Periodic Operation of a Bioreactor with Input Multiplicities

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The performance of a continuous bioreactor under periodic inlet substrate concentration is theoretically analyzed for productivity improvement which under conventional steady-state operation shows input multiplicities in the feed substrate concentration. Two values of feed substrate concentration give identical productivity under conventional steady-state operation. A periodic rectangular pulse is assumed for the feed substrate concentration. It is shown by simulation that under concentration forcing the average productivity is significantly different for these two substrate concentrations. The larger value of feed substrate concentration gives improved average productivity and shows a resonance with the period of oscillation. The effect of periodic operation on the average productivity under the input multiplicities in dilution rate is also analysed.

La performance d'un bioréacteur continu pour des concentrations d'alimentation en substrat périodique a été analysée de façon théorique afin d'améliorer la productivité qui en régime permanent classique montre des multiplicités dans l'alimentation par rapport à la concentration en substrat d'alimentation. Deux valeurs de concentration en substrat d'alimentation donnent une productivité identique en régime permanent classique. On suppose une pulsation rectangulaire périodique pour la concentration en substrat d'alimentation. La simulation permet de montrer que si on force la concentration, la productivité moyenne est très différente pour ces deux concentrations. La plus grande de ces deux valeurs donne une meilleure productivité moyenne et montre une résonance avec la période d'oscillation. L'effet du fonctionnement périodique sur la productivité moyenne dans des conditions de multiplicités du taux de dilution dans l'alimentation est également analysé.

Keywords: bioreactor, productivity, substrate concentration.

oncentration forcing of many nonlinear chemical and biochemical processes gives a superior time-averaged performance to that obtained under conventional steady-state operation (Bailey, 1977; Renken, 1984; Silveston and Hudgins, 1987; Abulez and Lyberatos, 1989). Bailey (1977) and Renken (1984) have classified one important class of periodic operation in which the steady-state condition is chosen arbitrarily and the average value of the periodic input (say, in feed concentration) is the same as the value at the steady-state operation. The time-averaged performance (for example, in productivity) of the reactor under periodic operation is then compared with that obtained under steady-state operation. A number of theoretical and experimental studies are available on the periodic operation of bioreactors (Abulez and Lyberatos, 1987, 1989).

In all these studies, the steady-state condition under a given particular set of operating variables is only considered. Under certain specific growth rate model, the bioreactor shows input multiplicities behaviour. For example, more than one values of feed substrate concentration give identical productivity (Henson and Seborg, 1992). In general, input multiplicities arise due to the presence of competing effects in the process (Koppel, 1982, 1983; Agarwal and Lim, 1984; Henson and Seborg, 1992) or due to recycle structure (Liou and Chien, 1991; Koppel, 1983). Recently, Chidambaram (1992) has analyzed the periodic operation of a chemical reactor for a consecutive reaction under input multiplicities in flow-rate. In the present work, the performance of a continuous bioreactor under feed substrate concentration (S_f) cycling is analyzed, with the input multiplicities in S_f, to check whether the average productivity is the same or not. Similarly the effects of input multiplicities in dilution rate on the average productivity under feed concentration cycling is also analyzed.

Model equations and evaluation

A variety of fermentation can be described by the following unstructured model (Agarwal et al., 1989):

$$dX/dt = -DX + \mu X \qquad (1)$$

$$dS/dt = D(S_f - S) - (\mu X)/Y_{x/s} \qquad (2)$$

$$dP/dt = -DP + (\alpha\mu + \beta)X \qquad (3)$$

at $t = 0$,

$$X = X_0, \ S = S_0, \text{ and } P = P_0 \qquad (4)$$

Here μ is the specific growth rate, $Y_{x/s}$ is the cell mass yield, and α and β are yield parameters for the product. The specific growth model is assumed to exhibit both substrate and product inhibition:

$$\mu = \mu_m [1 - (P/P_m)] S / [K_m + S + (S^2/K_i)] \qquad (5)$$

where μ_m, P_m, and K_i are respectively the maximum specific growth rate, product saturation constant, and substrate inhibition constant. Many types of fermentations can be modelled by choosing the model parameters appropriately (Agarwal et al. 1989). For example, the product is non-growth associated if $\alpha \neq 0$ and $\beta = 0$. The nominal values of the parameters and the operating conditions used in the present work are the same as those reported by Agarwal et al. (1989) and Henson and Seborg (1992). These values are given here for easy reference.

