J. Sci. Soc. Thailand 12 (1986) 171-186

THE EFFECT OF THE SPECIFIC GROWTH RATES AND THE YIELD EXPRESSIONS ON OSCILLATIONS IN A TWO – TANK FERMENTOR

YONGWIMON LENBURY[a, c] AND PHILIP CROOKE[b]

[a]*Department of Physics & Mathematics, Faculty of Sciences, Mahidol University, Rama 6, Rd. Bangkok 10400, Thailand.*
[b]*Department of Mathematics, Vanderbilt University, Nashville, TN 37235, U.S.A.*

(Received 3 June 1986)

Abstract

Oscillations in the cells and substrate concentration in a two-tank continuous fermentation system are shown to be Hopf bifurcation in the underlying system of four ordinary differential equations. It is shown that, if other parameters are suitably fixed and the first tank yield is assumed constant, then a low first tank yield will result in a Hopf bifurcation to a periodic solution to the system. On the other hand, if the first yield depends linearly on the substrate level a more complex situation may develop. When the bifurcation parameter under consideration varies beyond a certain value, the existing periodic solution becomes unstable and a secondary bifurcation from this periodic solution occurs. This leads to an appearance of solutions on a torus in the four dimensional phase plane.

Introduction

Sustained oscillations in the cell concentration X and the substrate concentration S have been observed in continuous fermentation processes even though the feed concentration of substrate S_f, the dilution rate D, and other environmental conditions are kept constant[1-5]. Several mathematical models have been developed to investigate the continuous system, one of which consists of the system of ordinary differential equations:

$$\frac{dX}{dt} = X[\mu - D], \qquad X(0) = X^* \tag{1a}$$

$$\frac{dS}{dt} = D[S_f - S] - \frac{\mu X}{Y}, \quad S(0) = S^* \tag{1b}$$

[c] To whom correspondence should be addressed.

where Y is the cell substrate yield and μ is the specific growth rate. Extensive analysis of this model has been carried out[6-8] with μ being approximated by the Monod equation, i.e.,

$$\mu = \frac{\mu_{\max} S}{K_s + S}$$

where μ_{max}, the maximum growth rate, and K_s, the saturation constant, are positive constants, and the yield is assumed to depend linearly on S:

$$Y(S) = C_1 + C_2 S.$$

Here C_1 and C_2 are positive constants.

It was shown[7] that the model admits sustained oscillations in the X, S phase plane. Heinzle *et al.*[4] showed experimentally that the oscillations were dependent on the oxygen tension. However, the factors that determine the direction of the oscillation trajectory in the phase plane are still not well understood, although oxygen tension or aerobic/anaerobic consideration is most likely a candidate. Experimentally, both clockwise and counterclockwise oscillations have been observed. The data of Finn and Wilson[3] and Heinzel *et al.*[4] show counterclockwise oscillations, while that of Borzani, Gregori, and Vairo[2] indicates clockwise oscillations.

It was shown[9] that the model (1) leads only to clockwise oscillations, and a criterion was developed which differentiated between clockwise and counterclockwise oscillations. The analysis lead the authors[9] to propose a system which possesses counterclockwise oscillations, consisting of two connected continous flow tanks, each containing cells and substrate, (X_1, S_1), (X_2, S_2), respectively. It is assumed that the first tanks receives substrate at a concentration S_f. In this first tank, the dynamics of the cell mass X_1, and substrate S_1, are modelled by the following system:

$$\frac{dX_1}{dt} = X_1[\mu_1(S_1) - D], \qquad X_1(0) = X_1^* \qquad (2a)$$

$$\frac{dS_1}{dt} = D(S_f - S_1) - \frac{\mu_1(S_1)}{Y_1(S_1)} X_1, \quad S_1(0) = S_1^* \qquad (2b)$$

Here, D is the dilution rate, $Y_1(S_1)$ is the yield and $\mu_1(S_1)$ is the specific growth rate, described by the Monod equation:

$$\mu_1(S_1) = \frac{\mu_{\max_1} S_1}{K_{S_1} + S_1}.$$

In the second tank, cells are allowed to be digested to produce substrate so that the condition for a counterclockwise cycle, $\frac{d\mu(S)}{dS} < 0$ (found in ref. 9), is satisfied. The substrate enters the tank at a concentration $S_1(t)$ and cells at concentration $X_1(t)$. Thus, the model for this second tank is essentially (2) with X and S reversed. This is equivalent to reversing the time and hence the direction along the limit cycle. The model equations for the second tank are

$$\frac{dX_2}{dt} = D(X_1 - X_2) - \frac{\mu_2(X_2)}{Y_2(X_2)} S_2, \quad X_2(0) = X_2^* \qquad (3a)$$

