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Optimization of glucose isomerase reactor: optimum operating temperature mode

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Abstract The optimum temperature operation mode required to achieve high fructose productivity is studied for immobilized glucose isomerase (GI) packed bed reactor. In this study, the reactor design equation based on reversible Michaelis-Menten kinetics assumes both thermal enzyme deactivation and substrate protection. The optimization problem is formulated as a discretized constrained nonlinear programming problem (NLP). The formulation is expressed in terms of maximization of fructose productivity as the objective function subject to reactor design equation, kinetic parameter equations, substrate protection factor equation and feasibility constraints. The constraints are discretized along the reactor operating period by employing piecewise polynomial approximations. Approximately 7% improvement in terms of fructose productivity is achieved when running the reactor at the optimum decreasing temperature operation mode as compared to the constant optimum isothermal operation.

List of symbols

a		residual enzyme activity
$b_{k+1,j}$		jth coefficient of second degree polynomial defined on element $k+1$
E	[mg/l]	concentration of active enzyme
E_0	[mg/l]	initial concentration of active enzyme
k_d	[h^{-1}]	first order thermal deactivation rate constant
k_e		equilibrium constant
k_m	[mole/l]	apparent Michaelis constant
k_p	[mole/l]	Michaelis constant for product
k_s	[mole/l]	Michaelis constant for substrate
n		number of time intervals
NE		number of elements
s'	[mole/l]	apparent substrate concentration
s_0	[mole/l]	substrate concentration at reactor inlet
$P_{k+1}(t)$		a polynomial defined on element $k+1$
Pr	[mole fructose/lh]	time average reactor productivity
T	[K]	temperature
T^{Lower}	[K]	lower temperature bound
T^{Upper}	[K]	upper temperature bound
t	[h]	operating time
t_f	[h]	operating period
t_i	[h]	operating time at node point i
v_m	[mole/lh]	maximum apparent reaction rate
v_p	[mole/lh]	maximum reaction rate for product
v_s	[mole/lh]	maximum reaction rate for substrate
x		substrate fractional conversion
x_e		substrate fractional conversion at equilibrium

Greek symbols

ε		very small positive real number
ϕ_i		a function of time defined on interval i
θ		dimensionless operating time
θ_i		dimensionless operating time at node point i
τ	[h]	residence time
σ		substrate protection factor

Special symbols

$[\ ]_i$	the expression in parenthesis is a function of the dimensionless operating time θ_i at node point i

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1 Introduction

The problem of determining the optimum operation mode for immobilized enzyme reactors is important when it is desired to improve the operational economics and product yield. This operational problem of reactors with deactivating catalysts can be stated as: how to best operate the reactor during a run. There are various factors affecting

biochemical reactor operation such as temperature and pH. Since temperature is one of the most important factors affecting enzyme activity, substrate protection factor, kinetic parameters, and reaction rate, this operational problem reduces to finding the best temperature progression mode during the run. This operational problem leads to two types of temperature operation modes, either a rising temperature mode with time, or the maximum allowable temperature [1]. If enzyme deactivation is very temperature sensitive, then the operation mode to use is a rising temperature with time so as to keep the outlet conversion from the reactor constant during the run [1]. When the outlet conversion can no longer be maintained during the run time, the conversion level must be adjusted accordingly. One such desired reactor operation is to achieve high product productivity subjected to enzyme thermal deactivation. Determining the optimum temperature operation mode of the reactor is of practical and industrial interest. As an example of such commercial process in the bio-industry is the production of high fructose corn syrup (HFCS). In such a process, glucose is converted into fructose by the enzyme glucose isomerase (GI) while passing through the reactor packed with immobilized glucose isomerase [2]. The isomerization of glucose syrup to fructose syrup is described by a reversible Michaelis- Menten kinetics.

Most of the published work on determining the optimum temperature operation mode for a continuous reactor are about obtaining high product productivity at a fixed conversion [3, 4, 5], or a preprogrammed optimal temperature operation mode [6, 7]. The optimization method employed is based on Pontryagin's maximum principle. The main disadvantage of the methods derived from the maximum principle is in the tedious preparation of the problem [8].

As a variation to the above modes of operation is to find the actual temperature progression with time so as to maximize product yield while staying within certain temperature bounds. The objective of this work is to determine the optimum temperature operation mode of glucose isomerase (GI) reactor under enzyme deactivation and substrate protection, such that maximum fructose productivity is obtained. Since the optimization formulation is a function of operating time, the problem is formulated as a discretized constrained nonlinear programming problem (NLP). The constraints are discretized along the reactor operating period by employing piecewise polynomial approximations.

2
Problem formulation via nonlinear programming

In order to achieve high fructose productivity, the immobilized glucose isomerase packed bed reactor based on reversible Michaelis-Menten kinetics subject to the design equation with enzyme deactivation and substrate protection can be operated optimally. There are various factors affecting reactor operations such as temperature and pH. Temperature is one of the most important factors affecting the enzyme activity, substrate protection factor, kinetic parameters, and the isomerization reaction rate. The problem is to select the actual temperature operation mode i.e. temperature profile to operate the reactor which gives the highest time average productivity over the operating period. For a given residence time τ and initial glucose (substrate) concentration s_0, selection of the optimal temperature mode, $T(t)$, which maximizes the time average productivity Pr of glucose to fructose over the operating period t_f, $t \in [0, t_f]$ is an optimization problem. The problem formulation is published in a previous publication [5], and can be stated as:

$$\underset{T(t),x(t)}{\text{Maximize}} \ \ \mathrm{Pr} = \left(\frac{s_0}{\tau}\right)\left[\frac{\int_0^{t_f} x(t)\,\mathrm{d}t}{\int_0^{t_f} \mathrm{d}t}\right] \ .$$

