k_{-1} + k_2}{k_{-2}}; \qquad k_e = \frac{V_s k_p}{V_p k_s};$$

$$x_e = k_e/(1 + k_e); \qquad x = \left(C_{s0} - C_s\right)/C_{s0}$$

Note that: $E'_p = E_p/R$; $E'_s = E_s/R$; $E'_{vp} = E_{vp}/R$; $E'_e = E_e/R$ and $E'_{vs} = E_{vs}/R$.

Eq. (2) can be rearranged to:

$$r(C_s) = \frac{k(C_s - C_{se})}{1 + K'_m(C_s - C_{se})} = \frac{kC_{s0}(x_e - x)}{1 + K'_m C_{s0}(x_e - x)} \tag{3}$$

where: $k = V_m/k_m$ and $K'_m = 1/k_m$

As it can be seen from Eq. (3), the reaction rate reduces to a pseudo-first order reversible reaction when $k_p = k_s$ [2, 5–7, 9, 11–13]. The operating temperature at which $k_p = k_s$ is called the characteristic temperature, T_L. At this characteristic temperature, the reversible Michaelis-Menten reaction follows steady state mechanism in both forward and reverse directions and approaches the equilibrium state. For the isomerization of glucose to fructose, the values of the kinetic parameters k_s and k_p are almost of the same order of magnitude in the temperature range of practical industrial

1) List of symbols at the end of the paper.

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applications (60 to 80 °C), and they are equal at the characteristic temperature T_L = 70.22 °C [2, 12, 13]. Based on this observation, the validity of assuming pseudo linear kinetics is verified experimentally by Palazzi and Converti [11] for the isomerization of glucose to fructose within the temperature range (60 to 80 °C) and glucose concentration (500 to 3000 mol/m^3) that are of practical interest. In this way the reversible Michaelis-Menten kinetics is reduced to a pseudo-first order reversible reaction. Thus, the actual rate of the isomerization of glucose to fructose, can be described by the following pseudo linear kinetics:

$$r(C_s) = k(C_s - C_{se}) = kC_{s0}(x - x_e) \tag{4}$$

Where the kinetic parameter, k, is a pseudo first order rate constant. The pseudo kinetic parameter is a function of the initial glucose concentration, C_{s0}, and temperature and can be written as [11]:

$$k = k'\,k'' \tag{5}$$

$$k' = \frac{1+k_e}{k_e}\,\frac{V_s}{k_s} \tag{6}$$

and k'' is given by:

$$k'' = \frac{1}{1+\lambda' C_{s0}} \tag{7}$$

where

$$\lambda' = \frac{2\lambda_0+\lambda_e}{3}; \qquad \lambda_0 = \frac{1}{k_s}; \qquad \lambda_e = \lambda_0 - \frac{k_e}{k_e+1}\Delta;$$

and $\Delta = \dfrac{1}{k_s} - \dfrac{1}{k_p}$

In this work, the experimental data published by Palazzi and Converti [11] for a given initial glucose concentation are utilized to show the linear dependency of the kinetic parameter k'' on temperature. Accordingly, we can write the slope of k'' as a function of temperature:

$$\frac{dk''}{dT} = -\left(\frac{C_{s0}}{(1+\lambda' C_{s0})^2}\right)\left(\frac{d\lambda'}{dT}\right) = -C_{s0}(k'')^2\left(\frac{d\lambda'}{dT}\right) \tag{8}$$

where

$$\frac{d\lambda'}{dT} = \frac{1}{3}\left(2\frac{d\lambda_0}{dT} + \frac{d\lambda_e}{dT}\right)$$

$$\frac{d\lambda_e}{dT} = \frac{d\lambda_0}{dT} - \left(\frac{k_e}{1+k_e}\right)\left(\frac{d\Delta}{dT}\right) + \Delta\frac{d}{dT}\left(\frac{k_e}{1+k_e}\right)$$

$$\frac{d\Delta}{dT} = \frac{d}{dT}\left(\frac{1}{k_s} - \frac{1}{k_p}\right) = -\left(\frac{E'_s}{T^2}\right)\left(\frac{1}{k_s}\right) + \left(\frac{E'_p}{T^2}\right)\left(\frac{1}{k_p}\right)$$

$$\frac{d\lambda_0}{dT} = \frac{d}{dT}\left(\frac{1}{k_s}\right) = -\left(\frac{E'_s}{T^2}\right)\left(\frac{1}{k_s}\right) = -\left(\frac{E'_s}{T^2}\right)\lambda_0 \tag{9}$$

