

Reduced order dynamical modelling of reaction systems : a singular perturbation approach

Vincent VAN BREUSEGEM* and Georges BASTIN

Center for Systems Engineering and Applied Mechanics
Université Catholique de Louvain
Bât. Maxwell, Place du Levant, 3, B-1348 Louvain-La-Neuve, Belgium

Abstract. Reaction systems constitute a class of non-linear dynamical systems relevant in many engineering fields such as chemical engineering, biotechnology and ecology. In this paper, we address the problem of the reduction of the order of such systems under the assumption that some reaction rates are much faster than the others. This can be achieved through a change of coordinates which transforms the system in a two-time-scale standard form.

Introduction.

The concept of reaction system refers to a class of non-linear dynamical systems of interest in various fields such as chemical engineering, biotechnology and ecology. The dynamics of reaction systems are commonly described by a set of ordinary differential equations (under the form of a state-space model) arising from mass balance equations. This is called the *natural mass-balance model* (in short : the natural model) in the sequel.

The starting point for building the natural model of a reaction system is the *reaction network* which encodes the reactions that are supposed to occur in the system.

In many applications, the assumption is made that some of the reactions of the network proceed at much faster rate than the others. This often leads to the so-called *quasi-steady-state approximation* which allows a reduction of the dimension of the mathematical model of the system. From an engineering viewpoint, reduced order models may allow to solve problems (e.g. parameter identification, control design, ...) which would be untractable otherwise.

However, the derivation of a reduced order model from the principle of quasi-steady-state approximation is not straightforward. The reason is that the separation into slow and fast reactions does not induce directly a clear separation between small and large time constants in the

natural model. It is therefore necessary, by an appropriate change of coordinates, to transform the natural model into the so-called two-time-scale standard form of the singular perturbation theory ([6]) in order to explicit the model reduction. An additional difficulty lies in the fact that this change of coordinates depends on the structure of the reaction network.

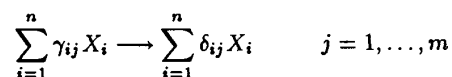
To our knowledge, a general convincing, theoretically funded, method for the derivation of this transformation has never been proposed in the literature. Only empirical and intuitive approaches have been followed to solve the problem in particular cases (e.g. [3],[7],[8]). An early and famous example is the justification of the approximate Michaelis-Menten model for enzymatic catalysis by Briggs and Haldane (1925)([4]).

Our purpose, in this paper, is to propose a general method for the characterization of the two-time-scale properties of reaction systems. Our contribution is twofold.

- 1) To present a systematic method for transforming the natural mass-balance model of reaction systems with slow and fast reactions into the two-time-scale standard form of singular perturbation theory.
- 2) To explicit algebraic conditions on the structure of the underlying reaction network under which the transformation exists.

1. Reaction networks.

The *reaction network* (or the *mechanism*) of a reaction system describes the relations between components and reactions. Let X_1, X_2, \dots, X_n designate the components, numbered in an arbitrary order. The reaction network is basically a set of m reactions of the following form (e.g. [2],[5]).

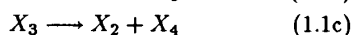
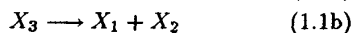


where the nonnegative real numbers $\gamma_{ij} (\geq 0)$ and $\delta_{ij} (\geq 0)$ are the stoichiometric coefficients. They express the nominal quantity of component X_i which is consumed

*Chargé de Recherches F.N.R.S. This paper presents research results of the Belgian Programme on Interuniversity Poles of Attraction initiated by the Belgian State, Prime Minister's Office, Science Policy Programming. The scientific responsibility rests with its authors.

(δ_{ij}) or produced (γ_{ij}) by the j^{th} reaction. Obviously, if a component is not involved in the j^{th} reaction, the corresponding stoichiometric coefficient is zero. The *reactants* of a reaction are the components which appear in the left hand side with non zero stoichiometric coefficients ($\gamma_{ij} > 0$) while the *products* of this reaction are the components which appear in the right hand side also with non zero stoichiometric coefficients ($\delta_{ij} > 0$).