subject to:

$$s_0 x(t) - k_m(T(t)) \ln\left[1 - \frac{x(t)}{x_e(T(t))}\right] = v_m(T(t))\tau\, a(t) \ ,$$

$$k_p = 1.7539 * 10^9 * \mathrm{e}^{-7360.939/T(t)} \ ,$$

$$k_s = 431.6294 * \mathrm{e}^{-2138.035/T(t)} \ ,$$

$$v_s = 1.1696798 * 10^{10} * \mathrm{e}^{-7163.882/T(t)} \ ,$$

$$v_p = 1.5503 * 10^{14} * \mathrm{e}^{-10469.39/T(t)} \ ,$$

$$k_d = 6.2716819 * 10^{23} * \mathrm{e}^{-20551.81/T(t)} \ ,$$

$$k_e = 385.7142 * \mathrm{e}^{-1996.4/T(t)} \ ,$$

$$x_e(T(t)) = \frac{k_e}{1 + k_e} \ ,$$

$$a = \frac{E}{E_0} = e^{-(1-\sigma(x(t),T(t)))k_d(T(t))t} \ ,$$

$$v_m(T(t)) = \left(\frac{v_s k_p}{k_p - k_s}\right)\left(1 + \frac{1}{k_e}\right) \ ,$$

$$k_m(T(t)) = \left(\frac{k_p k_s}{k_p - k_s}\right)\left[1 + \left(\frac{k_e}{k_p} + \frac{1}{k_s}\right)\left(\frac{s_0}{1 + k_e}\right)\right] \ ,$$

$$\sigma(x(t), T(t)) = \frac{0.5\left[k_p\left(1 + \frac{s'(1+k_e)}{s_0}\right) + k_s k_e\left(1 - \frac{s'(1+k_e)}{k_e s_0}\right)\right]}{\left[k_p k_s\left(\frac{(1+k_e)}{s_0}\right) + k_p\left(1 + \frac{s'(1+k_e)}{s_0}\right) + k_s k_e\left(1 - \frac{s'(1+k_e)}{k_e s_0}\right)\right]} \ ,$$

$$s' = s_0(x_e(T(t)) - x(t)) \ ,$$

$$T^{\text{Lower}} \le T(t) \le T^{\text{Upper}} \quad \text{for all } t \in [0, t_f] \ ,$$

$$0.0 \le x(t) \le x_e(T(t)) \quad \text{for all } t \in [0, t_f] \ .$$

Note that, in the above formulation, the variables $T(t)$ and $x(t)$ are functions of operating time t, for which we do not know explicitly their functional forms. The reactor design equation, substrate protection factor σ, and the kinetic parameters functional relationships to operating temperature i.e. k_p, k_s, v_s, v_p, k_d, k_e, x_e, v_m, and k_m are published in reference [9].

In order, to solve the above optimization problem, you can think of the true optimal temperature profile, $T(t)$, being approximately represented by some functional form given as [10]:

$$T(t) = b_0\phi_0(t) + b_1\phi_1(t) + \ldots + b_n\phi_n(t) = \sum_{i=0}^{n} b_i\phi_i(t) \quad , \tag{1}$$

where $\phi_i(t)$, $i = 0, 1, \ldots, n$ are functions of time and the form of $\phi_i(t)$ must be *specified*. This approximation results in $n+1$ variables $b_0, b_1, \ldots, b_n$ that must be adjusted to fit the desired temperature profile $T(t)$ according to the above objective function. The selection of the form of $\phi_i(t)$ requires more physical insight of the problem at hand. In the absence of a physical feeling for the optimum temperature profile, $T(t)$, a very general functional form such as a polynomial may be used.

Let the operating period t_f, $t \in [0, t_f]$, be discretized into $n+1$ distinct node points $t_0, t_1, \ldots, t_n$ such that: $t_0 < t_1 < t_2 < \ldots < t_n$. The operating period $[0, t_f]$, is divided into n different time intervals $[t_0, t_1], [t_1, t_2], \ldots [t_{n-1}, t_n]$. In this case, the temperature profile, $T(t)$, would be approximated by a polynomial of degree n, defined as:

$$T(t) = b_0 + b_1 t + b_2 t^2 + \ldots + b_n t^n = \sum_{i=0}^{n} b_i t^i \quad . \tag{2}$$

For an accurate approximation, this would require that the number of intervals, n, to be very large. Thus, instead of approximating the temperature profile, $T(t)$, by one polynomial covering the whole range of operating period t_f, $t \in [0, t_f]$, we use *piecewise polynomial approximations* defined on time intervals. This representation would result in more accurate approximation of the temperature profile.

To begin discussion of piecewise polynomial approximations, let $\{P_{k+1}(t) \mid k = 0, 1, 2, \ldots, NE-1\}$ be a sequence of NE second degree polynomials. Each $P_{k+1}(t)$ is defined over an element $k+1$ and its corresponding piecewise temperature profile $T(t)$ over element $k+1$ is given by:

$$T(t) = P_{k+1}(t) = b_{k+1,0} + b_{k+1,1}t + b_{k+1,2}t^2 = \sum_{j=0}^{2} b_{k+1,j}\, t^j \quad t_{2k} \le t \le t_{2k+2} \quad k = 0, 1, \ldots, NE-1 \quad . \tag{3}$$

Where NE is the total number of elements. An element consists of 2 adjacent time intervals, and elements do not overlap. For element $k+1$, the two adjacent intervals are $[t_{2k}, t_{2k+1}]$ and $[t_{2k+1}, t_{2k+2}]$ and it is given by $[t_{2k}, t_{2k+1}] \cup [t_{2k+1}, t_{2k+2}]$. For each element $k+1$, we have three variables $b_{k+1,0}$, $b_{k+1,1}$ and $b_{k+1,2}$ that must be adjusted. A total of $3NE$ variables $b_{1,0}, b_{1,1}, b_{1,2}, b_{2,0}, b_{2,1}, b_{2,2}, \ldots, b_{NE,0}$, $b_{NE,1}, b_{NE,2}$ are introduced in the formulation.

