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# Dynamic Behavior Classification of a Model for a Continuous Bio-Reactor Subject to Product Inhibition

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**Abstract**—The dynamic behavior of the continuous biological reactor subject to product inhibition is analysed and classified in terms of multiplicity and stability of steady states and existence and stability character of limit cycles. Various boundary conditions are derived which delineate the parameter space into regions of dynamically different behavior. The predicted types of behavior are then illustrated by numerical computation of cells and product concentration trajectories.

## INTRODUCTION

Dynamic behaviors of the continuous fermentation have been studied theoretically by several workers for different types of specific growth rate functions. In some fermentations, inhibition of microbial growth is observed at a high concentration of its product, for example, as in the lactic acid fermentation [1]. Experimental evidence for the formation of such inhibitory products during growth has been found for the green alga *Chlorella* as well as fungi [2]. A model for such a chemostat in which the growth of a microorganism is inhibited by its product was presented and theoretically studied in a paper by Yano and Koga [1] where the specific growth rate was assumed to have the form

$$\mu = \frac{\mu_m S}{(K_S + S)\left[1 + (P/K_p)^n\right]}$$

in order to cover wider problems of product inhibition. They then described the single-vessel continuous fermentation system by the following system of differential equations:

$$\frac{dX}{dt} = \mu X - DX \tag{1}$$

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

$$\frac{dP}{dt} = (\eta_1 + \eta_2 \mu) X - DP \tag{3}$$

where $X(t)$ denotes the cells concentration at time $t$; $S(t)$ the substrate concentration at time $t$; $P(t)$ the product concentration at time $t$; $S_F$ the concentration of the feed substrate; $Y$ the cells to substrate yield; $D$ the dilution rate; and $\eta_1$ and $\eta_2$ are constants for product formation.

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They noted that, while $\eta_1$ should not be negative, $\eta_2$ may be so, as in the case of the biotin-limited glutamic acid fermentation (negative-growth associated). Moreover, if the growth limiting substrate ($S$) is supplied in sufficient amount so that $S \gg K_S$ at any moment, then the concentration change of $S$ has little effect on $\frac{dX}{dt}$ and $\frac{dP}{dt}$. The system described by Equations (1)–(3) will be reduced to the following two-variable system:

$$\frac{dX}{dt} = \mu(P)X - DX \tag{4}$$

$$\frac{dP}{dt} = [\eta_1 + \eta_2\mu(P)]\, X - DP. \tag{5}$$

Lenbury and Chiaranai [3] later carried out a theoretical study of the two-dimensional model with $\eta_1 = 0$; namely

$$\frac{dX}{dt} = \mu X - DX, \qquad X(0) = X_0 \tag{6}$$

$$\frac{dP}{dt} = \frac{\mu}{Y_p} X - DP, \qquad P(0) = P_0. \tag{7}$$

If $Y_p$ is assumed constant, it can be shown [4] that the system of Equations (6) and (7) will not admit periodic behavior. It was also shown by Lenbury and Chiaranai [3] that if $Y_p$ is a linear function of the product concentration, sustained oscillation in $X$ and $P$ is possible due to a Hopf bifurcation in the system of differential equations which comprises the model. Some recent studies on these types of models can be found in the work of Alsholm [5] and that of Cheng-Fu [6]. In this paper, we shall therefore consider the system of Equations (6) and (7) with

$$Y_p = A - BP, \tag{8}$$

where $A$ and $B$ are constants, allowing for the negative-growth associated situation.

Following the work of Poore [7] and Uppal et al. [8,9] and later that of Agrawal et al. [10] on dynamic behavior of continuous stirred tank biological reactors, the criterion for periodic behavior of continuous cultures originating from Friedrich's [11] sufficient condition for the existence of limit cycles will be derived. While Agrawal et al. [10] employed first the monod's model and then the so-called one hump substrate inhibition function

$$\mu = kS \exp\left(-\frac{S}{K}\right)$$

for the specific growth rate in their work on continuous stirred tank reactors, we adopt for simplicity the function

$$\mu = \mu_0 \left(1 + \frac{P}{k_m} - \frac{P^2}{k_p}\right), \tag{9}$$

where $\mu_0$, $k_m$, and $k_p$ are positive constants, which exhibits the same characteristics as the usual product inhibition model [1,2] in the range where the function has positive value. In fact, the function in (9) results from linearizing the exponential term in the 'one hump' product inhibition model

$$\mu = k(P + 1) \exp\left(-\frac{P}{K}\right). \tag{10}$$

Different types of dynamic behavior of the continuous biological reactor subject to product inhibition, modelled by Equations (6) and (7) with (8) and (9), shall be classified in terms of a Damköhler number and two other system parameters.

