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Reachability of nonlinear fed-batch fermentation processes

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SUMMARY

The reachability of a simple nonlinear fed-batch fermentation process model is investigated in this paper. It is shown that the known difficulties of controlling such processes are primarily caused by the fact that the rank of the reachability distribution is always less than the number of state variables.

Furthermore, a co-ordinates transformation is calculated analytically that shows the nonlinear combination of the state variables which is independent of the input. The results of the reachability analysis and that of the co-ordinates transformation are independent of the source function in the system model.

The results are extended to the four state variable non-isotherm case, and to nonlinear fed-batch chemical reactors with general reaction kinetics. Copyright © 2002 John Wiley & Sons, Ltd.

KEY WORDS: nonlinear systems; reachability; co-ordinates transformations

1. INTRODUCTION

The methods for analysing local reachability of nonlinear concentrated parameter systems given their state space model in input-affine form is theoretically well established and widely known. The notion of controllability in the nonlinear sense was formulated and investigated mathematically in e.g. References [1–3].

However, the proposed methods for calculating the reachability distribution and the related co-ordinates transformation for transforming the system model into its canonical form suffer from the computational difficulties and high computational complexity. In some cases, however, the special structure of the underlying state space model enables to perform the calculation analytically. The process system analysed in this paper exhibits such a special structure.

Bio-processes in general and fermentation processes in particular are difficult to model and to control even in the simplest cases. The dynamic behaviour of fermenters is usually highly nonlinear and they have poor dynamic properties that make them difficult to control [4, 5]. Many successful methods for the control of fermenters have been reported in the literature (see

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e.g. References [6–8]). However, these papers do not contain exact nonlinear analysis neither about the open loop system nor about the operating region and robustness of the proposed controllers.

On the other hand, there are very few publications on the controllability analysis of fermentation processes. In Reference [9] different reactor configuration for continuous fermenters are examined in terms of their controllability properties using linearized process models. It is shown that using an additional inlet stream (which does not contain any growth limiting substrate) as a control input leads to superior control compared to a single stream fermenter. In Reference [10] the controllability of continuous fermentation to ethanol was studied experimentally, where the outlet glucose concentration was controlled with a PI controller.

Nonlinear analysis techniques are applied to analyse the dynamic properties of a class of continuous biotechnological processes for maximize the dimension of the linear system and get stable zero dynamics in Reference [11] and to base feedback linearization controllers based thereon. An algebraic method for characterizing state accessibility (a version of reachability) is proposed in Reference [12] for continuous fermenters with general reaction kinetics which is also based on nonlinear reachability analysis results.

The aim of this paper is to use rigorous nonlinear analysis of a simple fed-batch fermenter model for analysing its reachability properties and to relate them to the physico-chemical phenomena taking place in the reactor.

The paper is organized as follows. In Section 2, the dynamic state space model of a fed-batch fermenter based on first engineering principles is presented. Section 3 contains the calculations related to the nonlinear reachability analysis. In Section 4, the coordinates transformation for the decomposition of the system model is derived. Section 5 deals with the generalizations and the practical aspects of the results. In Section 6, the most important conclusions are drawn. The notations used in the paper are summarized in Section 7. For a detailed explanation of these notions the authors recommend the excellent book of Isidori [13].

2. NONLINEAR STATE SPACE MODEL

The state equations are derived from dynamic conservation balances of the overall mass, component masses and energy if applicable.

The simplest dynamic model of a fed-batch fermenter consists of three conservation balances for the mass of the cells (e.g. yeast to be produced), that of the substrate (e.g. sugar which is consumed by the cells) and for the overall mass.

Here, we assume that the fermenter is operating under isotherm conditions, that is no energy balance is needed. The cell growth rate is described by a nonlinear static function μ. The speciality of a fermentation model appears in the so-called source function which is highly nonlinear and non-monotonous in nature.

Initially a solution containing both substrate and cells is present in the fermenter. During the operation we feed a solution of substrate with a given feed concentration S_{f} to the reactor.

Under the above assumptions the nonlinear state space model of the fermentation process can be written in the following input-affine form [5]

$$\dot{x} = f(x) + g(x)u \tag{1}$$

where

$$x = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \end{bmatrix} = \begin{bmatrix} X \\ S \\ V \end{bmatrix}, \quad u = F \tag{2}$$

$$f(x) = \begin{bmatrix} \mu(x_2)x_1 \\ -\frac{1}{Y}\mu(x_2)x_1 \\ 0 \end{bmatrix} = \begin{bmatrix} \dfrac{\mu_{\max}x_2x_1}{k_1 + x_2 + k_2x_2^2} \\ -\dfrac{\mu_{\max}x_2x_1}{(k_1 + x_2 + k_2x_2^2)Y} \\ 0 \end{bmatrix}, \quad g(x) = \begin{bmatrix} -\dfrac{x_1}{x_3} \\ \dfrac{S_f - x_2}{x_3} \\ 1 \end{bmatrix} \tag{3}$$

and

$$\mu(x_2) = \frac{\mu_{\max}x_2}{k_1 + x_2 + k_2x_2^2} \tag{4}$$

The variables and parameters of the model are described in Section 7.