To make the problem well posed, an additional set of equations is added to make the set of polynomials $P_{k+1}(t)$ continuous at the common interior node points, t_{2k+2}, between two adjacent elements, $k+1$, and, $k+2$. This is done by enforcing the following constraints:

$$b_{k+1,0} + b_{k+1,1}t_{2k+2} + b_{k+1,2}(t_{2k+2})^2 = b_{k+2,0} + b_{k+2,1}t_{2k+2} + b_{k+2,2}(t_{2k+2})^2 \quad k = 0, 1, \ldots, NE-2 \quad . \tag{4}$$

As for the conversion $x(t)$, since it is a function of operating time t, it will be discretized at the node points as $x(t_0), x(t_1), x(t_2), \ldots, x(t_n)$. In this case, an additional $n+1$ variables will be introduced.

From the definition of the residual enzyme activity, it can be seen that, $a(t)$, decreases exponentially with time. To reflect this fact in the above formulation so that a feasible solution can be obtained, i.e. a physically possible reactor operation, we enforce the following feasibility constraints on the residual enzyme activity at the discretized node points:

$$a(t_i) > a(t_{i+1}) \quad . \tag{5}$$

The above residual enzyme feasibility constraints will be converted into inequalities as follows:

$$a(t_i) \ge a(t_{i+1}) + \varepsilon \quad i = 0, 1, \ldots, n-1 \quad , \tag{6}$$

where ε is a very small positive real number, and this introduces an extra n inequalities.

Let θ be a dimensionless time, defined as $\theta = \frac{t}{t_f}$, where $\theta \in [0, 1]$. With this change of variables and the above added constraints, the original optimization problem will be formulated as a nonlinear programming problem (discretized NLP) as follows:

$$\underset{T(\theta), x(\theta)}{\text{Maximize}}\ \Pr = \left(\frac{s_0}{\tau}\right)\left[\int_0^1 x(\theta)\mathrm{d}\theta\right] = \left(\frac{s_0 t_f}{\tau}\right)\left[\sum_{i=0}^{n-1}\left(\frac{x(\theta_i) + x(\theta_{i+1})}{2}\right)(\theta_{i+1} - \theta_i)\right] \quad ,$$

subject to:

$$s_0 x(\theta_i) - k_m(T(\theta_i)) \ln\left[1 - \frac{x(\theta_i)}{x_e(T(\theta_i))}\right] = v_m(T(\theta_i)) * \tau * a(\theta_i) \quad i = 0, 1, \ldots, n \quad ,$$

$$T(\theta_i) = b_{k+1,0} + b_{k+1,1}(t_f\theta_i) + b_{k+1,2}(t_f\theta_i)^2 = \sum_{j=0}^{2} b_{k+1,j}(t_f\theta_i)^j \quad i = 2k, 2k+1, 2k+2 \quad k = 0, 1, \ldots, NE-1 \quad ,$$

$$b_{k+1,0} + b_{k+1,1}(t_f\theta_{2k+2}) + b_{k+1,2}(t_f\theta_{2k+2})^2 = b_{k+2,0} + b_{k+2,1}(t_f\theta_{2k+2}) + b_{k+2,2}(t_f\theta_{2k+2})^2 \quad k = 0, 1, \ldots, NE-2 \quad ,$$

$$k_p(\theta_i) = 1.7539 * 10^9 * \mathrm{e}^{-7360.939/T(\theta_i)} \quad i = 0, 1, \ldots, n \quad ,$$

$$k_s(\theta_i) = 431.6294 * \mathrm{e}^{-2138.035/T(\theta_i)} \quad i = 0, 1, \ldots, n \quad ,$$

$$v_s(\theta_i) = 1.1696798 * 10^{10} * \mathrm{e}^{-7163.882/T(\theta_i)} \quad i = 0, 1, \ldots, n \quad ,$$

$$v_p(\theta_i) = 1.5503 * 10^{14} * e^{-10469.39/T(\theta_i)} \quad i = 0, 1, \ldots, n \ ,$$
$$k_d(\theta_i) = 6.2716819 * 10^{23} * e^{-20551.81/T(\theta_i)} \quad i = 0, 1, \ldots, n \ ,$$
$$k_e(\theta_i) = 385.7142 * e^{-1996.4/T(\theta_i)} \quad i = 0, 1, \ldots, n \ ,$$
$$x_e(T(\theta_i)) = \left[\frac{k_e}{1+k_e}\right]_i \quad i = 0, 1, \ldots, n \ ,$$
$$a(\theta_i) = e^{-(1-\sigma(x(\theta_i),T(\theta_i)))k_d(T(\theta_i))t_f\theta_i} \quad i = 0, 1, \ldots, n \ ,$$
$$a(\theta_i) \geq a(\theta_{i+1}) + \varepsilon \quad i = 0, 1, \ldots, n-1 \ ,$$
$$v_m(T(\theta_i)) = \left[\left(\frac{v_s k_p}{k_p - k_s}\right)\left(1 + \frac{1}{k_e}\right)\right]_i \quad i = 0, 1, \ldots, n \ ,$$
$$k_m(T(\theta_i)) = \left[\left(\frac{k_p k_s}{k_p - k_s}\right)\left[1 + \left(\frac{k_e}{k_p} + \frac{1}{k_s}\right)\left(\frac{s_0}{1+k_e}\right)\right]\right]_i \quad i = 0, 1, \ldots, n \ ,$$
$$\sigma(x(\theta_i), T(\theta_i)) = \left[\frac{0.5\left[k_p\left(1 + \frac{s'(1+k_e)}{s_0}\right) + k_s k_e\left(1 - \frac{s'(1+k_e)}{k_e s_0}\right)\right]}{\left[k_p k_s\left(\frac{(1+k_e)}{s_0}\right) + k_p\left(1 + \frac{s'(1+k_e)}{s_0}\right) + k_s k_e\left(1 - \frac{s'(1+k_e)}{k_e s_0}\right)\right]}\right]_i \quad i = 0, 1, \ldots, n \ ,$$
$$s'(\theta_i) = s_0(x_e(T(\theta_i)) - x(\theta_i)) \quad i = 0, 1, \ldots, n \ ,$$
$$0.0 \leq x(\theta_i) \leq x_e(T(\theta_i)) \quad i = 0, 1, \ldots, n \ ,$$
$$-\infty < b_{k+1,j} < +\infty \quad j = 0, 1, 2;\ k = 0, 1, \ldots, NE-1 \ ,$$
$$T^{\text{Lower}} \leq T(\theta_i) \leq T^{\text{Upper}} \quad i = 0, 1, \ldots, n \ .$$

