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A COMPARISON OF VARIOUS CONTROL SCHEMES FOR CONTINUOUS BIOREACTOR

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Abstract. A controller-independent controllability measure, the partial disturbance gain (PDG), is used for evaluating a continuous bioreactor's sensitivity to disturbances. Five control schemes for continuous bioreactors are examined based on controllability analysis with respect to disturbance rejection. At substrate-limited growth conditions, the turbidostat using the feed substrate concentration as manipulated variable is the best control scheme. The conventional turbidostat should be avoided to use. When the cell growth is not substrate limited, all these control schemes are effective except the nutristat using feed substrate concentration as manipulated variable which is not feasible no matter whether the growth is substrate limited or not.

Key Words. Continuous bioreactor; turbidostat; nutristat; controllability analysis; disturbance rejection.

1 INTRODUCTION

Bioreactor control has become an active area of research in recent years. Much emphasis has been placed on the control of fed-batch bioreactors because of their prevalence in industry. However, when production of biomass or metabolic product is to be optimized, continuous operation is desirable.

Unforeseen disturbances in a bioreactor may result in a failure of the reactor, such as *washout*, and require a new start-up procedure. Therefore, there is a strong economic incentive to develop efficient control schemes that would enable rapid start-up and stabilization of steady states in continuous bioreactors subject to disturbances.

Problem formulation. As already noted the primary objective of a continuous bioreactor control system is usually to avoid that the reaction stops due to washout. This may be done by closing one feedback loop and controlling the cell mass or substrate concentrations (x or s [g/l]). In addition, in order to optimize the production and maintain the quality of the product, one may as the secondary control objective want to keep both x and s at some desired value. To do this two degrees of freedom are available, namely the total feed flow rate F [l/h] (which is usually normalized with the reactor volume to get the dilution rate, $D = F/V$ [1/h]) and the feed substrate concentration, s_f [g/l]. One obvious solution is then to implement a 2×2 control system. However, this is expensive and probably not necessary, and in this paper the main consideration is on whether one may achieve acceptable control performances of both outputs by controlling only one of them.

This is actually a quite general control strategy problem where one is faced with a "partial control problem", that is, to use a subset of the available inputs to control a subset of the outputs. Define $y = [y_c \quad y_u]^T$ and $u = [u_c \quad u_u]^T$, where

y_c - controlled outputs

y_u - uncontrolled outputs

u_c - manipulated inputs used to control y_c

u_u - unused inputs

The problem is to select the controlled outputs (y_c), and the unused inputs (u_u). Issues are:

1) Use of u_c to control y_c should yield satisfactory control performance (u_c should have a "large" effect on y_c to avoid input constraints; delays and RHP-zeros from u_c to y_c should not conflict with the desired bandwidth needed for disturbance rejection and setpoint tracking).

2) With these control loops closed (i.e., with y_c approximately constant) and with the unused inputs u_u constant, the uncontrolled outputs y_u should be relatively insensitive to disturbances.

Issue 1 is a conventional feedback control problem where dynamic issues generally are most important, while steady-state considerations are often more important for issue 2. To evaluate both these issues a controllability analysis of the alternative structures needs to be performed. A useful tool when considering issue 2 is the partial disturbance gain (Skogestad and Wolff, 1992) which is the effect of a disturbance on the uncontrolled output when the controlled outputs are kept constant, i.e., $PDG = (\partial y_u/\partial d)_{u_u, y_c}$ (see Section 2).

Such strategy decisions arise frequently in process control. One extensively studied problem is the control configuration selection for distillation columns (e.g., Skogestad and Morari, 1987) where the problem involving u_c and y_c is the level control problem. For distillation columns it is well known that some configurations have better "built-in" disturbance rejection ability than others, i.e., the sensitivity of the uncontrolled outputs (which in this case are product compositions) with respect to disturbances is less.

The issue of disturbances has not been widely discussed in the literature on the controllability analysis for bioreactors. The objective of this paper is then to make a comparison of various control schemes for continuous bioreactors based on a controllability analysis with respect to disturbance rejection.