Example. The classical example of the conversion of a substrate X_1 into a product X_4 by a two-step enzymatic reaction ([1]) is described by the following reaction network :



where X_2 is the enzyme and X_3 the so-called substrate-enzyme complex. We thus have $m = 3$ reactions and $n = 4$ components. We note that reactions (1.1a) and (1.1b) can be interpreted as a reversible reaction of the form



Throughout the paper, we shall consider the reaction network (1.1) as a prototype example ■

2. Dynamics of reaction systems.

The dynamics of the components involved in a reaction system are usually expressed through material balances. The quantity of component X_i in the system at time t is denoted $x_i(t)$. The material balance combines two mechanisms : reaction kinetics and transport dynamics.

The reaction kinetics are characterized by reaction rates which express the rates of reactant consumption and product formation in the reactor, according to the reaction network. A reaction rate $r_j(t)$ is associated to each reaction of the network ($j = 1, \dots, m$).

The transport dynamics refer to the supply of reactants to the system from the outside and the removal of components from the system. If the components are withdrawn at a specific volumetric rate D and if $u_i(t)$ denotes the supply feedrate of component i (0 if the component is not a reactant), it is easily shown that the mass balance of the components in the reactor is represented by the following state space model :

$$\frac{d\mathbf{x}}{dt} = C\mathbf{r} - D\mathbf{x} + \mathbf{u} \quad (2.1)$$

where \mathbf{x} is the n -vector of the component concentrations, C is the characteristic matrix of the system, i.e. the $n \times m$ matrix with entries $\delta_{ij} - \gamma_{ij}$, \mathbf{r} is the m -vector of reaction rates and \mathbf{u} is the n -vector of the feedrates of the supplied reactants.

Example (continued). The state space model associated with the reaction network (1.1) is then :

$$\begin{pmatrix} \frac{dx_1}{dt} \\ \frac{dx_2}{dt} \\ \frac{dx_3}{dt} \\ \frac{dx_4}{dt} \end{pmatrix} = \begin{pmatrix} -1 & 1 & 0 \\ -1 & 1 & 1 \\ 1 & -1 & -1 \\ 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} r_1 \\ r_2 \\ r_3 \end{pmatrix} - D \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix} + \begin{pmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \end{pmatrix} \quad (2.2)$$

The only supplied reactants are the substrate X_1 and the enzyme X_2 . We have then $u_3 = 0$ and $u_4 = 0$ ■

3. Modelling of the reaction rates.

3.1. Application of a mass-action principle.

Each reaction rate $r_j(t)$ may be a highly complex non-linear function of the component quantities $x_i(t)$ and of physico-chemical environmental factors (Temperature, pH, ...). In this paper, we assume further that the reaction rates can be expressed under the following form:

$$(A.1) \quad r_j(\mathbf{x}, t) = k_j \varphi_j(\mathbf{x}, t) \prod_{i \sim j} (x_i)^{\gamma_{ij}} \quad \forall j$$

where k_j is the *rate constant* of the reaction and $\prod_{i \sim j}$ means that the product is taken over the components with index i which are reactants of reaction j . Following a mass-action principle, each reaction rate $r_j(\mathbf{x}, t)$ is expressed as being proportional to the product of the reactant concentrations, each raised to a power equal to its stoichiometric coefficient γ_{ij} in the reaction j .

We assume furthermore that $\varphi_j(\mathbf{x}, t)$ is positive whatever the component quantities :

$$(A.2) \quad \varphi_j(\mathbf{x}, t) > 0 \quad \forall j, \forall \mathbf{x}$$

This means that a reaction rate is identically zero only if a reactant is not present in the reactor and never otherwise. If we denote

- $K = \text{diag}\{k_j, j = 1, \dots, m\}$ the $m \times m$ diagonal matrix containing the rate constants

$$\bullet \quad \Phi = \begin{pmatrix} \varphi_1 \prod_{i \sim 1} (x_i)^{\gamma_{i1}} \\ \varphi_2 \prod_{i \sim 2} (x_i)^{\gamma_{i2}} \\ \vdots \\ \varphi_m \prod_{i \sim m} (x_i)^{\gamma_{im}} \end{pmatrix}$$

the mass balance dynamics (2.1) can be rewritten as

$$\frac{d\mathbf{x}}{dt} = C\mathbf{K}\Phi - D\mathbf{x} + \mathbf{u} \quad (3.1)$$

For the sake of simplicity, the dependencies of the variables w.r.t. t and \mathbf{x} will be most often omitted in the sequel of the paper.