$$\alpha = 2.2 \text{ g/g}, \ \beta = 0.2 \text{ h}^{-1}, \ \mu_m = 0.48 \text{ h}^{-1}, \ P_m = 50 \text{ g/L},$$

$$K_m = 1.2 \text{ g/L}, \ K_i = 22 \text{ g/L}, \ Y_{x/s} = 0.4 \text{ g/g}$$
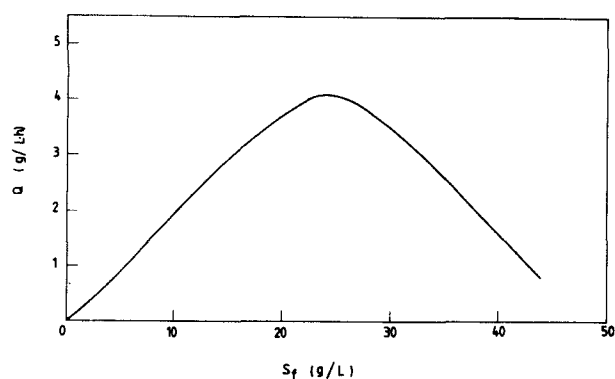
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Figure 1 — Productivity versus substrate feed concentration under steady-state operation.

Figure 2 — Concentration forcing function.

If the biomass and substrate are of negligible value compared to the product, the productivity Q can be defined as the amount of product cells produced per unit time (Henson and Seborg, 1992):

$$Q = DP \quad \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \quad (6)$$

The steady-state solution of equations (1) to (3) can be written in terms of the productivity as a function of feed substrate concentration (S_f):

$$Q = \xi(S_f) \quad \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \quad (7)$$

Then the necessary condition for occurrence of input multiplicities is given by (Koppel, 1983; Agarwal and Lim, 1989):

$$dQ/dS_f = 0 \quad \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \quad (8)$$

The Appendix gives the detailed derivation in terms of the system parameters and operating conditions under which input multiplicities in S_f occur. It is shown that input multiplicities exist because of the particular form of growth rate kinetics.

For the operating conditions and the parameters values given in Figure 1, the steady-state values of X, S and P and hence Q are calculated. The results are given in Figure 1 (Henson and Seborg, 1992). The system exhibits input multiplicities in S_f. For example, $S_f = 15.55$ g/L and $S_f = 32.99$ g/L give identical value of $Q = 3.0$ (g/L h). Our interest is to analyze the average value of productivity $(\bar{Q})$ under S_f cycling using these mean values of S_f.

The feed substrate concentration forcing function assumed here is a rectangular pulse (of period τ) as shown in Figure 2. In this Figure, $S_{f,p}$ is the amplitude of pulse and $\bar{S}_f$ is the feed substrate concentration used at the conventional steady-state operation. The pulse width, γ, is expressed as a fraction of period (τ). The value of $\gamma = 1$ represents the conventional steady-state operation and $\gamma < 1$ represents the periodic operation. From the Figure 2 we get,

$$S_{f,p} = \bar{S}_f / \gamma \quad \dots \dots \dots \dots \dots \dots \dots \dots \dots \dots \quad (9)$$

To evaluate the time-averaged yield under periodic operation, Equations (1) to (5) are solved numerically by Gear routine with the concentration cycling given in Figure 2. The average value of productivity $(\bar{Q})$ is calculated only after identical productivity profile is obtained for consecutive cycles (it takes about 5 to 10 cycles). $\bar{Q}$ versus period of
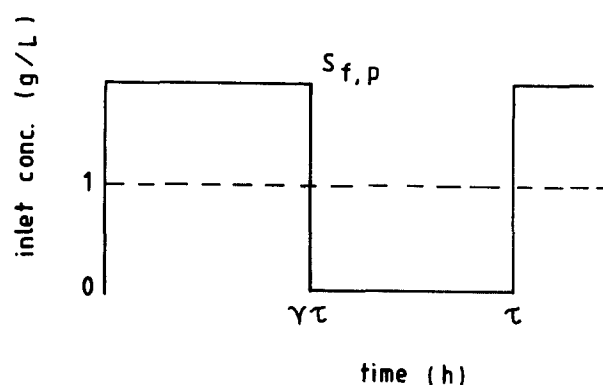