Previous work. Numerous control schemes for continuous bioreactors have been proposed. The two most common control schemes are the conventional turbidostat and nutristat with the dilution rate (D) as

a manipulated input. In a turbidostat the cell mass concentration (x) is controlled (in practice, the optical density is used to infer x). In a nutristat the residual substrate concentration (s) is controlled. Edwards et al. (1972) analyzed and compared these two schemes for a bioreactor with substrate inhibition kinetics and they concluded that the conventional nutristat is superior to the conventional turbidostat in many applications. Agrawal and Lim (1984) evaluated the conventional turbidostat, nutristat and other control schemes based on local controllability, local stability, input multiplicity and steady state gains. They concluded that the conventional turbidostat and nutristat are feasible only at those conditions where growth is not substrate limited. They then proposed a modified turbidostat where the dilution rate of the pure water stream (D_w) (which is mixed with the concentrated-substrate stream (D_s) to form the total feed) is used as a manipulated input instead of the total dilution rate (D). They found this modified turbidostat to be superior to the conventional turbidostat in that it can operate under all growth conditions. Menawat and Balachander (1991) proposed to use the feed substrate concentration (s_f) as the manipulated variable and claim that this control scheme improves the control performance for control of both x and s compared to using D as the manipulated variable.

Control Schemes Studied. In this paper five control schemes are examined:

1. Conventional turbidostat ($D \rightarrow x$ – scheme). Dilution rate (D) is used to control the cell mass concentration (x).

2. Conventional nutristat ($D \rightarrow s$ – scheme). D is used to control the substrate concentration (s).

3. Concentration turbidostat ($s_f \rightarrow x$ – scheme). Feed substrate concentration (s_f) is used to control x (Menawat and Balachander, 1991).

4. Concentration nutristat ($s_f \rightarrow s$ – scheme). s_f is used to control s (Menawat and Balachander, 1991).

5. Modified turbidostat ($D_w \rightarrow x$ – scheme). Dilution rate of the pure water (D_w) is used to control x (Agrawal and Lim, 1984).

2 CONTROLLABILITY MEASURES

In this paper simple frequency-dependent tools are used to study the inherent control characteristics. In particular, the open-loop disturbance gain $G_d(j\omega)$ (for selecting the "controlled" pairings) and the partial disturbance gain PDG (for selecting the "uncontrolled" pairings) are considered.

Tools. Consider a linear model of the form

$$y(s) = G(s)u(s) + G_d(s)d(s) \tag{1}$$

The open-loop disturbance sensitivity for an output y_i and a disturbance d_k is

$$\left(\frac{\partial y_i}{\partial d_k}\right)_u = [G_d]_{ik} \tag{2}$$

The corresponding disturbance sensitivity with all other outputs $y_{l\neq i}$ perfectly controlled can be expressed as

$$PDG_{ijk} = \left(\frac{\partial y_i}{\partial d_k}\right)_{u_j, y_{l\neq i}} = [G^{-1}G_d]_{jk}/[G^{-1}]_{ji} \tag{3}$$

where y_i— uncontrolled output
u_j— left in manual
$y_{l\neq i}$— other outputs under perfect control

For a particular disturbance d_k one should check if there exists a particular paring of y_i and u_j with the PDG_{ijk} less than 1 in magnitude such that the effect of disturbance d_k on the uncontrolled output y_i is acceptable. For simultaneous disturbances the worst overall effect may be evaluated by taking the sum of element magnitudes for each "pairing". This gives rise to a combined PDG-matrix, denoted C_{PDG}, with elements

$$[C_{PDG}]_{ij} = \sum_k |[PDG]_{ijk}| \tag{4}$$

Summary of controllability analysis. The variables should first be scaled with respect to their allowed range such that all variables are less than 1 in magnitude. The objective of the controllability analysis in this paper is to find the best partial control scheme, i.e., to select the controlled output (y_c) and unused input (u_u) as discussed in the introduction. The controllability analysis then consists of two main steps:

1. Analysis of "controlled" subsystem with "controlled pairing" $u_m - y_l$.

(a) To get the acceptable speed of response: Prefer pairings where G_{lm} has no delays and RHP-zeros within the desired bandwidth range. The desired bandwidth range is (at least) the frequency range where for some disturbance d_k $|G_{d_{lk}}(j\omega)| > 1$.