Note that, the objective function is in the form of an integral which is estimated by employing numerical integration at the discretized node points. In the above formulation trapezoidal rule is used.

If the reactor is run isothermally all the time i.e. at a constant temperature profile mode, then all kinetic parameters k_p, k_s, v_s, v_p, k_d, k_e, x_e, v_m, and k_m are specified. The discretized NLP is reduced in size and consists only of the design equation and the sigma constraints as a function of the discretized conversion $x(\theta_i)$. The reduced discretized NLP is given as:

$$\underset{x(\theta_i)}{\text{Maximize}} \quad \text{Pr} = \left(\frac{s_0 t_f}{\tau}\right)\left[\sum_{i=0}^{n-1}\left(\frac{x(\theta_i) + x(\theta_{i+1})}{2}\right)(\theta_{i+1} - \theta_i)\right] \ ,$$

subject to:

$$s_0 x(\theta_i) - k_m \ln\left[1 - \frac{x(\theta_i)}{x_e}\right] = v_m \tau\, e^{-(1-\sigma(x(\theta_i)))k_d t_f \theta_i} \quad i = 0, 1, \ldots, n \ ,$$
$$\sigma(x(\theta_i)) = \left[\frac{0.5\left[k_p\left(1 + \frac{s'(1+k_e)}{s_0}\right) + k_s k_e\left(1 - \frac{s'(1+k_e)}{k_e s_0}\right)\right]}{\left[k_p k_s\left(\frac{(1+k_e)}{s_0}\right) + k_p\left(1 + \frac{s'(1+k_e)}{s_0}\right) + k_s k_e\left(1 - \frac{s'(1+k_e)}{k_e s_0}\right)\right]}\right]_i \quad i = 0, 1, \ldots, n \ ,$$
$$s'(\theta_i) = s_0(x_e - x(\theta_i)) \quad i = 0, 1, \ldots, n \ ,$$
$$0.0 \leq x(\theta_i) \leq x_e \quad i = 0, 1, \ldots, n \ .$$

3
Example of the discretized NLP formulation

To show how piecewise polynomial approximations is used in the discretized NLP, consider the case when the number of node points, $n + 1 = 11$, number of intervals $n = 10$, and the total number of elements, $NE = 5$. The node points are $\theta_0, \theta_1, \ldots, \theta_{10}$ such that: $\theta_0 = 0.0 < \theta_1 < \theta_2 < \ldots < \theta_{10} = 1.0$. The corresponding formulation to maximize fructose productivity is as follows:

$$\text{Objective function: } \underset{T(\theta_i), x(\theta_i)}{\text{Maximize}} \quad \left(\frac{s_0 t_f}{\tau}\right) \times \left[\sum_{i=0}^{9}\left(\frac{x(\theta_i) + x(\theta_{i+1})}{2}\right)(\theta_{i+1} - \theta_i)\right] \ ,$$

Design equation constraints for the first and last node points are:

$$s_0 x(\theta_0) - k_m(T(\theta_0)) \ln\left[1 - \frac{x(\theta_0)}{x_e(T(\theta_0))}\right] = v_m(T(\theta_0))\tau\, a(\theta_0) \ ,$$
$$s_0 x(\theta_{10}) - k_m(T(\theta_{10})) \ln\left[1 - \frac{x(\theta_{10})}{x_e(T(\theta_{10}))}\right] = v_m(T(\theta_{10}))\tau\, a(\theta_{10}) \ .$$

Kinetic parameters constraints for the first node point are:

