Optimal Temperature Policy for Reversible Reactions with Deactivation: Applied to Enzyme Reactors

The optimal temperature policy which will maximize the final catalyst activity that gives a fixed conversion of reactants in a specified time for batch operation was determined by the formulation of a calculus of variations problem following the technique of Szepé and Levenspiel (1968). The method was applied to the general case of first-order reversible reactions which occur in the presence of catalysts deactivating by an irreversible first-order mechanism. To reduce trial and error estimations and circumvent numerical instabilities, the two-point boundary value variational problem was reformulated in terms of an initial value problem with a parameter which includes the initial value of temperature. This initial value problem was solved by a regression technique.

These techniques were applied to the industrially important enzymatic reaction of the isomerization of D-glucose to D-fructose catalyzed by glucose isomerase in solution. Kinetic and deactivation data are available for this endothermic reaction which obeys first-order reversible kinetics and for the isomerase denaturation which appears to be first order. The optimal temperature operational policy as stated above maximized final enzyme activity such that 10% less denaturation of glucose isomerase occurred when compared to final isomerase activity yielding the same conversion for the same reaction time when the reactor is operated at the optimal isothermal temperature.

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SCOPE

The problem of the optimal operation policy for chemical reactors is important when it is desired to improve the operational economics and product yield. Accordingly these problems have received attention in the recent literature where investigators have employed calculus of variations methods to the analysis of batch and tubular plug flow reactors. Irreversible nth order reactions with concentration independent and recently concentration dependent deactivation models were examined. Numerical methods and theoretical developments treated in the format of Pontryagin's Maximum Principle were applied to the problem of reversible reactions with concentration independent decaying catalysts in a tubular reactor. Biochemical reactions catalyzed by denaturable enzymes which may be in solution or immobilized on inert supports are of emerging interest in recent literature. The determination of the optimal policies of reactor operation for these biochemical reaction systems is as important as in previous needs because of the high costs of enzyme catalysts and the temperature sensitivity of enzyme denaturation.

The work described herein applies the calculus of variations formulation to the problem of determining the optimal temperature policy which will maximize the final catalyst activity that gives a fixed conversion of reactants in a specified time for a batchwise operated reactor. The technique can also be applied to the mathematically equivalent problem of maximizing conversion with a specified final catalyst activity in a given reaction time. General first-order reversible reaction with separable catalyst deactivation which is first order and concentration independent was studied. The computations were conducted by employing the rate parameters of the industrially important isomerization of D-glucose to D-fructose catalyzed by glucose isomerase in solution. Analytical solutions were obtained for the optimal temperature policy for nth order irreversible kinetics since the rate expression is factorable. An analytical solution could not be obtained for the reversible reaction studied as the rate expression is not factorable. Therefore, a numerical technique was employed with the calculus of variations formulation to obtain the optimal policy. The problem of estimating the initial temperature was circumvented and numerical instabilities were minimized by transformation of the two-point boundary value variational problem to an initial value problem with a parameter which includes the initial value of temperature. This initial value problem was solved by a regression technique. The methods developed may be applied to optimize reactor operation for a wide range of catalyzed reversible reactions for which catalyst deactivation occurs.

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CONCLUSIONS AND SIGNIFICANCE

The optimal temperature policy which will maximize the final catalyst activity that gives a preset conversion in a specified time for batchwise operation is determined by the solution of a calculus of variations problem. The method is applied to the general case of catalyzed first-order reversible reactions. Deactivation kinetics are assumed first order, have an Arrhenius temperature dependence, and are concentration independent. The two-point boundary value variational problem which arises from this formulation encounters the numerical difficulties of estimating the initial reactor temperature and instabilities. These difficulties can be circumvented by reformulation of the two point boundary value problem into an initial value problem (which has the initial value of temperature as a parameter), whose solution can be obtained by regression methods.

The technique is applied to the industrially important enzyme isomerization of D-glucose to D-fructose. It is shown that, for this free enzyme reaction, there is 10% less enzyme deactivation when the reactor is operated according to the optimal varying temperature policy as opposed to operating at the optimal isothermal temperature policy. If the enzyme is readily separable from the reaction mixture and can be reused in part, as in the case of cell bound enzyme or enzyme covalently attached to inert supports, this savings in operation costs may be significant.

