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Improving bioreactor performance: are two CSTBs always better than one?

Harvinder Sidhu
University of New South Wales

Mark Nelson
University of Wollongong, mnelson@uow.edu.au

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We investigate a bioreactor cascade consisting of two reactors. For a given total residence time, we study how the performance of the reactor (measured either as the cell mass concentration or the reactor productivity) depends upon the feed substrate concentration and the residence time in the first reactor. The bioreactor model in this study uses a growth rate that is given by a Monod expression with a yield coefficient that is a linear function of the substrate concentration. Previous researchers have compared the performance o f a two-reactor system against a single reactor with the same total residence time. The main focus of this paper is to show that the performance o f a two-reactor cascade should not be gauged in this manner, as comparisons using this criterion can give grossly misleading results. Our analysis shows that before maximising the performance o f a cascade, we must first consider the performance o f a single reactor system as a benchmark.

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Improving Bioreactor Performance: Are Two CSTBs Always Better Than One?

H.S. Sidhu
School of Physical, Environmental and Mathematical Sciences
University of New South Wales at The Australian Defence Force Academy
Canberra ACT2600
AUSTRALIA
E-mail: h.sidhu@adfa.edu.au
M.I. Nelson
School of Mathematics and Applied Statistics
The University of Wollongong
Wollongong, NSW 2522
AUSTRALIA
E-mail: nelsonm@member.ams.org

Abstract

We investigate a bioreactor cascade consisting of two reactors. For a given total residence time, we study how the performance of the reactor (measured either as the cell mass concentration or the reactor productivity) depends upon the feed substrate concentration and the residence time in the first reactor. The bioreactor model in this study uses a growth rate that is given by a Monod expression with a yield coefficient that is a linear function of the substrate concentration. Previous researchers have compared the performance of a two-reactor system against a single reactor with the same total residence time. The main focus of this paper is to show that the performance of a two-reactor cascade should not be gauged in this manner, as comparisons using this criterion can give grossly misleading results. Our analysis shows that before maximising the performance of a cascade, we must first consider the performance of a single reactor system as a benchmark.

1. INTRODUCTION

The past four decades have seen extensive research aimed at improving product yields in chemical reactors. Many studies, both experimental and theoretical, have shown that periodic forcing is an appropriate engineering tool to improve the conversion or selectivity of a desired product (Silveston *et al* 1995; Stankiewicz and Kuczynski 1995). However, the additional complications and costs associated with implementing external periodic operation have limited the industrial uptake of this technique (Silveston *et al* 1995; Stankiewicz and Kuczynski 1995).

The possibility of combining the advantages of periodic operation with the benefits of using two reactors arranged in series through the use of 'natural oscillations' have been investigated by several authors (Yang and Su, 1993, Chen *et al* 1995, Ray 1995, Balakrishnan and Yang 1998, Jianqiang and Ray 2000). By 'natural oscillations' it is meant that the process parameters are chosen so that a *steady input* of reactants into the first reactor generates *self-sustained oscillations* in its output. This output then forces the second reactor. Improvements in reactor performance are therefore achieved without the additional costs associated with external periodic forcing. Consequently, this approach harnesses all the advantages of periodic forcing without the expense of implementing such perturbations. Significant increases in product yields have been shown to be theoretically possible, when this approach is applied to various biochemical processes.

1.1. Review of related work

The model considered in this study was previously studied by Yang and Su (1993), Chen *et al* (1995) and Balakrishnan and Yang (1998). These authors investigated how the performance of two continuous-flow tank bioreactors (CSTBs) changes as the residence time in the first reactor is varied, assuming that the total residence time of the system is fixed. The behaviour of the model in a single reactor was investigated numerically by Balakrishnan and Yang (2002).

Yang and Su (1993) considered equal residence

times in each reactor as their baseline. As the residence time in the first reactor was varied, they found that the performance of the cascade could be improved significantly (more than six-fold when compared to their baseline). Furthermore, they concluded that the two CSTBs connected in series is *always* better than the one CSTB of equal dilution rate.