## SYSTEM MODEL

Introducing for convenience a new set of variables, namely,

$$x_1 = \frac{X}{k_m Y_p(0)}, \qquad x_2 = \frac{P}{k_m}, \qquad T = Dt, \qquad \mathrm{Da} = \frac{\mu(0)}{D},$$
$$M(x_2) = \frac{\mu(k_m x_2)}{\mu(0)}, \qquad y(x_2) = \frac{Y_p(k_m x_2)}{Y_p(0)},$$
$$\alpha = \frac{k_m^2}{k_p}, \qquad \beta = \frac{A}{Bk_m},$$

the Equations (6) through (9) become

$$\frac{dx_1}{dT} = -x_1 + \mathrm{Da}M(x_2)x_1 \tag{11}$$
$$\frac{dx_2}{dT} = -x_2 + \frac{\mathrm{Da}M(x_2)x_1}{y(x_2)} \tag{12}$$
$$y(x_2) = \frac{(\beta - x_2)}{\beta} \tag{13}$$
$$M(x_2) = 1 + x_2 - \alpha x_2^2. \tag{14}$$

Letting

$$\Sigma(x_2) = \frac{M(x_2)}{y(x_2)} \tag{15}$$
$$f_1(x_1, x_2, \mathrm{Da}) = -x_1 + \mathrm{Da}M(x_2)x_1 \tag{16}$$
$$f_2(x_1, x_2, \mathrm{Da}) = -x_2 + \mathrm{Da}\Sigma(x_2)x_1, \tag{17}$$

Equations (11) and (12) may be recast in vector form as

$$\frac{d\mathbf{x}}{dT} = \mathbf{f}(\mathbf{x}, \mathrm{Da}). \tag{18}$$

We investigate the dynamic as well as steady state behavior of the system described by Equation (18). Of particular interest are the existence of limit cycles and their stability.

## STABILITY OF STEADY STATE SOLUTIONS

Solving the equation

$$\mathbf{f}(\mathbf{x}_s, \mathrm{Da}) = \mathbf{0}$$

for $\mathbf{x}_s = (x_{s1}, x_{s2})$, we obtain the steady state solutions as

(a) trivial (washout) steady state: $x_{s1} = x_{s2} = 0$,

(b) nontrivial steady state ($s$): $x_{s1} = y(x_{s2})x_{s2}$, $M(x_{s2}) = 1/\mathrm{Da}$.

Let $\mathbf{J}$ be the Jacobian matrix of $\mathbf{f}$ evaluated at the steady state of interest,

$$\mathbf{J}(\mathbf{x}_s, \mathrm{Da}) = \begin{bmatrix} -1 + \mathrm{Da}M(x_{s2}) & \mathrm{Da}M'(x_{s2})x_{s1} \\ \mathrm{Da}\Sigma(x_{s2}) & -1 + \mathrm{Da}\Sigma'(x_{s2})x_{s1} \end{bmatrix}, \tag{19}$$

where the prime denotes differentiation with respect to $x_2$. The necessary and sufficient conditions for local stability of a steady state are that eigenvalues have negative real parts, which are equivalent to

$$\det \mathbf{J} > 0, \quad \text{and } \operatorname{tr} \mathbf{J} < 0.$$

At the washout steady state,

$$\text{tr }\mathbf{J} = -2 + \text{Da}$$
$$\det \mathbf{J} = 1 - \text{Da}.$$

It follows, therefore, that the washout steady state is stable if Da $< 1$ and a saddle point for Da $> 1$.