The technique developed can also be applied to the mathematically equivalent problem of maximizing conversion in a given reaction time at the expense of nearly exhausting enzyme (catalyst) activity. This problem is important when the enzyme (catalyst) can be discarded at the end of the operating cycle. The analysis can be applied to other industrially important reactions which are described by first-order reversible kinetics and the above mentioned catalyst deactivation kinetics.

Several optimization problems arise in the operation of catalytic reactors. In general, they can be classified in two categories—the regeneration policy and the operational policy.

The regeneration policy describes the operating cycle in regard to when the catalyst should be regenerated or discarded. This problem includes economic factors such as feed and product value, the cost of catalyst and the cost of time needed to regenerate, as well as the effectiveness of the regeneration technique. A number of authors (Aris, 1961; Roberts, 1960; Smith and Dresser, 1957; Walton, 1961) have addressed this problem for arbitrary operational policies. It becomes an ordinary calculus problem that determines the cycle length and final activity on an economic basis. Therefore, it is a point optimization problem.

The optimal operational policy is a defined path that must be described for each controllable independent parameter. Two general methods, direct and indirect, can be used to locate this path.

The direct methods, such as the gradient method, use a search technique and repeated computations to locate the desired path. Indirect methods proceed by finding the points or functions that satisfy the necessary and/or sufficient conditions needed to specify the optimal path. The indirect calculus of variation method has the great advantage in that the solution is applicable to an entire class of problems. This eliminates the necessity for repeated direct solutions when the optimal operating policy is combined with the regeneration policy to determine the overall reactor control scheme.

Temperature is one of the most important controllable variables that affect the activity of a catalyst and the reaction rate. Numerous authors (Bilous and Amundson, 1956; Denbigh, 1958; Katz, 1960; Horn, 1961) determined the optimal temperature policy for noncatalytic reactors, and more recently the problem concerning catalyst deactivation has been solved for an irreversible reaction with concentration independent deactivation (Szepe and Levenspiel, 1968; Chou, Ray, and Aris 1967) and cases of concentration dependent deactivation (Chandra and Pommersheim, 1973). Numerical methods and theoretical developments treated in the format of Pontryagin's Maximum Principle were applied to the problem of reversible reactions with concentration independent decaying catalysts in a tubular reactor (Drouin, 1969).

In this work, the optimal temperature policy will be presented for a catalyzed reversible first-order reaction taking place in an ideally mixed batch or plug flow system. The results presented are applied to the enzymatic isomerization of D-glucose by glucose isomerase from *Streptomyces* sp. Data obtained under a range of isothermal conditions and presented by Takasaki (Takasaki, Kasugo, and Kambayashi, 1969) were used to evaluate the temperature dependent parameters that appear in the rate equations and to determine the order of enzyme deactivation.

RATE EQUATIONS

The reaction rate of the first-order reversible reaction

$$G \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} F \tag{1}$$

can be written in the form

$$-r_0 = \frac{d(G)}{dt} = -(k_1 + k_{-1})(G) + k_{-1}(G)_0 \tag{2}$$

when the initial concentration of F is zero.

The rate constants k_1 and k_{-1} are temperature dependent and are represented by the Arrhenius form:

$$k_1 = k_{10} \exp\left(\frac{-E_1}{RT}\right) \tag{3}$$

and

$$k_{-1} = k_{-10} \exp\left(\frac{-E_{-1}}{RT}\right) \tag{4}$$

The rate equation for a catalyzed reaction must reflect the condition of the catalyst, which relates to its past history, as well as the present operating conditions. Szepe and Levenspiel (1968) have illustrated this and shown a formulation that is convenient when the catalyst state and the reaction rate can be separated. Using that formulation, the separable rate equation for a catalyzed reaction can be written

$$r = r_0(\text{present conditions}) \cdot a(\text{past history})$$

The catalyst activity a is described by

$$-\frac{da}{dt} = \rho(T, \overline{C}, a) \tag{5}$$

where the variables T, $\overline{C}$, and a represent the operating conditions and the catalyst condition. The deactivation rate is described by

$$\rho = \kappa(T)\varphi(\overline{C})\psi(a) \tag{6}$$

but for the case where activity is changed to a new steady value very rapidly by the concentration of a component in the reaction mixture (such as pH affects an enzyme) the function $\varphi(\overline{C})$ can be represented by a constant. The activity dependent function is