$$\frac{dS_2}{dt} = S_2[\mu_2(X_2) - D] + DS_1, \qquad S_2(0) = S_2^* \qquad (3b)$$

where

$$\mu(X_2) = \frac{\mu_{\max_2} X_2}{K_{S_2} + X_2}$$

and

$$Y_2(X_2) = C_3 + C_4 X_2$$

A computer simulation of (2) and (3) is shown in Figure 1, which shows a counterclockwise limit cycle in the phase plane. In this paper, such oscillation in the two-tank system is shown to be a Hopf bifurcation in the underlying system of four ordinary differential equations. The case where Y_1 is assumed constant is first considered. It is show that, if other parameters are suitably fixed, a low yield Y_1 in the first tank results in a Hopf bifurcation to a periodic solution in the second tank.

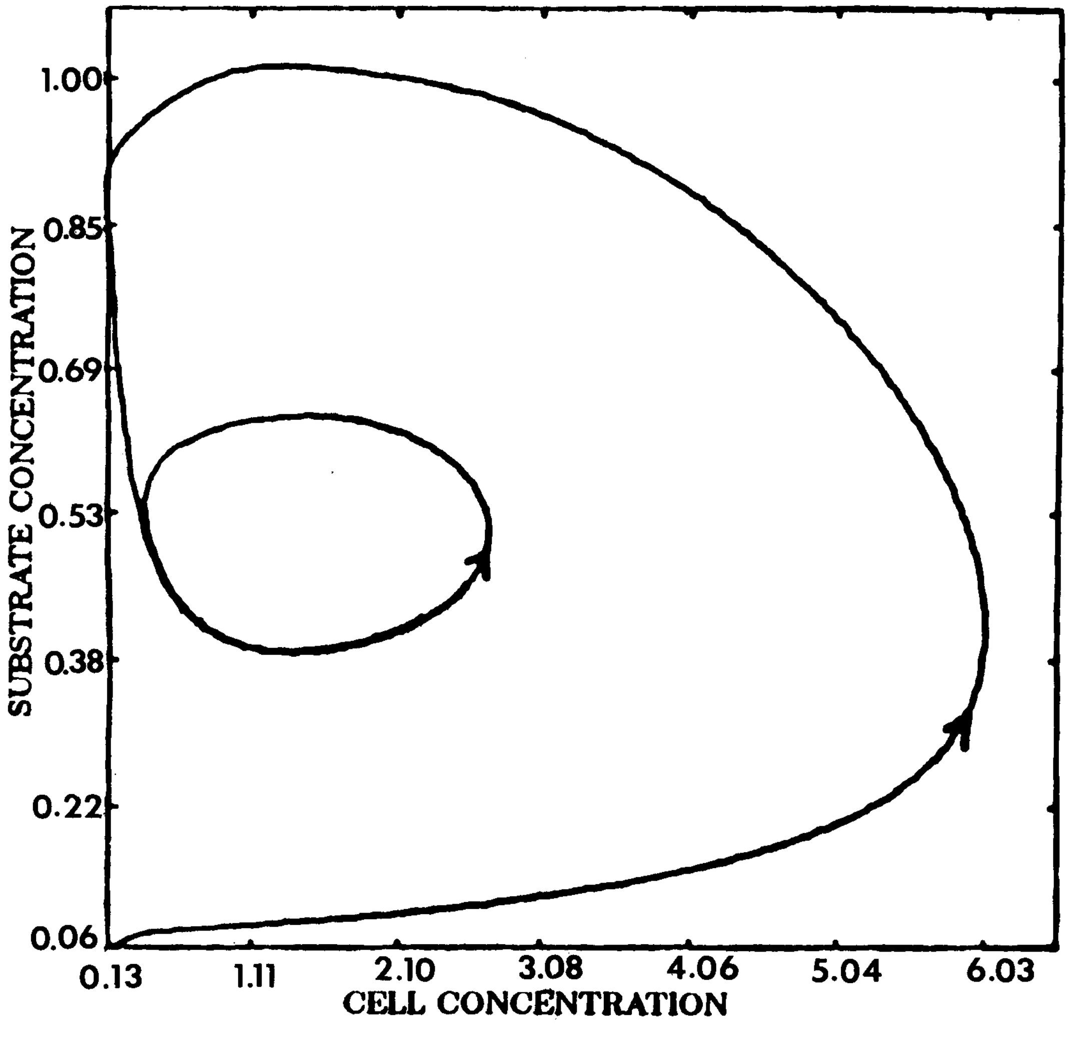

Figure 1. Computer simulation of (1a), (1b), (2a), (2b) with $\mu_{max1} = 1.14$, $K_{s1} = 0.14$, $\mu_{max2} = 0.3$, $K_{s2} = 1.75$, $C_1 = 0.5$, $C_2 = 0.01$, $C_4 = 0.03$, $D = 0.14$, and $S_f = 20$.