Motivated by the work of the previous authors, Chen *et al* (1995) investigated the performance enhancement in a two CSTB system, due to the generation of natural oscillation in the first CSTB. They found that for a single CSTB, the time-averaged performance of the Monod system operated in the oscillatory regime is always less than that operated at the optimal stable steady state. They concluded that it is not profitable to split the bioreactor system into a cascade for these types of models. However, Balakrishnan and Yang (1998) revisited the Monod-growth model whilst investigating two more complex microbial systems. These authors contradicted the findings of Chen *et al* (1995) and speculated that the performance of a two-reactor configuration may in general be better than that of a single CSTB with the same total residence time. They claimed that for the more complex systems, the two CSTBs arranged in series out-performs a single reactor of the same residence time.

In this paper we re-investigate the Monod growth model with a variable yield coefficient in both the single and the double CSTB cases. We study how the performance of these systems depends on the substrate concentration and residence times. A critical issue in assessing the performance of the cascade configuration is the determination of a suitable criterion for comparing the performance of the double CSTB with that of a single reactor. We measure the reactor performance by either the time-averaged reactor productivity, or the time-averaged cell mass concentration leaving the reactor. However to ensure that the comparison is meaningful, we compare the performance of a cascade against a single reactor operated at a residence time that is no greater than the total residence time in the cascade. In other words, if the optimal value of the residence time in the single reactor is *less* than the total residence time in the cascade, then the single reactor performance at that optimal residence time is used in the comparison against the two-reactor system. However, if the optimal residence time for the single reactor is *greater* than the total residence time in the cascade, then the performance of the single reactor that corresponds to the total residence time of the cascade is used for any comparison.

2. MODEL EQUATIONS

The biochemical model represents the growth of a biological species (X) through consumption of a substrate species (S). The specific growth rate is given by a Monod expression with variable yield coefficient but without product and substrate inhibition. Here we assume that the feed is sterile (X_0=0), so that the steady-state cell mass concentration in the first reactor may become zero. This occurs at 'low' residence times, corresponding to 'high' flowrates, and is known as washout. The governing equations for the Monod model described above are given by:

$$V_1 \frac{dS_1}{dt} = F(S_0 - S_1) - V_1 X_1 \frac{\mu(S_1)}{Y(S_1)}, \quad (1)$$

$$V_1 \frac{dX_1}{dt} = F(X_0 - X_1) + V_1 X_1 \mu(S_1), \quad (2)$$

$$V_2 \frac{dS_2}{dt} = F(S_1 - S_2) - V_2 X_2 \frac{\mu(S_2)}{Y(S_2)}, \quad (3)$$

$$V_2 \frac{dX_2}{dt} = F(X_1 - X_2) + V_2 X_2 \mu(S_2). \quad (4)$$

The specific growth rate is given by $\mu_i = \mu_m S_i/(K_S + S_i)$, and the yield coefficient $Y(S_i) = \alpha + \beta S_i$ (Essajee and Tanner 1979). The subscript i takes the value 1 or 2 and refers to a property of the i^{th} reactor. The flowrate through the reactor is given by F (lhr^{-1}), K_s is the Monod constant (gl^{-1}), S_i is the substrate concentration (gl^{-1}), S_0 is the substrate concentration in the feed (gl^{-1}), V_i is the volume (l), X_i is the cell mass concentration (gl^{-1}), X_0 is the cell mass concentration in the feed (gl^{-1}), $Y(S_i)$ is the cell mass yield coefficient (-), t is time (h), α is a constant in the yield coefficient (-), β is a constant in the yield coefficient (lg^{-1}), $\mu(S_i)$ is the specific growth rate (hr^{-1}), μ_m is the maximum specific growth rate (hr^{-1}). Following Yang and Su (1993), Chen *et al* (1995), Balakrishnan and Yang (2002) and Nelson and Sidhu (2003), we take $K_s = 1.75 gl^{-1}$, $X_0 = 0 gl^{-1}$, $\alpha = 0.01$,