3. REACHABILITY ANALYSIS

First, we give the general form of the algorithm for constructing the reachability distribution as it is described in Lemmas 1.8.1 and 1.8.2 in Reference [13]. Given a distribution Δ and vector fields $\{h_1, h_2, \ldots, h_m\}$ construct the sequence:

$$\Delta_0 = \Delta$$

$$\Delta_k = \Delta_{k-1} + \sum_{i=1}^{m} [h_i, \Delta_{k-1}]$$

The sequence terminates at $k = k'$ if $\Delta_{k'+1} = \Delta_{k'}$ such that $\Delta_{k'} = \langle h_1, h_2, \ldots, h_m | \Delta \rangle$.

The above algorithm can be applied to the model of the fermenter in the following way:

$$\Delta_0 = \text{span}\{g\} \tag{5}$$

$$\Delta_1 = \Delta_0 + [f, \Delta_0] = \text{span}\{g, [f, g]\} \tag{6}$$

$$\Delta_2 = \Delta_1 + [f, \Delta_1] + [g, \Delta_1] = \text{span}\{g, [f, g], [f, [f, g]], [g, [f, g]]\} \tag{7}$$

The calculation of the Lie-products in Δ_1 and Δ_2 is as follows:

$$[f, g](x) = \frac{\partial g}{\partial x} f(x) - \frac{\partial f}{\partial x} g(x) \tag{8}$$

Since

$$\frac{\partial g}{\partial x} f(x) = \begin{bmatrix} -\dfrac{1}{x_3} & 0 & \dfrac{x_1}{x_3^2} \\ 0 & -\dfrac{1}{x_3} & \dfrac{x_2 - S_f}{x_3^2} \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} f_1(x) \\ -\frac{1}{Y}f_1(x) \\ 0 \end{bmatrix} = \begin{bmatrix} -\dfrac{1}{x_3}f_1(x) \\ \dfrac{1}{Y}\dfrac{1}{x_3}f_1(x) \\ 0 \end{bmatrix} \tag{9}$$

and

$$\frac{\partial f}{\partial x} g(x) = \begin{bmatrix} \mu(x_2) & \frac{\partial \mu}{\partial x_2} & 0 \\ -\frac{1}{Y}\mu(x_2) & -\frac{1}{Y}\frac{\partial \mu}{\partial x_2} & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} g_1(x) \\ g_2(x) \\ 0 \end{bmatrix} = \begin{bmatrix} \mu(x_2) g_1(x) + \frac{\partial \mu}{\partial x_2} g_2(x) \\ -\frac{1}{Y}(\mu(x_2) g_1(x) + \frac{\partial \mu}{\partial x_2} g_2(x)) \\ 0 \end{bmatrix} \tag{10}$$

the Lie-product $[f, g]$ has the form

$$\begin{bmatrix} [f,g]_1 \\ [f,g]_2 \\ [f,g]_3 \end{bmatrix} = \begin{bmatrix} [f,g]_1 \\ -\frac{1}{Y}[f,g]_1 \\ 0 \end{bmatrix} \tag{11}$$

where $[f, g]_i$ denotes the ith co-ordinate function of the vector field $[f, g]$.

It follows from Equations (8)–(11) that the distributions $[f,[f,g]]$ and $[g,[f,g]]$ will also have the same form as (11), i.e.

$$[f,[f,g]] = \begin{bmatrix} [f,[f,g]]_1 \\ -\frac{1}{Y}[f,[f,g]]_1 \\ 0 \end{bmatrix} \tag{12}$$

and

$$[g,[f,g]] = \begin{bmatrix} [g,[f,g]]_1 \\ -\frac{1}{Y}[g,[f,g]]_1 \\ 0 \end{bmatrix} \tag{13}$$

On the basis of the above we can denote the co-ordinate functions of the vector fields spanning Δ_2 at a given point x of the state space as follows:

$$\Delta_2(x) = \text{span}\left\{ \begin{bmatrix} \delta_{11}(x) & \delta_{12}(x) & \delta_{13}(x) & \delta_{14}(x) \\ \delta_{21}(x) & \delta_{22}(x) & \delta_{23}(x) & \delta_{24}(x) \\ \delta_{31}(x) & \delta_{32}(x) & \delta_{33}(x) & \delta_{34}(x) \end{bmatrix} \right\} \tag{14}$$

where

$$\delta_{31} = 1, \quad \delta_{32}(x) = \delta_{33}(x) = \delta_{34}(x) = 0 \tag{15}$$

and

$$\delta_{22}(x) = -\frac{1}{Y}\delta_{12}(x) \tag{16}$$

$$\delta_{23}(x) = -\frac{1}{Y}\delta_{13}(x) \tag{17}$$

$$\delta_{24}(x) = -\frac{1}{Y}\delta_{14}(x) \tag{18}$$

i.e.

$$\Delta_2(x) = \operatorname{span}\left\{ \begin{bmatrix} \delta_{11}(x) & \delta_{12}(x) & \delta_{13}(x) & \delta_{14}(x) \\ \delta_{21}(x) & -\frac{1}{Y}\delta_{12}(x) & -\frac{1}{Y}\delta_{13}(x) & -\frac{1}{Y}\delta_{14}(x) \\ 1 & 0 & 0 & 0 \end{bmatrix} \right\} \tag{19}$$

which means that we could not increase the dimension of the reachability distribution in the second step and the rank of Δ_2 is at most 2 in any point of the state space.