When the yield Y_1 is allowed to depend in a linear fashion on the substrate level S_1 according to the equation

$$Y_1(S_1) = C_1 + C_2 S_2$$

a more complex situation may develop. When the parameter C_1 decreases past a certain value, the existing periodic solution in the second tank becomes unstable and a secondary bifurcation from this periodic solution occurs. This leads to an appearance of solutions on a torus in the four dimensional phase plane. Further bifurcations are believed to lead to turbulence. This is when the time dependence of the solution becomes complicated, irregular and chaotic. Such behavior, although commonly observed in nature, is generally difficult to analyze and model. Our system, however, possesses sufficient degree of symmetries that the phenomenon can be explained by bifurcation theory.

Hopf Bifurcation in the Second Tank

Introducing dimensionless variables, $u = \frac{X_1}{S_f}$, $v = \frac{S_1}{S_f}$, $\omega = \frac{X_2}{S_f}$, $z = \frac{S_2}{S_f}$, $T = Dt$, and dimensionless contants, $\alpha = \frac{\mu_{max_1}}{d}$, $\beta = \frac{K_{S_1}}{S_f}$, $\nu = \frac{\mu_{max_2}}{D}$, $\epsilon = \frac{K_{S_2}}{S_f}$, $A = C_1$, $B = C_2 S_f$, $E = C_3$, $H = C_4 S_f$, (2) and (3) become

$$\frac{du}{dT} = u[g(v) - 1], \qquad u(0) = u^* = \frac{X^*}{S_f} \tag{4a}$$

$$\frac{dv}{dT} = 1 - v - \frac{g(v)}{G_1(v)} u, \qquad v(0) = v^* = \frac{S_1^*}{S_f} \tag{4b}$$

$$\frac{d\omega}{dT} = u - \omega - \frac{h(\omega)\ z}{G_2(\omega)}, \qquad \omega(0) = \omega^* = \frac{X_2^*}{S_f} \tag{4c}$$

$$\frac{dz}{dt} = z(h(\omega) - 1) + v, \qquad z(0) = z^* = \frac{S_1^*}{S_f} \tag{4d}$$

where

$$g(v) = \frac{\alpha v}{\beta + v} \tag{5}$$

$$h(\omega) = \frac{\nu\omega}{\epsilon + \omega} \tag{6}$$

$$G_1(v) = A + Bv \tag{7}$$

and

$$G_2(\omega) = E + H\omega. \tag{8}$$

To locate a critical point $(u_0, v_0, \omega_0, z_0)$ of the system (4) in the first quadrant, we set $\frac{du}{dT} = \frac{dv}{dT} = \frac{d\omega}{dT} = \frac{dz}{dT} = 0$. We find the resulting nonlinear equations decouple to

$$v_0 = \frac{\beta}{\alpha - 1} \tag{9}$$

$$u_0 = \frac{(\alpha - \beta - 1)(A + Bv_0)}{\alpha - 1} \tag{10}$$

$$\omega_0 + \frac{h(\omega_0)}{G_2(\omega_0)} z_0 = u_0 \tag{11}$$

and

$$z_0 = \frac{v_0}{1 - h(\omega_0)} \tag{12}$$

Using (11) and (12), we arrive at the following cubic equation in ω_0:

$$H(1-\nu)\omega_0^3 + \{H[\epsilon - u_0(1-\nu)] + E(1-\nu)\}\omega_0^2$$

$$+ \{E[\epsilon - u_0(1-\nu)] - \epsilon u_0 H + \nu v_0\}\omega_0 - \epsilon u_0 E = 0 \tag{13}$$

where u_0 is given in (10). Equation (13) gives ω_0, once A, B, α, β, and ϵ are specified. The Jacobian matrix of (4) about $(u_0, v_0, \omega_0, z_0)$ is

$$(u_0, v_0, \omega_0, z_0) =$$

$$\begin{bmatrix} 0 & u_0 g'(v_0) & 0 & 0 \\ \frac{1}{G_1(v_0)} & -1-\left(\frac{g}{G_1}\right)'(v_0)u_0 & 0 & 0 \\ 1 & 0 & -1-\left(\frac{h}{G_2}\right)(\omega_0)z_0 & \frac{-h(\omega_0)}{G_2(\omega_0)} \\ 0 & 1 & z_0 h'(\omega_0) & h(\omega_0)-1 \end{bmatrix} \quad (14)$$