3.2. Slow and fast reactions.

Assume that p reactions are fast and $(m-p)$ reactions are slow, irrespective of the component concentrations. This means that p rate constants are much greater than the remaining ones. We furthermore assume that the fast reactions have indices 1 to p while the $(m-p)$ slow reactions have indices $(p+1)$ to m . The assumption is

then technically stated as follows.

(A.3) k_i and k_j have the same order of magnitude if i and $j \in [1, p]$ or if i and $j \in [p + 1, m]$

(A.4) $k_i \gg k_j$ if $i \in [1, p]$ and $j \in [p + 1, m]$

Example (continued). We assume, as usual, that the reversible reaction (1.2) is in equilibrium or otherwise stated that reactions (1.1a) and (1.1b) are much faster than reaction (1.1c) in which X_4 is produced. We have then $k_3 \ll k_1$ and $k_3 \ll k_2$ ■

4. Slow and fast kinetics in the natural model.

Each column of the matrices C, K and Φ^T is related to a given reaction. These matrices can be partitioned into "fast" (with index f) and "slow" (with index s) sub-matrices related to fast and slow reactions, respectively.

- $C = [C_f, C_s]$ where C_f and C_s are $(n \times p)$ and $(n \times (m - p))$ matrices, respectively.
- $K = \begin{bmatrix} K_f & O_{m-p}^p \\ O_p^{m-p} & K_s \end{bmatrix}$ where K_f and K_s are $p \times p$ and $(m - p) \times (m - p)$ diagonal matrices, respectively.
- $\Phi^T = [\Phi_f, \Phi_s]$ where Φ_f and Φ_s are $(p \times 1)$ and $((m - p) \times 1)$ vectors.

Using this partition, the general dynamical model becomes

$$\frac{dx}{dt} = C_f K_f \Phi_f + C_s K_s \Phi_s - D x + u \quad (4.1)$$

where the fast and the slow kinetics are now clearly separated.

Example (continued). Equation (2.2) becomes :

$$\begin{pmatrix} \frac{dx_1}{dt} \\ \frac{dx_2}{dt} \\ \frac{dx_3}{dt} \\ \frac{dx_4}{dt} \end{pmatrix} = \begin{pmatrix} -1 & +1 \\ -1 & +1 \\ +1 & -1 \\ 0 & 0 \end{pmatrix} \begin{pmatrix} k_1 & 0 \\ 0 & k_2 \end{pmatrix} \begin{pmatrix} \varphi_1 x_1 x_2 \\ \varphi_2 x_3 \end{pmatrix} + \begin{pmatrix} 0 \\ +1 \\ -1 \\ +1 \end{pmatrix} k_3 x_3 \varphi_3 - D \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix} + \begin{pmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \end{pmatrix} \quad (4.2)$$

5. Model order reduction.

5.1. Two-time-scale standard form : definition.

Our purpose, in the sequel, will be to transform the model (4.1) into the so-called two-time-scale standard form of singular perturbation theory which authorizes the order reduction. In this section, we give a formal

definition of this concept.

We consider $(v + w)$ -dimensional models which are written in the following state-variable form

$$\frac{dy}{dt} = f(y, z, \epsilon, t) \quad y \in \mathbb{R}^v, y(t_0) = y^0 \quad (5.1)$$

$$\epsilon \frac{dz}{dt} = g(y, z, \epsilon, t) \quad z \in \mathbb{R}^w, z(t_0) = z^0 \quad (5.2)$$

in which the derivatives of some of the states are multiplied by a small positive scalar ϵ . f and g are assumed to be sufficiently many times differentiable functions of their arguments y, z, ϵ . The scalar ϵ represents all the small parameters to be neglected.

The model (5.1)-(5.2) is a step towards *reduced-order modelling*. The order reduction from $(v + w)$ to v is converted into a parameter perturbation (called *singular*). When we set $\epsilon = 0$, the differential equation (5.2) degenerates into the algebraic or transcendental equation

$$0 = g(\bar{y}(t), \bar{z}(t), 0, t) \quad (5.3)$$

where the bar is used to indicate that the variables belong to a system with $\epsilon = 0$.