(b) To avoid input constraints: Find pairings where $|G_{lm}| > |G_{d_{lk}}|$ for all disturbances within the desired bandwidth range.

2. Analysis of "uncontrolled" subsystem with "uncontrolled pairing" $u_j - y_i$. To get the acceptable disturbance sensitivity for the uncontrolled outputs: Prefer pairings where the ij-th element in the combined PDG-matrix, C_{PDG}, is less than 1 at all frequencies.

3 DYNAMIC MODEL

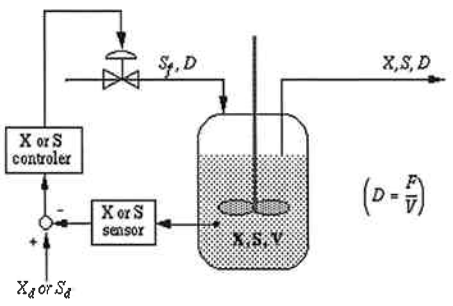

Fig. 1: Continuous bioreactor

A schematic diagram of a continuous bioreactor is shown in Fig. 1. From a chemical engineering point of view it can be viewed as a continuous stirred tank reactor (CSTR) with perfect mixing and constant volume. The most important overall reaction for this study is the growth of the microorganism population on the substrate

$$substrate \longrightarrow cells + metabolic\ products$$

From a chemical engineering point of view this reaction is autocatalytic, and the rate r [g cells/l,h] for formation of new cells is usually assumed to be proportional to the concentration of cells x, i.e., $r = \mu(s)x$. Here the specific growth rate μ [1/h] depends on the substrate concentration s. For Monod kinetics which is most frequently used:

$$\mu(s) = \frac{\mu_m s}{k_s + s}$$

where μ_m and k_s represent the maximum specific growth rate and the saturation constant respectively. Macroscopic material balances for the substrate and cells lead to the following "unstructured" model:

$$\frac{dx}{dt} = \mu(s)x - Dx \tag{5}$$

$$\frac{ds}{dt} = D(s_f - s) - \frac{\mu}{Y}x \tag{6}$$

Here x and s are the state variables representing the cell mass and the substrate concentrations, respectively. Y is the yield coefficient [g cells / g substrate] which in this paper is assumed constant.

3.1 Steady state behavior

From eqs. (5) and (6), the steady state values of cell mass and substrate concentrations can be calculated[1]:

$$\frac{dx}{dt} = 0 \Rightarrow \mu(\bar{s}) = \bar{D} \Rightarrow \bar{s} = \frac{k_s \bar{D}}{\mu_m - \bar{D}} \tag{7}$$

$$\frac{ds}{dt} = 0 \Rightarrow \bar{x} = Y(\bar{s}_f - \bar{s}) \tag{8}$$

Here the overbar ($^-$) denotes steady-state values. The steady-state relationship is shown in Fig. 2.

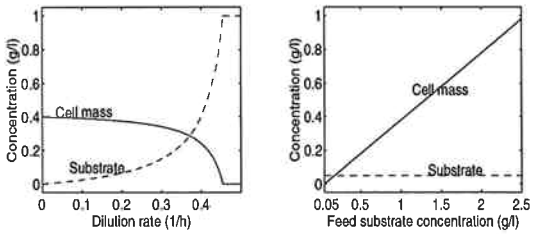

Fig. 2: Steady state values of x and s. Left plot: As a function of D with s_f = 1 g/l. Right plot: As a function of s_f with D=0.17 h^{-1}. Values of μ_m, k_s and Y from Table 1.