The eigenvalues of this 4 × 4 matrix are

$$\lambda_{1,2} = \left[-\Gamma \pm \sqrt{\Gamma^2 - 4\left[\frac{(\alpha-1)^2-(\alpha-1)\beta}{\alpha\beta}\right]}\right] \quad (15)$$

where

$$\Gamma = 1 + \frac{(\alpha-1)(\alpha-1-\beta)}{\alpha\beta} - \frac{B(\alpha-1-\beta}{A(\alpha-1)+B\beta} \quad (16)$$

and

$$\lambda_{3,4} = \Theta + i\sqrt{I(\Theta)} \quad (17)$$

where

$$\Theta = \frac{1}{2}\left[-1-\left(\frac{h}{G_2}\right)'(\omega_0)z_0 - \frac{v_0}{z_0}\right] \quad (18)$$

and

$$I(\Theta) = \frac{h(\omega_0)h'(\omega_0)}{G_2(\omega_0)}z_0 + \frac{v_0}{z_0}\left[1+\left(\frac{h}{G_2}\right)'(\omega_0)z_0\right] - \Theta^2. \quad (19)$$

With Θ as the bifurcation parameter, a bifurcation to a periodic solution will occur at

$$\Theta = 0 \tag{20}$$

if

$$I(\Theta = 0) = \frac{h(\omega_0)h'(\omega_0)}{G_2(\omega_0)} z_0 + \frac{v_0}{z_0}\left[1 + \left(\frac{h}{G_2}\right)'(\omega_0) z_0\right] > 0. \tag{21}$$

If (20) and (21) are satisfied, then the system (4) has a family of periodic solutions whose periods are approximately $\frac{2\pi}{\sqrt{I(0)}}$. Further, if

$$\Gamma > 0 \tag{22}$$

then the eigenvalues $\lambda_{1,2}$ have negative real parts, and there is a neighborhood N of the point, $(u, v, \omega, z, 0) = (u_0, v_0, \omega_0, 0)$ in $\mathbf{R}^4 \times \mathbf{R}^4$ such that any closed orbit in N is one of those above.

At this point, assuming that (22) is satisfied, we make the following observations:

a) If G_2 is constant $(G_2(\omega) \equiv E, H = 0)$ then

$$\Theta = \frac{1}{2}\left[-2\{2 - h(\omega_0)\} - \frac{\epsilon \nu z_0}{(\epsilon + \omega_0)^2 E}\right] < 0. \tag{23}$$

Therefore, the system does not admit a Hopf bifurcation in the case that G_2 (the dimensionless yield in the second tank) is constant.

b) If the dimensionless specific growth rate $h(\omega)$ is constant $(h(\omega) \equiv \nu, \epsilon = 0)$, then $h'(\omega) = 0$ and when $\Theta = 0$,

$$I(0) = -\left(\frac{v_0}{z_0}\right)^2 < 0. \tag{24}$$

This means that, for the case that the dimensionless specific growth rate function in the second tank is constant, the condition (21) is not satisfied and we do not have a Hopf bifurcation to a periodic solution at $\Theta = 0$.

c) If the yield term G_1 in the first tank is constant $(G_1(v) \equiv A, B = 0)$, then we find from (11) and (12) that

$$z_0 = \frac{\omega_0 - 1}{A(h(\omega_0) - 1) - \frac{h(\omega_0)}{G_2(\omega_0)}} \tag{25}$$

using (9) and (10). Assuming that (21) holds in a neighborhood of $\Theta = 0$, we have bifurcation when $\Theta > 0$, that is,

$$A < Q \equiv \frac{(\omega_0 - 1)\frac{h(\omega_0)}{G_2(\omega_0)} - \frac{h(\omega_0)}{G_2(\omega_0)}(2 - h(\omega_0))}{(1 - h(\omega_0))(2 - h(\omega_0))} \tag{26}$$

Condition (26) tells us that, once ω_0, ν, ϵ, E, and H (and hence Q) are specified, then a bifurcation to a periodic solution occur when the yield $G_1 \equiv$ A decreases beyond the value Q.

Variable Yield G_1

Here, we consider the case when G_1 depends in a linear fashion on the substrate level S_1 according to (7) with both A and B nonzero. We will investigate the effect of the parameter A on the oscillatory behavior of the two-tank system. For simplicity of the following analysis, we assume that $E = 0$ (that is, $G_2(\omega) \equiv H$), and $\nu = 1$.