Definition (Kokotovic *et al.*, 1986). A dynamical model is said to be in a two-time-scale standard form if and only if

- There exists a change of coordinates such that, in the new coordinates, the model can be written in the form (5.1)-(5.2).
- In a domain of interest, the associated algebraic equation (5.3) can explicitly be solved with respect to \bar{z} , that is it has $k \geq 1$ distinct ("isolated") roots :

$$\bar{z}(t) = \bar{\phi}_i(\bar{y}(t), t) \quad i = 1, 2, \dots, k$$

- Define as $\tilde{z} = z - \bar{z}$, the so-called "boundary-layer correction". The equilibrium $\tilde{z}(\tau) = 0$ of the "boundary-layer system"

$$\frac{d\tilde{z}}{d\tau} = g(y^0, \tilde{z} + \bar{z}(t_0), 0, t_0) \quad (5.4)$$

expressed in the fast time scale $\tau = t/\epsilon$ is asymptotically stable uniformly in y^0 and t_0 and $z^0 - \bar{z}(t_0)$ belongs to its domain of attraction. $\bar{z}(t_0)$ is given by

$$\bar{z}(t_0) = \bar{\phi}(y^0, t_0)$$

- The eigenvalues of $\partial g / \partial z$ evaluated, for $\epsilon = 0$, along $\bar{y}(t), \bar{z}(t)$ have strictly negative real parts, i.e. $Re \lambda \{ \partial g / \partial z \} < 0$ ■

Conditions C.1 to C.4 ensure that the *reduced-order* model, sometimes called the *quasi-steady-state* model,

$$\frac{d\bar{y}}{dt} = f(\bar{y}, \bar{\phi}_i(\bar{y}, t), 0, t) \quad \bar{y}(t_0) = y^0 \quad (5.5)$$

is a valid approximation of the dynamical model (5.1)-(5.2) for all $t \in [t_0, T]$. This result is most often referred as to as "Tikhonov's theorem".

5.2. Definition of a small scalar parameter.

We define the mean rate constant of the fast reactions, \bar{k}_f , by

$$\bar{k}_f = 1/p \sum_{i \in [1, p]} k_i \quad (5.6)$$

Each of the large rate constants k_i is related to \bar{k}_f by

$$k_i = \alpha_i \bar{k}_f \quad \forall i \in [1, p] \quad (5.7)$$

where $\alpha_i = k_i/\bar{k}_f$ is a known positive constant. We assume further that these rate constants are expressed in appropriate units such that

$$(A.5) \quad k_i \gg 1 \quad \forall i \in [1, p]$$

It follows that $\bar{k}_f \gg 1$ and we can therefore define the small scalar parameter ϵ as

$$\epsilon = 1/\bar{k}_f \quad (5.8)$$

Remark. Later on, we shall set this coefficient ϵ to zero in various equations to perform model reduction. It must be clearly understood that we shall suppose that $\epsilon \rightarrow 0$ while the α_i 's are kept constant ■

Example (continued). We have $\epsilon = \frac{2}{k_1+k_2}$, $\alpha_1 = \frac{2k_1}{k_1+k_2}$ and $\alpha_2 = \frac{2k_2}{k_1+k_2}$ ■

5.3. Model order reduction in natural coordinates.

We denote n_z and ρ , the number of zero rows and the rank of C_f , respectively. The zero rows are related to those of the components which are not involved at all in the p fast reactions. These components form a n_z -vector denoted \mathbf{x}_z , while we denote \mathbf{x}_f the $(n - n_z)$ -vector of the remaining components which are certainly involved in the fast reactions and possibly in the slow ones (\mathbf{u}_z and \mathbf{u}_f will denote the associated partition of \mathbf{u}). According to the partition of \mathbf{x} , C_f and C_s are partitioned as follows

$$C_f = \begin{pmatrix} C_{ff} \\ O_{n_z}^p \end{pmatrix}, \quad C_s = \begin{pmatrix} C_{sf} \\ C_{ss} \end{pmatrix}$$

where C_{ff}, C_{sf} , have $(n - n_z)$ rows and p , $(m - p)$ and q columns, respectively. C_{ss} has n_z rows and $(m - p)$ columns. Using this partition, the natural model (4.1) is splitted into the following two equations :

$$\frac{d\mathbf{x}_f}{dt} = C_{ff}K_f\Phi_f + C_{sf}K_s\Phi_s - D\mathbf{x}_f + \mathbf{u}_f \quad (5.9)$$

$$\frac{d\mathbf{x}_z}{dt} = C_{ss}K_s\Phi_s - D\mathbf{x}_z + \mathbf{u}_z \quad (5.10)$$