As can be seen from Eq. (7), the steady-state substrate concentration ($\bar{s}$) is independent of the feed concentration ($\bar{s}_f$). This unusual feature is due to the autocatalytic reaction. Thus $\bar{s}$ depends only on the dilution rate ($\bar{D}$). On the other hand, $\bar{x}$ depends also on $\bar{s}_f$ as given by Eq. (8). Another phenomena caused by the autocatalytic reaction is the possibility for washout. Mathematically, washout corresponds to the case when the above steady-state equations have no physical solution. Specifically, $\bar{x}$ in Eq. (8) must be positive, that is, we must require that $\bar{s}_f > \bar{s}$. Inserting this requirement into Eq. (7) we find that the dilution rate $\bar{D}$ must be less than a critical value D_c which depends on s_f:

$$D_c = \frac{\mu_m s_f}{k_s + s_f} = \mu(s_f)$$

Physically, at high dilution rates $D > D_c$, the cells can not grow fast enough to keep up with its dilution, and the culture is washed out of the reactor.

Similarly, there is another critical value at very low but nonzero dilution rates, where the reaction stops because a large fraction of the cells may die from starvation, but this effect is not reflected by our simple model since no maintenance term is included.

For many continuous bioreactors the objective is to maximize the productivity $P = Dx$ [g cells/l,h] The productivity increases when s_f increases, but for changes in D it has a maximum value (set $dP/dD = 0$) corresponding to:

$$D_{opt} = \mu_m(1 - \sqrt{\frac{k_s}{k_s + s_f}})$$

The nominal model parameter values and steady state data for two operating points are given in Table 1.

Table 1: Steady State Data

Operating Point	D (h^{-1})	s_f (g/l)	x (g/l)	s (g/l)	$P = Dx$ ($g/h \cdot l$)
No. I	0.17	1.0	0.38	0.05	0.065
No. II	0.35	1.0	0.31	0.23	0.109
washout	> 0.46	1.0	0	1.00	0
Nominal model parameter	μ_m (h^{-1}) 0.5		k_s (g/l) 0.1		Y (g/g) 0.4

Here operating point No. I is the one studied by Menawat and Balachander (1991) and operating point No. II corresponds to the maximum productivity.

3.2 Linearized model

Linearizing equations (5) and (6) around a nontrivial steady state yields the transfer function model:

$$y(\lambda) = G(\lambda)u(\lambda) + G_d(\lambda)d(\lambda) \tag{9}$$

$$y = \begin{bmatrix} \Delta x \\ \Delta s \end{bmatrix}; \quad u = \begin{bmatrix} \Delta D \\ \Delta s_f \end{bmatrix}$$

$$d = \left[\Delta\mu_m, \Delta k_s, \Delta Y, \Delta D_d, \Delta s_{fd}\right]^T$$

where the outputs (states) y, inputs u and disturbances d represent deviations from the steady state. In addition to possible disturbances in the manipulated inputs D and s_f, we have included disturbances in the model parameters μ_m, k_s and Y which may stem from variations in the environment conditions such as temperature, pH, aeration rate etc. λ is used to denote the Laplace variable to distinguish it from the substrate concentration s. The input-output transfer matrix is

$$G(\lambda) = \begin{bmatrix} \frac{-x}{\lambda+a} & \frac{\mu x}{(\lambda+a)(\lambda+D)}\frac{d\mu}{ds} \\ \frac{x}{(\lambda+a)Y} & \frac{\lambda D}{(\lambda+a)(\lambda+D)} \end{bmatrix} \tag{10}$$

where $a = \frac{x}{Y}\frac{d\mu}{ds}$. Here the overbar on the steady-state values has been dropped to simplify notation.

[1] For other kinetic schemes, like the substrate inhibition kinetics (Edwards et al, 1972) multiple steady states may exist.