For pseudo linear kinetics, as the operating temperature approaches the characteristic temperature, T_L, the value of k'' approaches the actual value of k'' at T_L. That is, when $k_p = k_s$ at $T = T_L$ then $\Delta = 0$, $\lambda_e = \lambda_0$, $\lambda' = \lambda_0 = (1/k_s)|_{T_L} = 1.175$ and $(k'')|_{T_L} = \dfrac{1}{1+\lambda_0 C_{s0}}$. And since the rate expression at T_L is linear, a linear function of temperature for k'' can be constructed at T_L and from the slope of k'' evaluated at T_L. Accordingly, we can write:

$$k'' = \beta(T - T_L) + \alpha \tag{10}$$

where:

$$\alpha = k''|_{T_L} = \frac{1}{1+\lambda_0 C_{s0}} = \frac{1}{1+1.175\,C_{s0}} \tag{11}$$

$$\beta = \frac{dk''}{dT}|_{T_L} = -C_{s0}\left((k'')^2\left(\frac{d\lambda'}{dT}\right)\right)_{T_L} =$$

$$-\left(\frac{C_{s0}}{(1+\lambda_0 C_{s0})^2}\right)\left(\frac{d\lambda'}{dT}\right)_{T_L} = \frac{0.031\;C_{s0}}{(1+1.175\;C_{s0})^2} \tag{12}$$

and:

$$\left(\frac{d\lambda'}{dT}\right)_{T_L} = -\left(\frac{1}{3}\,\frac{\lambda_0\left(E'_p - E'_s\right)}{T^2}\left(\frac{k_e}{1+k_e}\right) + \frac{E'_s\,\lambda_0}{T^2}\right)_{T_L}$$

In fact, it is found that the relative error in the above approximation increases linearly as a function of glucose concentration with a maximum value of 0.95 % at C_{s0} =3 mol/L in the temperature range of (60 to 80 °C).

In the presence of enzyme deactivation and substrate protection the actual reaction rate of the isomerization of glucose to fructose is given by:

$$r'(C_s) = r(C_s)a \tag{13}$$

The residual enzyme activity, $a = C_E/C_{E0}$, at any time t, assuming first order enzyme thermal deactivation with substrate protection [8, 18] can be written as:

$$\frac{da}{dt} = -k_d(1 - \sigma)a \qquad \text{at } t = 0,\ a = 1 \tag{14}$$

where the enzyme thermal deactivation rate constant, k_d, is given by:

$$k_d = k_{d0}e^{-E_d/RT} \tag{15}$$

The substrate protection factor for glucose isomerase is given by [8]:

$$\sigma = 0.5\,\frac{k_p\left[1+\frac{s'(1+k_e)}{C_{s0}}\right] + k_s k_e\left[1-\frac{s'(1+k_e)}{k_e C_{s0}}\right]}{k_s k_p\frac{1+k_e}{C_{s0}} + k_p\left[1+\frac{s'(1+k_e)}{C_{s0}}\right] + k_s k_e\left[1-\frac{s'(1+k_e)}{k_e C_{s0}}\right]} \tag{16}$$

$$s' = C_{s0}(x_e - x) \tag{17}$$

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2.2 Reactor Model

The modeling of the continuous immobilized enzyme packed bed reactor is expressed in terms of the recycle ratio, *Rc*. This ratio is defined according to Levenspiel [15], as the ratio of the volume of fluid returned to the reactor entrance to the net volume of fluid leaving the reactor configuration. Where the recycle ratio varies from zero to infinity, when ($Rc = 0$), the reactor corresponds to plug flow reactor, while ($Rc \to \infty$), the reactor approaches mixed flow reactor. Thus, this type of reactor provides means for obtaining various degrees of backmixing with the plug flow reactor. The following assumptions were used in modeling the reactor performance [1, 5, 19]: the enzyme deactivation is a rather slow process when compared to the mean residence time of reactants; no diffusional limitations; and the residual enzyme activity is considered as a weak function of substrate concentration along the reactor. These simplifying assumptions result in the following performance equation of the plug flow reactor with recycle [15]:

$$\frac{\tau_0}{C_{s_0}} = (Rc+1) \int_{(\frac{Rc}{Rc+1})x_e}^{x_e} \frac{dx}{r'(x)} \qquad 0 \le x \le x_e \tag{18}$$

Where τ_0 is the residence time in the reactor, x is the substrate conversion. And for pseudo linear kinetics the above performance equation could be reduced to the following algebraic form:

$$k\tau_0\ a + \ln\left(\frac{x_e - x}{x_e - \left(\frac{Rc}{Rc+1}\right)x}\right)^{Rc+1} = 0 \tag{19}$$

Accordingly, we can solve for the substrate conversion x, at any instant of time, t:

$$x(t) = x_e\left(\frac{1-e^{-k\tau_R a}}{1-\varphi\ e^{-k\tau_R a}}\right) \tag{20}$$

where

$$\varphi = \frac{Rc}{Rc+1} \qquad \text{and} \qquad \tau_R = \frac{\tau_0}{Rc+1} \tag{21}$$

Depending on the value of the recycle ratio, *Rc*, we can write:

$$x(t) = \begin{cases} x_e\left(1 - e^{-k\,\tau_0\ a}\right) & \text{if} \quad Rc \to 0 \\ x_e\left(\dfrac{k\tau_0\ a}{1+k\tau_0\ a}\right) & \text{if} \quad Rc \to \infty \end{cases}$$

For a specified residence time, τ_0, operating time period, t_f, feed substrate concentration, $C_{s0,}$ and $\theta = t/t_f$, the reactor performance is measured by the time-averaged productivity, which is defined as:

$$Pr(T) = \left(\frac{C_{s0}}{\tau_0}\right)\left[\int_0^{t_f} x(t)dt \Big/ \int_0^{t_f} dt\right] = \left(\frac{C_{s0}}{\tau_0}\right)\int_0^1 x(T,\theta)d\theta \tag{22}$$

2.3 Reactor Optimization by Disjoint Policy

For a given residence time and initial glucose concentration, the reactor productivity can be maximized. The optimization problem is formulated as a constrained nonlinear programming problem. The formulation is in terms of maximization of fructose productivity as the objective function given by Eq. (22). The constraints are reactor performance Eq. (19), enzyme deactivation Eq. (14), and the bounds on the reactor operating temperature (T^L and T^U).