Singular points: There are, however, points in the state space where the rank of the reachability distribution Δ_2 is less than 2:

- $x_1 = 0$: In this case Δ_2 is of dimension 1. This case means that there is no biomass in the system and since the inlet flow contains only substrate, the biomass concentration cannot be influenced by manipulating the input.

During the following analysis, we will consider the open region of the state space where Δ_1 is nonsingular and the value of state vector has real physical meaning (the concentrations and the liquid volume are positive) i.e.

$$U = \{x_1, x_2, x_3 | x_1 > 0, x_2 > 0, x_3 > 0\} \tag{20}$$

4. CALCULATION OF THE CO-ORDINATES TRANSFORMATION

The basis for our further calculations is the following general result (Proposition 1.7.1 in Reference [13]).

Let Δ be a non-singular involutive distribution of dimension d and assume that Δ is invariant under the vector fields $f, g_1, \ldots, g_m$. Moreover, suppose that the distribution $\operatorname{span}\{g_1, \ldots, g_m\}$ is contained in Δ. Then, for each point x^0 it is possible to find a neighbourhood U^0 of x^0 and a local co-ordinates transformation $z = \Phi(x)$ defined on U^0 such that, in the new co-ordinates, the state equation (1) is represented by equations of the form

$$\dot{\zeta}_1 = f_1(\zeta_1, \zeta_2) + \sum_{i=1}^{m} g_{1i}(\zeta_1, \zeta_2) u_i$$

$$\dot{\zeta}_2 = f_2(\zeta_2)$$

where $\zeta_1 = (z_1, \ldots, z_d)$ and $\zeta_2 = (z_{d+1}, \ldots, z_n)$.

Now, we will apply this decomposition theorem to the model of the fermenter. Since the generation of the reachability distribution stopped in the second step

$$\Delta_1 = \operatorname{span}\{g, [f, g]\}$$

is the smallest distribution invariant under f, g and containing the vector field g. Since $\langle f, g | \operatorname{span}\{g\} \rangle$ is nonsingular on U and involutive we may use it to find a co-ordinates transformation $z = \Phi(x)$ where $z = [z_1\ z_2\ z_3]^{\mathrm{T}}$. Thus, the system in the new co-ordinates will be represented by equations of the following form:

$$\dot{\zeta}_1 = \bar{f}_1(\zeta_1, \zeta_2) + \bar{g}(\zeta_1, \zeta_2)u \tag{21}$$

$$\dot{\zeta}_2 = \bar{f}_2(\zeta_2) \tag{22}$$

where $\zeta_1 = (z_1, z_2)$ and $\zeta_2 = z_3$ in our case.

To calculate Φ, we have to integrate the distribution Δ_1 first, that is to find a single ($\dim(x) - \dim(\Delta_1) = 3 - 2 = 1$) real valued function λ such that $\mathrm{span}\{d\lambda\} = [\langle f, g | \mathrm{span}\{g\} \rangle]^{\perp}$, where

$$\mathrm{d}\lambda = \begin{bmatrix} \frac{\partial \lambda}{\partial x_1} & \frac{\partial \lambda}{\partial x_2} & \frac{\partial \lambda}{\partial x_3} \end{bmatrix}$$

Since

$$[f, g](x) = \begin{bmatrix} -\dfrac{\left(\dfrac{\mu_{\max} x_1}{k_1 + x_2 + k_2 x_2^2} - \dfrac{\mu_{\max} x_2 x_1 (1 + 2k_2 x_2)}{(k_1 + x_2 + k_2 x_2^2)^2}\right)(S_{\mathrm{f}} - x_2)}{x_3} \\ -\dfrac{\left(-\dfrac{\mu_{\max} x_1}{(k_1 + x_2 + k_2 x_2^2)Y} + \dfrac{\mu_{\max} x_2 x_1 (1 + 2k_2 x_2)}{(k_1 + x_2 + k_2 x_2^2)^2 Y}\right)(S_{\mathrm{f}} - x_2)}{x_3} \\ 0 \end{bmatrix} \tag{23}$$

this amounts to solve the partial differential equations (PDEs)

$$\begin{bmatrix} \frac{\partial \lambda}{\partial x_1} & \frac{\partial \lambda}{\partial x_2} & \frac{\partial \lambda}{\partial x_3} \end{bmatrix} \begin{bmatrix} -\dfrac{x_1}{x_3} & -\dfrac{\left(\dfrac{\mu_{\max} x_1}{k_1 + x_2 + k_2 x_2^2} - \dfrac{\mu_{\max} x_2 x_1 (1 + 2k_2 x_2)}{(k_1 + x_2 + k_2 x_2^2)^2}\right)(S_{\mathrm{f}} - x_2)}{x_3} \\ \dfrac{S_{\mathrm{f}} - x_2}{x_3} & -\dfrac{\left(-\dfrac{\mu_{\max} x_1}{(k_1 + x_2 + k_2 x_2^2)Y} + \dfrac{\mu_{\max} x_2 x_1 (1 + 2k_2 x_2)}{(k_1 + x_2 + k_2 x_2^2)^2 Y}\right)(S_{\mathrm{f}} - x_2)}{x_3} \\ 1 & 0 \end{bmatrix} = [0 \quad 0] \tag{24}$$

