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## Model reduction by extended quasi-steady-state approximation

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**Abstract.** We extend the quasi-steady-state approximation (QSSA) with respect to the class of differential systems as well as with respect to the order of approximation. We illustrate the first extension by an example which cannot be treated in the frame of the classical approach. As an application of the second extension we prove that the trimolecular autocatalator can be approximated by a fast bimolecular reaction system. Finally we describe a class of singularly perturbed systems for which a higher order QSSA can easily be obtained.

### 1. Introduction

Mathematical modeling of processes with different time scales leads in general to singularly perturbed systems (SPS) of the form

$$\begin{aligned}\dot{x} &= f(x, y, t, \varepsilon), \\ \varepsilon \dot{y} &= g(x, y) + \varepsilon \tilde{g}(x, y, t, \varepsilon),\end{aligned}\tag{1}$$

where  $x \in \mathbb{R}^m$ ,  $y \in \mathbb{R}^n$ ,  $0 < \varepsilon \ll 1$ ,  $f, \tilde{g}$  are bounded as  $\varepsilon$  tends to zero. The first equation is called the slow subsystem and the second represents the fast one. A variety of perturbation methods have been developed to investigate singularly perturbed systems: matched asymptotic expansions [15], WKB-methods [16], multiple scale methods [11], boundary layer functions [24], averaging [2]. Renormalization group theory is a new unifying method for global asymptotic analysis [4].

Geometric singular perturbation theory is another approach for the qualitative analysis of singularly perturbed systems [7], especially it provides a mathematical justification for the reduction of system (1). It is based on the existence of an invariant manifold  $\mathcal{M}$  of the form

$$y = \psi(x, t, \varepsilon) = \psi_0(x) + \varepsilon \psi_1(x, t) + \mathcal{O}(\varepsilon^2)\tag{2}$$

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for systems of type (1) and reduces (1) to the regularly perturbed system (RPS) of lower order

$$\dot{x} = f(x, \psi(x, t, \varepsilon), t, \varepsilon) . \quad (3)$$

A necessary condition for the existence of this so-called slow manifold (2) is that the associated system

$$\dot{y} = g(x, y) \quad (4)$$

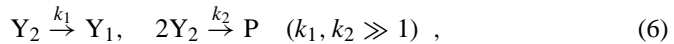
to (1) possesses a family  $y = \psi_0(x)$  of hyperbolic steady states where  $x$  has to be considered as a parameter. If this condition is fulfilled, system (1) is called a regular singularly perturbed system (RSPS). If furthermore the hyperbolic fixed points are asymptotically stable and the considered initial values lie in their domain of attraction, then the long-time dynamics of system (1) can be approximated by the regularly perturbed system (3) [7,23]. Under the (simple) quasi-steady-state approximation (QSSA) we understand the approximation of the dynamics of (1) by the system

$$\dot{x} = f(x, \psi_0(x), t, 0) , \quad (5)$$

where  $y = \psi_0(x)$  is the family of asymptotically stable steady states of (4). The higher order QSSA takes into account also higher order terms of (2).

The QSSA is sometimes called pseudo-steady-state hypothesis, Bodenstein's method or method of adiabatic elimination. It plays a prominent role in modeling biological [9], chemical [6,19,22] (especially in atmospheric chemistry [10] and combustion chemistry [17]) and physical [8,21] systems. The QSSA is the key assumption in deducing the velocity equations in enzyme kinetics [12,20] and can be used in the homogeneous [3] as well as in the nonhomogeneous case [14].

There are, however, systems containing fast and slow processes whose associated system (4) has no hyperbolic fixed point. As an example we consider an arbitrary chemical reaction system with two very fast reactions



where P is assumed to have constant concentration. Under the assumption of spatial homogeneity and mass-action kinetics the reaction system is described by the differential equations

$$\begin{aligned} \dot{x} &= f(x, y_1, y_2) , \\ \varepsilon \dot{y}_1 &= y_2 + \varepsilon \tilde{g}_1(x, y_1, y_2) , \\ \varepsilon \dot{y}_2 &= -y_2 - ay_2^2 + \varepsilon \tilde{g}_2(x, y_1, y_2) , \end{aligned} \quad (7)$$

where  $\varepsilon = 1/k_1 \ll 1$ ,  $a = 2k_2/k_1 = \mathcal{O}(1)$  and  $f, \tilde{g}_1, \tilde{g}_2$  are smooth functions. The corresponding associated system

$$\begin{aligned} \dot{y}_1 &= y_2 , \\ \dot{y}_2 &= -y_2 - ay_2^2 \end{aligned}$$

has a continuum of steady states described by  $y_2 = 0$ . Systems with such a property are called singular singularly perturbed systems (SSPS). The condition described above for the applicability of the QSSA is not fulfilled for SSPS.