For the nontrivial steady states, $\mathbf{x}_s \neq \mathbf{0}$,

$$\det \mathbf{J} = -\text{Da}M'(x_{s2})x_{s2} \tag{20}$$

and

$$\text{tr }\mathbf{J} = -1 + \text{Da}\Sigma'(x_{s2})x_{s1}. \tag{21}$$

Therefore, the necessary and sufficient conditions for local stability are

$$M'(x_{s2}) < 0 \tag{22}$$

and

$$\Sigma'(x_{s2}) < \frac{1}{\text{Da}x_{s1}}. \tag{23}$$

## BIFURCATION OF LIMIT CYCLES

The Hopf bifurcation occurs at a steady state $\mathbf{x}_s = \mathbf{x}_s^*$ if J evaluated at $\mathbf{x}_s^*$ has purely imaginary eigenvalues, which requires that

$$\det \mathbf{J} > 0 \quad \text{and} \quad \text{tr }\mathbf{J} = 0. \tag{24}$$

For the nontrivial steady states, the condition (24) becomes

$$M'(x_{s2}^*) < 0 \tag{25}$$

and

$$\text{Da}\Sigma'(x_{s2}^*)x_{s1}^* - 1 = 0. \tag{26}$$

Applying conditions (25) and (26) to the functions in Equations (13) and (14), we find that for positive det $\mathbf{J}$ the following condition must be satisfied:

$$1 - 2\alpha x_{s2}^* < 0, \tag{27}$$

while tr $\mathbf{J} = 0$ is equivalent to the requirement that

$$g(x_{s2}^*) \equiv (1 - \alpha\beta)(x_{s2}^*)^2 + 2x_{s2}^* - \beta = 0 \tag{28}$$

as the other factors in tr $\mathbf{J}$ do not change signs.

The function $g(x_{s2}^*)$ will have two distinct positive real roots $x_{s2}^* = r_1$ and $r_2$, with $r_1 < r_2$, if

$$\frac{1}{\beta} > \alpha\beta - 1 > 0. \tag{29}$$

On the other hand, if $\alpha\beta - 1 < 0$, then $g(x_{s2}^*)$ has only one positive real root $r_1$, which, from Equation (28), is given by

$$x_{2s}^* = \frac{\beta}{2} - \frac{(\alpha\beta - 1)(x_{s2}^*)^2}{2} < \frac{\beta}{2} < \frac{1}{2\alpha}.$$

Therefore, $M'(x_{s2}^*) = -2\alpha x_{s2}^* + 1 > 0$ here, in which case no bifurcation occurs. In other words, $M'(x_{s2}^*)$, and correspondingly det $\mathbf{J}$, changes signs when

$$\alpha\beta - 1 = 0, \tag{30}$$

at which point the number of positive roots of $g(x_{s2}^*)$ also reduces from two roots to only one.

Finally, onset of instability of steady states $\mathbf{x}_s$ is realized when tr $\mathbf{J} = 0$ and (tr $\mathbf{J})' = 0$ which, from Equation (28), occurs when

$$\alpha\beta^2 - \beta - 1 = 0. \tag{31}$$

## STABILITY OF LIMIT CYCLES

Applying the Poincaré's criterion and Friedrich's bifurcation theory [11], we may derive the following condition for the stability of the periodic solution which bifurcates from the point $x_{s2} = x^*_{s2}$:

$$3\Sigma'''(x^*_{s2})x^*_{s2} < \Sigma''(x^*_{s2}) \left\{ 1 + \frac{4M''(x^*_{s2})x^*_{s2}}{3M'(x^*_{s2})} \right\}. \tag{32}$$

According to Agrawal *et al.* [10], it can be shown that if a bifurcated periodic solution surrounds an unstable critical point, it is stable. If it surrounds a stable critical point, it is unstable.

Evaluating $M''$, $\Sigma''$, and $\Sigma'''$ and substituting into Equation (32), we arrive at the following stability condition:

$$9\left[(1-\alpha\beta)x^*_{s2} + 1\right](x^*_{s2})^2 < \frac{(\beta - x^*_{s2})^2(3 - 14\,\alpha\, x^*_{s2})}{(3 - 6\alpha\, x^*_{s2})}. \tag{33}$$

From Equation (28), we have

$$(1-\alpha\beta)r_{1,2} + 1 = \pm\sqrt{1 - \beta(\alpha\beta - 1)}. \tag{34}$$

Therefore, for $x^*_{s2} = r_2$, the left hand side of the inequality in (33) reads

$$-9\sqrt{1-\beta(\alpha\beta-1)}\, r_2^2,$$

which is always negative. On the other hand, we need have $1 - 2\alpha x^*_{s2} < 0$ for bifurcation, in which case we must have

$$3 - 14\,\alpha\, x^*_{s2} < 3 - 6\,\alpha x^*_{s2} < 0.$$

This in turns implies

$$\frac{(3 - 14\,\alpha\, x^*_{s2})}{(3 - 6\,\alpha\, x^*_{s2})} > 1,$$

and therefore the right hand side of (33) is always positive. This means that a limit cycle bifurcating from the bifurcation point $x^*_{s2} = r_2$ is always stable.

