

ORDER REDUCTION IN BIOPROCESS MODELLING: A SINGULAR PERTURBATION SOLUTION*

V. Van Breusegen† and G. Bastin

Centre for Systems Engineering and Applied Mechanics, Université Catholique de Louvain,
Bâtiment Maxwell, Place du Levant 3, B-1348 Louvain-la-Neuve, Belgium

Abstract. This paper deals with the order reduction of mass balance dynamical models of bioprocesses under the assumption that some reactions proceed at much faster rates than the others. It is shown that this can be generically achieved by using singular perturbations. The proposed methodology requires, in the one hand, the definition of a small scalar parameter related to small and fast reaction rates and, in the other hand, the definition of a suitable change of coordinates which transforms the system into a form which clearly separates its two time-scales. A prototype example dealing with anaerobic digestion is used throughout the paper to illustrate the proposed methodology.

Keywords. biotechnology, model reduction, singular perturbations

INTRODUCTION.

In many reaction systems, the assumption that some of the reactions proceed at much faster rate than the others can be made. The reduced-order modelling solution that we propose aims to introduce such an assumption in the mass-balance dynamical model of a reaction system in order to reduce its complexity. It has been shown in Van Breusegem and Bastin (1992) that this objective can be achieved by applying a singular perturbation to the model modified by a well-defined change of coordinates. The theory of singular perturbations (*see e.g.* Kokotovic and others, 1986) is indeed a convenient tool to easily convert a set of differential equations into algebraic equations by setting a small scalar parameter to zero. Moreover, this theory provides stability conditions which ensure that the reduced order model is still a valid approximation of the initial dynamics.

The aim of the present paper is to specialize the theoretical results of Van Breusegem and Bastin (1992) to the particular case of bioprocess models.

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†Senior Research Assistant of the National Fund for Scientific Research (Belgium)

Results will be presented through a representative illustrative example : the anaerobic digestion process.

1 DESCRIPTION OF THE ANAEROBIC DIGESTION PROCESS.

The anaerobic digestion is a biological treatment process of organic wastes with methane gas production. In this paper, we consider a two-step biological model of the methanogenesis process (Andrews and Graef, 1971). In the first step, organic compounds are fermented into intermediary metabolites (volatile fatty acids) by a group of fermentative bacteria. In the second step, a group of methanogenic bacteria converts the volatile fatty acids into methane. The process can be therefore described by the following reaction scheme :



where S_1 and S_2 represent organic compounds and volatile fatty acids, respectively. X_1 and X_2 represent fermentative and methanogenic bacteria, respectively. Finally, methane is denoted by P .

The mass balance dynamics of the compo-

nents of a bioprocess taking place in a stirred tank reactor can be described by the following nonlinear state space model (see e.g (Bastin and Dochain, 1990)):

$$\dot{\mathbf{x}} = \mathbf{C}\mathbf{r}(\mathbf{x}) + \mathbf{u} \quad (1.2)$$

where, for the particular case of the reaction scheme (1.1a)-(1.1b),

- the vector of the component concentrations (also referred to as natural coordinates in the sequel) $\mathbf{x}^T = [x_1, s_1, x_2, s_2, p]$
- the characteristic matrix, made up of the yield coefficients ($c_{ij} > 0$) associated to each reaction and to each component,

$$\mathbf{C}^T = \begin{bmatrix} 1 & -c_{12} & 0 & c_{14} & 0 \\ 0 & 0 & 1 & -c_{24} & c_{25} \end{bmatrix}$$

- the vector of the reaction rates $\mathbf{r}^T = [r_1, r_2]$
- the vector of the net balances between the supply feedrates and the withdrawal rates of the components
 $\mathbf{u}^T = [-Dx_1, -Ds_1 + Ds_{in}, -Dx_2, -Ds_2, -Dp - Q_p]$
 where s_{in} is the influent substrate concentration, D is the dilution rate and Q_p is the methane gas outflow rate.