Instead of using constrained nonlinear programming methods, fructose productivity, *Pr(T)*, can be maximized using the calculus of variations and in particular by applying the disjoint policy [13]. According to this policy, it is sufficient to maximize $x(T(\theta))$ at each value of θ in order to determine the optimal operating temperature profile $T(\theta)$, which maximizes the reactor productivity. As a result of using this policy the necessary condition of optimality leads to a pair of coupled nonlinear first-order differential equations (ODEs) of the initial value type. This differential equation system defines the optimal temperature profile completely (see Appendix A). Accordingly, for packed bed reactors with recycle, the necessary condition of optimality leads to:

$$\frac{dT}{d\theta} = \frac{t_f k_d(1-\sigma)a}{\left(\frac{a}{k}\right)\left(\frac{dk}{dT}\right) + \frac{\left(1-e^{-k\tau_R a}\right)\left(1-\varphi e^{-k\tau_R a}\right)}{k\,x_e\tau_R(1-\varphi)e^{-k\tau_R a}}\left(\frac{dx_e}{dT}\right)} \tag{23}$$

$$\frac{da}{d\theta} = -t_f k_d(1-\sigma)a \tag{24}$$

$$T = T_0 \qquad \text{and} \qquad a = 1 \qquad \text{at} \qquad \theta = 0$$

Depending on the value of the recycle ratio, we can write:

– For the plug flow reactor:

$$\frac{dT}{d\theta} = \frac{t_f k_d(1-\sigma)a}{\left(\frac{a}{k}\right)\left(\frac{dk}{dT}\right) + \frac{\left(1-e^{-k\tau_0 a}\right)}{k\,x_e\tau_0\ e^{-k\,\tau_0\ a}}\left(\frac{dx_e}{dT}\right)} \tag{25}$$

– For the mixed flow reactor:

$$\frac{dT}{d\theta} = \frac{t_f k_d(1-\sigma)a}{\left(\frac{a}{k}\right)\left(\frac{dk}{dT}\right) + \frac{a}{x_e}(1+k\,\tau_0\ a)\left(\frac{dx_e}{dT}\right)} \tag{26}$$

The maximum fructose productivity can be achieved, if the initial temperature, T_0, which is bound between T^L and T^U, is selected in such a way that the solution of Eqs. (24) and (25) (plug flow reactor), or Eqs. (24) and (26) (mixed flow reactor), satisfy the optimality condition [13]. This can be stated mathematically as:

$$\underset{T^L \le T_0 \le T^U}{\text{Maximize}} \quad Pr(T_0) \tag{27}$$

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3 Numerical Examples

The production of high fructose corn syrup using immobilized glucose isomerase (IGI) is considered as one of the most important commercial applications of immobilized enzymes. The literature on the isomerization of glucose to fructose with immobilized glucose isomerase is quite comprehensive [1, 2, 5–9, 11–13]. The kinetic parameters for this reaction are reported for the temperature range of (60, 80 °C) [13] and they are listed in Tab.1.

Table 1. Kinetic parameters for the isomerization of glucose into fructose [13].

Kinetic parameter	k_0	E_a/R (K)
k_s *(mol/L)*	*431.63*	*2138.0*
k_p *(mol/L)*	1.7539×10^9	*7360.9*
k_e *(–)*	*385.71*	*1996.4*
V_s *(mol/L ·h)*	1.16968×10^{10}	*7163.9*
V_p *(mol/L · h)*	1.55×10^{14}	*10469.0*
k_d (h^{-1})	6.2717×10^{23}	*20551.8*

For both plug and mixed flow immobilized reactors, the optimal reactor productivity, which is a measure of the reactor performance, is calculated at different operating periods and residence times. Accordingly, the optimal operating temperature profiles could be determined. Operating the reactor at such optimal profiles is necessary to achieve maximum fructose productivity.

The typical initial glucose concentration, C_{s0}, of 2.8 mol/L, is used [1, 5]. The lower and upper bounds on the temperature profile are 55 °C and 80 °C, respectively [5]. For the pseudo steady state hypothesis to be valid, the reactor residence time, τ, is in the order of hours. However, it is in the order of 1 to 100 days of magnitude with respect to the enzyme deactivation [5]. Accordingly, the reactor residence times of 0.5 and 1.0 h, and different operating periods of 50, 100, 500, and 1000 h are considered, where the reactor operation period is specified based on the characteristic life curve of the immobilized enzyme. The optimal initial temperature, T_0 that maximizes the reactor productivity given by Eq. (22) can be found by solving Eqs. (24) and (25), or Eqs. (24) and (26) using the above initial conditions. The solution proceeds numerically using the fourth and fifth orders Runge-Kutta methods with variable integration step, and the quadratic interpolation search algorithm [20].