$$\psi(a) = a^m \tag{7}$$

where m is the deactivation order. The deactivation temperature dependent rate constant also has the Arrhenius form

$$\kappa(T) = \kappa_0 \exp\left(\frac{-E_d}{RT}\right) \tag{8}$$

The reaction rate for an idealized batch reactor with no catalyst or reactant residence time distribution can be described by two coupled differential equations:

$$\frac{d(G)}{dt} + r = 0 \tag{9}$$

where

$$r = r_0 a$$

and

$$\frac{da}{dt} + \rho = 0$$

OPTIMIZATION PROBLEM

A calculus of variation solution that defines an optimal temperature policy for a first-order reversible reaction is a Bolza problem with separated end conditions (Szepe and Levenspiel, 1968). When byproducts are not of concern, the optimum temperature policy is that which minimizes the concentration of feed in a fixed reaction time and final catalyst activity. This is identical to minimizing reaction time to obtain a fixed conversion of feed at a fixed final catalyst activity or maximizing the final catalyst activity that gives a fixed conversion of feed in a specified reaction time (Szepe and Levenspiel, 1968).

The problem can be stated mathematically as shown in Table 1. An augmented function is formed using Lagrangian multipliers

$$F = \lambda_1\varphi_1 + \lambda_2\varphi_2 \tag{10}$$

The path that extremizes the objective function must satisfy the Euler-Lagrange equations in addition to the constraints listed in Table 1.

Two calculation techniques are available at this point that will result in the Bolza problem solution. The Euler-Lagrange equations reduce to two ordinary differential equations and one algebraic equation in terms of the Lagrangian multipliers λ_1 with the end conditions on λ_1 specified. These equations are coupled to the constraints through (G), T, and a. Therefore, these five simultaneous equations can be solved for (G), T, a, λ_1, and λ_2 as functions of time (Lee, 1968).

TABLE 1. MATHEMATICAL DESCRIPTION OF DEACTIVATING CATALYST OPTIMIZATION PROBLEM

Variables	$[G(t)], a(t), T(t)$
Constraints	$\varphi_1 = (\dot{G}) + r_0\,[T, (G)]\,a(T) = 0$ $\varphi_2 = \dot{a} + \rho(a, T) = 0$
End conditions	$t = 0;\ a = a_0;\ (G) = (G)_0$ $t = t_f;\ a = a_f$
Objective function	$\psi = (G)_0{}^f$

The other technique was followed by Szepe (Szepe and Levenspiel, 1968). Using the end conditions and the constraints, the Lagrangian multipliers can be eliminated and the Euler-Lagrange equations reduce to

$$\frac{\partial\rho}{\partial y}\left[\dot{r}\frac{\partial\rho}{\partial y} - \dot{\rho}\frac{\partial r}{\partial y} - \rho\frac{d}{dt}\left(\frac{\partial r}{dy}\right)\right] + \frac{\partial r}{\partial y}\rho\frac{d}{dt}\left(\frac{\partial\rho}{\partial y}\right) = \frac{\partial\rho}{\partial y}\left(\rho\frac{\partial r}{\partial y} - r\frac{\partial\rho}{\partial y}\right)\frac{\partial r}{\partial(G)} \tag{11}$$

where $y = 1/T$.

Equation (11) must be satisfied to give the optimal temperature policy.

The Legendre-Clebsch condition is a necessary condition for defining a stationary solution. A formulation of this problem is given (Szepe and Levenspiel, 1968) by using a method (Miele, 1958) of substituting z for y in the Legendre-Clebsch equations. An optimum policy is defined by Equation (11) if

$$\left\{\frac{r_f\left(\frac{\partial\rho}{\partial y}\right)_f - \rho_f\left(\frac{\partial r}{\partial y}\right)_f}{\left(\frac{\partial\rho}{\partial y}\right)_f}\right\}\left\{\frac{\frac{\partial\rho}{\partial y}\,\frac{\partial^2 r}{\partial y^2}}{\rho\frac{\partial r}{\partial y} - r\frac{\partial\rho}{\partial y}} - \frac{\frac{\partial^2\rho}{\partial y^2}}{\rho} - \frac{\frac{\partial\rho}{\partial y}\,\frac{\partial^2\rho}{\partial y^2}\,\frac{r}{\rho}}{\rho\frac{\partial r}{\partial y} - r\frac{\partial\rho}{\partial y}}\right\} \geqslant 0 \tag{12}$$