Now, for the point $x^*_{s2} = r_1$, the stability condition (32) for the limit cycle becomes

$$9\sqrt{1-\beta(\alpha\beta-1)}\, r_1^2 < (\beta - r_1)^2 \frac{(3 - 14\,\alpha\, r_1)}{(3 - 6\alpha\, r_1)}. \tag{35}$$

Substituting the appropriate root $r_1$ in (35), we find that a loss of stability of the periodic solution which bifurcates from $x_{s2} = r_1$ occurs when

$$\beta = (1+c)\frac{(-14\,c^2 + 68\,c - 54)}{(3\,c^2 - 38\,c + 27)}, \tag{36}$$

where $c = \sqrt{1 - \beta(\alpha\beta - 1)}$.

## POSITIONS OF BIFURICATION POINTS

Since different location of the bifurcation points $r_1$ and $r_2$ on the curve

$$\frac{1}{\text{Da}} = M(x_{s2}) \tag{37}$$

is also closely related to the multiplicity of steady states and dynamic behavior which may be possible for the system, we derive another boundary condition which will delineate the parameter space further into regions of different dynamic behavior.

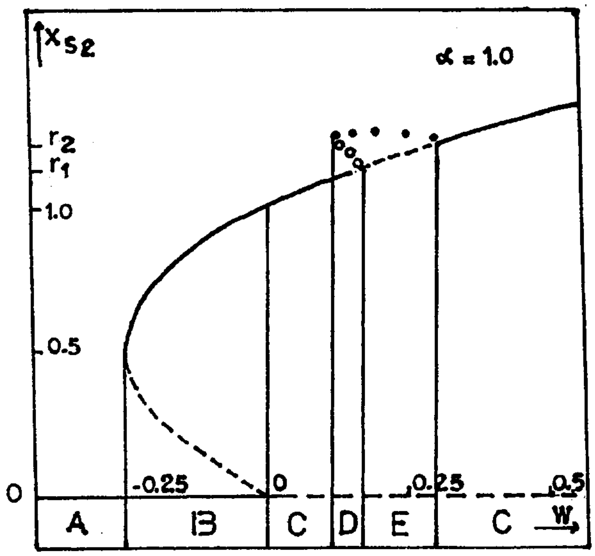


Figure 1. Typical $w$ vs. $x_{s2}$ curve: — stable steady state; - - - unstable steady state; • • • stable limit cycle; o o o unstable limit cycle.

Letting

$$w = 1 - \frac{1}{\mathrm{Da}}, \tag{38}$$

equation (37) becomes

$$w = \alpha(x_{s2})^2 - x_{s2}, \tag{39}$$

the graph of which is shown in Figure 1. We see that $w = 0$ at $x_{s2} = 0$ and $1/\alpha$.

By condition (29) for two positive real roots we must have

$$\beta(\alpha\beta - 1) < 1 \quad \text{and} \quad \alpha\beta > 1$$

so that

$$\frac{(\alpha\beta - 1)}{\alpha^2} < \beta^2(\alpha\beta - 1) < \beta.$$

Thus, we have

$$r_1 r_2 = \frac{\beta}{(\alpha\beta - 1)} > \frac{1}{\alpha^2},$$

which means that if $r_1 < 1/\alpha$ then $r_2 > 1/\alpha$. On the other hand, if $r_1 > 1/\alpha$ then $r_2 > r_1 > 1/\alpha$. In other words, $r_2$ is always greater than the value $1/\alpha$, while $r_1$ may be either less than or greater than that value. Substituting $1/\alpha$ for $x^*_{s2}$ in Equation (28), we find that $r_1$ will be equal to $1/\alpha$ when

$$\alpha\beta = \frac{1 + 2\alpha}{1 + \alpha}. \tag{40}$$

If $\alpha\beta$ is less than the quantity on the right of Equation (40) then $r_1 < 1/\alpha$, which is the case shown in Figure 1. As $w$ increases, $x_{s2}$ increases until the value $r_1$ is reached where tr $\mathbf{J} = 0$, then bifurcation occurs at this value of $w_1$ which corresponds to the critical Damköhler number $\mathrm{Da}_1^*$ through equation (38). If the parametric values $\alpha$ and $\beta$ satisfy condition (33) also, then the bifurcation originating at this critical Damköhler number $\mathrm{Da}_1^*$ is stable. Between the two critical Damköhler numbers $\mathrm{Da}_1^*$ and $\mathrm{Da}_2^*$ at which points tr $\mathbf{J} = 0$, the steady state is unstable, which is represented by a dashed line, while the stable limit cycles existing between these two $\mathrm{Da}^*$'s are denoted by dots. The distance between the dot and the dashed line approximately represents the average amplitude (in $x_2$) of the limit cycle surrounding the unstable steady state.