The optimal profiles of temperature, conversion, and residual enzyme activity are shown in Figs.1 through 6 at different reactor residence times and operating periods for both reactors. The variable optimal temperature of operation is characterized by an increasing temperature profiles, which is in agreement with the previous works and constant conversion for most of the operating periods followed by reduction in conversion [13, 17, 21]. As it can be seen from these figures, at low operating periods, the temperature profiles hit the upper temperature bound, while it tends to move away from it at long operating periods. For the mixed flow reactor, the substrate conversion is lower than that for the plug flow reactor. Due to this, the residual enzyme activity in the mixed flow reactor is higher than of the plug flow reactor because of the enzyme substrate protection at low operating periods (see Fig. 5a). This protection is a complex function of temperature and glucose concentration and has a significant effect on the enzyme stability.

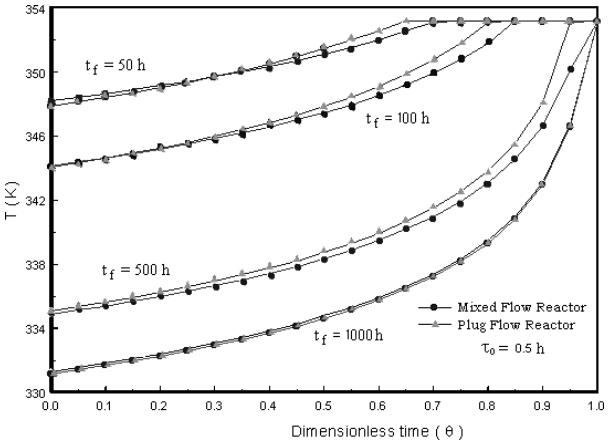

Figure 1. Optimal temperature profiles for mixed and plug flow glucose isomerase reactors under varying temperature operation at τ_0 = 0.5 h.

As it can be seen from Fig. 5a at τ_0 = 1.0 h and low operating periods, the residual enzyme activity in the mixed flow reactor is higher than that for the plug flow reactor. This allows the mixed flow reactor to operate at lower temperature than the plug flow reactor, which is evident in Fig. 4. As the operating period increases, the conversion in the mixed flow reactor increases in comparison with the conversion at τ_0 = 0.5 h (see Figs. 3 and 6). Accordingly, there is less glucose to protect the enzyme thus resulting in lower enzyme activity as indicated by Fig. 5, which is manifested by the increase in the temperature profile as a function of time as shown in Fig. 4. This means that the two reactors after a long period of operation have not enough substrate concentration to protect the enzyme due to a high level of conversion and both have almost the same optimal temperature profiles. For small values (τ_0 = 0.5 h) the degrees of conversions are not so high relative to that at τ_0 = 1.0 h during the operating period of time and hence the effect of substrate protection on the enzyme stability is almost the same for both reactors (see Figs. 2 and 5).

The optimal productivities for the constant optimal temperature and that under variable temperature of operation are compared in Tabs. 2, 3, 4, and 5. It is clear that the rising temperature profile improves the productivity of both plug flow and mixed flow reactor. On the other hand the improvement in reactor productivity for the plug flow reactor is significant in comparison with the mixed flow reactor for both operating policies, where an average improvement of

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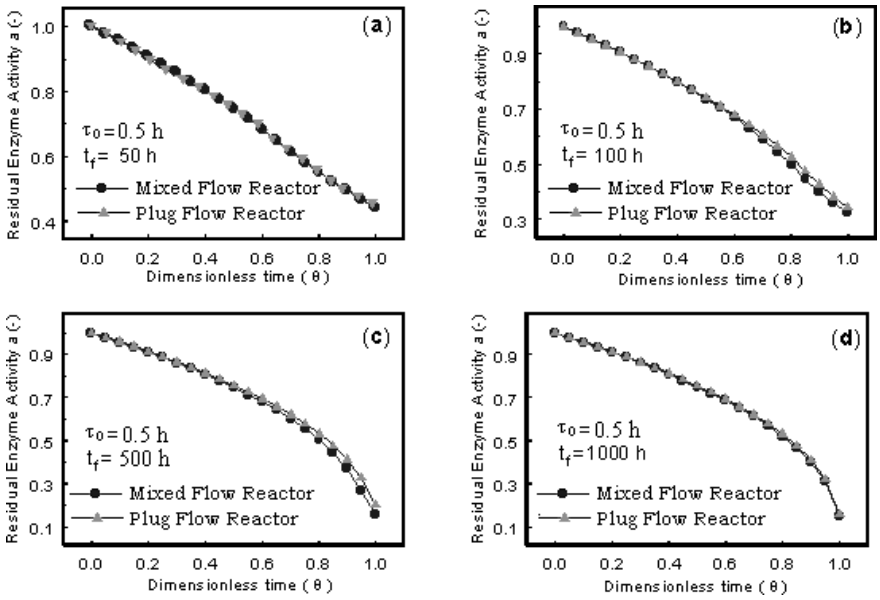

Figure 2. Time course of IGI enzyme deactivation of plug and mixed flow glucose isomerase reactors under varying optimal temperature operation at $\tau_0 = 0.5$ h.