Equation (5.10) gives the dynamics of the components which are involved only in the $(m - p)$ slow reactions while equation (5.9) gives the dynamics of the remaining components which are involved in the fast reactions but also in the slow ones. Using (5.7) and (5.8), equation (5.9) is easily rewritten as

$$\epsilon \frac{d\mathbf{x}_f}{dt} = C_{ff}A\Phi_f + \epsilon C_{sf}K_s\Phi_s - \epsilon D\mathbf{x}_f + \epsilon \mathbf{u}_f \quad (5.11)$$

where $A = \text{diag}\{\alpha_i, \forall i \in [1, p]\}$ is a matrix of positive constants.

Equations (5.10) and (5.11) clearly show that the natural model satisfies condition C.1. By setting $\epsilon = 0$ in equation (5.11), we obtain the following algebraic equation

$$C_{ff}A\bar{\Phi}_f = O_{n-n_z}^1 \quad (5.12)$$

where $O_{n-n_z}^1$ denotes the $n - n_z \times 1$ null matrix. This equation should be solved with respect to the fast variables $\bar{\Phi}_f$, i.e. the components which are involved in the fast reactions.

We have the following result which shows that condition C.2. is generally not satisfied in natural coordinates.

Lemma 5. 1 *A necessary condition for the existence of distinct roots for equation (5.12) is that $n - n_z = \rho$*

Proof. See ([9]) ■

Example (continued). From equation (4.2), it is easily checked that $n - n_z = 3$ and $\rho = 1$. It follows that condition C.2. is not satisfied in natural coordinates. ■

5.4. Model order reduction through a change of coordinates.

In this section, we shall show how to define a change of coordinates which lead to the two-time-scale standard form. Each column of C_f is related to a fast reaction. We separate further the set of fast reactions into *dependent* and *independent* fast reactions.

The i^{th} reaction is independent of the others if $c_j^i \notin \text{span}[c_j^j, j \neq i]$ where c_j^i denotes the i^{th} column of C_f or dependent of the others if $c_j^i \in \text{span}[c_j^j, j \neq i]$. For the sake of simplicity, let us assume that the p_1 fast reactions indexed 1 to p_1 are dependent while the $p_2 = p - p_1$ remaining ones (indexed $p_1 + 1$ to p) are independent. Hence, C_f can be partitioned as $C_f = (C_{f_1} \ C_{f_2})$ where C_{f_1} and C_{f_2} are related to dependent and independent fast reactions, respectively. C_{f_1} and C_{f_2} are of rank ρ_1 and ρ_2 , respectively, with $\rho_1 + \rho_2 = \rho$.

Example (continued). The fast reactions (1.1a) and (1.1b) are dependent since we have $p_1 = p = 2$, $p_2 = 0$, $\rho_1 = \rho = 1$ and $\rho_2 = 0$. ■

Let C_f^* denote a matrix obtained by permuting the rows of C_f and such that its ρ first rows form a submatrix of rank ρ . C_f^* is partitioned as follows

$$C_f^* = \begin{pmatrix} C_{f_{11}} & C_{f_{12}} \\ C_{f_{21}} & C_{f_{22}} \\ C_{f_{31}} & C_{f_{32}} \end{pmatrix} \quad (5.13)$$

where $C_{f_{11}}$ is $(\rho_1 \times \rho_1)$, $C_{f_{12}}$ is $(\rho_1 \times \rho_2)$, $C_{f_{21}}$ is $(\rho_2 \times \rho_1)$, $C_{f_{22}}$ is $(\rho_2 \times \rho_2)$, $C_{f_{31}}$ is $((n-\rho) \times \rho_1)$ and $C_{f_{32}}$ is $((n-\rho) \times \rho_2)$. Similarly to C_f^* , C_s^* , u^* and x^* are obtained by permuting the rows of C_s , u and x , respectively. Moreover, C_s^* is partitioned accordingly to the partition of C_f^*

This matrix which has the following property :

Property 5. 2

There exists (at least) one n -dimensional non singular matrix T such that

$$TC_f^* = \begin{pmatrix} C_{f_{11}} & C_{f_{12}} \\ O_{\rho_1}^{\rho_2} & -C_{f_{21}}C_{f_{11}}^+C_{f_{12}} + C_{f_{22}} \\ O_{\rho_1}^{n-\rho} & O_{\rho_2}^{n-\rho} \end{pmatrix}$$

where $C_{f_{11}}^+$ is a right pseudoinverse of $C_{f_{11}}$.