$\beta = 0.03 \text{lg}^{-1}$, and $\mu_m = 0.3 hr^{-1}$. By introducing dimensionless variables for the substrate concentrations ($S_i^* = S_i / K_S$), the cell mass concentrations ($X_i^* = X_i / (\alpha K_S)$) and time ($t^* = \mu_m t$), the system of differential equations (1 - 4) can be written down in the dimensionless form

$$\frac{dS_1^*}{dt^*} = \frac{1}{\tau_1^*}(S_0^* - S_1^*) - \frac{S_1^* X_1^*}{(1+\beta^* S_1^*)(1+S_1^*)}, \quad (5)$$

$$\frac{dX_1^*}{dt^*} = \frac{1}{\tau_1^*}(X_0^* - X_1^*) + \frac{S_1^* X_1^*}{1+S_1^*}, \quad (6)$$

$$\frac{dS_2^*}{dt^*} = \frac{1}{\tau_2^*}(S_1^* - S_2^*) - \frac{S_2^* X_2^*}{(1+\beta^* S_2^*)(1+S_2^*)}, \quad (7)$$

$$\frac{dX_2^*}{dt^*} = \frac{1}{\tau_2^*}(X_1^* - X_2^*) + \frac{S_2^* X_2^*}{1+S_2^*}, \quad (8)$$

where the total dimensionless residence time $\tau_{tot}^* = \tau_1^* + \tau_2^*$. The value of β^* is determined by the choice of the microbial system and is assumed fixed. Using the values of earlier authors this equals 5.25. A feature of our non-dimensionalization is that there is a one-to-one relationship between our dimensionless variables and their dimensional counterparts. Henceforth we write, for example "the residence time", rather than "the dimensionless residence time".

3. PERFORMANCE INDICATORS

The aim of this paper is to determine a suitable criterion that can be utilized to assess the performance of two-reactor cascade systems. Only by using a meaningful criterion can one make comparisons of the performances of these configurations. The crux of our approach is to determine the *best* performance of a single CSTB (provided that the optimal residence time is no greater than the total residence time in the two CSTB case), and then to use this indicator as a benchmark for comparison with performances for the double-reactor system. If the optimal residence time for the single reactor is greater than the total residence time of the cascade, we then use the output of the single reactor when the residence time *equals* the total residence time for the double CSTB. Previous researchers (such as Yang and Su, 1993) compared the performance of the two-reactor system to that of a single reactor configuration with the *same* residence time, and showed that an appropriate choice of the residence time in the first reactor can produce considerable improvements in product yield (up to 1420%) when compared to utilising equal residence times in each of the two reactors. Here we shall use two definitions to gauge the performance of the double-reactor CSTB: (i) reactor productivity, and (ii) cell mass concentration leaving the reactor. Before studying each of these indicators in greater detail, we note that the cell mass concentrations will be time-averaged values if the reactor performance is maximized for parameter values at which the stable attractor is a periodic solution. For the Monod system studied here, the maximum values of the cell mass concentration leaving the reactor for both the single and cascade configurations *always occur* at the stable equilibrium solution.