Remarks about the model: 1) The model is stable at all nontrivial steady states. At washout conditions we have $\bar{x} = 0$ and $a = 0$ and the linearized model contains a pure integrator. 2) The steady-state gain matrix is obtained by setting $\lambda = 0$. As expected s_f has no steady-state effect on s and therefore should not be used to control s. 3) Except for this zero gain between s_f and s, neither the transfer function nor any of its elements contains RHP-zeros. However, measurement delays in obtaining x or s have not be included which will limit the achievable performance. 4) One of the eigenvalues is fixed at $-\bar{D}$ irrespective of the reaction, and it can be easily shown that there is a combined state, e.g. $z = x + Ys$, representing a reaction invariant. From the transfer matrix the effect of D is first order and does not affect this combined state. Thus, the system is not "*state* controllable" with D as an input. Physically, if D is used to control x (or s) the uncontrollable combined state z will "drift away" by itself unaffected by the feedback using D. Menawat and Balachander (1991) indicate that this may be a problem. However, as pointed out by Agrawal and Lim (1984) it may not have any practical significance since the uncontrollable model is stable, and any control problems associated with it will appear in the controllability analysis of the uncontrolled output.

4 CONTROLLABILITY STUDY

4.1 Scaling of variables

The scaled transfer matrices are derived by scaling all variables with respect to their maximum allowed changes.

$$G' = \begin{bmatrix} \bar{\Delta}x & 0 \\ 0 & \bar{\Delta}s \end{bmatrix}^{-1} G \begin{bmatrix} \bar{\Delta}D & 0 \\ 0 & \bar{\Delta}s_f \end{bmatrix} \tag{11}$$

$$G'_d = \begin{bmatrix} \bar{\Delta}x & & \\ & \bar{\Delta}s & \end{bmatrix}^{-1} G_d \begin{bmatrix} \bar{\Delta}\mu_m & & & & \\ & \bar{\Delta}k_s & & & \\ & & \bar{\Delta}Y & & \\ & & & \bar{\Delta}D_d & \\ & & & & \bar{\Delta}s_{fd} \end{bmatrix} \tag{12}$$

(in the following the prime (′) used to denote the scaled matrices is deleted to simplify notation). The allowed maximum output changes are

$$\bar{\Delta}x = 10\%\,\bar{x}; \quad \bar{\Delta}s = 20\%\,\bar{s}$$

The allowed maximum input changes are

$$\bar{\Delta}D = 30\%\,\bar{D}; \quad \bar{\Delta}s_f = 35\%\,\bar{s}_f$$

The expected maximum disturbance changes are

$$\bar{\Delta}\mu_m = 10\%\,\bar{\mu}_m; \; \bar{\Delta}k_s = 20\%\,\bar{k}_s; \; \bar{\Delta}Y = 25\%\,\bar{Y}$$

$$\bar{\Delta}D_d = 20\%\,\bar{\Delta}D; \quad \bar{\Delta}s_{fd} = 20\%\,\bar{\Delta}s_f$$

4.2 Controllability analysis results

Operating Point No. I. In this operating point the cell growth is substrate limited. The steady-state gain matrices in terms of scaled variables are

$$G(0) = \begin{bmatrix} -0.24 & 3.68 \\ 2.25 & 0 \end{bmatrix}$$

$$G_d(0) = \begin{bmatrix} 0.08 & -0.11 & 2.5 & -0.05 & 0.74 \\ -0.75 & 1 & 0 & 0.45 & 0 \end{bmatrix}$$

The time constants at this operating point are $1/a = 0.5$ h and $1/D = 5.9$ h. The corresponding frequency response plots for the open-loop system are shown in Fig. 3.