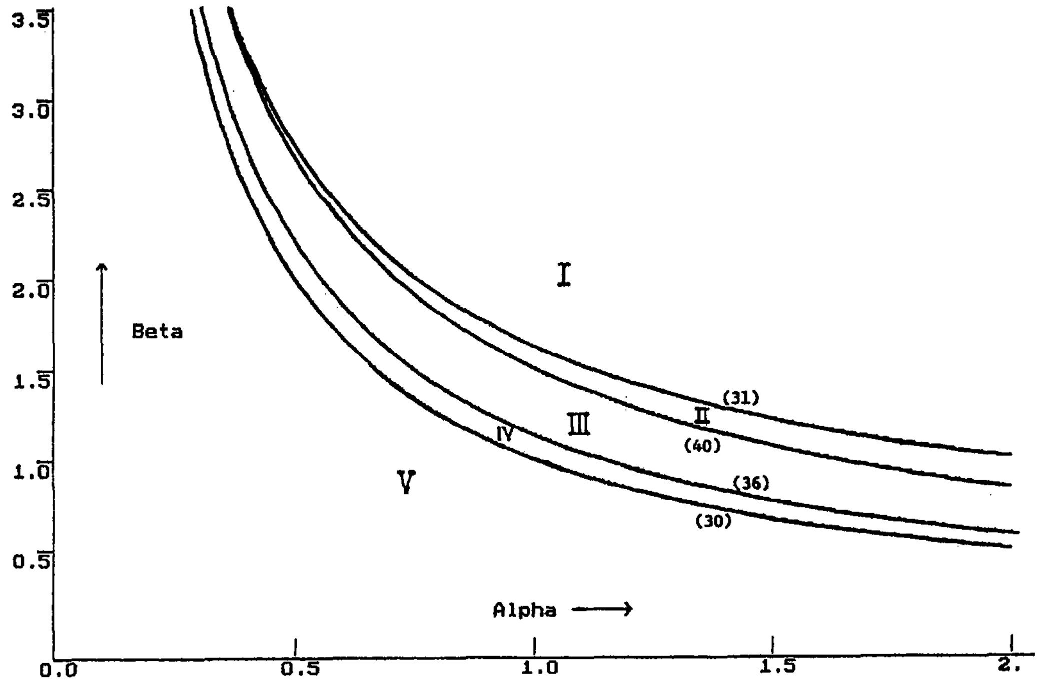


Figure 2. The $(\alpha, \beta)$ plane delineated by graphs of Equations (30), (31), (36), and (40) into 5 regions of qualitatively different dynamic behavior.

Table 1. Typical phase plots.

| | A | B | C | D | E | F | G | H | I | J | K |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Stable washout (node) | 1 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 1 | 1 | 1 |
| Unstable washout (saddle pt.) | 0 | 0 | 1 | 1 | 1 | 1 | 1 | 0 | 0 | 0 | 0 |
| Stable normal (node or focus) | 0 | 1 | 1 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 |
| Unstable normal (saddle pt. or focus) | 0 | 1 | 0 | 0 | 1 | 0 | 1 | 1 | 2 | 1 | 2 |
| Stable limit cycle | 0 | 0 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 0 | 0 |
| Unstable limit cycle | 0 | 0 | 0 | 1 | 0 | 1 | 0 | 1 | 0 | 1 | 0 |
| Total invariants | 1 | 3 | 2 | 4 | 3 | 3 | 2 | 5 | 4 | 4 | 3 |

## PARAMETER SPACE CLASSIFICATION

As discussed above, the two system parameters $\alpha$ and $\beta$ determine the stability regions of bifurcating periodic solutions. Figure 2 shows the $(\alpha, \beta)$ plane divided into 5 regions by the graphs of Equations (30), (31), (36) and (40). Following the representation used by Uppal *et al.* [8] we also show in Figure 3 typical steady state and limit cycle plots of $x_{s2}$ vs. $w$ for each region. There can be as many as eleven different types of qualitative phase planes which are possible for different ranges of $w$, and correspondingly the Damköhler numbers. These are labelled A through K in Table 1.