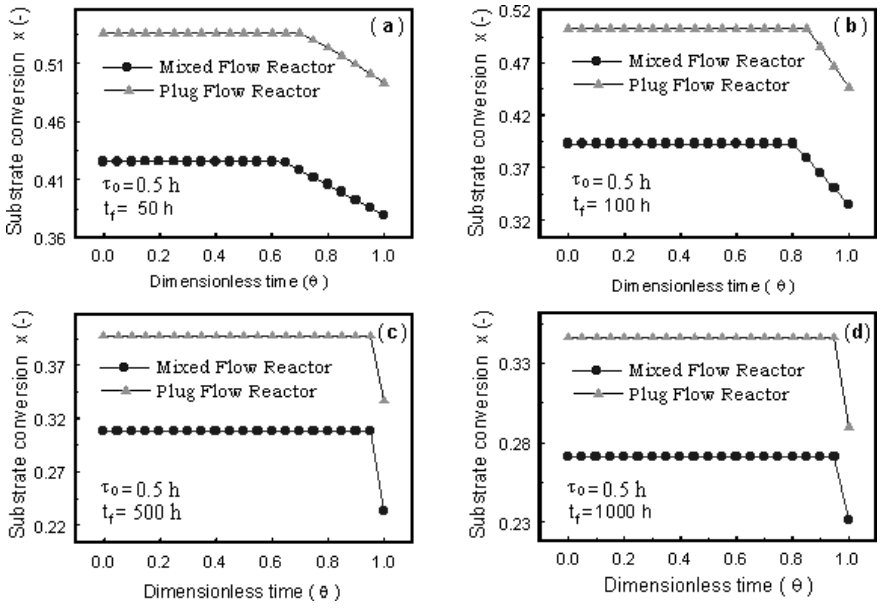

Figure 3. Substrate conversion of plug and mixed flow glucose isomerase reactors under varying optimal temperature operation at $\tau_0 = 0.5$ h.

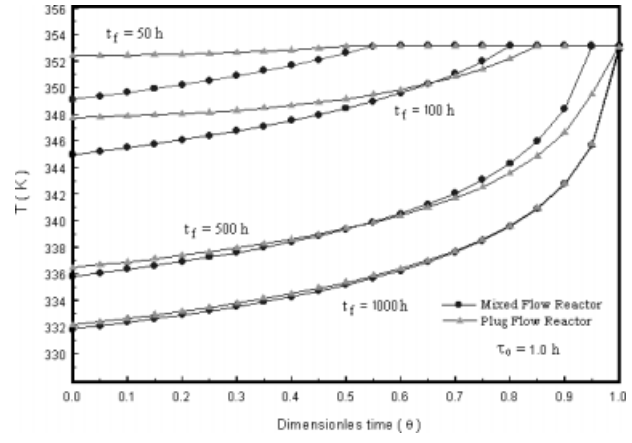

Figure 4. Optimal temperature profiles for mixed and plug flow glucose isomerase reactors under varying temperature operation at $\tau_0 = 1.0$ h.

28 % at τ_0 of 0.5 h, and of 24 % at τ_0 of 1 h, respectively. For the plug flow reactor, the productivity improvement in comparison with the constant optimal temperature is about 1.2 % to 6.3 % at a residence time of 0.5 h, and from 1.2 % to 4.4 % at a residence time of 1.0 h. Whereas the improvement in productivity for mixed flow reactor ranges from 1.3 % to 5.5 % at τ_0 of 0.5 h, and from 0.6 % to 4.3 % at τ_0 of 1 h, respectively.

As it can be seen from the results that the optimum productivity under constant and variable temperature of operation seems to be nearly equal for short operating periods (say less than 100 h). This is because of less enzyme deactivation, where at 50 % of the operating time the enzyme activity is around 80 %, as it can be seen from Figs. 2 and 5, respectively. Under these conditions the loss of enzyme activity is rather slow, and hence the substrate conversion

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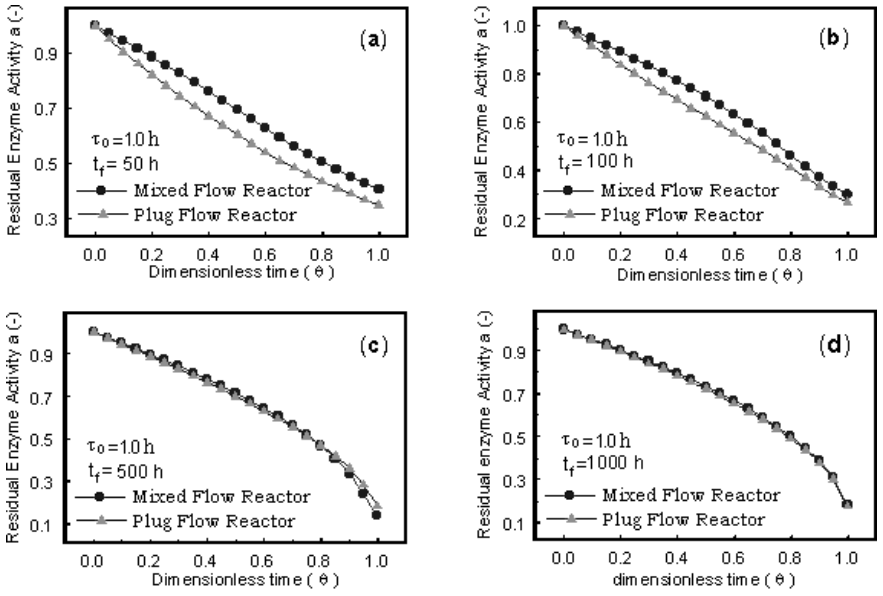

