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DYNAMIC BEHAVIOR OF THE CHEMOSTAT SUBJECT TO PRODUCT INHIBITION

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Theoretical study was made on the transient behavior of a single-vessel continuous fermentation in which the growth of a microorganism is inhibited by its product. When the product formation was negatively growth-associated, occurrence of diverging as well as damped oscillations was shown with the analog computer. No oscillation could be observed, on the other hand, when the product formation was either completely growth-associated, completely non-growth associated, or partially growth-associated. The present model for a product-inhibited chemostat covers the Stepanova-Romanovskii model as one of its special cases, while it is in parallel with the Ramkrishna-Fredrickson-Tsuchiya model that deals with a chemostat in which one of its products has a cell-killing effect on the microorganism.

Our preceding papers (*1*, *2*) discussed the dynamic nature of the chemostat in which the specific growth rate of a microorganism depended only on the concentration of a substrate. This paper discusses the nature of the chemostat in which the specific growth rate depends on the concentrations of both a substrate and an inhibitory product of a microorganism.

In this regard, STEPANOVA and ROMANOVSKII (*3*) discussed the continuous lactic acid fermentation assuming that (a) dependence of the specific growth rate on the concentration of an inhibitory product is similar to that of the enzyme reaction rate on the concentration of a non-competitive inhibitor, and (b) the type of product formation is that of the so-called growth-associated. They used the following expression for their continuous fermentation system.

$$\mu = \frac{\mu_m S}{(K_S + S)\left(1 + \dfrac{P}{K_P}\right)} \tag{1}$$

$$\begin{cases} \dfrac{dX}{dt} = \mu X - DX & (2) \\ \dfrac{dS}{dt} = D(S_R - S) - \dfrac{1}{Y}\mu X & (3) \\ \dfrac{dP}{dt} = \eta\mu X - DP & (4) \end{cases}$$

They showed by using the analog computer that an overshoot could be observed in the time course of the biomass (X) and lactate concentration (P), but not any oscillations.

THEORETICAL

Mathematical model

We assumed the specific growth rate equation as follows so as to cover wider problems of product inhibition; this is what one usually does for general analysis of the enzyme reaction under the effect of a non-competitive inhibitor.

$$\mu = \frac{\mu_m S}{(K_S + S)\left\{1 + \left(\dfrac{P}{K_P}\right)^n\right\}} \tag{5}$$

Eq. (5) could also be generalized as for S in the manner shown in one (*2*) of the preceding papers. This, however, does not add any significant information to those available for studying the effect of the inhibitory product on the dynamic character of the chemostat. The simple Monod function is, therefore, left in Eq. (5) as it usually stands.

Eq. (4) assumes the growth-associated product formation as mentioned above. The rate of product formation will be better expressed by the following equation, since it covers the "non-growth associated" as well as the growth-associated production.

$$\frac{1}{X}\left(\frac{dP}{dt}\right)_{\text{production}} = \eta_1 + \eta_2\mu \qquad (>0) \tag{6}$$

LUEDEKING and PIRET (*5*) claimed that Eq. (6) held for the lactic acid fermentation. Note that the right hand side of Eq. (6) is the linear approximation to any function of μ.

By using Eqs. (5) and (6), the single-vessel continuous fermentation system can be described as follows:

$$\left\{\begin{aligned} &\mu=\frac{\mu_m S}{(K_S+S)\left\{1+\left(\frac{P}{K_P}\right)^n\right\}} &&(5)\\ &\frac{dX}{dt}=\mu X-DX &&(7)\\ &\frac{dS}{dt}=D(S_R-S)-\frac{1}{Y}\mu X &&(8)\\ &\frac{dP}{dt}=(\eta_1+\eta_2\mu)X-DP &&(9)\end{aligned}\right.$$

Obviously, the model coincides with that given by Eqs. (1)–(4), if $n=1$ and $\eta_1=0$.

Types of product formation

Before going into analysis of the present chemostat model, it seems convenient here to classify the types of product formation. Usually production is called "growth-associated" if $\eta_1=0$ in Eq. (6), and "non-growth associated" if $\eta_1>0$ and $\eta_2=0$. Looking at Eq. (6) carefully, however, one will see that η_1 should not be negative because the right hand side of the equation must be positive for any small value of μ, while η_2 may be negative as seen, for example, in the biotin-limited glutamic acid fermentation. The types of product formation can now be classified in more general terms as shown in Table 1.