4.1. Solution by the method of characteristics

The method of characteristics [14, 15] is used for solving the above resulted first-order linear homogeneous partial differential equation in the following general form:

$$\sum_{i=1}^{n} \phi_i(x) \partial_i \lambda(x) = 0, \quad \partial_i \lambda = \frac{\partial \lambda}{\partial x_i} \tag{25}$$

or briefly

$$\phi(x)\partial\lambda'(x) = 0 \tag{26}$$

where $U \subset \mathbb{R}^n$ is a domain, $x \in U$, ϕ_i, $i = 1, \ldots, n$ are known functions and λ is the unknown. The characteristic equation system of (26) is the following set of ordinary differential equations:

$$\dot{\xi} = \phi(\xi) \tag{27}$$

We call the $\xi : \mathbb{R} \to \mathbb{R}^n$ solutions of (27) characteristic curves. A $\lambda \in C^1(T)$ function is called the first integral of (27) if $t \to \lambda(\xi(t))$ is constant along any characteristic curve. In order to solve (26) we have to find $(n-1)$ linearly independent solutions $(\lambda_1, \lambda_2, \ldots, \lambda_{n-1})$ of it. Then the general solution of (26) will be in the form $\lambda = \Psi(\lambda_1, \lambda_2, \ldots, \lambda_{n-1})$, where $\Psi \in C^1(\mathbb{R}^{n-1})$ is an arbitrary function. We know that a first integral of (27) satisfies (26), therefore we have to find $(n-1)$ linearly independent first integrals to obtain the general solution. This can be done without solving (27) as it is illustrated below in our case.

To solve the first PDE, namely

$$\frac{\partial\lambda}{\partial x_1}\left(-\frac{x_1}{x_3}\right) + \frac{\partial\lambda}{\partial x_2}\left(\frac{S_f - x_2}{x_3}\right) + \frac{\partial\lambda}{\partial x_2} = 0 \tag{28}$$

we start from the following set of ordinary differential equations:

$$\dot{x}_1 = -\frac{x_1}{x_3}$$

$$\dot{x}_2 = \frac{S_f - x_2}{x_3}$$

$$\dot{x}_3 = 1$$

It's easy to observe that

$$\dot{x}_1 x_3 = -x_1$$

and

$$\dot{x}_1 x_3 + \dot{x}_3 x_1 = (x_1 x_3)' = 0$$

since $\dot{x}_3 = 1$. Therefore $x_1 x_3 = \text{const.}$ Moreover

$$\dot{x}_2 x_3 = S_f - x_2$$

and

$$\dot{x}_2 x_3 + x_2 \dot{x}_3 - S_f \dot{x}_3 = (x_2 x_3)' - S_f \dot{x}_3 = 0$$

from which it follows that

$$x_2 x_3 - S_f x_3 = \text{const.}$$

We can see from the above that the solution of (28) will be in the form

$$\lambda(x_1, x_2, x_3) = \Psi(x_1 x_3, x_2 x_3 - S_f x_3)$$

with an arbitrary C^1 function Ψ.

To solve the second PDE we first remember that in the reachability distribution

$$\delta_{22} = -\frac{1}{Y}\delta_{12} \quad \text{and} \quad \delta_{32} = 0$$

and then it's enough to write the PDE as

$$\frac{\partial \lambda}{\partial x_1}\delta_{12}(x) + \frac{\partial \lambda}{\partial x_2}\left(-\frac{1}{Y}\delta_{12}(x)\right) = 0 \tag{29}$$

The characteristic equations are written as

$$\dot{x}_1 = \delta_{12}(x)$$

$$\dot{x}_2 = -\frac{1}{Y}\delta_{12}(x)$$

$$\dot{x}_3 = 0$$

It's easy to see that

$$-\frac{1}{Y}\dot{x}_1 - \dot{x}_2 = 0$$

and

$$\dot{x}_3 = 0$$

Therefore, the solution of (29) is in the form

$$\lambda(x_1, x_2, x_3) = \Phi^*\left(-\frac{1}{Y}x_1 - x_2,\ x_3\right) \tag{30}$$

with an arbitrary C^1 function Φ^*. To give a common solution for both (28) and (29) we propose the function

$$\lambda(x_1, x_2, x_3) = x_3\left(-\frac{1}{Y}x_1 - x_2 + S_f\right) = -\frac{1}{Y}x_1x_3 - (x_2x_3 - S_fx_3) \tag{31}$$

from which we can see that it indeed satisfies both PDEs. With the help of λ we can define the local (and luckily global) co-ordinates transformation $\Phi : \mathbb{R}^n \to \mathbb{R}^n$

$$\begin{bmatrix} z_1 \\ z_2 \\ z_3 \end{bmatrix} = \Phi(x_1, x_2, x_3) = \begin{bmatrix} x_1 \\ x_2 \\ -\frac{1}{Y}x_1x_3 - x_2x_3 + S_fx_3 \end{bmatrix} \tag{32}$$