The derivation of the above is outlined in Appendix II.*

SOLUTION FOR THE FIRST-ORDER REVERSIBLE REACTION WITH CATALYST DEACTIVATION

The rate of a first-order reversible catalyzed reaction can be written

$$r = \frac{-d(G)}{dt} = a[(k_1 + k_{-1})(G) - k_{-1}(G)_0] \tag{13}$$

for the separable case. For first-order dependency on activity the rate of deactivation is

$$\rho = \frac{-da}{dt} = \kappa a \tag{14}$$

After the mathematical operations described by Equation (11) are performed and that equation is rearranged, the optimal temperature policy is described by a third coupled differential equation

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* Appendices 1 and 2 have been deposited as Document No. 02375 with the National Auxiliary Publications Service (NAPS), c/o Microfiche Publications, 305 E. 46 St., New York, N.Y. 10017 and may be obtained for $1.50 for microfiche or $5.00 for photocopies.

$$\frac{dy}{dt} = \frac{N}{D} \tag{15}$$

where

$$\begin{aligned} N = {} & \{k_1 + k_{-1}\} \\ & \{-a(G)E_1k_1 - a(G)E_{-1}k_{-1} + a(G)_0E_{-1}k_{-1}\} \\ & - E_d\kappa(G)(k_1 + k_{-1}) + E_dk_{-1}\kappa(G)_0 + \kappa E_1k_1(G) \\ & + \kappa E_{-1}k_{-1}(G) - \kappa E_{-1}k_{-1}(G)_0 + r(E_1k_1 + E_{-1}k_{-1}) \end{aligned} \tag{16}$$

and

$$\begin{aligned} D = {} & \{E_d(G)(E_1k_1 + E_{-1}k_{-1}) - E_dE_{-1}k_{-1}(G)_0 \\ & - E_1{}^2(G)k_1 - E_{-1}{}^2k_{-1}(G) + E_{-1}{}^2k_{-1}(G)_0\} \left[\frac{1}{R}\right] \end{aligned} \tag{17}$$

The reactant conversion rate, the temperature policy, and the catalyst deactivation rate are defined by three ordinary first-order, nonlinear differential Equations (13), (14), and (15) subjected to the Legendre-Clebsch conditions. A numerical solution to this set of equations can be determined easily if the initial conditions of the dependent variables, (G), a, T, are known. In this problem $(G)_0$ and a_0 can be specified, but to satisfy the criterion established for the optimal temperature policy a final condition must be stated for one of these variables while an optimum value is determined for the other. Therefore, no end conditions are specified for the temperature.

A simple change of variables converts this boundary value problem to a more readily solvable regression problem. A set of ordinary differential equations

$$\frac{d\bar{z}}{dt} = \bar{f}(\bar{z}, t) \tag{18}$$

where

$$\bar{z} = (z_1, z_2, \ldots\ldots, z_n)'$$

$$\bar{f}(\bar{z}, t) = [f_1(\bar{z}, t), f_2(\bar{z}, t), \ldots\ldots, f_N(\bar{z}, t)]'$$

subject to the boundary conditions

$$\bar{z}(t) = \bar{z}(\tau) \tag{19}$$

where τ is some final value of time, can be converted to an initial value problem. The initial value problem can be solved using the regression routine outlined in Appendix I* by the following technique. The initial values of the dependent variables $z_i(0)$ are unknown constants and can be written

$$\bar{z}(0) = \bar{K}$$

where

$$\bar{K} = (k_1, k_2, \ldots\ldots, k_N)'$$

A new variable vector $\bar{Y}$ can be defined with elements

$$y_i = \frac{z_i - k_i}{z_i(\tau) - k_i} \tag{20}$$

Thus

$$\bar{Y}(0) = \bar{0} \tag{21}$$

and

$$\bar{Y}(\tau) = \bar{I} \tag{22}$$

The set of equations can be written in terms of this new variable vector as

$$\frac{d\bar{Y}}{dt} = \bar{g}(\bar{Y}, \bar{K}, t) \tag{23}$$

where

$$g_i(\bar{Y}, \bar{K}, t) = \frac{1}{z_i(t) - k_i} f_i(\bar{Y}, \bar{K}, t) \tag{24}$$

subject to the boundary conditions

$$\bar{Y}(0) = \bar{0} \tag{25}$$

and

$$\bar{Y}(\tau) = \bar{I} \tag{26}$$

The values of $\bar{K}$ are determined by the regression routine shown in Appendix I.*

The regression problem was solved using an algorithm by Marquardt (1963) that combines the features of the gradient search and the Newton-Raphson methods to assure absolute convergence (Appendix I).