The goal of this note is to extend the class of differential equations to which the QSSA can be applied. In section 2 we prove that the existence of some conservation property (linear or nonlinear first integrals) of the corresponding associated system allows the transformation of a SSPS into a RSPS generically. Moreover, in section 3 we demonstrate that under some circumstances it is necessary to apply higher order QSSA. As an interesting example we treat the simplified ‘Brusselator’ model which shows that trimolecular reactions can be approximated by fast bimolecular ones. In section 4 we characterize a class of singularly perturbed systems where higher order QSSA can simply be determined only by means of the fast subsystem.

**2. Extension of the QSSA with respect to the class of SPS**

We consider the class of singularly perturbed systems of the form (1) under the assumptions

- (A<sub>1</sub>).  $f, g, \tilde{g}$  are continuous and locally lipschitzian in  $x \in R^m$  and  $y \in R^n$ .
- (A<sub>2</sub>). The associated system (4) to (1) has a first integral  $\kappa : R^m \times R^n \rightarrow R^k, k \leq n$ , such that there exists a splitting  $y = (y_1, y_2)$  with  $\dim y_1 = k$  and the property that the derivative  $\kappa_{y_1}$  is invertible and  $\|\kappa_{y_1}^{-1}\|$  is uniformly bounded on its domain.

**Theorem.** *Assume hypotheses (A<sub>1</sub>), (A<sub>2</sub>) are satisfied. Then the SPS (1) can be transformed into a SPS whose number of fast variables is  $n - k$ .*

*Proof.* Using the splitting  $y = (y_1, y_2)$  we rewrite (1) as

$$\begin{aligned} \dot{x} &= f(x, y_1, y_2, t, \varepsilon) , \\ \varepsilon \dot{y}_1 &= g_1(x, y_1, y_2) + \varepsilon \tilde{g}_1(x, y_1, y_2, t, \varepsilon) , \\ \varepsilon \dot{y}_2 &= g_2(x, y_1, y_2) + \varepsilon \tilde{g}_2(x, y_1, y_2, t, \varepsilon) . \end{aligned} \tag{8}$$

Since  $\kappa$  is a first integral of (4) it satisfies the relation

$$\kappa_y(x, y) g(x, y) = 0 . \tag{9}$$

Thus, we have by (1)

$$\begin{aligned} \varepsilon \dot{\kappa} &= \kappa_x \varepsilon \dot{x} + \kappa_y \varepsilon \dot{y} = \varepsilon \kappa_x f(x, y, t, \varepsilon) + \kappa_y g(x, y) + \varepsilon \kappa_y \tilde{g}(x, y, t, \varepsilon) \\ &= \varepsilon \left( \kappa_x f(x, y, t, \varepsilon) + \kappa_y \tilde{g}(x, y, t, \varepsilon) \right) . \end{aligned} \tag{10}$$

Now we introduce new coordinates by  $x = x, y_2 = y_2, \sigma = \kappa(x, y_1, y_2)$ . From hypothesis (A<sub>2</sub>) it follows that  $\sigma = \kappa(x, y_1, y_2)$  can be solved globally for  $y_1$ ,

$$y_1 = w(x, \sigma, y_2) . \tag{11}$$

Thus, we have

$$\begin{aligned} \varepsilon \dot{\sigma} &= \varepsilon \left( \kappa_x(w(x, \sigma, y_2), y_2) f(x, w(x, \sigma, y_2), y_2, t, \varepsilon) \right. \\ &\quad \left. + \kappa_y(w(x, \sigma, y_2), y_2) \tilde{g}(x, w(x, \sigma, y_2), y_2, t, \varepsilon) \right) . \end{aligned}$$

Hence, system (8) is equivalent to

$$\begin{aligned} \dot{x} &= f(x, w(x, \sigma, y_2), y_2, t, \varepsilon) , \\ \dot{\sigma} &= \kappa_x(w(x, \sigma, y_2), y_2)f(x, w(x, \sigma, y_2), y_2, t, \varepsilon) \\ &\quad + \kappa_y(w(x, \sigma, y_2), y_2)\tilde{g}(x, w(x, \sigma, y_2), y_2, t, \varepsilon) , \\ \varepsilon\dot{y}_2 &= g_2(x, w(x, \sigma, y_2), y_2) + \varepsilon\tilde{g}_2(x, w(x, \sigma, y_2), y_2, t, \varepsilon) \end{aligned} \tag{12}$$

having  $n - k$  fast variables.