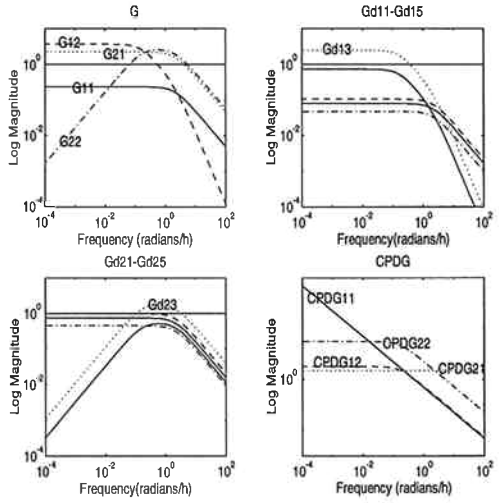

Fig. 3: Frequency responses in operation point No. I

We now proceed with the controllability analysis in order to evaluate the five control schemes by following the controllability analysis procedures described in Section 2.

1. Controlled output.

a. Input constraints. The first requirement is that the open-loop gain, $|G_{lm}|$ for the "controlled pairing" should be larger than the disturbance gains $|G_{d_{lk}}|$ to avoid input constraints. We first note that the steady-state gain from s_f to s is zero ($G_{22}(0) = 0$) which means that s_f can not be used to control s. The steady-state gain from D to x is only -0.24 whereas the gain for a disturbance in yield (Y) is about 2.5. This means that the control action in D needed to reject the largest disturbance in Y (which corresponds to a change in Y of 25%) is about $2.5/0.24 \approx 10$ times higher than what is allowed. The conventional turbidostat is therefore not recommended in operating point No. I where the cell growth is substrate limited. This is consistent with the conclusion of Agrawal and Lim (1984). The corresponding frequency-dependent plots in Fig. 3 are consistent with the steady-state values. The main exception is that at frequencies (> 0.1 rad/h) a disturbance in Y has a large effect also on s and may cause problems for the conventional nutristat.

b. Bandwidth requirements. From the frequency-dependent plots of the elements in G_d, the bandwidth requirement to achieve acceptable rejection for disturbances in Y (the worst disturbance) is 0.4 rad/h for x (response time of better than 2.5 h required), and 3 rad/h for s (response time of better than 0.3 h required). In practice, this means that it may be favor-

able to control x if very long measurement delays are expected.

2. Uncontrolled output.

The effect of disturbances on the uncontrolled outputs are given by the PDG. The steady-state PDG values are listed for individual disturbances in Table 2, and their corresponding combined effect (C_{PDG}) is shown as a function of frequency in Fig. 3.

Table 2: PDG in operating point No. I

Scheme:	$s_f \rightarrow s$	$D \rightarrow s$	$s_f \rightarrow x$	$D \rightarrow x$
d_k	PDG_{11k}	PDG_{12k}	PDG_{21k}	PDG_{22k}
μ_m	∞	0	-0.75	0
k_s	∞	0	1	0
Y	0	2.5	0	23.75
D	∞	0	0.45	0
s_f	0	0.74	0	7

From the steady-state PDG values in Table 2 and the frequency response of C_{PDG}, the best scheme is the $s_f \rightarrow x$ – scheme. However, the $D \rightarrow s$ – scheme is better at higher frequencies. Again, the $s_f \rightarrow s$ – scheme is not feasible since the sensitivity to some disturbances is infinite, while the $D \rightarrow x$ – scheme is unacceptable with large sensitivity to disturbances in Y (24 times larger than acceptable) and in s_f (7 times larger than acceptable).

If the feed substrate concentration is difficult to manipulate, the $D_w \rightarrow x$ – scheme (modified turbidostat) proposed by Agrawal and Lim (1984) is quite effective. The steady-state gain from D_w to x (with D_s constant) is -1.70. The steady-state PDG values giving the effect of various disturbances on the uncontrolled s are

$$\begin{bmatrix} d_k \\ PDG_{22k} \end{bmatrix} = \begin{bmatrix} \mu_m & k_m & Y & D_w & s_f & D_s \\ -0.7 & 0.93 & 1.66 & 0 & 0.49 & 0.42 \end{bmatrix}$$

which is almost acceptable. In particular, we note that the effects of disturbances in Y and in s_f on the uncontrolled output s ($PDG_{223} = 1.6, PDG_{225} = 0.49$) are much less than for the conventional turbidostat ($PDG_{223} = 23.75, PDG_{225} = 7$). Thus, using the dilution rate of the pure water stream (D_w) to control x gives much better control performance than using the total dilution rate (D) (conventional turbidostat).