A. Primary Bifurcation

We first consider system:

$$\frac{d\omega}{dT} = u_0 - \omega - \frac{h(\omega)}{G_2(\omega)}z, \quad \omega(0) = \omega^* \tag{27a}$$

$$\frac{dz}{dT} = (h(\omega) - 1) + v_0, \quad z(0) = z^* \tag{27b}$$

which are in fact equations (4c) and (4d) with (u , v) set equal to (u_0 , v_0), the critical point of (4a), (4b). The critical point of (27) is still (ω_0 , z_0), as given in (11), (12). The Jacobian of (27) about (ω_0 , z_0) is

$$J_1(\omega_0, z_0) = \begin{bmatrix} -1 - \left(\frac{h}{G_2}\right)'(\omega_0)z_0 & \frac{-h(\omega_0)}{G_2(\omega_0)} \\ z_0 h'(\omega_0) & h(\omega_0) - 1 \end{bmatrix} \tag{28}$$

Comparing (28) with the matrix J (u_0 , v_0 , ω_0 , z_0) in (14), it is clear that the eigenvalues of J_1(ω_0 , z_0) are exactly $\lambda_{3,4}$ given in (17), (18) and (19). Thus, we have a Hopf bifurcation to a periodic solution for the system (27) when (20) and (21) are satisfied. For the case that $E = 0$ and $\nu = 1$, (20) becomes

$$v_0 > (\omega_0 + 2\epsilon)\epsilon H. \tag{29}$$

Equation (13) becomes

$$H\epsilon\omega_0^2 - (\epsilon u_0 H - v_0)\omega_0 = 0 \tag{30}$$

Solving for ω_0 in (30), we find

$$\omega_0 = u_0 - \frac{v_0}{H\epsilon}. \tag{31}$$

Using (31) and (10), (29) becomes

$$A + Bv_0 < P \equiv \frac{2(v_0 - \epsilon^2 H)}{\epsilon H(1 - v_0)} \tag{32}$$

or

$$A < P - \frac{B\beta}{\alpha - 1} \tag{33}$$

This means that if α , β, ϵ , and H are given, then we must be in the region below the line $A + Bv_0 = P$ in the (B, A) parameter plane for a bifurcation to occur in the second tank (see Figure 2), with the first tank running under the conditions such that the cells are fed into the second tank at the constant concentration u_0, and the substrate at the constant concentration v_0.

In other words, if (21) and (33) are satisfied then there is a periodic solution $(\bar{\omega}(T), \bar{z}(T))$ to the system (27). Since (u_0, v_0) is a stationary point of (4a) and (4b), the periodic function $(u_0, v_0, \bar{\omega}(T), \bar{z}(T))$ is a solution to the system (4). Figure 3 shows a computer simulation of (4) with $(u^*, v^*, \omega^* z^*) = (v_0, v_0 \omega^*, z^*)$ and $A + Bv_0 < P$, showing a bifurcating limit cycle in the (ω, z) phase plane (the second tank).

B. Secondary Bifucation

We have seen above how a fixed point $(u_0, v_0 \omega_0, z_0)$ of (4) may be replaced by a closed orbit $p(T) = (u_0, v_0 \bar{\omega}(T) \bar{z}(T))$ when the parameter A decreases beyond the value $P - Bv_0$ (see Figure 3). We consider now the next bifurcation. It is quite concievable that for A close to $P - Bv_0$, the closed orbit might be stable, but for smaller A it might become unstable and a stable torus takes its place. To investigate when this might happen for system (4), we note that the periodic solution $p(T) = (u_0, v_0, \bar{\omega}(T), \bar{z}(T))$ to (4) occurs at the stationary solution (u_0, v_0) of the system (4a), (4b). Thus we only have to investigate the stability of the stationary solution (u_0, v_o) of (4a), (4b) to find the condition for secondary bifurcation of the closed orbit $p(T)$ into a torus in the four dimensional phase plane. To do this, consider now the system (4a), (4b). The Jacobian of this system about (u_0, v_0) is

$$J_2(u_0, v_0) = \begin{bmatrix} 0 & u_o g'(v_0) \\ \frac{1}{G_1(v_0)} & -1 - \left(\frac{g}{G_1}\right)'(v_0)u_0 \end{bmatrix} \qquad (34)$$

Comparing (34) with the matrix in (14), it is clear that the eigenvalues of (34) are exactly $\lambda_{1,2}$ given in (15), (16).

The stationary solution (u_0, v_0) (and hence the periodic solution $p(T)$ will be stable if

$$\Gamma > 0$$

when the eigenvalues of $J_0(u_0, v_0)$ both have negative real parts. The stationary solution (u_0, v_0) loses its stability at $\Gamma = 0$, resulting in a bifurcation for the system (4a), (4b) "on top of" the basic periodic solution which bifurcates from the stationary solution of (4). This, therefore, represents a bifurcation in the 4-dimensional coordinate space (u, v, ω, z). Using (16), we have a secondary bifurcation when

$$\frac{A}{B} < R \equiv \frac{\alpha\beta(1-\beta) - \beta(1+\beta)}{(\alpha-1)[(\alpha-1)^2+\beta]} \tag{35}$$

or

$$A < RB, \tag{36}$$

assuming that $\alpha > \beta + 1$ (so that $\lambda_{1,2}$ are non-real). In orther words, when

$$A < \min(RB, P - Bv_0) \tag{37}$$

there exists a family of bifurcating tori in the 4-dimensional phase plane. This means that in the *(B, A)* parameter space, the point *(B, A)* must be located in the region below both lines $A + Bv_0 = P$ and $A = RB$ (see Figure 2). where *P, R* and v_0 are fixed once α, β, ϵ and H are given.