Proof. See ([9]). ■

We define now the following change of coordinates

$$\xi = T x^* \quad (5.14)$$

where T which verifies Property 5.2, is given by

$$T = \begin{pmatrix} I_{\rho_1} & O_{\rho_1}^{\rho_2} & O_{\rho_1}^{n-\rho} \\ T_{21} & I_{\rho_2} & O_{\rho_2}^{n-\rho} \\ T_{31} & T_{32} & I_{n-\rho} \end{pmatrix} \quad (5.15)$$

I_{ρ_1} , I_{ρ_2} and $I_{n-\rho}$ are unit matrices of dimension ρ_1 , ρ_2 and $n-\rho$, respectively and T_{21} , T_{31} and T_{32} are defined as follows (see [9]):

$$T_{21} = -C_{f_{21}}C_{f_{11}}^+ \quad (5.16)$$

$$T_{32} = -(C_{f_{31}}C_{f_{11}}^+C_{f_{12}} - C_{f_{32}})(C_{f_{21}}C_{f_{11}}^+C_{f_{12}} - C_{f_{22}})^{-1} \quad (5.17)$$

$$T_{31} = (-C_{f_{31}} - T_{32}C_{f_{21}})C_{f_{11}}^+ \quad (5.18)$$

This state transformation is a diffeomorphism since T is non singular. The new coordinates are obviously linear combinations of the natural coordinates and conversely. The vector of the new state variables can be partitioned as follows :

$$\xi = (\xi_{f_1}, \xi_{f_2}, \xi_s)^T \quad (5.19)$$

where ξ_{f_1} , ξ_{f_2} and ξ_s are ρ_1 , ρ_2 and $(n-\rho)$ vectors, respectively.

We apply now the change of coordinates (5.14) and the partition (5.19) of the new state to the general dynamical

model (4.1). Using the property (5.2) and evidencing the small parameter ϵ , we obtain :

$$\epsilon \frac{d\xi_{f_1}}{dt} = C_{f_{11}}A_1\bar{\Phi}_{f_1} + C_{f_{12}}A_2\bar{\Phi}_{f_2} + \epsilon C_{s_1}K_s\bar{\Phi}_s - \epsilon D\xi_{f_1} + \epsilon u_{f_1}^* \quad (5.20)$$

$$\epsilon \frac{d\xi_{f_2}}{dt} = (T_{21}C_{f_{12}} + C_{f_{22}})A_2\bar{\Phi}_{f_2} + \epsilon(T_{21}C_{s_1} + C_{s_2})K_s\bar{\Phi}_s - \epsilon D\xi_{f_2} + \epsilon(T_{21}u_{f_1}^* + u_{f_2}^*) \quad (5.21)$$

$$\frac{d\xi_s}{dt} = (T_{31}C_{s_1} + T_{32}C_{s_2} + C_{s_3})K_s\bar{\Phi}_s - D\xi_s + T_{31}u_{f_1}^* + T_{32}u_{f_2}^* + u_s^* \quad (5.22)$$

where A_1 and A_2 are diagonal matrices of positive constants. $u_{f_1}^*$, $u_{f_2}^*$ and u_s^* are obtained by partitioning u^* similarly to ξ .

The general dynamical model, expressed in the new coordinates by the equations (5.20) to (5.22) clearly satisfies condition C.1. of the two-time-scale form definition. The change of coordinates (5.14) displays therefore fast (ξ_{f_1}, ξ_{f_2}) and slow (ξ_s) variables. Recall that the corresponding diffeomorphism was mainly defined by the choice of a full rank submatrix in C_f . This choice is generally not unique and there can exist therefore several changes of coordinates which lead to equations (5.20), (5.21) and (5.22) (see [9] for further details).

By setting $\epsilon = 0$ in equations (5.20) and (5.21), we obtain the following matrix relations :

$$C_{f_{11}}A_1\bar{\Phi}_{f_1} + C_{f_{12}}A_2\bar{\Phi}_{f_2} = O_1^{\rho_1} \quad (5.23)$$

$$(T_{21}C_{f_{12}} + C_{f_{22}})A_2\bar{\Phi}_{f_2} = O_1^{\rho_2} \quad (5.24)$$

which are made up of ρ nonlinear equations with exactly ρ unknowns : the fast variables $\bar{\xi}_{f_1}$ and $\bar{\xi}_{f_2}$. This system is therefore much better conditioned than the similar one obtained in natural coordinates.