Operating Point No. II. This operating point corresponds to the maximum productivity and the cell growth is not substrate limited. We have

$$G(0) = \begin{bmatrix} -2.95 & 4.52 \\ 4.97 & 0 \end{bmatrix}$$

$$G_d(0) = \begin{bmatrix} 0.98 & -0.59 & 2.5 & -0.59 & 0.91 \\ -1.65 & 1 & 0 & 0.99 & 0 \end{bmatrix}$$

The time constants at this operating point are $1/a = 2.8$ h and $1/D = 2.9$ h. We note immediately that the outputs are more sensitive to both inputs and disturbances than in operating point No. I. In particular, this is the case for changes in the dilution rate D where the gain for its effect on relative changes x has increased by more than a factor of 10. This means that tighter control is needed to reject disturbances in this case, and since the reactor is operating closer to washout, tighter control is needed also to maintain stability.

The PDG-values at the steady state are listed in Table 3.

Table 3: PDG in operating point No. II

Scheme:	$s_f \rightarrow s$	$D \rightarrow s$	$s_f \rightarrow x$	$D \rightarrow x$
d_k	PDG_{11k}	PDG_{12k}	PDG_{21k}	PDG_{22k}
μ_m	∞	0	-1.65	0
k_s	∞	0	1	0
Y	0	2.5	0	4.21
D	∞	0	0.99	0
s_f	0	0.91	0	1.53

For this operating point there is no big difference in the controllability of various control schemes (except for the $s_f \rightarrow s$ – scheme which is still not feasible), and also the $D \rightarrow x$ – scheme may be used. If one should pick one scheme, then from the PDG values and in particular the frequency response of C_{PDG} (not shown), the $D \rightarrow s$ – scheme is preferable.

5 SIMULATION RESULTS

In this section we present nonlinear simulation results to confirm the validity of the conclusions from the linear controllability analysis presented in the previous section. All simulations are for operating point No. I and a simple PI controller is used for the controlled output.

Fig. 4 shows step responses to a disturbance of 25% decrease in the yield factor (Y) from 0.4 to 0.3 [g/g]. Fig. 5 shows step responses to a disturbance of 10% decrease in specific growth rate (μ_m) from 0.5 to 0.45 [1/h]. Overall, the best performance is obtained by using the concentration turbidostat (curve no. 3 in the plots). This confirms the linear controllability analysis. We see that with this scheme the cell mass and substrate concentrations remain within their allowable bounds, and so does the feed substrate concentration (s_f) without violating the input constraints.

From simulation results we also find:

The system can not be left uncontrolled (curve no. 5) because of disturbances in Y.

For a disturbance in Y the conventional turbidostat (curve no. 1) is unacceptable because the uncontrolled output s exceeds its bound (in fact s goes to zero and so does the dilution rate D, which means there is no production).

For a disturbance in Y the conventional nutristat (curve no. 2) is poor because the uncontrolled output x exceeds its bound.

For a disturbance in μ_m the concentration nutristat (curve no. 4) is unacceptable because the uncontrolled output x exceeds its bound and eventually the reaction will stop: s_f has to be continuously lowered in order to try to keep s constant, however, it is not possible to

keep s constant in the long run because s is independent of s_f at stesdy state , and finally s_f will reach 0 and results in a failure of the reactor.

A careful comparison shows that *all* these results are consistent with the linear controllability analysis in the previous section.