Figure 4 shows a limit cycle bifurcating from the stationary solution (u_0, v_0) in the first tank when (37) is satisfied. Such bifurcation on top of the original periodic solution (shown in Figure 3) results in an appearance of a torus in the four dimensional phase plane. The projection of the torus onto the (w, z) plane is shown in Figure 5, in which both (33) and (36) are satisfied (corresponding to the shaded region in Figure 2).

CONCLUSIONS

In this paper, it is shown that oscillations in the two-tank continuous system is a Hopf bifurcation in the underlying system of ordinary differential equations. When G_2 (corresponding to the yield term in the second tank) is contant, we observe that the system does not admit a Hopf bifurcation if the paramters α, β, A, and B are such that $\Gamma > 0$. Also, we do not have two pure imaginary eigenvalues when $\Gamma = 0$ if the specific growth rate in the second tank is constant. Thus, no bifurcation to a periodic solution occurs.

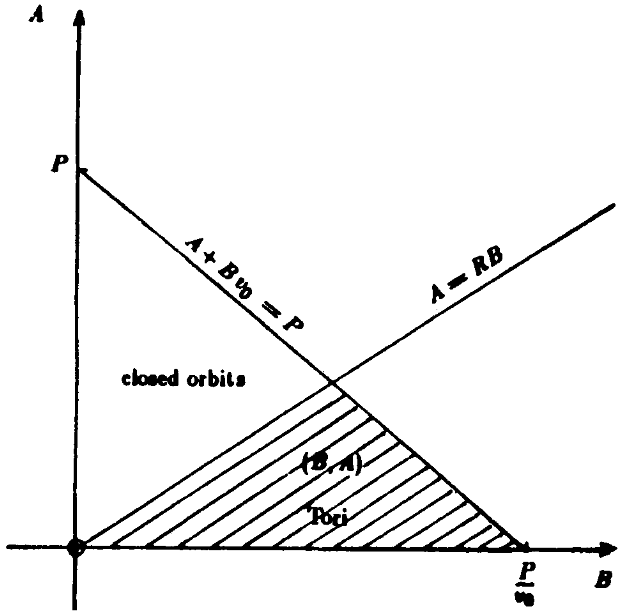

Figure 2. Plot of the lines $A+B\,v_0 = P$ and $A = RB$, showing the shaded region in the (B, A) plane where a secondary bifurcation to a torus is possible.

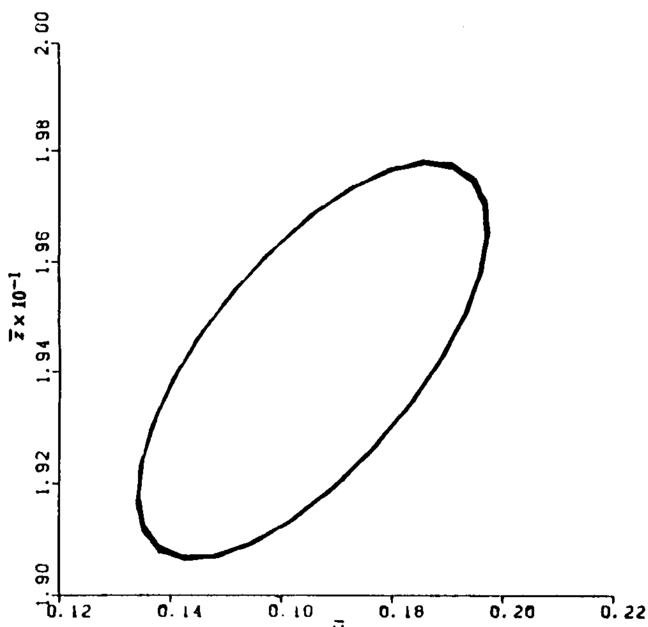

Figure 3. Computer simulation of (1a), (1b), (2a), (2b) with $\nu = 1$, E = 0, E = 4.0, $\alpha = 4.0$, $\beta = 0.5$, $\varepsilon = 1.0$, H = 1/13, A = 0.1407, B = 15.95, and $(u^*, v^*, \omega^*, z^*) = (v_0, v_0, \omega^*, z^*) = (2.33255, 0.1667, 0.155, 0.191)$, showing a limit cycle in the (ω, z) plane.