The reaction rates $r_i(\mathbf{x})$, ($i = 1, \dots, 2$) are very complex time varying functions of the state of the process. They are related to the specific reaction rates $\mu_i(\mathbf{x})$ as follows :

$$r_i(\mathbf{x}) = \mu_i(\mathbf{x})x_i \quad (1.3)$$

According to the fact that the growth of a population of microorganisms is intrinsically limited, irrespective of the environmental conditions, the specific growth rates $\mu_i(\mathbf{x})$ can be assumed to be upper bounded as :

$$(A.1) \quad 0 \leq \mu_i(\mathbf{x}) \leq \mu_i^* \quad \text{for all } \mathbf{x}$$

with the constants μ_i^* representing the maximal growth capacity of the bacteria population in each reaction. This implies also that

$$\mu_i(\mathbf{x}) = \mu_i^* \psi_i(\mathbf{x}) \quad \text{for all } \mathbf{x} \quad (1.4)$$

where $\psi_i(\mathbf{x})$ are positive bounded functions ($0 \leq \psi_i(\mathbf{x}) \leq 1$, for all \mathbf{x}). We assume furthermore that each reaction is stopped when and only when one or more of its reactants are missing. This is

formalised by factorising the normalized specific growth rates as :

$$(A.2a) \quad \psi_1(\mathbf{x}) = \phi_1(\mathbf{x})s_1$$

$$(A.2b) \quad \psi_2(\mathbf{x}) = \phi_2(\mathbf{x})s_2$$

Notice that the functions $\phi_i(\mathbf{x})$ are now strictly positive and bounded.

In the anaerobic digestion process, it is in good accordance with the physical reality to assume that the fermentative reaction (1.1a) proceeds at its maximal rate which is much faster than those of the methanogenesis reaction (1.1b). This assumption is mathematically expressed as :

$$(A.3) \quad \mu_1^* \gg \mu_2^*$$

According to assumption (A.3), we define

$$\epsilon = 1/\mu_1^* \ll 1/\mu_2^*$$

as the small scalar parameter representative of the existence of fast and slow reactions in the mechanism of the anaerobic digestion process. Hence, this parameter will be chosen as the singularly perturbed parameter of our singular perturbation design approach.

2 REDUCED ORDER MODEL REQUIREMENTS.

The objective of our reduced order modelling approach is to use assumption (A.3) to transform the state-space model (1.2) into a two-time scale standard form. From the singular perturbation theory, it is indeed well-known that, after a singular perturbation, a model set under this form provides a valid approximation of the initial dynamics. A two-time scale standard form has to satisfy the following conditions :

C.1 A two-time scale standard form model is written in the form :

$$\dot{\mathbf{x}}_s = \mathbf{f}(\mathbf{x}_s, \mathbf{x}_f, \epsilon) \quad (2.1a)$$

$$\epsilon \dot{\mathbf{x}}_f = \mathbf{g}(\mathbf{x}_s, \mathbf{x}_f, \epsilon) \quad (2.1b)$$

with $\dim(\mathbf{x}_s) + \dim(\mathbf{x}_f) = \dim(\mathbf{x})$.

C.2 When ϵ is set to 0, equation (2.1b) admits distinct roots w.r.t. \mathbf{x}_s , i.e

$$0 = \mathbf{g}(\mathbf{x}_s, \mathbf{x}_f, 0) \Leftrightarrow \mathbf{x}_f = \mathbf{h}(\mathbf{x}_s) \quad (2.2)$$

C.3 In the fast time scale $\tau = t/\epsilon$, the deviations from the candidate reduced order model

$$\dot{\mathbf{x}}_s = \mathbf{f}(\mathbf{x}_s, \mathbf{h}(\mathbf{x}_s), 0)$$

decrease asymptotically towards 0.

3 MODEL ORDER REDUCTION IN NATURAL COORDINATES.

It has been shown in Van Breusegem and Bastin (1992) that condition C.2 is generally not satisfied when the singular perturbation design of an admissible reduced order dynamical model (RODM) for reaction systems is attempted in natural coordinates. It is easily checked that this result holds for the anaerobic digestion process considered here.

Let us introduce $\epsilon = 1/\mu_1^*$ in the state space model (1.2):

$$\epsilon \dot{x}_1 = \phi_1(\mathbf{x})x_1s_1 - \epsilon Dx_1 \quad (3.1a)$$

$$\epsilon \dot{s}_1 = -c_{12}\phi_1(\mathbf{x})x_1s_1 - \epsilon Ds_1 + \epsilon Ds_{in} \quad (3.1b)$$

$$\epsilon \dot{s}_2 = c_{14}\phi_1(\mathbf{x})x_1s_1 - \epsilon c_{24}\mu_2^*\phi_2(\mathbf{x})x_2s_2 - \epsilon Ds_2 \quad (3.1c)$$