6 CONCLUSIONS

At the substrate-limited growth conditions (operating point No. I), the controllability analysis results indicate that using s_f to control x (the concentration turbidostat) is the best control scheme. This conclusion is consistent with the result of Menawat and Balachander (1991). The conventional turbidostat can not be used in this operating point because the cell concentration (x) is insensitive to changes in the dilution rate (D). The conventional nutristat is also not recommended from the controllability analysis, and it has the additional problem that it is difficult to accurately measure low values of substrate concentration (Agrawal and Lim, 1984).

At higher dilution rates close to the maximum specific growth rate (operating point No. II) the conventional nutristat is slightly better than the other schemes, consistent with the results of Agrawal and Lim (1984). However there is no big difference among the first three control schemes. Thus the conventional turbidostat is also effective.

The concentration turbidostat where s_f is used to control s (proposed by Menawat and Balachander, 1991) is unacceptable in all operating points because s_f has no steady-state effect on s.

In this paper we have not considered the measurement problem which is one of the main obstacles for effective control of bioreactors. However, a number of secondary measurements are often available, such as temperature, pH, CO_2 and O_2 in the exhaust gas, which may be used to estimate the cell mass and substrate concentrations.

The simulation results are consistent with the linear controllability analysis. This shows that the partial disturbance gain (PDG) is an effective tool for controllability analysis. The main advantage with a controllability analysis is that it is independent of controller parameter tuning and makes detailed simulations unnecessary.

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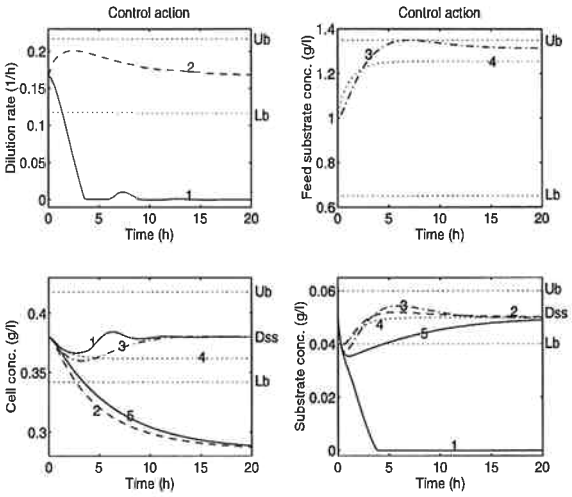

Fig. 4: Time responses for step disturbance in Y

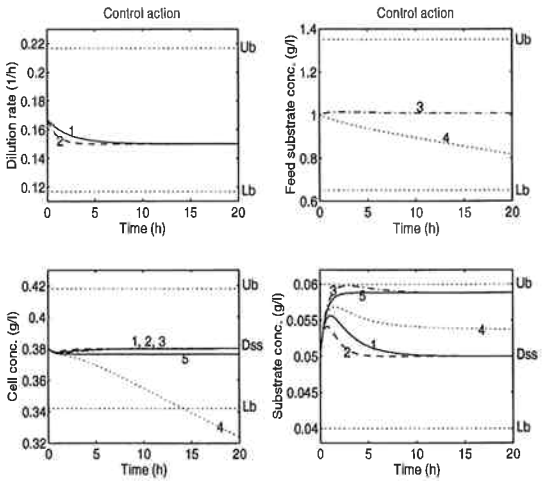

Fig. 5: Time responses for step disturbance in μ_m

Note. In Fig. 4 and Fig. 5:
1 — Conventional turbidostat ($K_c = -2$ in Fig. 4 and $K_c = -1$ in Fig. 5, $\tau_i = 0.5$)
2 — Conventional nutristat ($K_c = 1$, $\tau_i = 0.5$)
3 — Concentration turbidostat ($K_c = 8$, $\tau_i = 3$ in Fig. 4 and $K_c = 4$, $\tau_i = 4$ in Fig. 5)
4 — Concentration nutristat ($K_c = 6$ in Fig. 4 and $K_c = 1$ in Fig. 5, $\tau_i = 0.5$)
5 — No control action ($K_c = 0$)
Ub — Upper bound,
Lb — Lower bound
Dss — Desired steady state