Steady state

The non-zero steady solution to the set of Eqs. (7)–(9) is obtained by making all the differential terms zero.

$$\left\{\begin{aligned} &\mu_\infty=\frac{\mu_m S_\infty}{(K_S+S_\infty)\left\{1+\left(\frac{P_\infty}{K_P}\right)^n\right\}}=D &&(10)\\ &X_\infty=Y(S_R-S_\infty) &&(11)\\ &P_\infty=Y\left(\frac{\eta_1}{D}+\eta_2\right)(S_R-S_\infty) &&(12)\end{aligned}\right.$$

Although Eqs. (10)–(12) cannot be easily rearranged into explicit forms as for X_∞, S_∞, and P_∞, one will see from Fig. 1, a graphic expression of Eqs. (5), (10), and (12), that there exists only one real positive steady solution, if

$$0<D<\frac{\mu_m S_R}{K_S+S_R} \qquad (13)$$

Table 1. Classification of the types of product formation.

$$\frac{1}{X}\left(\frac{dP}{dt}\right)_{\text{production}}=\eta_1+\eta_2\mu>0$$

	η_1	η_2
Completely growth-associated	0	+
Completely non-growth associated	+	0
Partially growth-associated	+	+
Negatively growth-associated	+	−

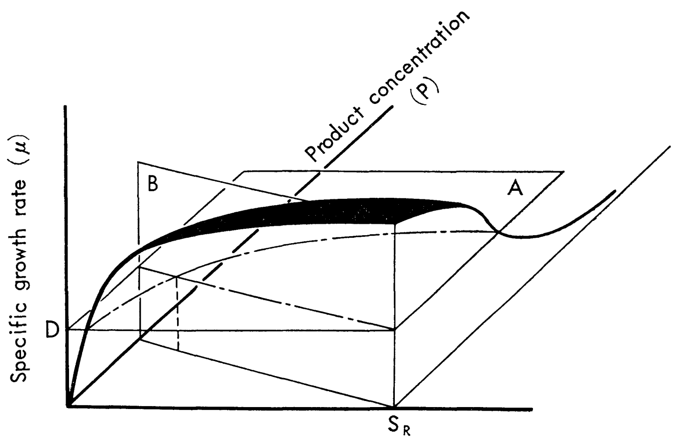


Fig. 1. Graphic expression of the steady solution.

Curved surface: Eq. (5) in the text

Plane A : $\mu=D$

Plane B : $P=Y\left(\frac{\eta_1}{D}+\eta_2\right)(S_R-S)$

This constraint is the same as that for the simple Monod model without inhibition.

Behavior of the system in the neighborhood of the steady solution

Local stability of the steady solution and transient nature of the system can be studied in the same way as already described (*1*, *2*, *4*, *6*). Linear approximation to the differential Eqs. (7)–(9) in the neighborhood of the non-zero steady solution gives

$$\left\{\begin{aligned} &\frac{dx}{dt}=a_{12}y-a_{13}z \\ &\frac{dy}{dt}=-\frac{D}{Y}x-\left(D+\frac{a_{12}}{Y}\right)y+\frac{a_{13}}{Y}z \\ &\frac{dz}{dt}=(\eta_1+\eta_2 D)x+\eta_2 a_{12}y-(D+\eta_2 a_{13})z \end{aligned}\right. \tag{14}$$

where

$$\left\{\begin{aligned} &x=X-X_\infty \\ &y=S-S_\infty \\ &z=P-P_\infty \end{aligned}\right. \tag{15}$$

and

$$\left\{\begin{aligned} &a_{12}=DX_\infty\left(\frac{1}{S_\infty}-\frac{1}{K_S+S_\infty}\right) \qquad >0 \\ &a_{13}=DX_\infty\frac{n\ P_\infty{}^{n-1}}{K_P{}^n+P_\infty{}^n} \qquad >0 \end{aligned}\right. \tag{16}$$

The solution to Eq. (14) is

$$\left\{\begin{aligned} &x=\sum_{j=1}^{3} C_{1j}\ e^{\lambda_j t} \\ &y=\sum_{j=1}^{3} C_{2j}\ e^{\lambda_j t} \\ &z=\sum_{j=1}^{3} C_{3j}\ e^{\lambda_j t} \end{aligned}\right. \tag{17}$$

where λ's are the roots of the characteristic equation of Eq. (14) given by

$$\begin{vmatrix} -\lambda & a_{12} & -a_{13} \\ -\dfrac{D}{Y} & -\left(D+\dfrac{a_{12}}{Y}\right)-\lambda & \dfrac{a_{13}}{Y} \\ (\eta_1+\eta_2 D) & \eta_2 a_{12} & -(D+\eta_2 a_{13})-\lambda \end{vmatrix}=0 \tag{18}$$