Since

$$x_3 = \frac{z_3}{-\frac{1}{Y}z_1 - z_2 + S_f}$$

and

$$\dot{z}_3 = \left(-\frac{1}{Y}x_1x_3 - x_2x_3 + S_f x_3\right)' = -\frac{1}{Y}(\dot{x}_1x_3 + x_1\dot{x}_3) - (\dot{x}_2x_3 + x_2\dot{x}_3) + S_f\dot{x}_3$$
$$= -\frac{1}{Y}(\mu(x_2)x_1x_3 - x_1 + x_1) - \left(-\frac{1}{Y}\mu(x_2)x_1x_3 + S_f - x_2 + x_2\right) + S_f = 0$$

the transformed form of the model (1)–(2) can be written as

$$\dot{z} = \tilde{f}(z) + \tilde{g}(z)u \tag{33}$$

where

$$\tilde{f}(z) = \begin{bmatrix} \tilde{f}_1(z) \\ \tilde{f}_2(z) \\ \tilde{f}_3(z) \end{bmatrix} = \begin{bmatrix} \dfrac{\mu_{\max} z_2 z_1}{k_1 + z_2 + k_2 z_2^2} \\ -\dfrac{\mu_{\max} z_2 z_1}{(k_1 + z_2 + k_2 z_2^2)Y} \\ 0 \end{bmatrix},$$

$$\tilde{g}(z) = \begin{bmatrix} \tilde{g}_1(z) \\ \tilde{g}_2(z) \\ \tilde{g}_3(z) \end{bmatrix} = \begin{bmatrix} -\dfrac{z_1}{z_3}(-\dfrac{1}{Y}z_1 - z_2 + S_f) \\ \dfrac{S_f - z_2}{z_3}(-\dfrac{1}{Y}z_1 - z_2 + S_f) \\ 0 \end{bmatrix}, \tag{34}$$

and $z_3 \neq 0$.

Using the notation of Equations (21) and (22) it's clear that

$$\bar{f}_1 = \begin{bmatrix} \tilde{f}_1 \\ \tilde{f}_2 \end{bmatrix}, \quad \bar{f}_2 = \tilde{f}_3, \quad \bar{g}_1 = \begin{bmatrix} \tilde{g}_1 \\ \tilde{g}_2 \end{bmatrix}, \quad \bar{g}_2 = \tilde{g}_3$$

5. DISCUSSION AND GENERALIZATIONS

The aim of this section is to show the reasons present in the original state space model which led to the reachability and state transformation above. This analysis enables to find other models of similar form with the same properties and points toward related problems of practical interest.

5.1. Physical analysis of the model and the solutions

The first important thing to observe is that the results of the reachability analysis and that of the co-ordinates transformation do not depend on the actual form of the function μ in Equation (4). The results utilized the following specialities of the original state space model (1)–(2).

(i) the constant coefficients in the third state equation, i.e.

$$f_3 = 0, \ \ g_3 = 1$$

where f_i and g_i are the ith entry of the vector functions f and g in the state space model. This property always holds for the overall mass balance of fed-batch reactors.

(ii) the relation between the first and the second state equation, namely

$$f_2 = -\frac{1}{Y} f_1 = C_f f_1$$

where C_f is a constant. Such a relationship exists if the two related state variables, x_1 and x_2 are concentrations of components related by a chemical reaction in the form, $(1/Y)S \to X$ [16].

Further, we may notice that the quantity λ in Equation (31) which is conserved independently of the input consists of two parts corresponding to the substrate mass and cell mass of the system as follows:

$$\lambda(x_1, x_2, x_3) = V(S_f - S) + \frac{1}{Y} V(X_f - X) \quad (35)$$

with X_f being the influent cell concentration which is now $X_f = 0$ because the feed does not contain any cells. The above two terms originate from the (weighted) convective terms in the component mass conservation balances respectively, that is such terms which are only caused by the feed as inflow.

5.2. Related problems of practical interest

In order to understand how one can use the results of the nonlinear reachability analysis to solve practical operability and control problems we can interpret the conserved extensive quantity in λ in Equation (35) in a geometric way. This equation means that the state variables may only move on a three-dimensional surface in $\mathbb{R}^3$ which depends on the initial values $x_1(0), x_2(0), x_3(0)$. Examples of such surfaces for different initial values can be seen in Figures 1 and 2. It is shown that if the initial liquid volume is too small then the possibilities to control the biomass concentration x_1 are dramatically worsening.