Gill's modification of the Runge-Kutta method was adapted to simultaneously perform the integration necessary to evaluate those derivatives used in correcting the parameters obtained with the regression routine.

When the numerical solution of Equations (13), (14), and (15) is obtained, the values of r, ρ, $\partial\rho/\partial y$, and $\partial r/\partial y$ at $t = \tau$ are substituted into the Legendre-Clebsch condition Equation (12), and the calculation is repeated for all values of time to insure this necessary condition is satisfied.

APPLICATION TO ENZYME REACTORS

Enzyme catalysts are important in biological reactions. Only recently has it been possible to produce and isolate sufficient quantities of relatively pure enzyme with potential use in commercial processes. One such enzyme catalyzed reaction of industrial importance is the isomerization of D-glucose to D-fructose via glucose isomerase, an endoenzyme obtained from various microbial sources such as *Streptomyces* sp. or *Bacillus* strains. Although one can describe this reaction mechanism in terms of reversible Michaelis-Menten kinetics (Takasaki, 1967; McKay, 1973), the reaction has been shown to follow first-order reversible kinetics where the rate constants exhibit Arrhenius temperature dependence. Glucose isomerase, as is the case with most enzymes, has an accelerating denaturation or deactivation process when the temperature exceeds a certain level. Data presented on free glucose isomerase activity (Takasaki, Kosugo, and Kambayashi, 1969) during isomerization at various temperature levels indicate first-order deactivation and Arrhenius temperature dependence.

The problem addressed in this study is to define an optimal temperature policy which will decrease the costs of reactor operation by prolonging enzyme catalyst life without a decrease in production rate.

PARAMETER ESTIMATION FROM DATA

The forward reaction is shown to be first-order in glucose by the linear relationship between the initial rate and the glucose concentration. Initial rate data (Takasaki et al., 1969) taken from batch runs made at 308, 322, 333, and 343°K were used to evaluate the forward reaction frequency factor and activation energy as 3.4×10^7 s^{-1} and 15,500 cal/g mole, respectively. The parameters for the reverse rate coefficient k_{-1} were determined from information given on the equilibrium constants at various temperatures. From the relationship

$$\ln K = \ln\left(\frac{k_{10}}{k_{-10}}\right) - \frac{(E_1 - E_{-1})}{RT} \tag{27}$$

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* See footnote on page 709.

The reverse reaction frequency factor and activation energy are calculated to be $k_{-10} = 7.9 \times 10^5$ s^{-1} and $E_{-1} = 13{,}120$ cal/g mole.

Data given on residual enzyme activity after 10 min. at 343, 348, 353, and 358°K were used to evaluate the activation energy for deactivation, E_d, and κ_0. The values of these constants were determined for a first-order deactivation mechanism,

$$\frac{da}{dt} = -\left[\kappa_0 \exp\left(\frac{-E_d}{RT}\right)\right] a \qquad (28)$$

as

$$E_d = 30{,}200 \text{ cal/g mole}$$

and

$$\kappa_0 = 2 \times 10^{17} \text{ s}^{-1}$$

OPTIMAL ISOTHERMAL TEMPERATURE

An optimal isothermal temperature for a batch or an ideal plug flow reactor is defined as that which results in the maximum conversion of feed in a fixed reaction time τ. The optimum is determined from ordinary calculus by solving Equations (13) and (14) to obtain

$$G = G(y, t) \qquad (29)$$

and then determine y such that

$$\left.\frac{\partial G}{\partial y}\right)_{t=t_f} = 0$$

or

$$\left.\frac{\partial G}{\partial y}\right)_{t_f} = 0 = \frac{k_1 (G)_0}{k_1 + k_{-1}} [A + B \cdot C] + H \cdot \frac{J}{K} \qquad (30)$$