By solving Eq. (18),

$$\left\{\begin{aligned}
\lambda_1&=-D && (19)\\
\lambda_2&=-\frac{D+\dfrac{a_{12}}{Y}+\eta_2 a_{13}}{2}+\sqrt{\frac{\left(D+\dfrac{a_{12}}{Y}+\eta_2 a_{13}\right)^2}{4}-\left\{\frac{a_{12}}{Y}D+a_{13}(\eta_1+\eta_2 D)\right\}}\\
&=-\frac{D+\dfrac{a_{12}}{Y}+\eta_2 a_{13}}{2}+\sqrt{\frac{\left(\dfrac{a_{12}}{Y}+\eta_2 a_{13}-D\right)^2}{4}-\eta_1 a_{13}} && (20)\\
\lambda_3&=-\frac{D+\dfrac{a_{12}}{Y}+\eta_2 a_{13}}{2}-\sqrt{\frac{\left(\dfrac{a_{12}}{Y}+\eta_2 a_{13}-D\right)^2}{4}-\eta_1 a_{13}} && (21)
\end{aligned}\right.$$

Since a_{12}, a_{13}, and $(\eta_1+\eta_2 D)$ are positive as will be seen from Eqs. (16), (6), and (13), one can discuss the stability of the system around the steady state as follows:

Case (1) If

$$0\leqq\eta_1\leqq\frac{1}{4\,a_{13}}\left(\frac{a_{12}}{Y}+\eta_2\,a_{13}-D\right)^2, \tag{22}$$

then all the λ's are real, and hence x, y, and z in Eq. (17) do not oscillate.

Case (2) If

$$\eta_1>\frac{1}{4\,a_{13}}\left(\frac{a_{12}}{Y}+\eta_2\,a_{13}-D\right)^2, \tag{23}$$

λ_2 and λ_3 are complex, and hence x, y, and z do oscillate.

Case (3) If

$$\eta_2>-\frac{D+\dfrac{a_{12}}{Y}}{a_{13}}, \tag{24}$$

all the λ's are of negative real parts, and hence x, y, and z converge to zero (*i.e.* the steady state is stable).

Case (4) If

$$\eta_2\leqq-\frac{D+\dfrac{a_{12}}{Y}}{a_{13}}, \tag{25}$$

λ_2 and λ_3 are of zero or positive real parts, and hence x, y, and z keep a certain periodical change or diverge (*i.e.*, the steady state is unstable).

One will see from the above analysis that, distinct from the system given by Eqs. (2)–(4), the present system has a feature of the possible occurrence of damped or even diverging oscillations. Although it is difficult to go into further analysis of the oscillations of this three-variable system, its basic nature can be studied with the following two-variable system.

TWO-VARIABLE APPROXIMATION

Suppose a case where 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 (dX/dt) and (dP/dt). The system described by Eqs. (7)–(9), therefore, will be reduced to the following two-variable system.

$$\left\{\begin{aligned} \frac{dX}{dt} &= \frac{\mu_m}{1+\left(\dfrac{P}{K_P}\right)^n} X - DX & (26) \\ \frac{dP}{dt} &= \left\{\eta_1 + \eta_2 \frac{\mu_m}{1+\left(\dfrac{P}{K_P}\right)^n}\right\} X - DP & (27) \end{aligned}\right.$$

The positive steady solution to Eqs. (26) and (27) is

$$\left\{\begin{aligned} P_\infty &= K_P \left(\frac{\mu_m}{D} - 1\right)^{1/n} & (28) \\ X_\infty &= \frac{K_P \left(\dfrac{\mu_m}{D} - 1\right)^{1/n}}{\dfrac{\eta_1}{D} + \eta_2} & (29) \end{aligned}\right.$$

where

$$0 < D < \mu_m \tag{30}$$

By linearizing Eqs. (26) and (27) in the neighborhood of the positive steady solution and solving the characteristic equation, one obtains

$$\lambda = -\frac{D}{2}\left\{1 + \frac{n\left(1 - \dfrac{D}{\mu_m}\right)}{1 + \dfrac{\eta_1}{\eta_2 D}}\right\} \pm \frac{D}{2}\sqrt{\left\{1 + \frac{n\left(1 - \dfrac{D}{\mu_m}\right)}{1 + \dfrac{\eta_1}{\eta_2 D}}\right\}^2 - 4n\left(1 - \frac{D}{\mu_m}\right)} \tag{31}$$

The behavior of this two-variable system was found as follows.

Case (1). Completely growth-associated system ($\eta_1 = 0$, $\eta_2 > 0$). Since the values of λ are both real negative, the only positive steady solution is stable, and no oscillation will be observed.