Figure 5. Time course of IGI enzyme deactivation of plug and mixed flow glucose isomerase reactors under varying optimal temperature operation at τ_0 = 1.0 h.

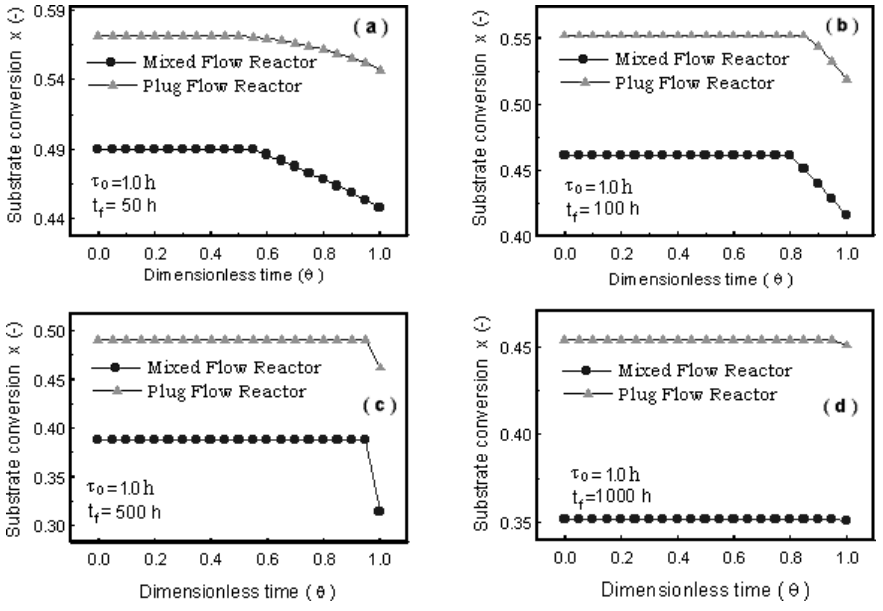

Figure 6. Substrate conversion of plug and mixed flow glucose isomerase reactors under varying optimal temperature operation at τ_0 = 1.0 h.

becomes nearly dependent on the reaction rate and on the temperature solely. This shifts the optimal operating temperature towards the maximum permissible ones as shown in Figs. 1 and 4, respectively.

4 Conclusion

In this work, it is shown that, from the numerical point of view, the present method is simple and also general for any immobilized packed bed reactor with linear reversible kinetics and first order enzyme deactivation. This method involves only the solution of two ODEs of the initial value type during a one-dimensional unconstrained optimization with bounds on the reactor operating temperature.

Appendix A: Derivation of the Optimal Temperature Profile Using the Disjoint Policy

According to the disjoint policy [22], to get maximum fructose productivity *Pr(T)*, the integral given by Eq. (22), it is sufficient to maximize the integrand $x(T(\theta))$ at each value of the dimensionless time θ. In this way the optimal operating temperature profile $T^*(\theta)$, which maximizes the reactor productivity could be determined. Mathematically, the dis-

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Table 2. Fructose productivity under constant optimal temperature operation of plug flow reactor with respect to mixed flow reactor at τ_0 = 0.5 h and C_{s0} = 2.8 mol/L.

t_f (h)	Plug flow reactor		Mixed flow reactor		% Improvement in *Pr*
	*T** (K)	*Pr* (mol/L·h)	*T** (K)	*Pr* (mol/L·h)	
50	351.6	2.936	351.8	2.308	27.2
100	347.4	2.714	347.6	2.109	28.7
500	338.4	2.101	338.6	1.636	28.4
1000	334.8	1.818	334.9	1.433	28.9

*T**: optimal constant temperature

Table 3. Fructose productivity under constant optimal temperature operation of plug flow reactor with respect to mixed flow reactor at τ_0 = 1.0 h and C_{s0} = 2.8 mol/L.

t_f (h)	Plug flow reactor		Mixed flow reactor		% Improvement in *Pr*
	*T** (K)	*Pr* (mol/L·h)	*T** (K)	*Pr* (mol/L·h)	
50	353.0	1.590	352.5	1.339	18.7
100	349.2	1.524	348.4	1.254	21.5
500	338.9	1.326	339.1	1.041	27.3
1000	335.0	1.216	335.3	0.944	28.8