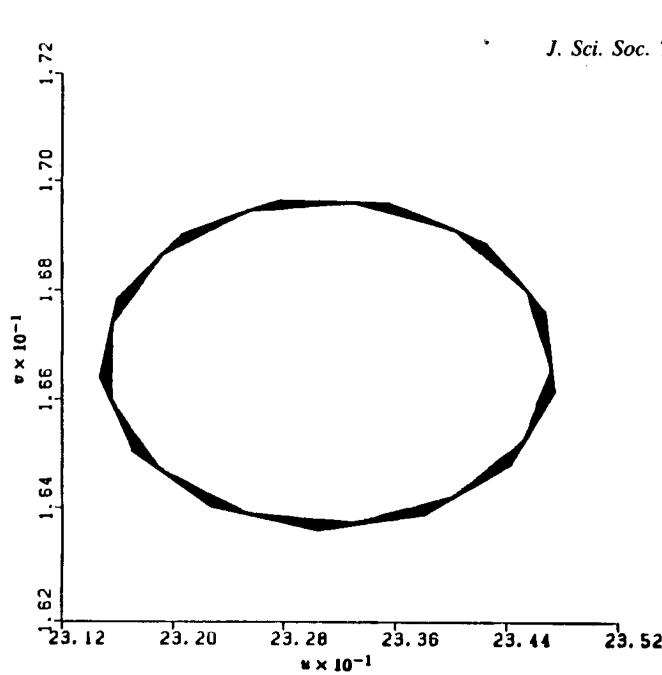

Figure 4. A plot of a limit cycle in the (u, v) plane after secondary bifurcation has occured for the system (1a), (1b), (2a), (2b), with ν = 1, E = 0, α = 4.0, ß = 0.5, ε = 1.0, H = 1/13, A = B/114.8, B = 15.95 and (u^*, v^* ω^*, z^*) = (2.347, 0.1667, 0.155, 0.191).

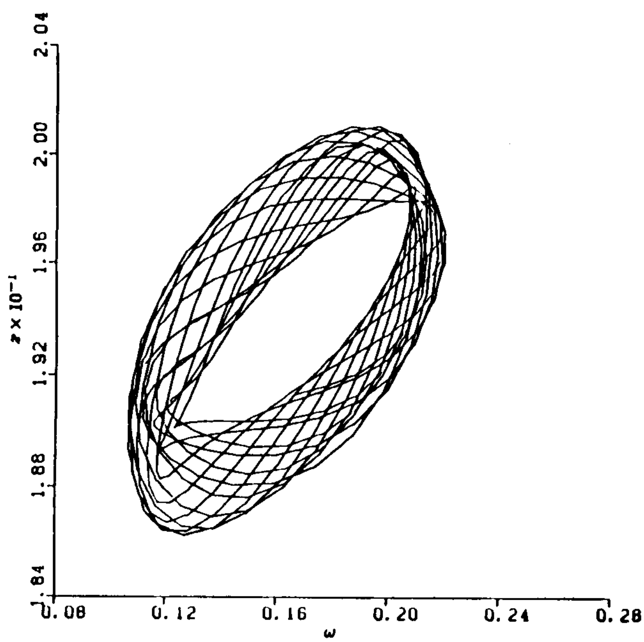

Figure 5. The projection onto the (w, z) plane of the bifurcating torus, ν = 1, E = 0, α = 4.0, ß = 0.5, ε = 1.0, H = 1/13, A = B/144.8, B = 15.95, and (u^*, v^* ω,* z^*) = (2.347, 0.1667, 0.155, 0.191).

The constant yield term $G_1 \equiv A$ in the first tank is shown to play an essential role in the bifurcation of the system. When ω_0, ε, ν, E, and H are fixed, Q is given in (26). When G_1 (equivalently A) decreases past the value Q then a Hopf bifurcation occurs.

On the other hand, if α, β, ε and H are fixed, in the case the $\nu = 1$ and $E = 0$, then P is given in (32). In this case, a Hopf bifurcation to a periodic solution occurs when A satisfies the inequality

$$A < P - \frac{B\beta}{\alpha - 1}$$

If A is allowed to decrease further, past the value RB, then a further bifurcation is expected from the basic closed orbit to a torus in the 4-dimensional phase plane.