Case (2). Completely non-growth associated system ($\eta_1 > 0$, $\eta_2 = 0$). Eq. (31)

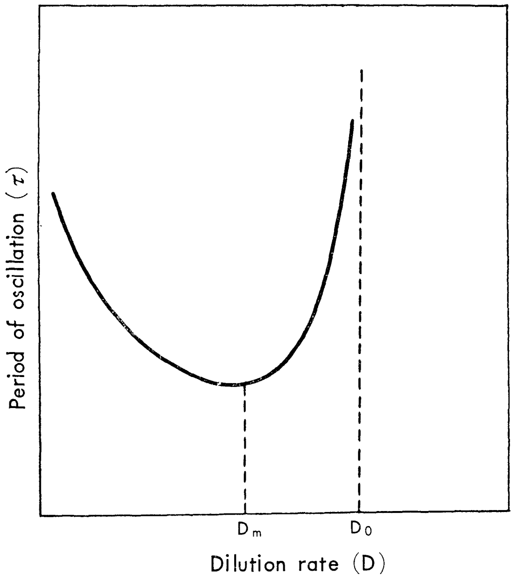


Fig. 2. Period of oscillation *vs.* dilution rate.

$$D_0 = \mu_m\left(1-\frac{1}{4n}\right)$$

$$D_m = \frac{4n-1}{6n}\mu_m$$

$$\tau_{\min}=\frac{24\pi n}{(4n-1)\mu_m\sqrt{\frac{1}{3}(4n-1)}}$$

becomes

$$\lambda= -\frac{D}{2}\pm\frac{D}{2}\sqrt{1-4n\left(1-\frac{D}{\mu_m}\right)} \tag{32}$$

The only positive steady solution is stable because the λ's are both real negative or complex with negative real parts. Oscillations may occur if

$$0<D<\mu_m\left(1-\frac{1}{4n}\right) \tag{33}$$

with the following period of oscillation and damping factor.

$$\tau=\frac{4\pi}{D\sqrt{4n\left(1-\frac{D}{\mu_m}\right)-1}} \tag{34}$$

$$f = \exp.\left\{-\frac{2\pi}{\sqrt{4n\left(1-\dfrac{D}{\mu_m}\right)-1}}\right\} \tag{35}$$

Eq. (34) is graphically shown in Fig. 2.

One may see from Eqs. (34) and (35) that, with a greater value of n, the period of oscillation becomes shorter and the damping factor greater. In practice, however, one will not observe the oscillation because it is highly damped as shown by the following sample calculation.

Suppose $n=3$, $\mu_m=0.4\,\mathrm{hr}^{-1}$, $\eta_1>0$, $\eta_2=0$. Then,

1) if $D=0.61\ \mu_m$,

$$\tau_{\min}=26.8\,\mathrm{hr} \quad \text{and} \quad f=\frac{1}{26.5}$$

This value of D corresponds to D_m in Fig. 2.

2) If $D=0.1\ \mu_m$,

$$\tau=100\,\mathrm{hr} \quad \text{and} \quad f=\frac{1}{7.4}$$

Case (3). Partially growth-associated system ($\eta_1>0$, $\eta_2>0$). The values of λ are either real negative or complex with negative real parts as will be seen from Eq. (31). The solution is thus stable as in Case (2), but the period of the possible oscillation is longer and the damping factor smaller than those in Case (2). One will hardly observe any oscillation either in this case.

Case (4). Negatively growth-associated system ($\eta_1>0$, $\eta_2<0$). The following relation holds even when $\eta_2<0$ for a value of D which satisfies Eq. (30) (see also Eq. (6)).

$$\eta_1+\eta_2 D>0$$

or

$$1+\frac{\eta_1}{\eta_2 D} \quad <0 \tag{36}$$

Let the first term in the right hand side of Eq. (31) be expressed by $f(D)$.

$$f(D)\equiv -\frac{D}{2}\left\{1+\frac{n\left(1-\dfrac{D}{\mu_m}\right)}{1+\dfrac{\eta_1}{\eta_2 D}}\right\}$$

$$=\frac{\mu_m}{2}\left(\frac{1}{1+\dfrac{\eta_1}{\eta_2 D}}\right)\left\{n\left(\frac{D}{\mu_m}\right)^2-(n+1)\frac{D}{\mu_m}-\frac{\eta_1}{\eta_2\,\mu_m}\right\} \tag{37}$$

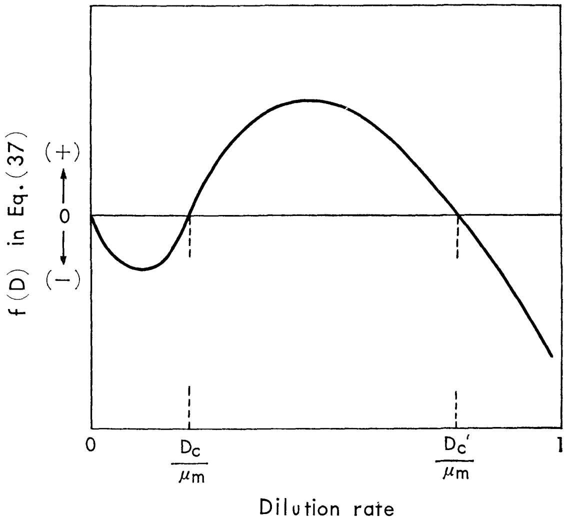


Fig. 3. $f(D)$ *vs.* (D/μ_m)

$$\frac{D_c}{\mu_m}=\frac{(n+1)-\sqrt{(n+1)^2+4n\frac{\eta_1}{\eta_2\ \mu_m}}}{2n}$$

$$\frac{D_c'}{\mu_m}=\frac{(n+1)+\sqrt{(n+1)^2+4n\frac{\eta_1}{\eta_2\ \mu_m}}}{2n}$$