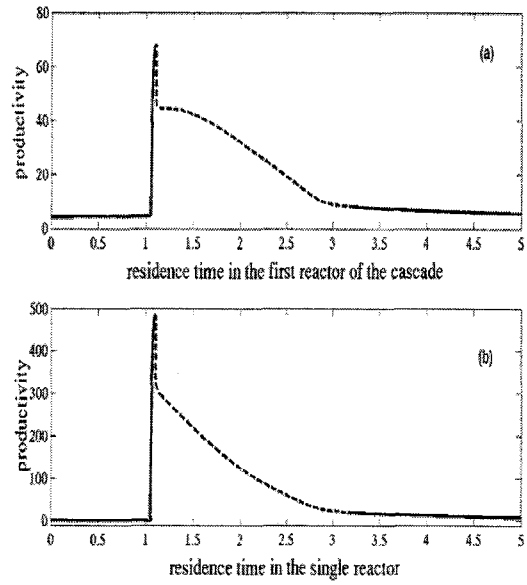

Figure 1: The reactor productivity plots for (a) the cascade system and (b) the single reactor arrangement for $S_0^* = 20$ and $\tau_{tot}^* = 8$. The solution branches in the dashed line represent the time-averaged reactor productivity obtained from stable periodic solutions. The solution branches in the solid line represent the productivity from stable equilibrium solutions.

3.1. Reactor Productivity

The reactor productivity is defined as the product of the flow rate through the reactor and the cell mass concentration. In terms of our dimensionless quantities, it is given by $P^* = \frac{X^*}{\tau^*}$. Figure 1 shows the reactor productivity for the double-reactor cascade and the single reactor. We have plotted only the reactor productivity corresponding

to the stable solutions. We can immediately see that the optimal reactor productivity in the single reactor is around seven-times larger than that of the double reactor cascade. The maximums occur at around the same values of residence time for both configurations. The productivity in the double reactor was obtained by dividing the cell mass concentration leaving the second reactor by the total residence time, which in this case is fixed at the value 8. Just to the left of the optimal operating conditions, we observe the regions in which washout occurs for both the systems. We define productivity efficiency of the double-reactor cascade as

productivity efficiency

$$=100\frac{P^*_{2,\max}(\tau^*_{tot})-P^*_{1,\max}(\tau^*_1\le\tau^*_{tot})}{P^*_{1,\max}(\tau^*_1\le\tau^*_{tot})}. \quad (9)$$

Here $P^*_{2,\max}(\tau^*_{tot})$ is the maximum productivity in the double-reactor cascade for a fixed total residence time, and feed substrate concentration, and $P^*_{1,\max}(\tau^*_1\le\tau^*_{tot})$ is the optimal productivity for the single reactor obtained for the same feed substrate concentration having a residence time no larger than τ^*_{tot}. Figure 2 shows the productivity efficiency plots for two values of feed substrate concentration, as the total residence time of the cascade is varied. We can see immediately that in most cases the double reactor cascade is inferior when compared to the single reactor. For feed substrate concentration $S^*_0=20$, we observe only a small range of total residence time (between 1.45 and 1.11) when the productivity of the cascade is marginally better than that of the single reactor. When the total residence time is around 1.09, the reactor productivities in both configurations are equal so that the productivity efficiency goes to zero. For low residence times washout occurs in the cascade and as a result we did not plot the productivity efficiency curves beyond that point. (This is also true for figure 3.)

As before, figure 3 shows that the reactor productivity for the single reactor is mostly superior to that of the cascade. Here we have fixed the total residence time of the cascade and varied the feed substrate concentration.

By using the reactor productivity as a performance indicator for the double-reactor cascade, it is clear that its performance is mostly inferior to that of the single reactor, and only marginally better in other cases. Based on these results, one may be tempted to conclude that the performance of the cascade is mostly inferior to the single CSTB.

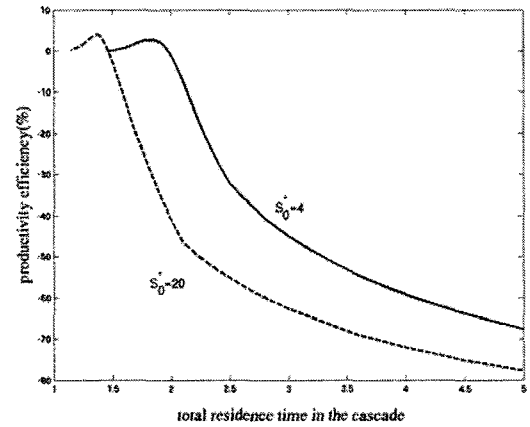

Figure 2: The productivity efficiency plot of the two-reactor cascade for two values of feed substrate concentration, as the total residence time in the two-reactor cascade is varied.