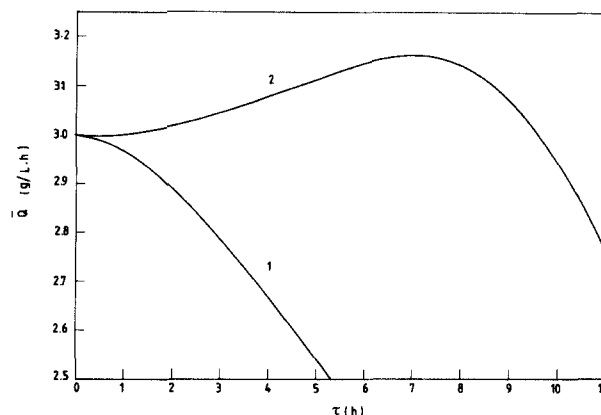Figure 3 — Average productivity versus period of oscillation under S_f cycling ($\gamma = 0.1$, 1: $\bar{S}_f = 15.55$ g/L; 2: $\bar{S}_f = 32.99$ g/L).
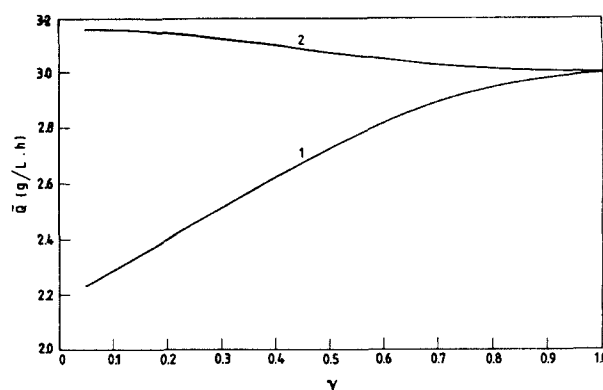

Figure 4 — Average productivity versus γ under S_f cycling ($\tau = 7$ h, 1: $\bar{S}_f = 15.55$ g/L; 2: $\bar{S}_f = 32.99$ g/L).