Then, if $f(D)<0$, the λ's in Eq. (31) are both either real negative or complex with negative real parts; hence the positive steady solution is uniquely obtained and stable without or with oscillations. If $f(D)>0$ on the other hand, at least one of the two λ's is either real positive or complex with positive real parts; hence the steady solution is unstable without or with oscillations. Finally, if $f(D)=0$ $(0<D<\mu_m)$, the λ's are both purely imaginary functions; hence a sustained oscillation will occur around the steady solution.

The sign of $f(D)$ is as follows:

1) If

$$(n+1)^2+4n\frac{\eta_1}{\eta_2\ \mu_m}<0, \tag{38}$$

the algebraic sum in the second braces in the right hand side of Eq. (37) is positive; and the term in the first parentheses is negative as shown by Eq. (36). Therefore, $f(D)$ is negative and the steady solution is positive and stable.

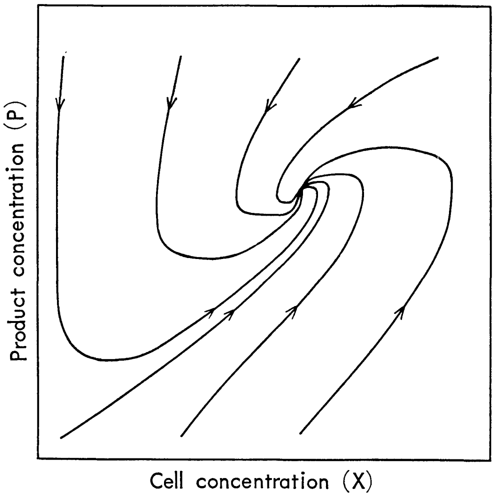


Fig. 4. Phase portrait for the two-variable, partially growth-associated system.

Parameters used are: $n=3$, $\mu_m=0.4\,\text{hr}^{-1}$, $D=0.5\,\mu_m$,

$$\frac{\eta_1}{\eta_2}=0.2\,\text{hr}^{-1},\ 0\leqq\frac{P}{K_P}\leqq 2.$$

$$\lambda=0.05(-3.5\pm\sqrt{11.75}\ i)\ \text{hr}^{-1}$$

2) If

$$(n+1)^2+4n\frac{\eta_1}{\eta_2\ \mu_m}>0, \tag{39}$$

the sign of $f(D)$ will change as shown in Fig. 3. Therefore;

a) a sustained oscillation will occur at the critical dilution rates of D_c and D_c' as indicated in Fig. 3,

b) a damped oscillation for D such as

$$0<D<D_c \qquad \text{and} \qquad D_c'<D<\mu_m,$$

and

c) a diverging oscillation for D such as

$$D_c<D<D_c'.$$

The oscillation may not occur if a given value of D is relatively far from D_c or D_c', because the λ's may become real numbers for such values of D.

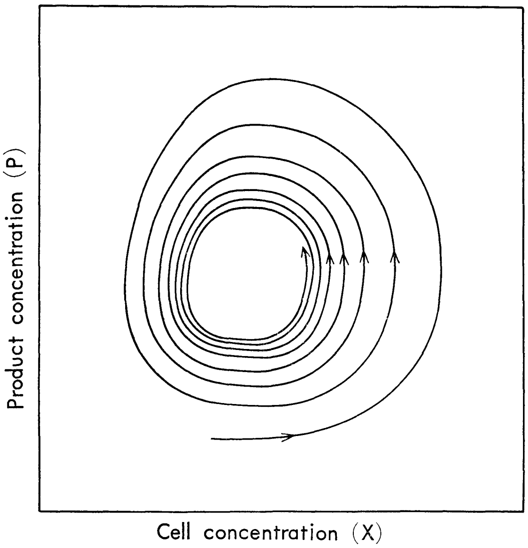


Fig. 5. Phase portrait for the two-variable, negatively growth-associated system (damped oscillation).