$$k_p(\theta_0) = 1.7539 * 10^{9} * e^{-7360.939/T(\theta_0)} \ ,$$
$$k_s(\theta_0) = 431.6294 * e^{-2138.035/T(\theta_0)} \ ,$$
$$v_s(\theta_0) = 1.1696798 * 10^{10} * e^{-7163.882/T(\theta_0)} \ ,$$
$$v_p(\theta_0) = 1.5503 * 10^{14} * e^{-10469.39/T(\theta_0)} \ ,$$
$$k_d(\theta_0) = 6.2716819 * 10^{23} * e^{-20551.81/T(\theta_0)} \ ,$$
$$k_e(\theta_0) = 385.7142 * e^{-1996.4/T(\theta_0)} \ ,$$
$$x_e(T(\theta_0)) = \left[\frac{k_e}{1+k_e}\right]_0 \ ,$$
$$v_m(T(\theta_0)) = \left[\left(\frac{v_s k_p}{k_p - k_s}\right)\left(1 + \frac{1}{k_e}\right)\right]_0 \ ,$$
$$k_m(T(\theta_0)) = \left[\left(\frac{k_p k_s}{k_p - k_s}\right)\left[1 + \left(\frac{k_e}{k_p} + \frac{1}{k_s}\right)\left(\frac{s_0}{1+k_e}\right)\right]\right]_0 \ ,$$
$$\sigma(x(\theta_0), T(\theta_0)) = \left[\frac{0.5\left[k_p\left(1 + \frac{s'(1+k_e)}{s_0}\right) + k_s k_e\left(1 - \frac{s'(1+k_e)}{k_e s_0}\right)\right]}{\left[k_p k_s\left(\frac{(1+k_e)}{s_0}\right) + k_p\left(1 + \frac{s'(1+k_e)}{s_0}\right) + k_s k_e\left(1 - \frac{s'(1+k_e)}{k_e s_0}\right)\right]}\right]_0 \ .$$

Piecewise second degree polynomials constraints for the first element, $[\theta_0, \theta_1] \cup [\theta_1, \theta_2]$ and last element, $[\theta_8, \theta_9] \cup [\theta_9, \theta_{10}]$ are:

$$T(\theta_0) = b_{1,0} \ ,$$
$$T(\theta_1) = b_{1,0} + b_{1,1}(t_f\theta_1) + b_{1,2}(t_f\theta_1)^2 \ ,$$
$$T(\theta_2) = b_{1,0} + b_{1,1}(t_f\theta_2) + b_{1,2}(t_f\theta_2)^2 \ ,$$
$$T(\theta_8) = b_{5,0} + b_{5,1}(t_f\theta_8) + b_{5,2}(t_f\theta_8)^2 \ ,$$
$$T(\theta_9) = b_{5,0} + b_{5,1}(t_f\theta_9) + b_{5,2}(t_f\theta_9)^2 \ ,$$
$$T(\theta_{10}) = b_{5,0} + b_{5,1}(t_f\theta_{10}) + b_{5,2}(t_f\theta_{10})^2 \ .$$

The continuity equations are:

$$b_{1,0} + b_{1,1}(t_f\theta_2) + b_{1,2}(t_f\theta_2)^2 = b_{2,0} + b_{2,1}(t_f\theta_2) + b_{2,2}(t_f\theta_2)^2 \ ,$$
$$b_{2,0} + b_{2,1}(t_f\theta_4) + b_{2,2}(t_f\theta_4)^2 = b_{3,0} + b_{3,1}(t_f\theta_4) + b_{3,2}(t_f\theta_4)^2 \ ,$$
$$b_{3,0} + b_{3,1}(t_f\theta_6) + b_{3,2}(t_f\theta_6)^2 = b_{4,0} + b_{4,1}(t_f\theta_6) + b_{4,2}(t_f\theta_6)^2 \ ,$$
$$b_{4,0} + b_{4,1}(t_f\theta_8) + b_{4,2}(t_f\theta_8)^2 = b_{5,0} + b_{5,1}(t_f\theta_8) + b_{5,2}(t_f\theta_8)^2 \ .$$

Residual enzyme activity constraints for the first and last node points are:

$$a(\theta_0) = 1.0 \ ,$$
$$a(\theta_{10}) = \mathrm{e}^{-(1-\sigma(x(\theta_{10}),T(\theta_{10})))k_d(T(\theta_{10}))t_f\theta_{10}} \ .$$

Feasibility residual enzyme activity constraints for the node points of index 0, 1, 2, 3, and 9 are:

$$a(\theta_0) \geq a(\theta_1) + \varepsilon \ ,$$
$$a(\theta_1) \geq a(\theta_2) + \varepsilon \ ,$$
$$a(\theta_2) \geq a(\theta_3) + \varepsilon \ ,$$
$$a(\theta_3) \geq a(\theta_4) + \varepsilon \ ,$$
$$a(\theta_9) \geq a(\theta_{10}) + \varepsilon \ ,$$
$$s'(\theta_i) = s_0(x_e(T(\theta_i)) - x(\theta_i)) \quad i = 0, 1, \ldots, 10 \ ,$$
$$0.0 \leq x(\theta_i) \leq x_e(T(\theta_i)) \quad i = 0, 1, \ldots, 10 \ ,$$
$$-\infty < b_{k+1,j} < +\infty \quad j = 0, 1, 2;\ k = 0, 1, \ldots, 4 \ ,$$
$$T^{\mathrm{Lower}} \leq T(\theta_i) \leq T^{\mathrm{Upper}} \quad i = 0, 1, \ldots, 10 \ .$$

4 Numerical examples, results and discussions

The time average productivity of enzymatic conversion of glucose to fructose by the enzyme glucose isomerase (GI) is studied under two optimum temperature profile modes used to run the continuous packed bed reactor. The first is the constant optimum temperature profile (isothermal) mode which corresponds to the maximum time average productivity, and the other is the optimum temperature profile mode i.e. varying the temperature as a function of operating time.

The typical initial glucose concentration s_0 of 2.8 mole/l of HFCS process is used [11]. Lower and upper bounds on the temperature profile $T(t)$ are 50 °C and 80 °C respectively. Residence times τ, of 0.5 and 1.0 h are considered and different operating periods t_f, of 100, 250, 500, 750, and 1000 h are used. The dimensionless operating time θ, is discretized into 11 node points: $\theta_0 = 0.0 < \theta_1 < \theta_2 < \ldots < \theta_9 < \theta_{10} = 1$. All time intervals are of equal length of 0.1. The discretized and reduced nonlinear programming problems (NLPs) are solved using the GAMS software [12].