In practical terms it means that if we want to reach a predefined state at the end of a batch and we only manipulate the inlet flowrate of the substrate solution of a given concentration then we need to choose an appropriate initial state for our goal to fit the set of reachable states (the reachability surface in Figures 1 and 2) accordingly.

5.3. Generalized state space models

We can generalize the original model in Equations (1)–(2) in two steps if we want to preserve the special dynamic properties of the model.

1. *General reaction rate function*: As the results do not depend on the function μ in Equation (4), we can replace the fermentation reaction by a general chemical reaction of the form

$$\frac{1}{Y} S \to X$$

where the reaction rate (source) function is $\mu^*(x_2)x_1$ with μ^* is an unspecified possibly nonlinear function.

2. *Non-isotherm case*: If we further release the assumption that the fermenter is operating under isothermal conditions, then we should include the energy conservation balance to

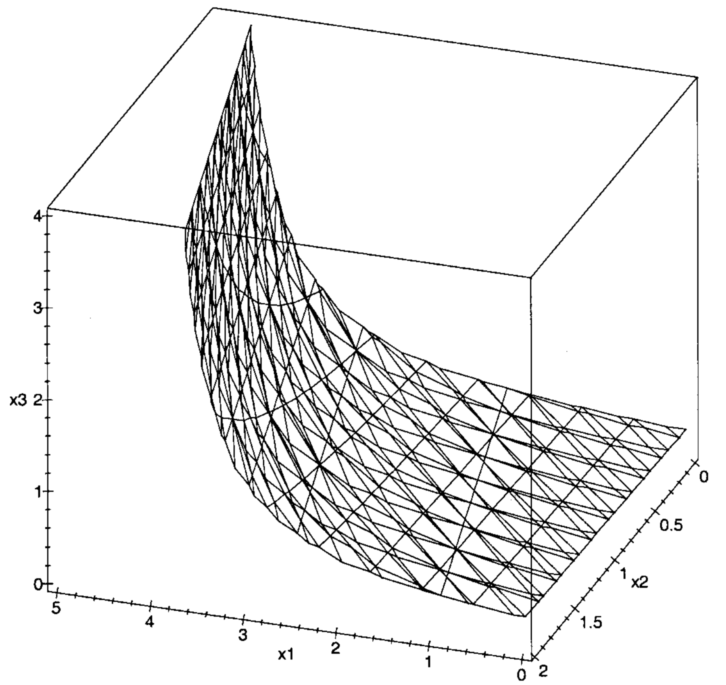

Figure 1. The reachability hypersurface of the fed-batch fermenter for initial conditions $x_1(0) = 2(g/l)$, $x_2(0) = 0.5(g/l)$, $x_3(0) = 0.5(g/l)$.

the original model. Then a four state model is obtained [16] in the following input-affine form:

$$\dot{x} = f^*(x) + g^*(x)u \tag{36}$$

where

$$x = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{bmatrix} = \begin{bmatrix} X \\ S \\ T \\ V \end{bmatrix}, \quad u = F \tag{37}$$

with T being the temperature in the fermenter.

$$f^*(x) = \begin{bmatrix} \mu^*(x_2, x_3)x_1 \\ c_1\mu^*(x_2, x_3)x_1 \\ c_2\mu^*(x_2, x_3)x_1 \\ 0 \end{bmatrix}, \quad g^*(x) = \begin{bmatrix} -\dfrac{x_1}{x_4} \\ \dfrac{S_f - x_2}{x_4} \\ \dfrac{T_f - x_3}{x_4} \\ 1 \end{bmatrix} \tag{38}$$

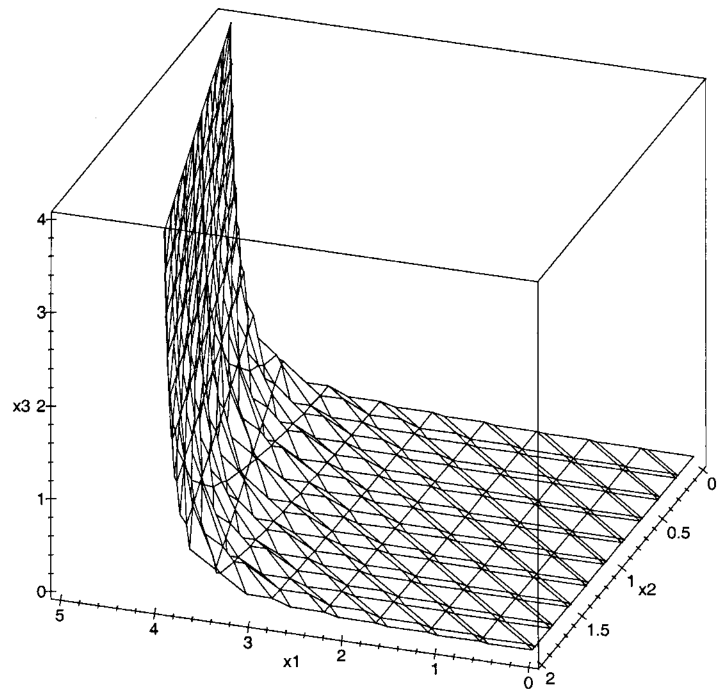

Figure 2. The reachability hypersurface of the fed-batch fermenter for initial conditions $x_1(0) = 2(g/l)$, $x_2(0) = 0.5(g/l)$, $x_3(0) = 0.1(g/l)$.

with $c_1 = -1/Y$ and the following additional constant parameters, c_2 the reaction enthalpy coefficient (m^3K/J) and $T_f = 293$ the influent temperature (K).