In Region I, there is no bifurcation ($\alpha\beta^2 - \beta - 1 > \mathbf{0}$). Three types of phase planes are possible: A, B and C. The type A shows only one stable washout steady state. The type B shows one stable washout, one unstable normal, and one stable normal, while the type C shows an unstable washout (saddle point) and a stable normal.

Region II is bounded above by the line $\alpha\beta^2 - \beta - 1 = \mathbf{0}$ and below by the graph of Equation (40). This region is also above the graph of Equation (36). Therefore, unstable bifurcation originates at the Damköhler number $\mathrm{Da}_1^*$ corresponding to the lower $w^*$ value $w_1^*$, with stable bifurcation

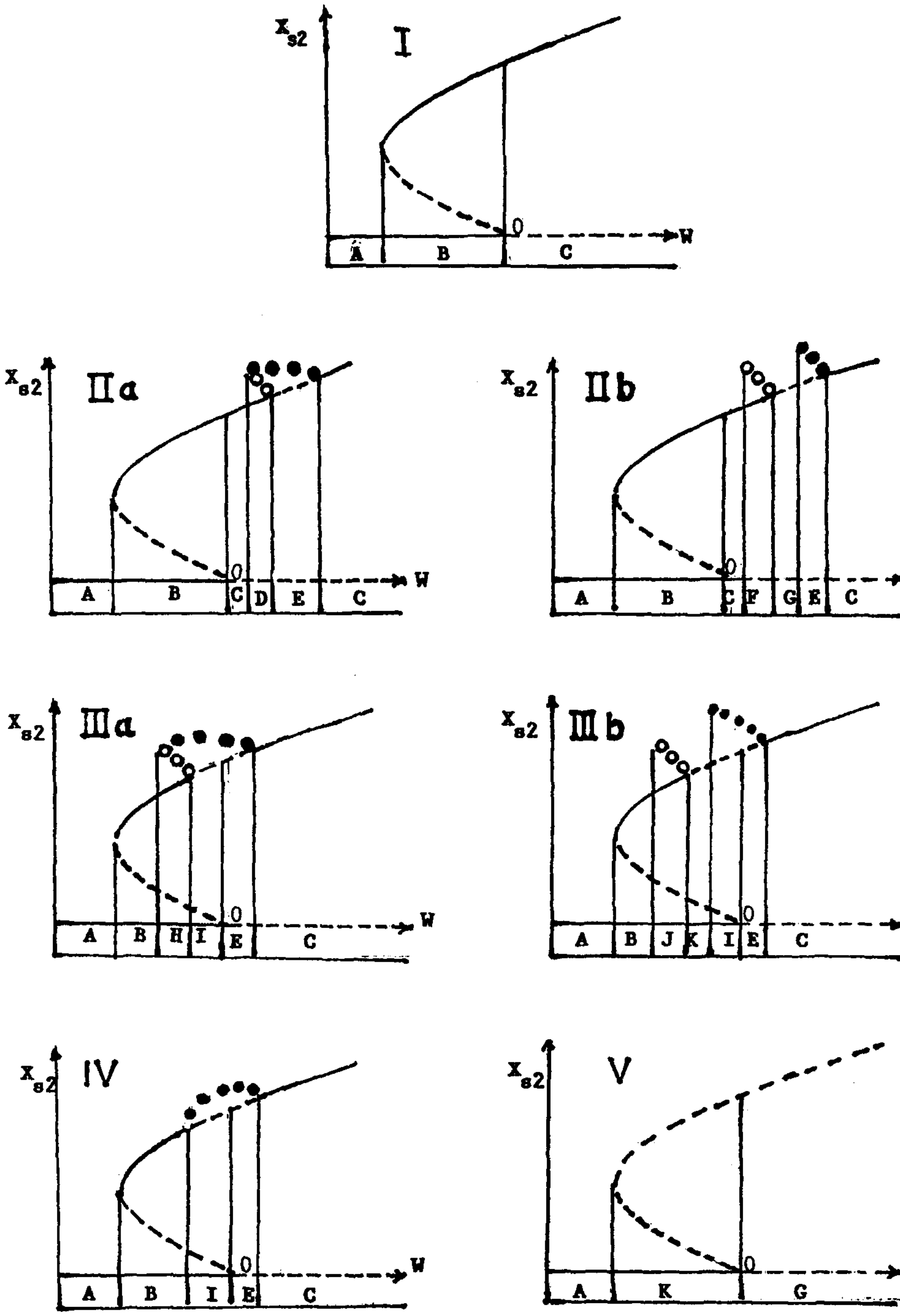


Figure 3. Typical plots of $w$ vs. $x_{s2}$ for each region of the $(\alpha, \beta)$ plane.