Parameters used are: $n=3$, $\mu_m=0.4\,\mathrm{hr}^{-1}$, $D=0.45\,\mu_m$,

$$\frac{\eta_1}{\eta_2}=-0.5\,\mathrm{hr}^{-1},\quad 0\leqq\frac{P}{K_P}\leqq 2.$$

COMPUTER SIMULATION

The mathematical discussion made so far is valid only in the neighborhood of the steady solution. To study the global transient behavior of the present product-inhibited chemostat system, the sets of Eqs. (26) and (27) as well as of Eqs. (7)–(9) have to be numerically solved. Sample solutions are shown here for some cases by the use of an analog computer.

Two-variable system

a) *Partially growth-associated* ($\eta_1>0$, $\eta_2>0$). A phase portrait of the system is shown in Fig. 4. Note that the system oscillates mathematically but not in practice as already discussed.

b) *Negatively growth-associated* ($\eta_1>0$, $\eta_2<0$). Fig. 5 shows a damped oscillation at $D=0.45\,\mu_m$, and Fig. 6 a diverging oscillation at $D=0.65\,\mu_m$. The critical dilution rates at which sustained oscillations could be observed are

$$D_c=\frac{1}{2}\mu_m,\qquad \text{and}\qquad D_c'=\frac{5}{6}\mu_m\,.$$

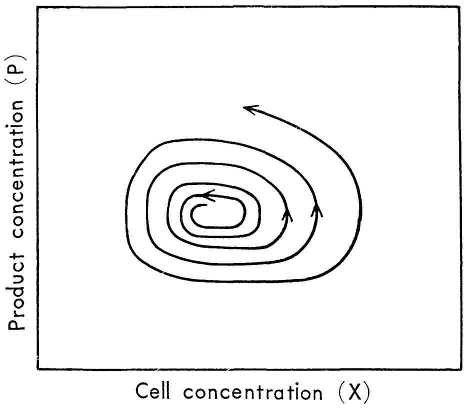


Fig. 6. Phase portrait for the two-variable, negatively growth-associated system (diverging oscillation).

Values of the parameters are the same as those in Fig. 5 except that $D=0.65\,\mu_m$.

Three-variable system

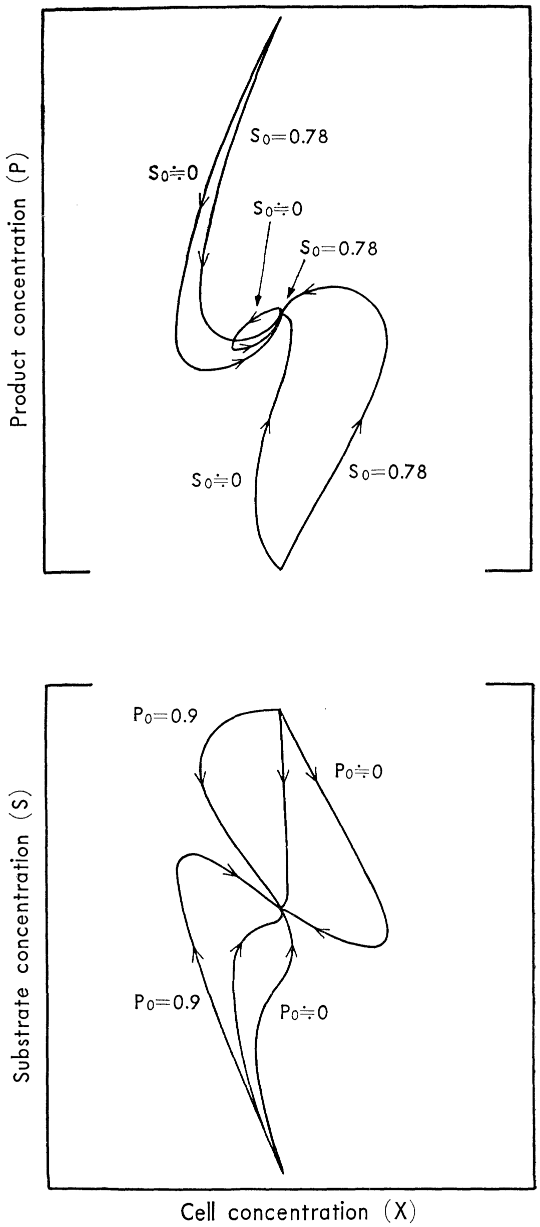
c) *Partially growth-associated* ($\eta_1>0$, $\eta_2>0$). Figs. 7 and 8 show six trajectories in the three-dimensional phase space and their time courses, respectively. No oscillations were observed.

d) *Negatively growth-associated* ($\eta_1>0$, $\eta_2<0$). Figs. 9 and 10 show damped oscillations for a three-variable system. Diverging oscillations can be shown by changing the value of D as already shown in Fig. 6 for a two-variable system.