Beautiful examples of periodic oscillations have been observed in chemical systems of biological origins. The physical phenomenon where the time dependence appears complicated, irregular and chaotic, however, might be easily overlooked in the chemical system as "messy, unusable data." In fluid dynamics, the phenomenon of turbulent fluid motion has recieved various mathematical interpretations. It was argued by Leray[11] that it leads to a breakdown of the validity of the Navier Stokes equations used to describe the system. Ruelle and Takens[12], however, argued that while such a breakdown may happen, it does not necessarily accompany turbulence. We hope that it has been demonstrated here that the phenomenon is, in fact, perfectly respectable and might have physiological-or pathological-significance in biological systems.

Acknowledgment

The authors would like to express their graditude to Gerando Montero who did some of the initial numerical studies on the problem. Also, we would like to thank Professor Robert Tanner who helped with the development of the two-tank model.

References

1. Bonomi, A., Aboutboul, H., and Schmidell, W. (1981). In *Biotechnology and Bioengineering Symp.* No. 11, Ed. C.D. Scott, New York, J. Wiley, pp. 333-357.
2. Borzani, W., Gregori, R.E., and Vairo, M.L.R. (1979). Some Observations on Oscillatory Changes in the Growth Rate of *Saccharomyces cerevisiae* in Aerobic Continuous Undisturbed Culture. *Biotechnol. Bioeng.* **19**, 1363-1374.

3. Finn, R.K. and Wilson, R.E. (1954). Population Dynamics of a Continuous Propagator for Microorganisms." *Journal of Agricultural and Food Chemistry* **2,** 66-69.

4. Heinzle, E., Dunn, I.J., Furukawa, K., and Tanner, R.D. (1983). Modelling of Sustained Oscillations Observed in Continuous Culture of *Saccharomyces cerevisiae. First IFAC Workshop on Modelling and Control of Biotechnical Pwocesses,* Helsinki, Finland, Ed. A. Palme, Pergamon Press, Oxford, pp. 57-65.

5. Kraepelin, G. (1973). In *Biological and Biochemical Oscillators,* Ed. B. Chance, E.K. Pye, A.K. Ghosh, and B. Hess, Academic Press, New York, pp. 419-427.

6. Crooke, P.S. and Tanner, R.D. (1982). Hopf Bifurcations for a Variable Yield Continuous Fermentation Model. *Int. J. Eng. Sci.* **20,** 439-443.

7. Crooke, P.S., Wei, C.J., and Tanner, R.D. (1980). The Effect of the Specific Growth Rate and Yield Expression on the Existance of Oscillatory Behavior of a Continuous Fermentation Model. *Chem. Eng. Commun.* **6,** 333,-347.

8. Essajie, C. K., and Tanner R. D. (1976). The Effect of Extracellular Variables on the Stability of the Continuous Baker's Yeast-Ethanol Fermentation Process. *Process Biochem.* **14,** 16-21.

9. Simon, F. A., Tanner, R. D., Crooke, P.S., and Heinzle, E. (1983). Criteria for Determining the Direction of the Sustained Oscillation Trajectory in the Cell-Substrate Phase Plane Describing Continuous Fermentation Systems. *Biotechnology and Bioengineering Symp.* No. 13, pp. 257-264.

10. Hassard, B.D., Kazarinoff, N.D., and Wan, Y-H. (1981). *Theory and Applications of Hopf Bifurcation,* Cambridge University Press, Cambridge, p. 16.

11. Leray, J. (1934). Sur le mouvement d'um liquide visquex emplissant l'espace. *Acta Math.* **63,** 193-248.

12. Ruelle, D. and Takens, F. On the Nature of Turbulence. (1971). *Commun. Math. Phys.* **20,** 167-192.

บทคัดย่อ

ถ้าแสดงว่าการเปลี่ยนแปลงขึ้น ๆ ลง ๆ ของความเข้มข้นของเซลและสารอาหารในระบบการหมักแบบต่อเนื่องในสองแท้งค์ เกิดมาจากปรากฏการณ์ Hopf bifurcation ของระบบสมการอนุพันธ์ธรรมดาสี่สมการ เราแสดงว่าถ้า parameters ต่าง ๆ มีค่าที่ถูกต้อง และให้ yield ในแท้งค์แรกมีค่าคงที่ ค่า yield ต่ำ ในแท้งค์แรกจะทำให้เกิด Hopf bifurcation เกิดเป็น periodic solution ขึ้น แต่ถ้า yield ในแท้งค์แรกเป็นฟังก์ชั่นเชิงเส้นของระดับสารอาหาร และ bifurcation parameter มีค่าเปลี่ยนแปลงไปจนเกินค่า ๆ หนึ่ง periodic solution ที่มีอยู่นั้นจะเริ่มไม่มีเสถียรภาพทำให้เกิด secondary bifurcation ขึ้นจาก periodic solution ดังกล่าวนั้น ปรากฏการณ์นี้ทำให้เกิดเป็น solutions บนรูป torus ใน phase plane ซึ่งเป็นสี่มิติ