With respect to the structure of this system, the admissible solutions to (5.23)-(5.24) generally depend on the kinetics of the fast reactions. That is most often the case when some reactions of the fast reaction subnetwork are dependent. That is not the case when the fast reaction subnetwork is made up of independent reactions only, as stated in the following lemma.

Lemma 5. 3 *If the fast reaction subnetwork is made up of independent reactions only and if an admissible solution exists, then this solution does not depend on the kinetics of the fast reactions, that is on the structure of the functions φ_j .*

Proof. See ([9]) ■

Example (continued). A possible choice for C_f^* is simply $C_f^* = C_f$. Since all the fast reactions are dependent, it follows that C_f^* reduces to

$$C_f^* = \begin{pmatrix} C_{f_{11}} \\ C_{f_{31}} \end{pmatrix} \text{ with } C_{f_{11}} = \begin{pmatrix} -1 \\ +1 \end{pmatrix}^T \text{ and } C_{f_{31}} = \begin{pmatrix} -1 & +1 \\ 0 & 0 \end{pmatrix}$$

From (5.15), (5.17) and (5.18), we obtain the new coordinates ξ

$$\begin{pmatrix} \xi_1 \\ \xi_2 \\ \xi_3 \\ \xi_4 \end{pmatrix} = \begin{pmatrix} 1 & 0 & 0 & 0 \\ -1 & 1 & 0 & 0 \\ 1 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \end{pmatrix}$$

The general dynamical model becomes:

$$\epsilon \frac{d\xi_1}{dt} = -\alpha_1 \varphi_1 \xi_1 (\xi_1 + \xi_2) + \alpha_2 \varphi_2 (\xi_3 - \xi_1) - \epsilon D \xi_1 + \epsilon u_1 \quad (5.25)$$

$$\frac{d\xi_2}{dt} = k_3 \varphi_3 (\xi_3 - \xi_1) - D \xi_2 + u_2 - u_1 \quad (5.26)$$

$$\frac{d\xi_3}{dt} = -k_3 \varphi_3 (\xi_3 - \xi_1) - D \xi_3 + u_3 + u_1 \quad (5.27)$$

$$\frac{d\xi_4}{dt} = k_3 \varphi_3 (\xi_3 - \xi_1) - D \xi_4 + u_4 \quad (5.28)$$

Setting ϵ to zero in (5.25), we get

$$-\alpha_1 \bar{\varphi}_1 \bar{\xi}_1 (\bar{\xi}_1 + \bar{\xi}_2) + \alpha_2 \bar{\varphi}_2 (\bar{\xi}_3 - \bar{\xi}_1) = 0 \quad (5.29)$$

This equation should be solved wrt the fast variable $\bar{\xi}_1$. For the sake of simplicity, we assume from now that $\bar{\varphi}_1$ and $\bar{\varphi}_2$ are constant. Then, equation (5.29) has two roots wrt to $\bar{\xi}_1$. Hence, there are two candidate reduced order dynamical models. However, one can quite easily check that conditions C.3 and C.4 are only satisfied for one of them :

$$\bar{\xi}_1 = -\frac{1}{2} \left(\bar{\xi}_2 + \frac{\alpha_2 \bar{\varphi}_2}{\alpha_1 \bar{\varphi}_1} \right) - \frac{1}{2} \sqrt{\left(\bar{\xi}_2 + \frac{\alpha_2 \bar{\varphi}_2}{\alpha_1 \bar{\varphi}_1} \right)^2 + 4 \frac{\alpha_2 \bar{\varphi}_2 \bar{\xi}_3}{\alpha_1 \bar{\varphi}_1}} \quad (5.30)$$