oscillation (τ) is calculated and the results are shown in Figure 3 for $\gamma = 0.1$. Figure 3 shows that for $\bar{S}_f = 15.55$ g/L and $\bar{S}_f = 32.99$ g/L we get distinct values of $\bar{Q}$, even though identical value of Q is obtained at the conventional steady-state operation. The larger value of $\bar{S}_f$ gives larger value of $\bar{Q}$. $\bar{Q}$ versus τ shows a resonance for the larger value of $\bar{S}_f$. The resonance in $\bar{Q}$ versus τ can be explained as the expression for μ is affected by S in both the numerator and in the denominator. The net effect depends on the value of S. For a lower values of τ the net effect is increasing in $\bar{Q}$ and for larger value of τ the net effect is decreasing. Figure 4 shows $\bar{Q}$ versus γ for the two values of $\bar{S}_f$. The larger value of $\bar{S}_f$ gives an improved productivity. Figure 5 shows S versus time behaviour, after invariant condition with respect to cycles, under S_f forcing for the two values of $\bar{S}_f$. The corresponding P versus time
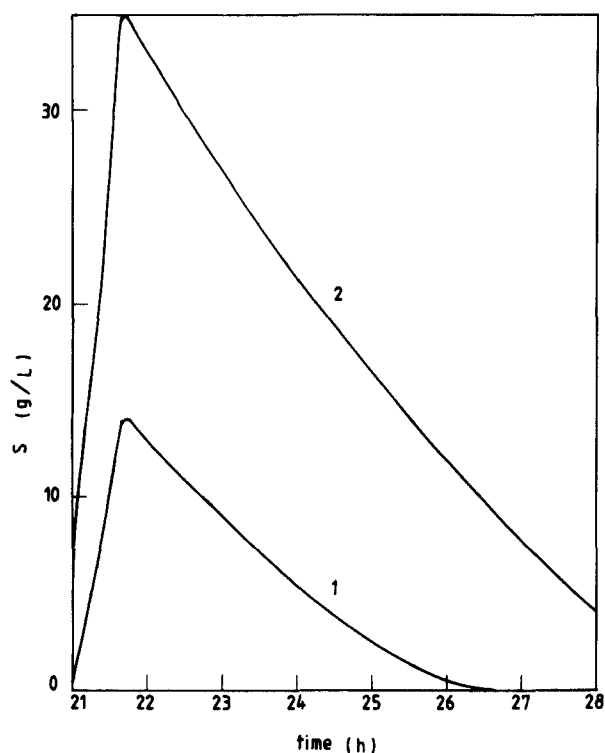
Figure 5 — S versus time under cycle-invariant condition for S_f cycling ($\tau = 7$ h; $\gamma = 0.1$, 1: $\bar{S}_f = 15.55$ g/L; 2: $\bar{S}_f = 32.99$ g/L).
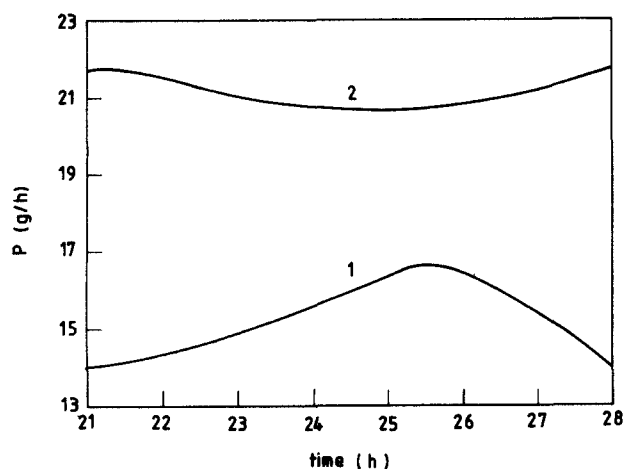

Figure 6 — P versus time under cycle-invariant condition for S_f cycling ($\tau = 7$ h; $\gamma = 0.1$, 1: $\bar{S}_f = 15.55$ g/L; 2: $\bar{S}_f = 32.99$ g/L).

Figure 7 — Average productivity versus τ under D cycling for input multiplicities in S_f ($\gamma = 0.5$, $\bar{D} = 0.15$ h^{-1}; 1: $S_f = 15.55$ g/L; 2: $S_f = 32.99$ g/L).

Figure 8 — Average productivity versus τ under S_f cycling for input multiplicities in D ($\gamma = 0.1$, $\bar{S}_f = 15.55$ g/L; 1: $D = 0.15$ h^{-1}; 2: $D = 0.248$ h^{-1}).

Figure 9 — Average productivity versus τ under D cycling for input multiplicities in D ($\gamma = 0.1$, $S_f = 15.55$ g/L; 1: $\bar{D} = 0.15$ h^{-1}; 2: $\bar{D} = 0.248$ h^{-1}).

response is shown in Figure 6. In the first γ fraction, the substrate inhibition is lesser particularly at the lower value of $\bar{S}_f$ whereas in the next $(1 - \gamma)$ fraction period substrate limitation occurs particularly at lower $\bar{S}_f$. The overall effects give deteriorating performance under periodic operation at lower value of $\bar{S}_f$. Whereas at higher value of $\bar{S}_f$ there is an improvement in $\bar{Q}$.