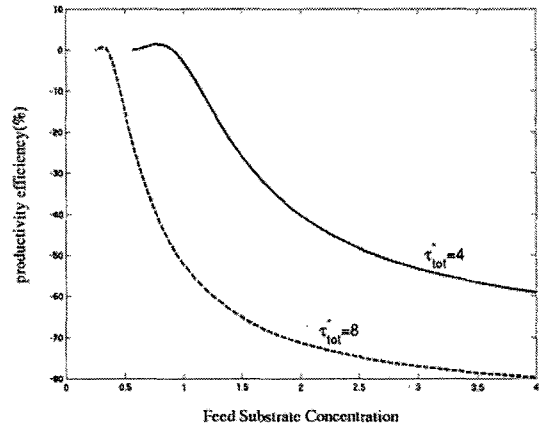

Figure 3: The productivity efficiency plot of the two-reactor cascade for two values of total residence time in the cascade, as the feed substrate concentration is varied.

3.2. Cell Mass Concentration

Here we compare the cell mass concentration leaving the two-reactor cascade with that of the single reactor by defining the cell mass efficiency of the two-reactor cascade as

cell mass efficiency

$$=100\frac{X^*_{2,\max}(\tau^*_{tot})-X^*_{1,\max}(\tau^*_1\le\tau^*_{tot})}{X^*_{1,\max}(\tau^*_1\le\tau^*_{tot})}, \quad (10)$$

where $X^*_{2,\max}(\tau^*_{tot})$ is the optimal value of the cell mass concentration leaving a two-reactor cascade that has total residence time τ^*_{tot}, and

$X^*_{1,\max}(\tau_1^* \le \tau^*_{tot})$ is the optimal value of the cell mass concentration leaving a single reactor that has a residence time of no larger than τ^*_{tot}. We note that if the optimal residence time for the single reactor is greater than the total residence time for the double-cascade, then the output will be evaluated at the residence time equal to the total residence time of the cascade, i.e. $X^*_{1,\max}(\tau_1^* = \tau^*_{tot})$.

The maximum cell mass concentration of the two-reactor cascade for $\tau^*_{tot} = 8$ and $S_0^* = 20$ is $X_2^* = 545.14$, occurring at $\tau_1^* = 1.10$. The output for the single reactor with the residence time fixed at 8 is 34.75, whereas the output for the double-reactor cascade with the residence time in each reactor being equal to 4 is 54.42. By comparing the optimal performance of the double reactor cascade with single reactor performance at the *same* residence time, we see that the cascade improves the reactor performance by 1469%. A double reactor cascade with equal residence time in each reactor, i.e. $\tau_1^* = \tau_2^* = 4$, is superior to that of a single reactor with residence time of 8 by around 57%. Such results lead Yang and Su (1993) to conclude that the performance of a double CSTB is *always better* than the single CSTB. However, by analysing the single reactor carefully, we find that its performance is maximized when the residence time in the single reactor is 1.10, and the output is 535.04. Now using (10), the improved cell mass efficiency of the double-reactor cascade is only 1.9%.

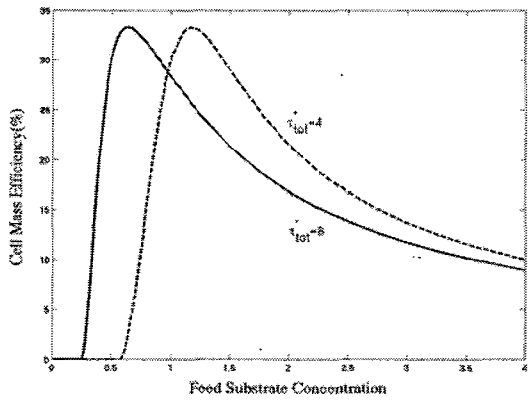

Figure 4: Shows how the cell mass efficiency varies with feed substrate concentration for two values of total residence time.