DISCUSSION

RAMKRISHNA *et al.* (*4*) presented a chemostat model different from ours. They assumed that viable cells (V) interact with a substrate (S) so as to produce the new viable cells and a cell-killing product (T), and this product interacts with viable cells to form dead cells (N) which in turn may or may not release the cell-killing product. Their mathematical formulation for the chemostat was

$$\left\{\begin{aligned} \frac{dV}{dt} &= \frac{\mu_m S}{K_S+S} V - KTV - DV && (40) \\ \frac{dS}{dt} &= D(S_R - S) - a_S \frac{\mu_m S}{K_S+S} V && (41) \\ \frac{dT}{dt} &= a_T \frac{\mu_m S}{K_S+S} V + Ka_{T1} TV - DT && (42) \end{aligned}\right.$$



Product concentration (P)
$S_0=0.78$
$S_0 \doteqdot 0$
$S_0 \doteqdot 0$
$S_0=0.78$
$S_0 \doteqdot 0$
$S_0=0.78$
Substrate concentration (S)
$P_0=0.9$
$P_0 \doteqdot 0$
$P_0=0.9$
$P_0 \doteqdot 0$
Cell concentration (X)

Fig. 7.

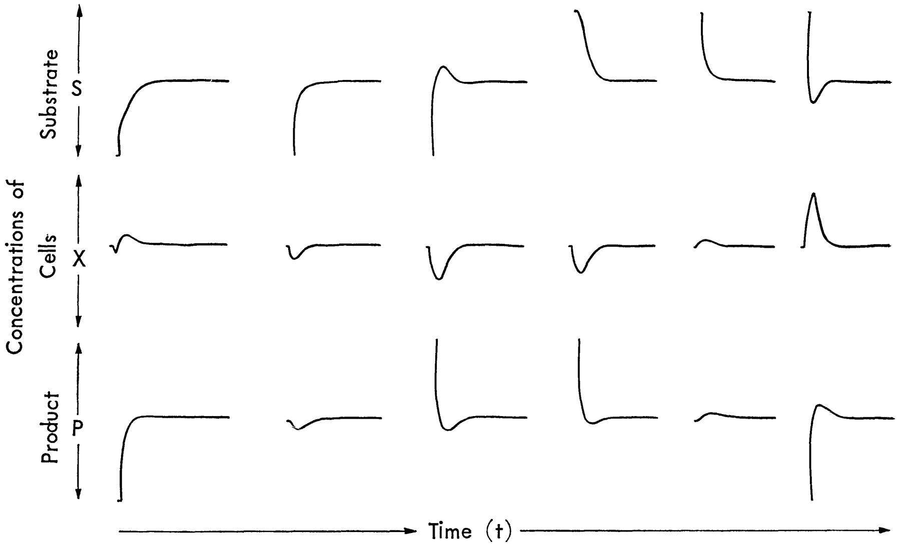


Fig. 8. Time course of the six trajectories shown in Fig. 7.

They discussed the possible occurrence of oscillations, if $a_{T1}>0$, in the time course of biomass, substrate, and product.

They were discussing the cell-killing effect of a product on the chemostat behavior, whereas the present model deals with a growth-inhibiting effect of a product and it comprises the Stepanova-Romanovskii model as one of its special cases where the inhibition is of the first order and production is completely growth-associated.

It should be noted that Eq. (6) is positive even when $S=0$. This situation indicates that the model studied in this paper concerns the case in which the product is made from a substance different from the growth-limiting sub-

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Fig. 7. Phase portrait for the three-variable, partially growth-associated system. Parameters used are: $n=3$, $\mu_m=0.4\,\text{hr}^{-1}$, $D=0.45\,\mu_m$,

$$\frac{S_R}{K_S}=3.6,\ \frac{\eta_1}{\eta_2}=0.2\,\text{hr}^{-1},\ 0\leqq\frac{P}{K_P}\leqq 2.$$

Initial conditions (relative values):