Substituting $\bar{\xi}_1$ by (5.30) in equations (5.26), (5.27) and (5.28), we can obtain a reduced order model in new coordinates. In natural coordinates, we finally get

$$\begin{aligned} \frac{d\bar{x}_2}{dt} &= \frac{(\alpha_1 \bar{\varphi}_1 \bar{x}_2)^2 (k_3 \bar{\varphi}_3 \bar{x}_3 - D(-\frac{\alpha_2 \bar{\varphi}_2 \bar{x}_3}{\alpha_1 \bar{\varphi}_1 \bar{x}_2} + \bar{x}_2)) + u_2 - u_1}{(\alpha_1 \bar{\varphi}_1 \bar{x}_2)^2 + \alpha_1 \bar{\varphi}_1 + \alpha_2 \bar{\varphi}_2} \\ &+ \frac{\alpha_2 \bar{\varphi}_2 (-D(\bar{x}_2 + \bar{x}_3) + u_2 + u_3)}{(\alpha_1 \bar{\varphi}_1 \bar{x}_2)^2 + \alpha_1 \bar{\varphi}_1 + \alpha_2 \bar{\varphi}_2} \\ \frac{d\bar{x}_3}{dt} &= \frac{(\alpha_1 \bar{\varphi}_1 \bar{x}_2)^2 (-k_3 \bar{\varphi}_3 \bar{x}_3 - D(\frac{\alpha_2 \bar{\varphi}_2 \bar{x}_3}{\alpha_1 \bar{\varphi}_1 \bar{x}_2} + \bar{x}_3)) + u_3 + u_1}{(\alpha_1 \bar{\varphi}_1 \bar{x}_2)^2 + \alpha_1 \bar{\varphi}_1 + \alpha_2 \bar{\varphi}_2} \\ &+ \frac{\alpha_1 \bar{\varphi}_1 (-D(\bar{x}_2 + \bar{x}_3) + u_2 + u_3)}{(\alpha_1 \bar{\varphi}_1 \bar{x}_2)^2 + \alpha_1 \bar{\varphi}_1 + \alpha_2 \bar{\varphi}_2} \\ \frac{d\bar{x}_4}{dt} &= k_3 \bar{\varphi}_3 \bar{x}_3 - D \bar{x}_4 + u_4 \end{aligned} \quad (5.31)$$

We have seen that in natural coordinates, there is generally no direct partition between fast and slow variables. It is therefore possible to write down equivalent reduced

order models by substituting \bar{x}_2 or \bar{x}_3 (which are also involved in the fast reactions) in place of \bar{x}_1 as it has been done to obtain the system (5.31) ■

Conclusion.

In this paper, we have addressed the problem of the reduction of order of natural mass-balance models which commonly describe the dynamics of reaction systems. This reduction subordinated to the presence of slow and fast reactions. We have shown that, in natural coordinates, a convenient partition of the state leading to a two-time-scale standard form which allows the order reduction by using the singular perturbation technique, does not generally exist. Moreover, we have proposed a convenient change of coordinates which is better suited to perform the order reduction. The theory has been illustrated by a prototype example.

References.

- [1] Bailey J.E. and D.F. Ollis. **Biochemical engineering fundamentals**, Mc Graw-Hill chemical engineering series (1977).
- [2] Bastin G. and D. Dochain. **On-line estimation and adaptive control of bioreactors**, Elsevier, Amsterdam (1990).
- [3] Bowen J.R., A. Acrivos and A.K. Oppenheim. Singular perturbation refinement to quasi-steady-state approximation in chemical kinetics. *Chemical Engineering Science*, **18**, 177-181 (1963).
- [4] Briggs G.E. and J.B.S. Haldane. A note on the kinetics of enzyme reaction. *Biochem. J.*, **19**, 338-341 (1925).
- [5] Feinberg, M., 1987, Chemical reaction network structure and the stability of complex isothermal reactors - I. the deficiency zero and the deficiency one theorems. *Chem. Engng Sci.*, **42**-10, 2229-2268 .
- [6] Kokotovic P.V., H.K. Khalil and J. O'Reilly. **Singular perturbation methods in control: analysis and design**, Academic Press, London (1986).
- [7] Lakin W.D. and P. Van Den Driessche. Time scales in population biology. *SIAM J. Appl. Math.*, **32**-3, 694-705 (1977).
- [8] Schauer M. and R. Heinrich. Quasi-steady-state approximation in the mathematical modelling of biochemical networks. *Mathematical Biosciences*, **65**, 155-170 (1983).
- [9] Van Breusegem V. and G. Bastin. Reduced order mathematical modelling of reaction systems : a singular perturbation approach (full version). Technical report (submitted for publication), Laboratoire d'Automatique, Dynamique et Analyse des Systèmes, University of Louvain (1991).