where

$$A = \frac{k_{-10} R}{k_{10}(E_1 - E_{-1})} \exp\left[(E_1 - E_{-1}) \frac{y}{R}\right]$$

$$B = \exp - \left\{ \frac{a_0 (k_1 + k_{-1})}{\kappa} [1 - \exp(-\kappa t_f)] \right\}$$

$$C = [-a_0 + a_0 \exp(-\kappa t_f)] \left[\frac{k_{10}(E_d - E_1)}{R} \exp\left(\frac{E_d - E_1}{\kappa} y\right) + \frac{k_{-10}(E_d - E_{-1})}{R\kappa} \exp\left(\frac{E_d - E_{-1}}{R}\right) y \right] \qquad (31)$$

$$H = \frac{k_{-1}}{k_1} + \exp\left\{ \frac{-a_0 (k_1 + k_{-1})}{\kappa} [1 - \exp(\kappa t_f)] \right\}$$

$$J = -G_0 R \frac{k_{-10}}{k_{10}(E_1 - E_{-1})} \exp\left[(E_1 - E_{-1}) \frac{y}{R}\right]$$

$$K = \left\{ 1 + \frac{k_{-10}}{k_{10}} \exp\left[\frac{(E_1 - E_{-1})}{R} y\right] \right\}$$

The optimum isothermal temperature calculated from Equation (30) with $\tau = 200$ min was 60°C. This result was verified by numerically integrating the set of simultaneous differential Equations (13) and (14) at constant temperatures between 50° and 70°C with $a_0 = 1$ and $G_0 = 2.8$ moles/liter. A plot of final glucose concentration G_f versus reaction temperature is shown in Figure 1.

Approximately 40% of the glucose, $G_f = 1.68$ g mole/liter, is converted to fructose by operating at the optimal isothermal temperature of 60°C for $\tau = 200$ min.

COMPARISON OF REACTOR PERFORMANCE: OPTIMAL TEMPERATURE POLICY VERSUS OPTIMAL ISOTHERMAL OPERATION

The optimal temperature policy was determined by simultaneously integrating Equations (13), (14), and (15) for $G_0 = 2.8$ g mole/liter, $a_0 = 1$, and $G_f = 1.68$ for $\tau = 200$ min. The integration was computed by employing the change of variables discussed earlier with the regression technique described in Appendix I subjected to the Legendre-Clebsch condition. The initial temperature for the optimal temperature policy was calculated to be 55°C.

Figures 2, 3, and 4 are plots of the time histories of G, a, and T for the optimal isothermal operating policy and the optimal varying temperature policy determined for equal final concentration of reactant after 200 min of reaction time. Approximately 10% less enzyme is expended using the varying temperature policy.

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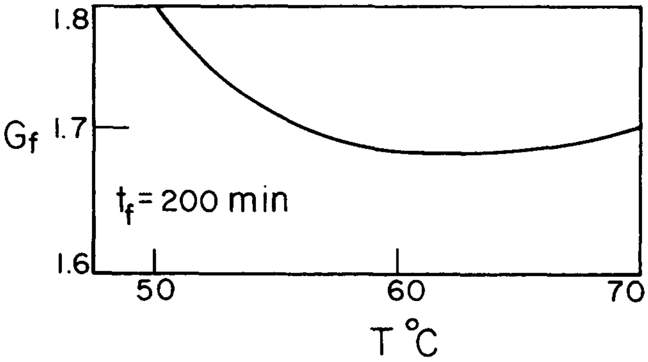

Fig. 1. Effect of reaction temperature on D-glucose concentration after 200 min.

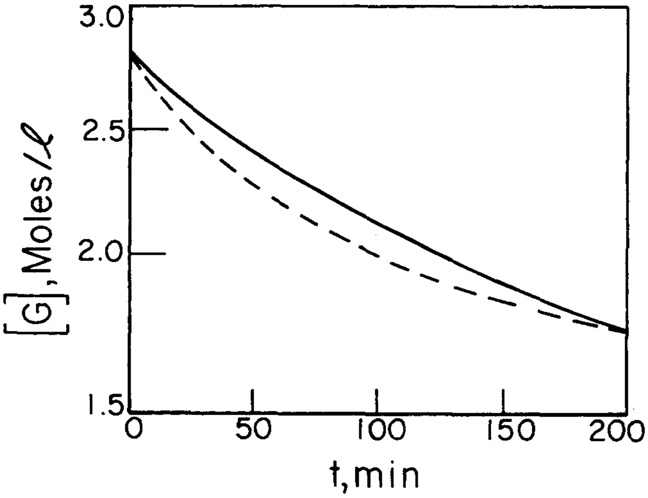

Fig. 2. D-Glucose concentration in a batch reactor: ——— optimal varying temperature; and - - - - - - optimal isothermal temperature.