$$\dot{x}_2 = \mu_2^*\phi_2(\mathbf{x})x_2s_2 - Dx_2 \quad (3.1d)$$

$$\dot{p} = c_{25}\mu_2^*\phi_2(\mathbf{x})x_2s_2 - Dp - Q_p \quad (3.1e)$$

These equations are in the form (2.1a)-(2.1b) so that condition C.1 is satisfied. However, it is easily checked that condition C.2 is *not* satisfied. Indeed, by setting $\epsilon = 0$ in (3.1) (singular perturbation), we obtain the following algebraic equation:

$$\phi_1(\bar{\mathbf{x}})\bar{x}_1\bar{s}_1 = 0 \quad (3.2)$$

where the bar is used to indicate variables that belong to a system with $\epsilon = 0$. Clearly, whatever the form of $\phi_1(\bar{\mathbf{x}})$, this equation cannot be solved uniquely for \bar{x}_1 , \bar{s}_1 and \bar{s}_2 . This means that condition C.2 is violated.

4 MODEL ORDER REDUCTION THROUGH A CHANGE OF COORDINATES.

Let us consider the following change of coordinates

$$\begin{aligned} \xi_1 &= x_1 \\ \xi_2 &= c_{12}x_1 + s_1 \\ \xi_3 &= x_2 \\ \xi_4 &= -c_{14}x_1 + s_2 \\ \xi_5 &= p \end{aligned} \quad (4.1)$$

Applying this change of coordinates to the nonlinear state space model (1.2) and evidencing the small parameter ϵ , we obtain :

$$\epsilon \dot{\xi}_1 = \phi_1(\mathbf{x})\xi_1(\xi_2 - c_{12}\xi_1) - \epsilon D\xi_1 \quad (4.2a)$$

$$\dot{\xi}_2 = -D\xi_2 + Ds_{in} \quad (4.2b)$$

$$\dot{\xi}_3 = \mu_2^*\phi_2(\mathbf{x})\xi_3(\xi_4 + c_{14}\xi_3) - D\xi_3 \quad (4.2c)$$

$$\dot{\xi}_4 = -c_{24}\mu_2^*\phi_2(\mathbf{x})\xi_3(\xi_4 + c_{14}\xi_3) - D\xi_4 \quad (4.2d)$$

$$\dot{\xi}_5 = \mu_2^*\phi_2(\mathbf{x})\xi_3(\xi_4 + c_{14}\xi_3) - D\xi_5 - Q_p \quad (4.2e)$$

These equations are also in the form (2.1a)-(2.1b). It results that only one of the new states has its derivative multiplied by ϵ ($dim(\mathbf{x}_f) = 1$). Setting $\epsilon = 0$ in this equation, we get the following equation :

$$\phi_1(\bar{\mathbf{x}})\bar{\xi}_1(\bar{\xi}_2 - c_{12}\bar{\xi}_1) = 0 \quad (4.3)$$

which has to be solved w.r.t. $\bar{\xi}_1$ in order that condition C.2 be satisfied in the new coordinates. Equation (4.3) admits two roots w.r.t. $\bar{\xi}_1$ ($\phi_1(\bar{\mathbf{x}}) > 0$):

$$\bar{\xi}_1 = 0 \quad (4.4a)$$

$$\bar{\xi}_1 = \bar{\xi}_2/c_{12} \quad (4.4b)$$

By combining (4.4a) or (4.4b) with the equations (4.2b) to (4.2e), it would be therefore admissible to obtain two RODMs provided that condition C.3 be satisfied in both cases.

Comments.

1. The new state variables which have their derivative multiplied by ϵ are referred to as fast variables. The others are called slow variables. The fast variables are also those which have to be expressed in terms of slow variables in order that condition C.2 be satisfied.
2. The change of coordinates (4.1) has been designed according to the procedure given in Van Breusegem and Bastin (1992). The design procedure is mainly related to the structure of the fast reaction scheme. The resulting change of coordinates is then such that the number of algebraic relations is equal to the number of fast variables and condition C.2 will be satisfied if the algebraic relations are solvable w.r.t. the fast variables. The existence of such a solution has also been discussed in Van Breusegem and Bastin (1992) w.r.t the structure of the reaction network.
3. The proposed change of coordinates is generally not unique. There exist therefore a set of equivalent changes of coordinates. However, all these state transformations are ϵ -independent, non singular and such that the slow variable subspace is invariant.