originating at the Damköhler number $\mathrm{Da}_2^*$ corresponding to the upper $w^*$ value $w_2^*$. In this region, two cases are possible, IIa and IIb, permitting seven types of phase planes, A through G. The type D shows one unstable washout (saddle point), a stable normal surrounded by one unstable limit cycle inside a stable one which bifurcates from the Damköhler number $\mathrm{Da}_2^*$. The type E shows one unstable washout, one unstable normal (focus), and a stable limit cycle which surrounds the steady state. The type F shows one unstable washout, one stable normal, and one unstable limit cycle. The type G shows one unstable washout and one unstable normal.

Figure 4 shows computer simulation of the system model for $\alpha = 1.0$ and $\beta = 1.6$, where the solution trajectories of the type F are seen to tend away from the unstable limit cycle whose approximate position is represented by the dashed line.

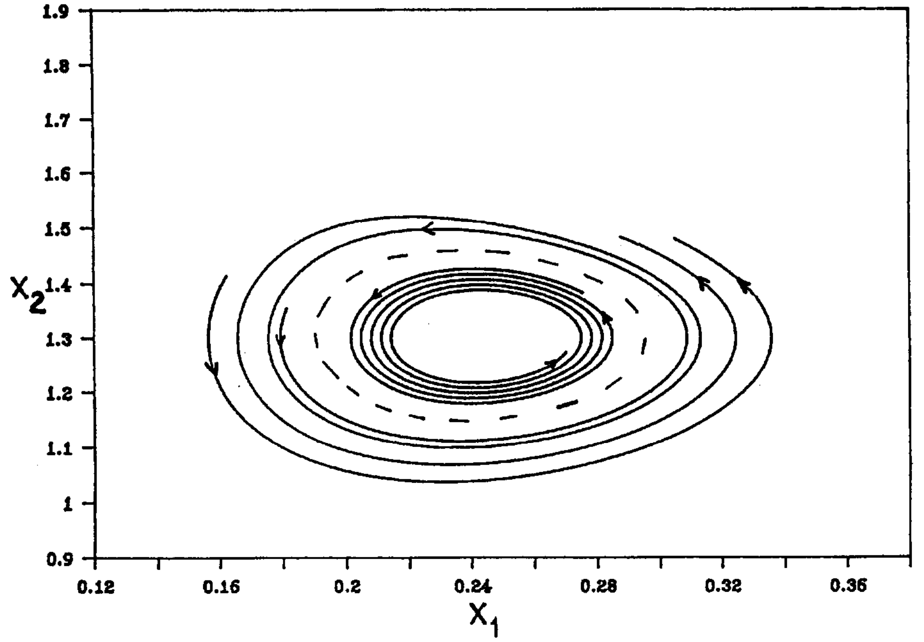


Figure 4. Computer simulation of the system model with $\alpha = 1.0$, $\beta = 1.6$, and Da = 0.61 (Region II, type F) showing solution trajectories tending away from the unstable limit cycle.