**Remark 1.** If the associated system to (12)  $\dot{y}_2 = g_2$  has a hyperbolic fixed point, then system (12) represents a RSPS to which the QSSA can be applied if this fixed point is stable.

**Remark 2.** The first integral of the associated system (4) can be found as a solution of the system of linear first-order PDE's (9). If it has no solution, then the associated system (4) does not possess a first integral.

**Remark 3.** If system (4) has a first integral, it always has a continuum of steady states. If we differentiate relation (9) with respect to  $y$  on the solution set of  $g(x, y) = 0$  we get the relation  $\kappa_y g_y = 0$ . Since  $\kappa_y$  is not identically zero it follows that  $g_y$  is singular on  $g(x, y) = 0$ .

**Remark 4.** In modeling biological, chemical and biochemical systems, linear transformations have been used to transform special SSPS into RSPS [9]. However, in many cases, as e.g. for the given example (6,7), no linear transformation can transform the system into a RSPS.

Now we illustrate our approach by considering system (7). The corresponding PDE (9) reads in our case

$$\kappa_{y_1}y_2 + \kappa_{y_2}(-y_2 - ay_2^2) = 0 , \tag{13}$$

which has the solution

$$\kappa(y_1, y_2) = y_1 + a^{-1} \ln(1 + ay_2) . \tag{14}$$

Because  $\kappa_{y_1} \equiv 1$ , we can use  $\sigma = \kappa(y_1, y_2)$  as **nonlinear** coordinate transformation in the whole phase plane. Substituting

$$y_1 = \sigma - a^{-1} \ln(1 + ay_2) \tag{15}$$

into (7) yields

$$\begin{aligned} \dot{x} &= \hat{f}(x, \sigma, y_2) , \\ \dot{\sigma} &= \hat{g}_1(x, \sigma, y_2) + (1 + ay_2)^{-1} \hat{g}_2(x, \sigma, y_2) , \\ \varepsilon\dot{y}_2 &= -y_2 - ay_2^2 + \varepsilon\hat{g}_2(x, \sigma, y_2) . \end{aligned} \tag{16}$$

This is a RSPS whose associated system  $\dot{y}_2 = -y_2 - ay_2^2$  has the hyperbolic stable fixed point  $y_2 = 0$  (we are only interested in non-negative steady states). After applying the (simple) QSSA we obtain the reduced system

$$\begin{aligned} \dot{x} &= \tilde{f}(x, \sigma, 0) , \\ \dot{\sigma} &= \hat{g}_1(x, \sigma, 0) + \hat{g}_2(x, \sigma, 0) , \end{aligned} \tag{17}$$

which has the same long-time dynamics as the original system (7) for  $0 < \varepsilon \ll 1$ .

### 3. Higher order QSSA

As mentioned above, the simple QSSA consists in using the zeroth order approximation of the invariant manifold  $\mathcal{M}$  in (2) to study the corresponding system (1). Sometimes this approach is not sufficient to get the desired information about the dynamics of (1). In these cases it is necessary to use higher order QSSA that is, instead of  $y = \psi_0(x)$  we use the  $n$ -th order approximation

$$y = \tilde{\psi}_n(x, t, \varepsilon) = \psi_0(x) + \varepsilon\psi_1(x, t) + \dots + \varepsilon^n\psi_n(x, t) \quad , \quad (18)$$

where the functions  $\psi_i$  are the coefficients in the representation (2) of the invariant manifold  $\mathcal{M}$ . To compute the functions  $\psi_i$  we substitute (18) into (1) and exploit the invariance property of  $\mathcal{M}$ . By this way we get