5 ADMISSIBLE REDUCED ORDER DYNAMICAL MODELS.

Once the model has been reduced, we have at our disposal a set of *Candidate* Reduced Order Dynamical Models (CRODMs), expressed in the new coordinates (one for each distinct solution of equation (2.2)).

The admissibility of these reduced models has now to be checked with respect to condition C.3. A way to do is to study the stability properties of the boundary layer system associated to each CRODM. A boundary layer model represents, in the fast time scale driven by $\tau = t/\epsilon$, the deviations from the slow behaviour predicted by a CRODM. Condition C.3. ensures that these deviations decrease asymptotically towards and remain close to zero.

The boundary layers associated to the anaerobic digestion process are of the following form :

$$\frac{d\tilde{\xi}_1}{d\tau} = \phi_1(\mathbf{x})(\tilde{\xi}_1 + \bar{\xi}_1)(\bar{\xi}_2 - c_{12}\tilde{\xi}_1 - c_{12}\bar{\xi}_1) \quad (5.1)$$

where $\tilde{\xi}_1 = \xi_1 - \bar{\xi}_1$ and where $\bar{\xi}_1$ is given either by (4.4a) or by (4.4b).

Let us analyze the both cases :

A) If $\bar{\xi}_1 = 0$, the boundary layer becomes :

$$\frac{d\tilde{\xi}_1}{d\tau} = \phi_1(\mathbf{x})\tilde{\xi}_1(\bar{\xi}_2 - c_{12}\bar{\xi}_1) \quad (5.2)$$

$\phi_1(\mathbf{x})$ is positive. The equilibrium $\tilde{\xi}_1 = 0$ of (5.2) is then asymptotically stable if $\bar{\xi}_2 < 0$. Since $\bar{\xi}_2 = c_{12}\bar{x}_1 + \bar{s}_1$ is necessarily positive, we conclude that the CRODM associated to $\bar{\xi}_1 = 0$ is not admissible.

B) If $\bar{\xi}_1 = c_{12}\bar{\xi}_2$, we obtain :

$$\frac{d\tilde{\xi}_1}{d\tau} = -c_{12}\phi_1(\mathbf{x})\tilde{\xi}_1(\tilde{\xi}_1 + \bar{\xi}_2/c_{12}) \quad (5.3)$$

The equilibrium $\tilde{\xi}_1 = 0$ of (5.3) is asymptotically stable provided that $\bar{x}_1 > 0$. The corresponding CRODM provides therefore a good approximation of the initial dynamics.

6 BACK IN NATURAL COORDINATES.

The last step of the design procedure consists of expressing the admissible CRODMs back in terms of natural coordinates. Since the state transformation is an ϵ -independent diffeomorphism, the corresponding RODMs always exist.

The reduced order dynamical model takes finally the following form :

$$\dot{\bar{s}}_1 = 0 \quad (6.1a)$$

$$\dot{\bar{x}}_1 = -D\bar{x}_1 + \frac{1}{c_{12}}Ds_{in} \quad (6.1b)$$

$$\dot{\bar{x}}_2 = r_2(\bar{\mathbf{x}}) - D\bar{x}_2 \quad (6.1c)$$

$$\dot{\bar{s}}_2 = -c_{24}r_2(\bar{\mathbf{x}}) + \frac{c_{14}}{c_{12}}Ds_{in} - D\bar{s}_2 \quad (6.1d)$$

$$\dot{\bar{p}} = c_{25}r_2(\bar{\mathbf{x}}) - D\bar{p} - Q_p \quad (6.1e)$$

Notice that this reduced order model is not really surprising : since the first reaction is much faster than the second one, the influent substrate is instantaneously transformed into biomass and volatile fatty acids. This shows that the reduced order modelling approach that we propose is also well suited for application to bioprocesses.

REFERENCES

- Andrews, J. and S.P. Graef (1971). Dynamical modeling and simulation of the anaerobic digestion process. *Advances in Chemistry Series 106*. 126-161. Am. Chem. Society .
- Bastin, G. and D. Dochain (1990). *On-line estimation and adaptive control of bioreactors*. Elsevier, Amsterdam.
- Kokotovic, P., H.K. Khalil and J. O'Reilly (1986). *Singular perturbation methods in control: analysis and design*. Academic Press, London.
- Van Breusegem, V. and G. Bastin (1992). A singular perturbation approach to the reduced order modelling of reaction systems. Technical Report 92-14 CESAME, Université Catholique de Louvain, Louvain-la-Neuve, Belgium.