	X_0	S_0	P_0
(1)	0.4	0.0	0.0
(2)	0.4	0.0	0.45
(3)	0.4	0.0	0.9
(4)	0.4	0.78	0.0
(5)	0.4	0.78	0.45
(6)	0.4	0.78	0.9

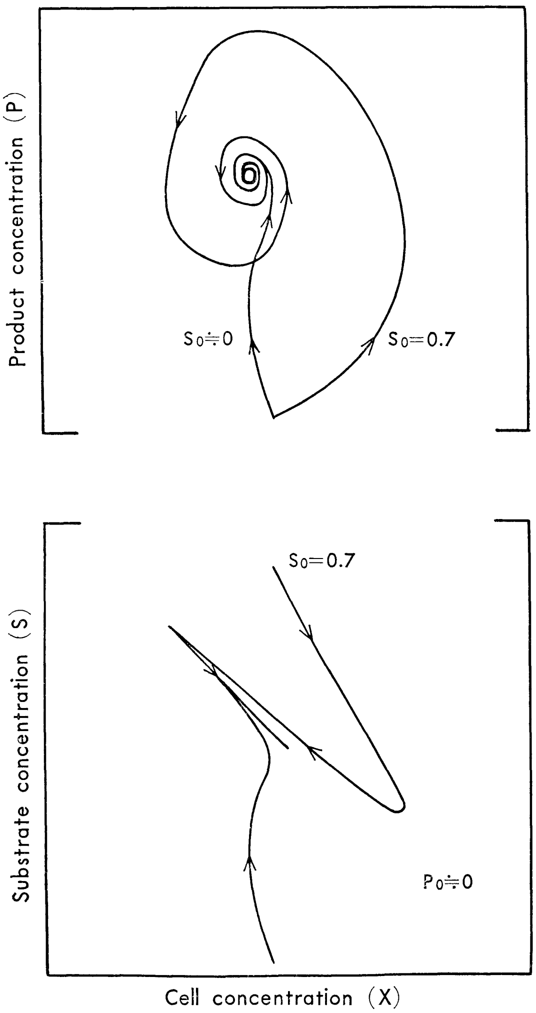

Fig. 9. Phase portrait for the three-variable, negatively growth-associated system (damped oscillation).

Parameters used are: $n=3$, $\mu_m=0.4\,\mathrm{hr}^{-1}$, $D=0.45\,\mu_m$,

$$\frac{S_R}{K_S}=3.6,\ \frac{\eta_1}{\eta_2}=-0.34\,\mathrm{hr}^{-1},\ 0\leqq\frac{P}{K_P}\leqq 2\,.$$

strate (S). If the product is made from the same substance as the growth-limiting substrate, the production mode can be taken as completely growth-associated in the present model because, in such a case, Eq. (6) must be zero when $S=0$.

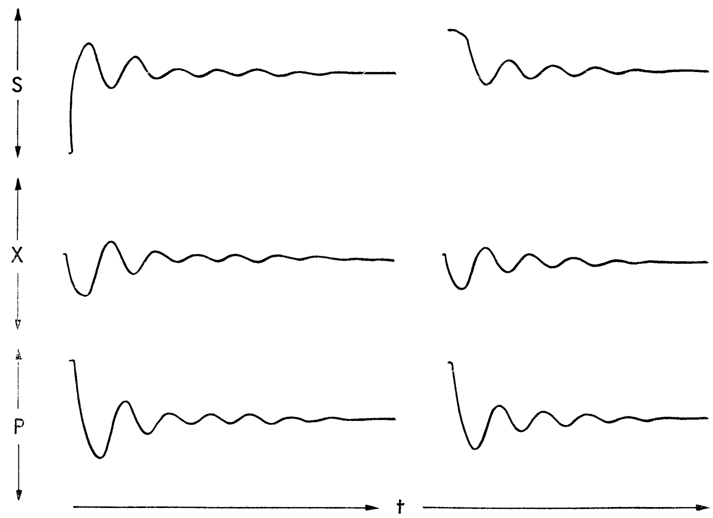

Fig. 10. Time course of the damped oscillation shown in Fig. 9.

NOMENCLATURE

a_{12}, a_{13}: Constants defined by Eq. (16).
a_S, a_T, a_{T1}: Stoichiometric constants
$C's$: Integral constants
D: Dilution rate, hr^{-1}
D_c, D_c': Critical dilution rates at which sustained oscillations occur, hr^{-1}
f: Damping factor, –
K: Rate constant, $(g/liter)^{-1}t^{-1}$
K_S, K_P: Constants, g/liter
n: Order of inhibition, –
N: Concentration of dead cells, g/liter
P: Concentration of product, g/liter
P_0: P at $t=0$, g/liter
P_∞: P at steady state, g/liter
S: Concentration of growth-limiting substrate in the fermentor, g/liter
S_0: S at $t=0$, g/liter
S_∞: S at steady state, g/liter
S_R: Concentration of growth-limiting substrate in the feeding solution, g/liter
t: Time, hr

T: Concentration of cell-killing product, g/liter
V: Concentration of viable cells, g/liter
X: Concentration of cells in the fermentation vessel, g/liter
X_0: X at $t=0$, g/liter
X_∞: X at steady state, g/liter
x, y, z: See Eq. (20) in the text
Y: Yield coefficient, g cells/g substrate
η, η_2: Constants for growth-associated product formation, g/g cells
η_1: Constants for non-growth associated product formation, g/g cells·hr
λ: Root of the characteristic equation, hr^{-1}
μ: Specific growth rate, hr^{-1}
μ_m: Maximum specific growth rate, hr^{-1}
μ_∞: Specific growth rate at steady state, hr^{-1}
τ: Period of oscillation, hr

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