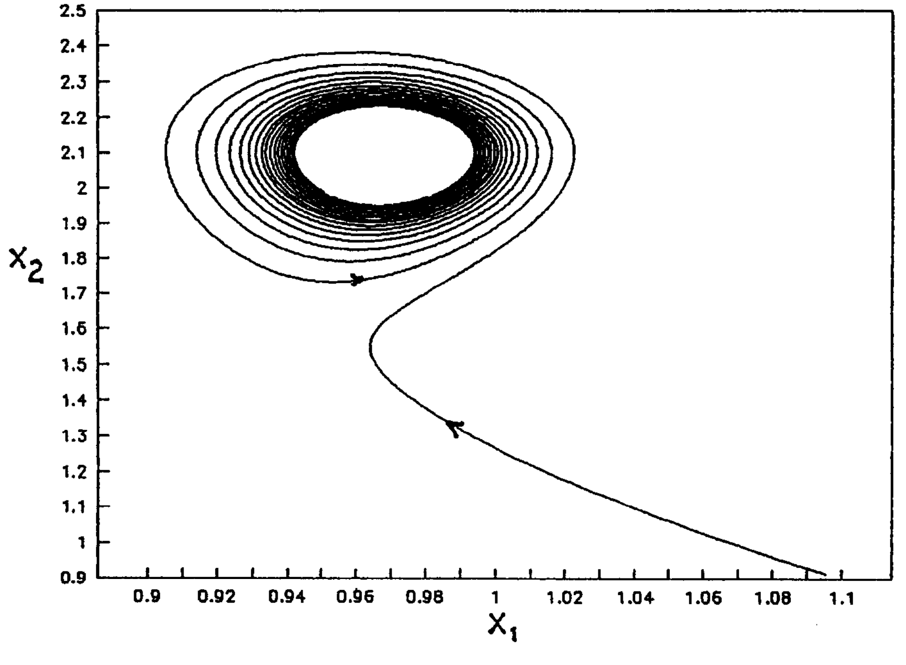


Figure 5. Computer simulation of the system model with $\alpha = 0.273997$, $\beta = 3.9$, and Da = 1.891370559 (Region IV, type I) showing trajectory approaching a stable limit cycle in the phase plane.

Region III is bounded above by the graph of Equation (40) and below by that of Equation (36). Here, $r_1$ lies below the value $1/\alpha$ and there can be two cases, IIIa and IIIb, in this region admitting eight types of phase planes, A through C, E, and H through K. The type H shows one stable washout, one unstable normal, and one stable normal (focus) surrounded by an unstable limit cycle inside a stable limit cycle. The type I shows one stable washout and two unstable normals, one of which is a focus surrounded by a stable limit cycle. The type J shows one stable washout, one unstable normal, one stable normal, and an unstable limit cycle. The type K shows one stable washout and two unstable normals.

Region IV is one of stable bifurcation at the Damköhler number $\mathrm{Da}_1^*$. Therefore, five types of phase plane trajectories are possible, A through C, E, and I. Figure 5 shows a computer simulation of the system model for $\alpha = 0.273997$ and $\beta = 3.9$ in this region IV and $\mathrm{Da} = 1.891370559$ of the type I, showing the predicted asymptotically stable limit cycle surrounding the unstable steady state.

Finally, in Region V, $\alpha\beta - 1 < 0$ and no bifurcation occurs. Tr $\mathbf{J}$ becomes positive at $x_{s2}$ for which $M'(x_{s2}) > 0$ so that the nonwashout steady states are always unstable. Thus, there are 3 possible types of phase planes in this region, A, G, and K.

## CONCLUSIONS

We have theoretically investigated steady state multiplicity and existence of limit cycle behavior of a continuous bio-reactor subject to product inhibition modelled by two mass balance equations over cells and product, in which the supply of substrate is assumed to be of a surplus amount so that the concentration change of $S$ has little effect on the rates of change in $X$ and $P$.

It is found that bifurcation to periodic solutions can occur only at the nontrivial steady state and not at the washout steady state. Asymptotically stable limit cycles exist for a significant range of the Damköhler number at appropriate system parametric values. While it is possible for bifurcation to originate at two Damköhler numbers $\mathrm{Da}_1^*$ and $\mathrm{Da}_2^*$, the one originating at the Damköhler number $\mathrm{Da}_2^*$ is always stable.

Employing a simple product inhibition form of the specific growth rate which results from linearizing the so called "one hump" function involving two parameters, phase plane trajectories have been completely classified and numerical examples given. A simple linearly decreasing "yield" coefficient $Y_p(P)$ was used which was sufficient to allow limit cycle behavior. In practice, the yield coefficient is known to vary for many organisms [10], and various researchers have adopted such linear form for the yield expression in their works with models of continuous fermentation processes [3,6,12–14]. It is also reasonable to expect that a high product concentration will have an inhibitory effect on the yield.

Our analysis of the influence of changing Damköhler number on the steady state and dynamic behavior of continuous bio-reactors subject to product inhibition yieds five dynamically different regions in the parameter plane and up to a combination of five possible invariants in a phase plane. It is expected that the results, as well as the analysis described, will be of some help in interpreting experimental data.

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