Figure 7 shows $\bar{Q}$ versus τ under cycling in D, (the forcing function in D is similar to that given in Figure 2), when the input multiplicities arise in S_f. The response shows a distinct behaviour for these two values of S_f. However, the periodic operation in D gives an inferior performance in $\bar{Q}$ for both the values of S_f when compared to the conventional steady-state and also when compared to that obtained due to periodic cycling in S_f.
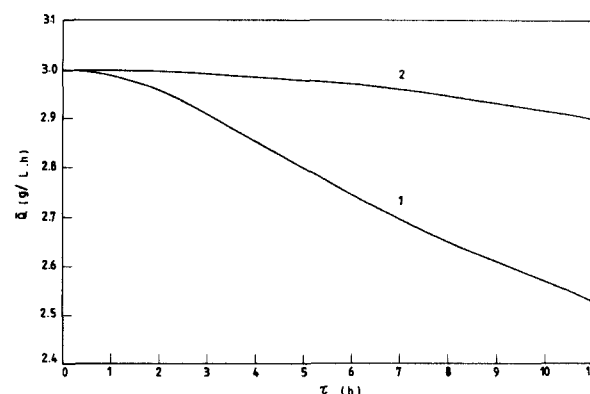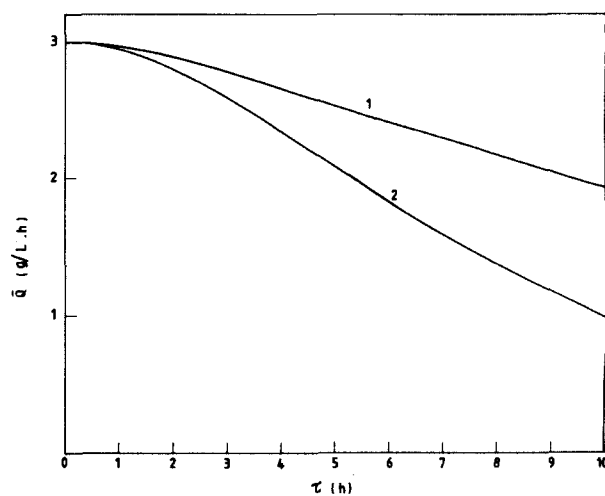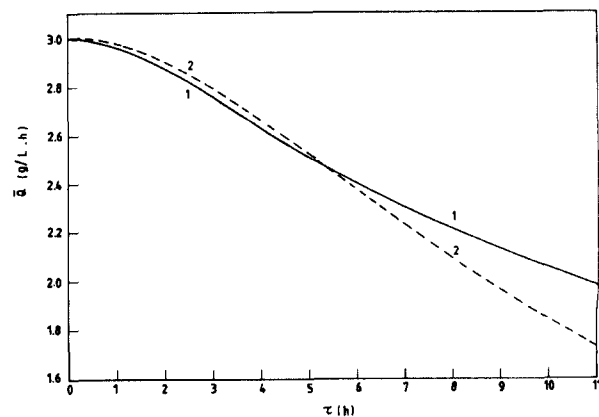
It is interesting to note that the reactor Equations (1) to (5) also give input multiplicities in D on Q (refer to Figure 2 of Henson and Seborg, 1992). For example when $S_f = 15.55$ g/L both the values of $D = 0.15$ and $D = 0.248$ h^{-1} give identical productivity of $Q = 3.0$. The average value of Q under S_f cycling for these two values of D give distinct behaviour as shown in Figure 8. However, there is a degradation in $\bar{Q}$ under periodic operation.

Similarly the forcing in the dilution rate also give distinct behaviour in $\bar{Q}$ for these two values of $\bar{D}$ (refer to Figure 9). However, there is a degradation in the average productivity under periodic operation.

Conclusion

Though two values of feed substrate concentration give identical productivity under conventional steady-state operation, the average productivity is distinctly different under feed concentration (S_f) cycling. Improvement in the average productivity is obtained for the larger value of $\bar{S}_f$. Even though two values of dilution rate give identical productivity under steady-state operation, the average productivity is distinctly different either under S_f cycling or under dilution rate cycling. However both the values of dilution rate give inferior performance under periodic operation.