In the case of constant optimum temperature profile mode, the reactor is run at all times under the specified temperature which corresponds to the maximum time average productivity. To find the corresponding optimum temperature, the reduced NLP is solved several times covering the range of temperature from 50 to 80 °C for different operating periods of 100, 250, 500, 750, and 1000 h under 0.5 and 1.0 h residence times. As an example, for a 100 h operating period, the time average productivity Pr as a function of temperature goes through a maximum. At this maximum productivity the corresponding optimum temperature is 74.5 °C for a given residence time of 0.5 h as shown in Fig. 1. At this optimum temperature, the reactor is run isothermally all the times

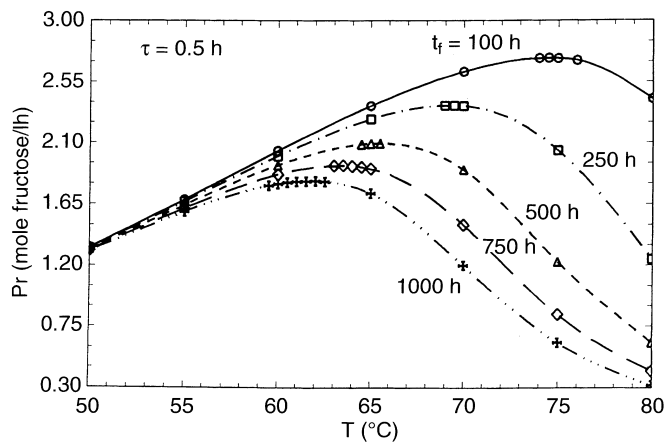

Fig. 1. Productivity profiles of glucose isomerase reactor under constant temperature operation mode at different operating periods

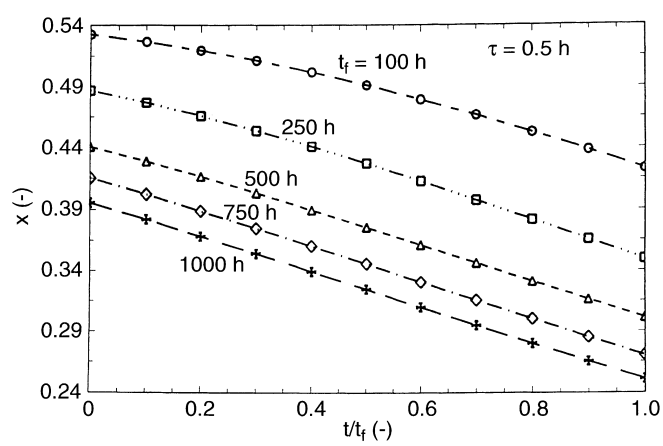

Fig. 2. Optimal conversion profiles of glucose isomerase reactor at constant optimum temperature operation at different operating periods

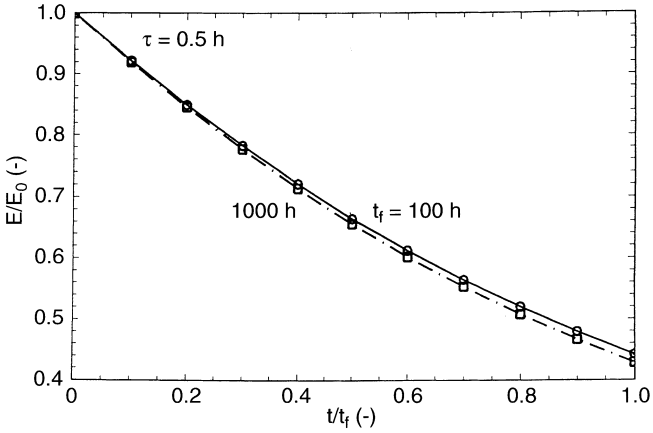

Fig. 3. Time course of GI deactivation of glucose isomerase reactor under constant optimum temperature operation

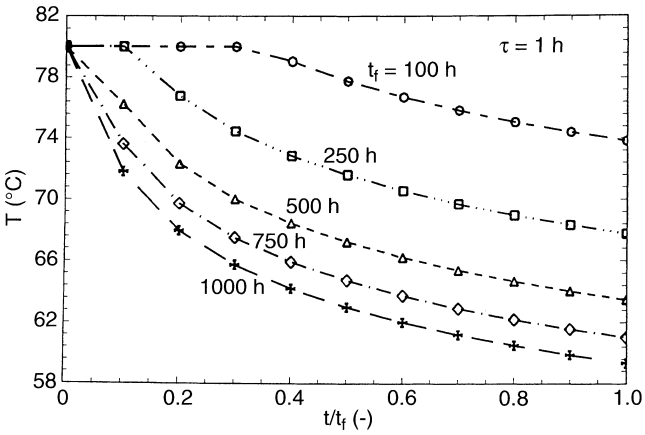

Fig. 4. Optimal temperature profiles of glucose isomerase reactor under varying temperature operation at different operating periods

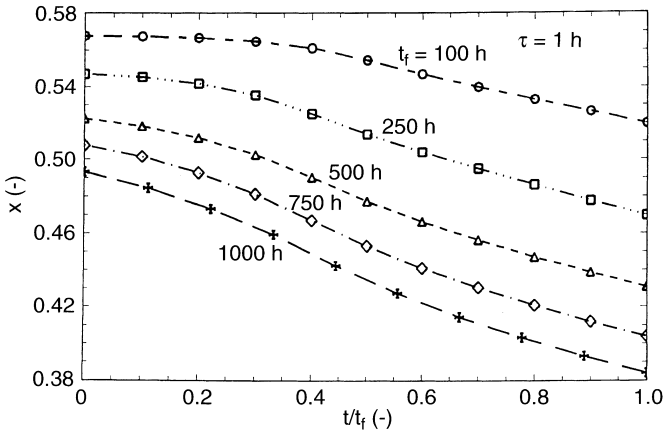

Fig. 5. Optimal conversion profiles of glucose isomerase reactor under varying temperature operation at different operating periods