$$\begin{aligned} \varepsilon \dot{y} &= g(x, \tilde{\psi}_n(x, t, \varepsilon)) + \varepsilon \tilde{g}(x, \tilde{\psi}_n(x, t, \varepsilon), t, \varepsilon) + \mathcal{O}(\varepsilon^{n+1}) \\ &= \varepsilon \left( \frac{\partial \psi_0}{\partial x} + \varepsilon \frac{\partial \psi_1}{\partial x} + \dots + \varepsilon^{n-1} \frac{\partial \psi_{n-1}}{\partial x} \right) f(x, \tilde{\psi}_n(x, t, \varepsilon), t, \varepsilon) \\ &\quad + \varepsilon^2 \left( \frac{\partial \psi_1}{\partial t} + \dots + \varepsilon^{n-2} \frac{\partial \psi_{n-1}}{\partial t} \right) + \mathcal{O}(\varepsilon^{n+1}) \quad . \end{aligned} \quad (19)$$

By comparing the coefficients multiplied by  $\varepsilon$  we get for  $\psi_1$  the relation

$$g_y(x, \psi_0(x))\psi_1(x, t) + \tilde{g}(x, \psi_0(x), t, 0) = \frac{\partial \psi_0}{\partial x} f(x, \psi_0(x), t, 0) \quad . \quad (20)$$

Thus, we have

$$\psi_1(x, t) = g_y^{-1}(x, \psi_0(x)) \left( \frac{\partial \psi_0}{\partial x} f(x, \psi_0(x), t, 0) - \tilde{g}(x, \psi_0(x), t, 0) \right) \quad . \quad (21)$$

To demonstrate the importance of the higher order QSSA we consider the trimolecular autocatalator which is a simplified ‘Brusselator’.

From the very beginning of modeling small mass-action kinetic systems, it has been supposed that two-component bimolecular systems cannot have limit cycles (The final proof has been given in [18].). Hence, for the sake of simplicity, two-component systems with trimolecular reactions, such as the famous ‘Brusselator’, has been studied. There is a vast literature devoted to the ‘Brusselator’ (cf. [13]). Nevertheless, such models often have been criticized because of their unrealistic trimolecularity. Thus, attempts have been undertaken to explain the trimolecular reaction as an approximation by bimolecular ones (cf.[5] and citations therein). In what follows we consider the well-known trimolecular autocatalator (also known as Higgins-Selkov-, Schnakenberg- or Gray-Scott-system [1]) which contains the same trimolecular reaction as the ‘Brusselator’:



where  $S$  and  $P$  denote substances with constant concentrations and  $k$  is a positive parameter. Under the assumptions of spatial homogeneity and mass-action kinetics the dynamic behavior is described by the differential equations

$$\begin{aligned}\dot{x} &= 1 - kxy^2, \\ \dot{y} &= kxy^2 - y.\end{aligned}\tag{23}$$

Here we have scaled out the reaction rates for the (constant) influx reaction for  $X$  and the efflux reaction for  $Y$ . We shall prove that the trimolecular autocatalator (22) can be understood as an approximation of the bimolecular reaction system



where  $k_1, k_{-1}, k_2$  are positive parameters,  $k_{-1}$  is assumed to be large. Under the same assumptions as for system (22) and by introducing the small parameter  $\varepsilon = 1/k_{-1}$ , the corresponding mathematical model reads

$$\begin{aligned}\dot{x} &= 1 - k_2xz, \\ \varepsilon\dot{y} &= -2\varepsilon k_1y^2 + 2z + \varepsilon(k_2xz - y), \\ \varepsilon\dot{z} &= \varepsilon k_1y^2 - z.\end{aligned}\tag{25}$$

The QSSA cannot be applied to system (25), because the associated system has no isolated steady state ((25) is a SSPS). However, with the coordinate transformation

$$\sigma = y + 2z,\tag{26}$$

system (25) can be transformed into a RSPS

$$\begin{aligned}\dot{x} &= 1 - k_2xz, \\ \dot{\sigma} &= k_2xz - (\sigma - 2z), \\ \varepsilon\dot{z} &= \varepsilon k_1(\sigma - 2z)^2 - z.\end{aligned}\tag{27}$$