Figure 4 shows how the cell mass efficiency varies as a function of the substrate concentration for two values of total residence time (τ^*_{tot}). For both cases the maximum cell mass efficiency of the cascade is around 33.33%. These results contradict one of the conclusions in Chen *et al* (1995) which states that performance enhancement by splitting the reactor into two smaller ones is infeasible for biological systems with Monod growth kinetics.

Our numerical results indicate that the maximum cell mass efficiency appears to be independent of the choice of total residence time, that is it is always around 33.33% as shown in figure 4. (For clarity purposes we have only shown the results for two values of total residence time.) Given the results above, it is important in practical terms to determine operating conditions that result in the global maximum of the cell mass efficiency curves shown in figure 4. The maximal operating conditions are presented in figure 5. This figure shows the dependence of the most efficient values for the feed substrate concentration (S_0^*) and the residence time in the first reactor of the cascade system (τ_1^*) upon the total residence time (τ^*_{tot}). Thus for a given total residence time, the graph enables one to determine values of the feed substrate concentration and the most efficient reactor design that would result in the maximum cell mass efficiency of around 33.33% over the best single reactor design. The bold curve in figure 5 shows that the feed substrate concentration at which the cascade is most efficient decreases rapidly initially as the total residence time increases, and while $\tau^*_{tot} \ge 10$, this value remains approximately constant. The dashed curve shows the size of the first reactor in the cascade for the most efficient reactor design as a percentage of the

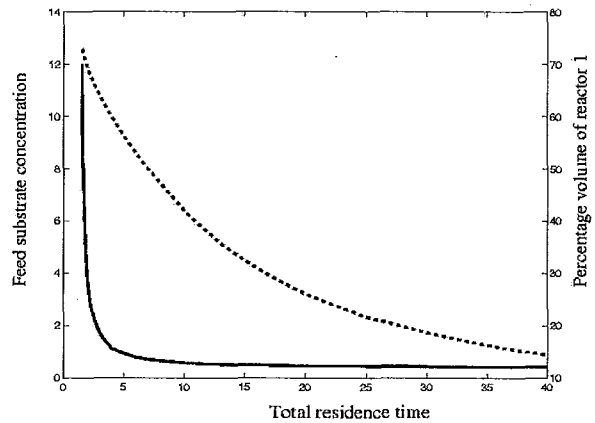

Figure 5: Shows the dependence of substrate concentration (solid line) and the reactor design (dashed line) upon the total residence time for the most efficient reactor design.

total volume of the cascade. This curve shows that when the total residence time is sufficiently low ($\tau^*_{tot} \leq 7$), the volume of the first reactor must be over 50% of the total volume in order to achieve the highest possible cell mass efficiency.

4. CONCLUSIONS

We have re-investigated a simple model for microbial growth with Monod growth kinetics and a variable yield coefficient in a single and double-reactor cascade, with the aim to compare the performances of these configurations. We have used two performance indicators, reactor productivity and cell mass concentration leaving the reactor, to compare the single and double-reactor systems. Earlier investigators (Balakirshnan and Yang 1998, Yang and Su 1993) studied the design of the cascade, through the choice of the residence time in the first reactor for a specified total residence time, and how the design changed the performance of the system, by comparing the cascade against a single reactor having the same total residence time. Using this criterion, an optimally designed cascade was found to significantly outperform a single reactor. However, using our criterion, it was found that the increase is performance was only marginal. If the comparison was made on the basis of reactor productivity, then the cascade is in fact *mostly inferior*. In fact our results show that when using the reactor productivity criterion, the cascade is mostly inferior to the single reactor for a majority of the parameter values, and is at best only marginally better than the single reactor case (up to only 4% for the cases investigated).

We therefore suggest that it does not make sense to compare the performance of a cascade unless the conditions that maximize the performance of a single reactor are fully understood. The latter can then be used as a benchmark to compare the performance of the cascade.

5. ACKNOWLEDGMENTS

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