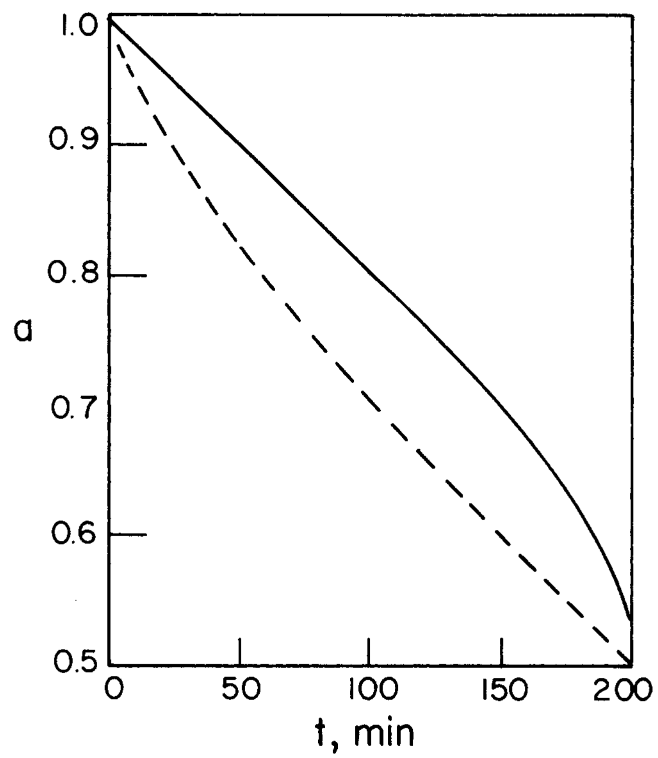

Fig. 3. Enzyme activity in a batch reactor: ——— optimal varying temperature; and - - - - - - optimal isothermal temperature.

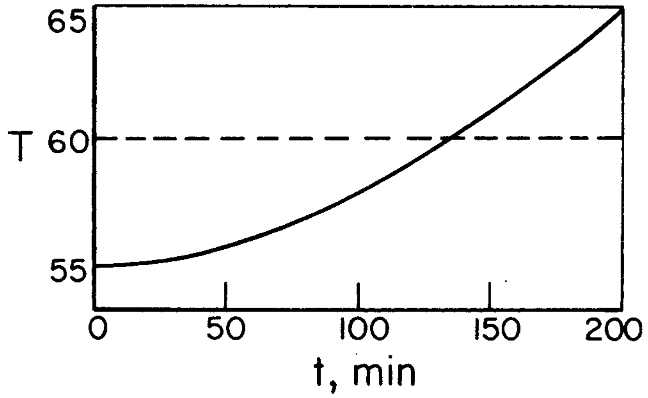

Fig. 4. Temperature of a batch reactor: ——— optimal varying temperature; and - - - - - - - optimal isothermal temperature.

NOTATION

a = catalyst activity
$(\dot{a})$ = da/dt
$\overline{C}$ = concentration set for all components
E_d = activation energy for deactivation
E_i = activation energy of k_i
f = final condition
F = augmented function
(F) = fructose concentration
(G) = glucose concentration
$(\dot{G})$ = $d(G)/dt$
k_i = Arrhenius rate coefficient of ith reaction
k_{i0} = frequency factor of k_i
m = deactivation order
0 = initial condition
r = reaction rate
r_0 = catalyst activity independent reaction rate
R = international gas constant
t = batch time or continuous space time
T = temperature, °K
y = $1/T$
y_i = dependent variable
$\overline{Y}$ = dependent variable vector

Greek Letters

κ = temperature dependent function
κ_0 = pre-exponential constant in Arrhenius function for deactivation
λ_i = ith Lagrangian multiplier
ρ = deactivation rate
τ = final time
$\varphi(c)$ = concentration dependent function
φ_i = ith constraint equation
ψ = activity dependent function

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