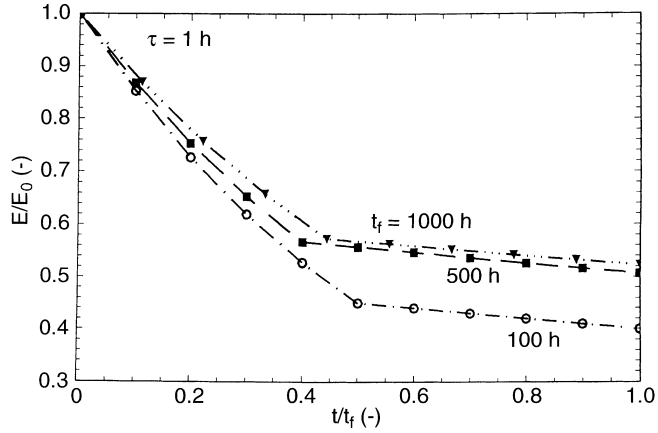

Fig. 6. Time course of GI deactivation of glucose isomerase reactor under varying temperature operation

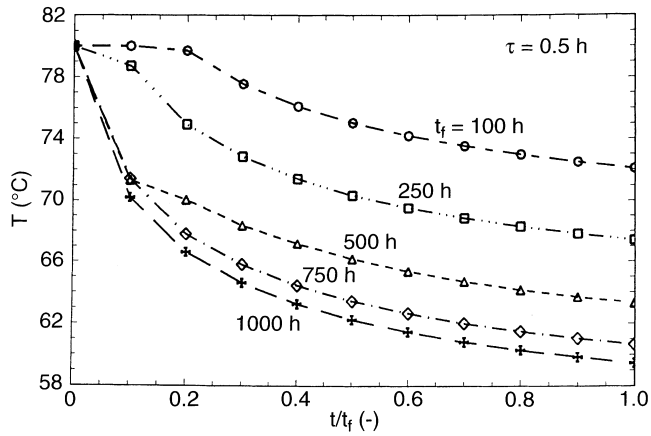

Fig. 7. Optimal temperature profiles of glucose isomerase reactor under varying temperature operation at residence time of 0.5 h

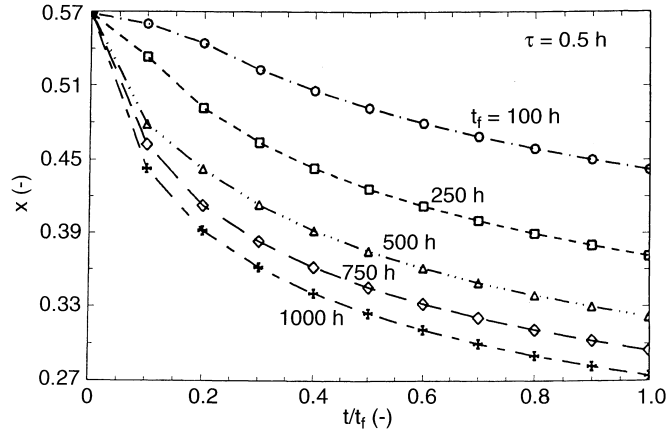

Fig. 8. Optimal conversion profiles of glucose isomerase reactor under varying temperature operation at residence time of 0.5 h

and this is what we call constant optimum temperature profile mode. Also, it can be seen from the figure that the optimum temperature which corresponds to the maximum productivity decreases as the reactor operating periods increases. The time average productivities are shown in Tables 1 and 2. The optimum discretized conversion $x(\theta_i)$, and the optimum residual enzyme activity $a(\theta_i) = E(\theta_i)/E_0$, are shown in Figures 2 and 3. From Fig. 2, at different operating periods of 100, 250, 500, 750, and 1000 h and given residence time of 0.5 h, the optimum conversion profiles are decreasing with time, and their corresponding time average conversions are 0.4865, 0.4240, 0.3739, 0.3446 and 0.3241 respectively.

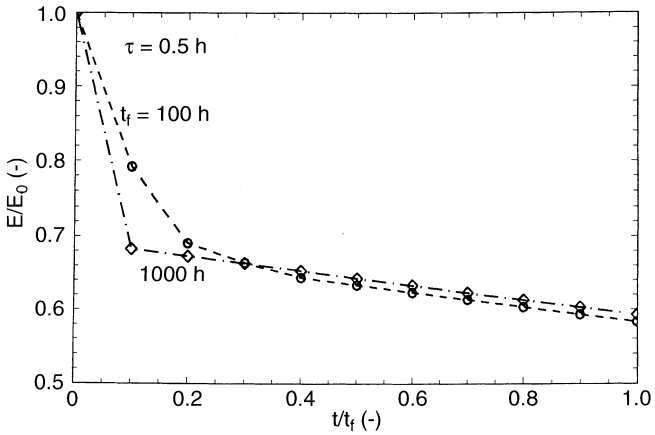

Fig. 9. Time course of GI deactivation of glucose isomerase reactor under varying temperature operation at residence time of 0.5 h