*T**: optimal constant temperature

Table 4. Fructose productivity under variable optimal temperature operation of plug flow reactor with respect to mixed flow reactor at τ_0 = 0.5 h and C_{s0} = 2.8 mol/L.

t_f (h)	Plug flow reactor		Mixed flow reactor		% Improvement in *Pr*
	T_0 (K)	*Pr* (mol/L·h)	T_0 (K)	*Pr* (mol/L·h)	
50	348.2	2.970	347.8	2.338	27.0
100	344.1	2.793	344.1	2.169	28.8
500	334.9	2.218	335.1	1.718	29.1
1000	331.2	1.933	331.3	1.512	27.8

T_0: optimal initial temperature for variable operation

Table 5. Fructose productivity under variable optimal temperature operation of plug flow reactor with respect to mixed flow reactor at τ_0 = 1.0 h and C_{s0} = 2.8 mol/L.

t_f (h)	**Plug flow reactor**		Mixed flow reactor		% Improvement in *Pr*
	T_0 (K)	*Pr* (mol/L·h)	T_0 (K)	*Pr* (mol/L·h)	
50	352.4	1.590	349.1	1.347	18.0
100	347.8	1.542	345.0	1.278	20.7
500	336.5	1.371	335.8	1.081	26.8
1000	332.1	1.269	331.8	0.985	28.8

T_0: optimal initial temperature for variable operation

joint policy states that: $x(T^*(\theta)) \geq x(T(\theta))$ for all θ, where the function $T(\theta)$ is any feasible temperature profile satisfying the constraints.

As a result of applying this policy [13], the necessary condition of optimality states that:

$$\left(\frac{dx}{dT}\right) = 0 \tag{A1}$$

Applying this condition to Eq. (20) we get:

$$\left(\frac{dx}{dT}\right) = \left(\frac{1-e^{-k\,\tau_R{}^a}}{1-\varphi e^{-k\,\tau_R{}^a}}\right)\left(\frac{dx_e}{dT}\right)$$

$$+\left(x_e\right)\left(\frac{d}{dT}\left(\frac{1-e^{-k\,\tau_R{}^a}}{1-\varphi e^{-k\,\tau_R{}^a}}\right)\right) = 0 \tag{A2}$$

where:

$$\frac{d}{dT}\left(\frac{1-e^{-k\,\tau_R{}^a}}{1-\varphi e^{-k\,R^a}}\right) = \frac{\left(\left(1-\varphi e^{-k\,\tau_R{}^a}\right)\frac{d}{dT}\left(1-e^{-k\,\tau_R{}^a}\right)\right)}{\left(1-\varphi e^{-k\,\tau_R{}^a}\right)^2}$$

$$-\frac{\left(\left(1-e^{-k\,\tau_R{}^a}\right)\frac{d}{dT}\left(1-\varphi e^{-k\,\tau_R{}^a}\right)\right)}{\left(1-\varphi e^{-k\,\tau_R{}^a}\right)^2} \tag{A3}$$

$$\frac{d}{dT}\left(1-\varphi e^{-k\,\tau_R{}^a}\right) = \left(\tau_R\ \varphi e^{-k\,\tau_R{}^a}\right)\left(\frac{d(ka)}{dT}\right) \tag{A4}$$

$$\frac{d}{dT}\left(1-e^{-k\,\tau_R{}^a}\right) = \left(\tau_R\ e^{-k\,\tau_R{}^a}\right)\left(\frac{d(ka)}{dT}\right) \tag{A5}$$

Accordingly, we can write Eq. (A2) as follows:

$$\left(\frac{dx_e}{dT}\right)\left(\frac{1-e^{-k\ \tau_R{}^a}}{1-\varphi e^{-k\ \tau_R{}^a}}\right) - \frac{\left((1-\varphi)\ x_e\ \tau_R\ e^{-k\ \tau_R{}^a}\right)\left(\frac{d(ka)}{dT}\right)}{\left(1-\varphi e^{-k\ \tau_R{}^a}\right)^2} = 0 \tag{A6}$$

Solving Eq. (A6) for $\frac{d(ka)}{dT}$, we can write:

$$\frac{d(ka)}{dT} = -\left(\frac{\left(1-e^{-k\ \tau_R{}^a}\right)\left(1-\varphi e^{-k\ \tau_R{}^a}\right)}{(1-\varphi)\ x_e\ \tau_R\ e^{-k\ \tau_R{}^a}}\right)\left(\frac{dx_e}{dT}\right) \tag{A7}$$

Since both *k* and *a* are functions of temperature we have:

$$\frac{d}{dT}(ka) = k\left(\frac{da}{dT}\right) + a\left(\frac{dk}{dT}\right) \tag{A8}$$

By using Eq. (A7), we can write Eq. (A8) as follows:

$$\frac{da}{dT} = -\left(\left(\frac{a}{k}\right)\left(\frac{dk}{dT}\right) + \frac{\left(1-e^{-k\ \tau_R{}^a}\right)\left(1-\varphi e^{-k\ \tau_R{}^a}\right)\left(\frac{dx_e}{dT}\right)}{(1-\varphi)k\ x_e\ \tau_R\ e^{-k\ \tau_R{}^a}}\right) \tag{A9}$$