APPENDIX

Derivation of a condition for the occurrence of input multiplicities in S_f on Q

From the Equations (1) to (5) under steady-state condition we get:

$$\mu = D \quad \dotfill \quad (A1)$$

$$X = Y_{x/s} (S_f - S) \quad \dotfill \quad (A2)$$

$$P = [\alpha + (\beta/D)] X \quad \dotfill \quad (A3)$$

$$= [\alpha + (\beta/D)] (S_f - S) Y_{x/s} \quad \dotfill \quad (A4)$$

$$D = Nr(P)/Dr(S) \quad \dotfill \quad (A5)$$

where

$$Nr(P) = \mu_m [1 - (P/P_m)] \quad \dotfill \quad (A6)$$

$$Dr(S) = (K_m/S) + 1 + (S/K_i) \quad \dotfill \quad (A7)$$

Differentiating Equation (A4) with respect to S_f we get,

$$dP/dS_f = Y_{x/s} [\alpha + (\beta/D)] (1 - dS/dS_f) \quad \dotfill \quad (A8)$$

Differentiating Equation (A5) we get,

$$D \{dDr/dS\} \{dS/dS_f\} = [-\mu_m/P_m] \{dP/dS_f\} \quad \dotfill \quad (A9)$$

For input multiplicities in S_f on Q (and hence on P for constant D) we should have

$$dP/dS_f = 0 \quad \dotfill \quad (A10)$$

For this condition, Equation (A8) requires

$$dS/dS_f = 1 \quad \dotfill \quad (A11)$$

Hence from Equation (A9) we get the condition (1) for input multiplicities in S_f on Q as

$$dDr/dS = 0 \quad \dotfill \quad (A12)$$

For the expression given by Equation (5) this condition is satisfied. It is to be noted that when $K_i = \infty$, (i.e., under no substrate inhibition) the condition is not satisfied.

From Equation (A4) we get,

$$a_1 S^2 - (a_1 + a_4 S_f) S - K_m = 0 \quad \dotfill \quad (A13)$$

where

$$a_1 = [(\mu_m a_2)/(DP_m)] - (1/K_i) \quad \dotfill \quad (A14)$$

$$a_3 = 1 - (\mu_m/D) \quad \dotfill \quad (A15)$$

$$a_4 = (\mu_m a_2)/(DP_m) \quad \dotfill \quad (A16)$$

$$a_2 = [\alpha + (\beta/D)] Y_{x/s} \quad \dotfill \quad (A17)$$

From Equation (A13) we get,

$$S = \{b + [b^2 + 4a_1 K_m]^{0.5}\} / (2a_1) \quad \dotfill \quad (A18)$$

where

$$b = a_3 + a_4 S_f \quad \dotfill \quad (A19)$$

To satisfy the condition $(dS/dS_f) = 1$, we should have,

$$a_4 + \{ [a_4 (a_3 + a_4 S_f)] / [(a_3 + a_4 S_f)^2 + 4a_1 K_m]^{0.5}\} = 2a_1$$
$$\dotfill \quad (A20)$$

It is to noted that when $P_m = \infty$, then S_f will not appear in Equation (A18) for S. Hence, the condition $(dS/dS_f) = 1$ will not be satisfied. Thus Equations (A12) and (A20) are the two conditions both of which are required for the occurrence of the input multiplicities.

Nomenclature

D = dilution rate (h^{-1})
K_i = substrate inhibition constant (g/L)
K_m = substrate saturation constant (g/L)
P = product concentration (g/L)
P_m = product saturation constant (g/L)
Q = product cell produced per unit time (g/h L)
S = substrate concentration (g/L)
S_f = feed substrate concentration (g/L)
$S_{f,p}$ = feed substrate concentration during γ fraction of a period (g/L)
t = time (h)
X = biomass concentration (g/L)
$Y_{x/s}$ = cell mass yield (g/g)

Greek letters

α = product yield parameter (g/g)
β = product yield parameter (h^{-1})
γ = pulse width expressed as a fraction of a period
μ = specific growth rate (h^{-1})
μ_m = maximum specific growth rate (h^{-1})
τ = period (h)
(bar)
$-$ = average value

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