Observe, that now the reaction rate function μ^* depends also on the temperature $x_3 = T$ giving rise to the source function $\mu^*(x_2, x_3)x_1$.

Furthermore, the required structural properties (i) and (ii) described in Section 5.1 are present in the generalized model. The property (i) now holds for the entries f_4^* and g_4^* which is the overall mass balance. There are two independent pairs, (f_1^*, f_2^*) (the two component mass balances) and (f_1^*, f_3^*) (a mass and an energy balance) which possess property (ii) with different constants.

5.4. The analysis of the generalized models

In the above four state variable case the final reachability distribution after four steps would be the following

$$\Delta = \text{span}\{g^*, [f^*, g^*], [f^*, [f^*, g^*]], [g^*, [f^*, g^*]], [f^*, [f^*, [f^*, g^*]]],$$
$$[g^*, [f^*, [f^*, g^*]]], [f^*, [g^*, [f^*, g^*]]], [g^*, [g^*, [f^*, g^*]]]\} \quad (39)$$

If we calculate the Lie-products $[f^*, g^*]$, $[f^*, [f^*, g^*]]$ and $[g^*, [f^*, g^*]]$ we find that

$$[f^*, g^*] = \begin{bmatrix} [f^*, g^*]_1 \\ c_1[f^*, g^*]_1 \\ c_2[f^*, g^*]_1 \\ 0 \end{bmatrix}, \quad [f^*, [f^*, g^*]] = \begin{bmatrix} [f^*, [f^*, g^*]]_1 \\ c_1[f^*, [f^*, g^*]]_1 \\ c_2[f^*, [f^*, g^*]]_1 \\ 0 \end{bmatrix} \tag{40}$$

and also

$$[g^*, [f^*, g^*]] = \begin{bmatrix} [g^*, [f^*, g^*]]_1 \\ c_1[g^*, [f^*, g^*]]_1 \\ c_2[g^*, [f^*, g^*]]_1 \\ 0 \end{bmatrix} \tag{41}$$

Therefore, the calculation of the reachability distribution stops here and it turns out that the dimension of the distribution is 2 in this case.

To find the decomposed system similarly to (34) we have to find two independent real-valued functions λ_1 and λ_2 such that

$$\begin{bmatrix} \frac{\partial \lambda_1}{\partial x_1} & \frac{\partial \lambda_1}{\partial x_2} & \frac{\partial \lambda_1}{\partial x_3} & \frac{\partial \lambda_1}{\partial x_4} \\ \frac{\partial \lambda_2}{\partial x_1} & \frac{\partial \lambda_2}{\partial x_2} & \frac{\partial \lambda_2}{\partial x_3} & \frac{\partial \lambda_2}{\partial x_4} \end{bmatrix} \begin{bmatrix} g_1^*(x) & [f^*, g^*]_1(x) \\ g_2^*(x) & c_1[f^*, g^*]_1(x) \\ g_3^*(x) & c_2[f^*, g^*]_1(x) \\ 1 & 0 \end{bmatrix} = \begin{bmatrix} 0 & 0 \\ 0 & 0 \end{bmatrix} \tag{42}$$

where the second multiplier matrix on the left-hand side of the above equation takes the following concrete form in our case:

$$\begin{bmatrix} -\frac{x_1}{x_4} & -\frac{1}{x_4}\mu^*(x_2, x_3)x_1 - \mu^*(x_2, x_3)g_1^*(x) - \frac{\partial \mu}{\partial x_2}x_1 g_2^*(x) - \frac{\partial \mu}{\partial x_3}x_1 g_3^*(x) \\ \frac{S_f - x_2}{x_4} & c_1(-\frac{1}{x_4}\mu^*(x_2, x_3)x_1 - \mu^*(x_2, x_3)g_1^*(x) - \frac{\partial \mu}{\partial x_2}x_1 g_2^*(x) - \frac{\partial \mu}{\partial x_3}x_1 g_3^*(x)) \\ \frac{T_f - x_3}{x_4} & c_2(-\frac{1}{x_4}\mu^*(x_2, x_3)x_1 - \mu^*(x_2, x_3)g_1^*(x) - \frac{\partial \mu}{\partial x_2}x_1 g_2^*(x) - \frac{\partial \mu}{\partial x_3}x_1 g_3^*(x)) \\ 1 & 0 \end{bmatrix}$$