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Note that Eq. (14) in terms of dimensionless time θ can be written as:

$$\frac{da}{d\theta} = -t_f k_d (1-\sigma) a \tag{A10}$$

Now, by making use of the chain rule:

$$\frac{da}{d\theta} = \left(\frac{dT}{d\theta}\right)\left(\frac{da}{dT}\right)$$

and by eliminating da/dT and $da/d\theta$ between Eqs. (A9) and (A10) we obtain the desired result:

$$\frac{dT}{d\theta} = \frac{t_f k_d (1-\sigma) a}{\left(\frac{a}{k}\right)\left(\frac{dk}{dT}\right) + \frac{\left(1-e^{-k\ \tau_R a}\right)\left(1-\varphi e^{-k\ \tau_R a}\right)}{k x_e\ \tau_R (1-\varphi) e^{-k\ \tau_R a}}\left(\frac{dx_e}{dT}\right)} \tag{A11}$$

$$\frac{da}{d\theta} = -t_f k_d (1-\sigma) a \tag{A12}$$

with the initial conditions:

$T = T_0$ and $a = 1$ at $\theta = 0$ with $T^L \le T_0 \le T^U$

where:

$$\frac{dk}{dT} = k'\left(\frac{dk''}{dT}\right) + k''\left(\frac{dk'}{dT}\right)$$

$$\frac{dk'}{dT} = \frac{V_s}{k_s}\left[\frac{1}{x_e}\left(\frac{E'_{vs} - E'_s}{T^2}\right) - \frac{1}{x_e^2}\left(\frac{dx_e}{dT}\right)\right]$$

$$\frac{dk''}{dT} = \beta;\ x_e = \frac{k_e}{1+k_e} \text{ and}$$

$$\frac{dx_e}{dT} = \left(\frac{E'_e}{T^2}\right)\left(\frac{x_e^2}{k_e}\right)$$

If $Rc = 0$, which corresponds to plug flow reactor, then $\phi = 0$ and $\tau_R = \tau_0$, we obtain Eq. (25). For mixed flow reactor, when $Rc \to \infty$, then $\phi = 1$ and $\tau_R \to 0$ and by applying L'Hopital's rule we get Eq. (26).

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Symbols used

a	[–]	residual enzyme activity
C_E	[mol/L]	concentration of active enzyme
C_{E0}	[mol/L]	initial concentration of active enzyme
C_s	[mol/L]	substrate concentration
C_{s0}	[mol/L]	initial substrate concentration
E	[–]	enzyme
E_a	[J/mol]	activation energy
E_e	[J/mol]	activation energy at equilibrium
E_p	[J/mol]	activation energy of Michaelis-Menten constant for product
E_s	[J/mol]	activation energy of Michaelis-Menten constant for substrate
E_{Vp}	[J/mol]	activation energy of maximum reaction rate for product
E_{Vs}	[J/mol]	activation energy of maximum reaction rate for substrate
ES	[–]	enzyme substrate complex
k	[1/h]	pseudo first order rate constant
k'	[1/h]	parameter defined in Eq.(6)
k''	[–]	parameter defined in Eq.(7)
k_1, k_{-2}	[L/(mol·h)]	rate constants
k_{-1}, k_2	[1/h]	rate constants
k_e	[–]	equilibrium constant
k_d	[1/h]	enzyme thermal deactivation rate constant
k_m	[mol/L]	apparent Michaelis-Menten constant
K'_m	[L/mol]	reciprocal of K_m
k_p	[mol/L]	Michaelis-Menten constant for product
k_s	[mol/L]	Michaelis-Menten constant for substrate
P	[–]	product
Pr	[mol/L · h]	fructose productivity
R	[J/mol · K]	ideal gas constant
Rc	[–]	recycle ratio
r	[mol/L · h]	reaction rate
r'	[mol/L · h]	reaction rate with enzyme deactivation
s'	[mol/L]	apparent substrate concentration defined as $s' = C_{s0}(x_e - x)$
T	[K]	temperature
T^L	[K]	lower temperature bound
T^U	[K]	upper temperature bound
T^*	[K]	optimum temperature
T_0	[K]	initial temperature
t	[h]	time
t_f	[h]	reactor operating period
V_m	[mol/L · h]	maximum apparent reaction rate
V_p	[mol/L · h]	maximum reaction rate for product
V_s	[mol/l · h]	maximum reaction rate for substrate
x	[–]	substrate conversion
x_e	[–]	equilibrium substrate conversion

Greek symbols

α	[–]	intercept of k'' defined in Eq. (11)
β	[1/K]	slope of k'' defined in Eq. (12)
Δ	[L/mol]	kinetic parameter
φ	[–]	parameter defined in Eq. (21)
λ'	[L/mol]	kinetic parameter
λ_0	[L/mol]	reciprocal of k_s
λ_e	[L/mol]	kinetic parameter
θ	[–]	dimensionless operating time
σ	[–]	substrate protection factor
τ_R	[h]	parameter defined in Eq.(21)
τ_0	[h]	reactor residence time

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Subscripts

e	equilibrium
p	product
s	substrate
0	initial or pre-exponential factor

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