The associated system  $\dot{z} = -z$  has the hyperbolic stable fixed point  $z = 0$ . Note that in contrast to the example (6,7) which requires the nonlinear coordinate transformation (15), here a linear transformation is suited to transform the SSPS (25) into the RSPS (27). However, the simple QSSA does not yield our desired result, as the zeroth order approximation is still too rough. We instead use the general asymptotic approximation of the slow manifold (2), which can be written in our case as

$$z = \psi(x, \sigma, \varepsilon) = \psi_0(x, \sigma) + \varepsilon\psi_1(x, \sigma) + \mathcal{O}(\varepsilon^2).\tag{28}$$

Inserting this Ansatz into (27) we obtain by comparing the corresponding coefficients  $\psi_0 = 0$ ,  $\psi_1 = k_1\sigma^2$  such that we have

$$z = k_1\sigma^2\varepsilon + \mathcal{O}(\varepsilon^2).\tag{29}$$

Inserting this into the first two equations of (27) we get the regularly perturbed system

$$\begin{aligned} \dot{x} &= 1 - \varepsilon k_1 k_2 x \sigma^2 + \mathcal{O}(\varepsilon^2) , \\ \dot{\sigma} &= \varepsilon k_1 k_2 x \sigma^2 - \sigma + 2\varepsilon k_1 \sigma^2 + \mathcal{O}(\varepsilon^2) , \end{aligned} \tag{30}$$

with the perturbation parameter  $\varepsilon = 1/k_{-1}$ . In order to get system (23) describing the trimolecular reaction (22) as  $\varepsilon$  tends to zero we have to fulfill the relations

$$\lim_{\varepsilon \rightarrow 0} \varepsilon k_1 k_2 = k, \quad \lim_{\varepsilon \rightarrow 0} \varepsilon k_1 = 0 . \tag{31}$$

(It follows from (29)  $\lim_{\varepsilon \rightarrow 0} z = 0$  and with (26)  $\lim_{\varepsilon \rightarrow 0} \sigma = y$ .) The last relation in (31) excludes  $k_1 = \mathcal{O}(k_{-1})$ , but we note that  $k_1$  must not be bounded as  $\varepsilon$  tends to zero,  $k_1$  can growth with order  $\mathcal{O}(k_{-1}^{1-\delta})$  where  $0 < \delta < 1$ . The given derivation is both, rigorous and simple compared with the approach in [5].

#### 4. Special case for the higher order QSSA

The computation of the coefficients for the higher order QSSA requires some effort. From the relation (19) which determines the coefficients  $\psi_i$  for the higher order QSSA we can derive special cases where the computation of these coefficients is based only on the fast subsystem. Concerning the first order QSSA we get the following result.

**Lemma.** *Consider the SPS (1). Suppose hypothesis (A<sub>1</sub>) is valid, and  $g$  is continuously differentiable with respect to  $y$ . Under the conditions that  $g(x, y) = 0$  has a solution  $y = \varphi_0$  where  $\varphi_0$  does not depend on  $x$  and that  $g_y(x, \varphi_0)$  is invertible for all  $x$  there is an invariant manifold  $\mathcal{M}$  to (1) which can be represented by*

$$y = \psi_1(t, x, \varepsilon) = \varphi_0 - \varepsilon g_y^{-1}(x, \varphi_0) \tilde{g}(x, \varphi_0, t, 0) + \mathcal{O}(\varepsilon^2) .$$

*Proof.* See Eq. (21).

As an example we consider the model of H. Haken [8]

$$\begin{aligned} \dot{x} &= -\sigma x - axy , \\ \varepsilon \dot{y} &= -y + \varepsilon bx^2 , \end{aligned}$$

which can be interpreted as a mass-action kinetic system with a very fast reaction  $Y \rightarrow P$ . It is easy to verify that this model fits into the scope of our Lemma. We get as the first-order QSSA  $y = \varepsilon bx^2$ , such that the system on the slow manifold  $\mathcal{M}$  can be approximated by  $\dot{x} = -\sigma x - \varepsilon abx^3$ .

#### 5. Summary

We have shown under which conditions the QSSA can be extended to SSPS. The corresponding coordinate transformation can be found as a solution of the system of linear first-order PDE's (9). We have presented a case study when the simple QSSA has to be replaced by a higher order QSSA. As an interesting side product we have got that trimolecular reaction systems can be approximated by fast bimolecular systems. Finally we have selected a class of SPS where the first-order QSSA

can be determined only by means of the fast subsystem. A known model due to H. Haken fits into that class.

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