It's easy to check that the two independent functions

$$\lambda_1(x) = x_4(c_1 x_1 - x_2 + S_f) \tag{43}$$

$$\lambda_2(x) = x_4(c_2 x_1 - x_3 + T_f) \tag{44}$$

satisfy the PDEs in Equation (43). Therefore the new co-ordinate vector z is given by the function $\Phi^* : \mathbb{R}^4 \to \mathbb{R}^4$

$$\begin{bmatrix} z_1 \\ z_2 \\ z_3 \\ z_4 \end{bmatrix} = \Phi^*(x) = \begin{bmatrix} x_1 \\ x_2 \\ x_4(c_1 x_1 - x_2 + S_f) \\ x_4(c_2 x_1 - x_3 + T_f) \end{bmatrix} \tag{45}$$

and the system (36)–(38) in the new co-ordinates is written as

$$\dot{z} = \bar{f}^*(z) + \bar{g}^*(z)u \tag{46}$$

where

$$\bar{f}^*(z) = \begin{bmatrix} \bar{\mu}^*(z_1, z_2, z_3, z_4) z_1 \\ c_1 \bar{\mu}^*(z_1, z_2, z_3, z_4) z_1 \\ 0 \\ 0 \end{bmatrix}, \quad \bar{g}^*(z) = \begin{bmatrix} -\dfrac{z_1(c_1 z_1 - z_2 + S_f)}{z_3} \\ \dfrac{(S_f - z_2)(c_1 z_1 - z_2 + S_f)}{z_3} \\ 0 \\ 0 \end{bmatrix} \tag{47}$$

and

$$\bar{\mu}^*(z_1, z_2, z_3, z_4) = \mu^*\left(z_2, c_2 z_1 + T_f - \frac{z_4(c_1 z_1 - z_2 + S_f)}{z_3}\right) \tag{48}$$

with the condition $z_3 \neq 0$.

5.5. Discussion on the analysis results of the non-isotherm case

The reachability analysis above for the non-isotherm fed-batch fermenter shows that the dimension of the reachability distribution remained the same, i.e. 2 despite of the fact that we have included a fourth state equation. This seems surprising from practical point of view and needs some discussion.

First we need to remember that although we included the energy balance as the fourth state equation we had not changed the set of input variables but use the inlet feed flowrate F as the only manipulated input variable. This is a rather restricted case and never occurs in practice: one usually manipulates another independent input variable, a heater or a cooling liquid flowrate to achieve temperature control.

However, for this purpose we need to include either a direct energy source term describing the direct heating or a heat transfer term and possibly another energy balance for the heating–cooling jacket [16]. It is not too difficult to see that these additional terms destroy the special dynamic properties (i) and (ii) of the model (see in Section 5.1) we have based our analysis upon. Therefore for the non-isotherm cases of practical interest the above analysis results will not be valid. Further investigations should be carried out to clarify this case.

6. CONCLUSION

Rigorous nonlinear analysis has been used in this paper for analysing the reachability properties of a simple fed-batch fermenter model and to relate them to the physico-chemical phenomena taking place in the reactor. With a help of this grey-box approach we have shown that the known difficulties of controlling such processes are primarily caused by the fact that the rank of the reachability distribution is always two which is less than the number of state variables being three.

Furthermore, a co-ordinates transformation is calculated analytically using the method of characteristics that shows the nonlinear combination of the state variables that is constant independently of the input. The co-ordinates transformation is independent of the most uncertain part of the state-space model: the source (μ) function, too.

The results are extended to the four state variable non-isotherm case, and to nonlinear fed-batch chemical reactors with general reaction kinetics. The rank of the reachability distribution remains two in this case giving rise to two conserved combination of the state variables independently of the input.

The structural properties of the process models enabling to apply the proposed analytical technique have also been described.

Further work will be directed towards the analytical investigation of the observability of simple fed-batch fermentation processes with different output selections.

The constant parameters and their values used for plotting Figures 1 and 2 are given in Nomenclature.

NOMENCLATURE

X	cell concentration (state) (g/l)
S	substrate concentration (state) (g/l)
V	volume (state) (l)
F	feed flow rate (input) (l/h)
Y	(0.5) yield coefficient
$\mu_{\max}$	(1) maximum growth rate (h^{-1})
k_1	(0.03) Monod constant (g/l)
k_2	(0.5) kinetic parameter (l/g)
S_f	(10) influent substrate concentration (g/l)
X_f	(0) influent cell concentration
c_1, c_2	reaction enthalpy coefficients
Δ	distribution
$[f, \Delta]$	denotes the distribution spanned by all the vector fields $[f, \gamma_i]$, i.e. $[f, \Delta] = \text{span}\{[f, \gamma_i],\ \gamma_i \in \Delta; i = 1, \ldots, q\}$
$\langle h_1, h_2, \ldots, h_m \vert \Delta \rangle$	the smallest distribution which contains Δ and is invariant under the vector fields $\{h_1, h_2, \ldots, h_m\}$
$\Delta^{\perp}$	annihilator of a distribution Δ at a point x, which is the set of all covectors which annihilates all vectors in $\Delta(x)$ $\Delta^{\perp}(x) = \{w^* \in (\mathbb{R}^n)^* : \langle w^*, v \rangle = 0 \text{ for all } v \in \Delta(x)\}$.

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