For varying temperature profile mode, the optimal results are shown in Figs. 4, 5, 6, 7, 8 and 9 for the discretized temperature, conversion, and the residual enzyme activity are illustrated for different operating periods of 100, 250, 500, 750, and 1000 h for τ of 0.5 h and 1 h. In Tables 3 through 7, the optimum values of the piecewise polynomial coefficients obtained from the solution of the discretized NLP's are listed. As it can be seen from the solution of the discretized NLP and Figs. 4 and 7, that maximum productivity of fructose is obtained when the optimal temperature profile mode is a decreasing profile with time. Also, it can be seen from the figures that the optimum temperature profile mode which corresponds to the maximum productivity decreases as the reactor operating periods increases. From Figs. 5 and 8, we observe that the conversion profile is also decreasing with time and decreases as a reactor operating period increases. It is noted that the optimum residual enzyme activity profile decreases with time, but does not change significantly with the operating periods, see Figs. 6 and 9. Reactor produc-

Table 1. Maximum average productivities under constant optimum temperature mode at different operating periods and residence time, τ, of 0.5 h

Operating period, t_f [h]	Maximum average productivity, Pr [mole fructose/lh]	Optimum temperature, T [°C]
100	2.7243	74.5
250	2.3744	69.5
500	2.0939	65.5
750	1.9296	63.5
1000	1.8151	62.0

Table 2. Maximum average productivities under constant optimum temperature mode at different operating periods and residence time, τ, of 1.0 h

Operating period, t_f [h]	Maximum average productivity, Pr [mole fructose/lh]	Optimum temperature T [°C]
100	1.5279	76.5
250	1.4201	70.5
500	1.3205	66.0
750	1.2549	64.0
1000	1.2054	62.0

Table 3. Optimal values of the piecewise polynomial coefficients, for τ of 0.5 h and t_f of 100 h

Element $k+1$	$b_{k+1,0}$	$b_{k+1,1}$	$b_{k+1,2}$
1	353.0000000	1.4556880	−14.5568803
2	359.0572395	−38.6559096	34.5701207
3	355.7463750	−21.2116159	11.6522892
4	353.7127518	−14.2817687	5.7514972
5	352.2396297	−10.5537056	3.3931717

Table 4. Optimal values of the piecewise polynomial coefficients, for τ of 0.5 h and t_f of 250 h

Element $k+1$	$b_{k+1,0}$	$b_{k+1,1}$	$b_{k+1,2}$
1	352.9985412	0.6190726	−1.28003E + 2
2	354.2258608	−37.8702085	33.7607286
3	357.7043837	−51.0488863	44.9666550
4	343.7672797	−1.3779630	0.8959605
5	343.2746650	−0.0771958	0.0397120

Table 5. Optimal values of the piecewise polynomial coefficients, for τ of 0.5 h and t_f of 500 h

Element $k+1$	$b_{k+1,0}$	$b_{k+1,1}$	$b_{k+1,2}$
1	343.2012882	1.6697384	−16.7983363
2	348.8722696	−36.6039902	32.7957724
3	345.7308341	−20.0537650	11.0541808
4	343.7980975	−13.4677902	5.4462689
5	342.3978645	−9.9241709	3.2046089

Table 6. Optimal values of the piecewise polynomial coefficients, for τ of 0.5 h and t_f of 750 h

Element $k+1$	$b_{k+1,0}$	$b_{k+1,1}$	$b_{k+1,2}$
1	353.0000000	−1.10629E+2	248.0788182
2	346.7564355	−36.2932660	32.4876836
3	343.6456448	−19.9047508	10.9588372
4	341.7309485	−13.3802981	5.4033501
5	340.3432913	−9.8685247	3.1818477

Table 7. Optimal values of the piecewise polynomial coefficients, for τ of 0.5 h and t_f of 1000 h

Element $k+1$	$b_{k+1,0}$	$b_{k+1,1}$	$b_{k+1,2}$
1	352.9999367	−1.28710E+2	308.7060346
2	345.5516751	−36.1952773	32.3412993
3	342.4569548	−19.8916666	10.9242747
4	340.5511685	−13.3976507	5.3947656
5	339.1691036	−9.9000673	3.1822628

Table 8. Operating temperature profile modes and average productivities, for τ of 0.5 h

Operating period, t_f [h]	Constant optimum temperature profile mode		Optimum temperature profile mode	Productivity improvement [%]
	Maximum average productivity, Pr [mole fructose/lh]	Optimum temperature, T [°C]	Maximum average productivity, Pr [mole fructose/lh]	
100	2.7243	74.5	2.7931	2.5
250	2.3744	69.5	2.4683	4.0
500	2.0939	65.5	2.1988	5.0
750	1.9296	63.5	2.0516	6.3
1000	1.8151	62.0	1.9411	6.9

Table 9. Operating temperature profile modes and average productivities, for τ of 1 h

Operating period, t_f [h]	Constant optimum temperature profile mode		Optimum temperature profile mode	Productivity improvement [%]
	Maximum average productivity, Pr [mole fructose/lh]	Optimum temperature, T [°C]	Maximum average productivity, Pr [mole fructose/lh]	
100	1.5279	76.5	1.5503	1.5
250	1.4201	70.5	1.4571	2.6
500	1.3205	66.0	1.3632	3.2
750	1.2549	64.0	1.3013	3.7
1000	1.2055	62.0	1.2548	4.1

tivity operating under constant optimum temperature profile is compared to that with optimum temperature profile mode. For τ of 0.5 h and t_f of 1000 h, under constant temperature, the optimal value of productivity is 1.8151 mole fructose/lh, while under optimum temperature mode it is 1.9411 mole fructose/lh. The optimum temperature profile mode improves the productivity by about 6.9% over the constant temperature mode. The results of constant and optimal temperature profile modes and productivity improvement are given in Tables 8 and 9.

In this work, it is shown that the varying optimum operating temperature profile mode, significantly affects the reactor performance, which is expressed in terms of fructose productivity for the glucose isomerase reactor operation subject to enzyme deactivation and substrate protection.

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