

Model complexity reduction of chemical reaction networks using mixed-integer quadratic programming[☆]

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Abstract

The model complexity reduction problem of large chemical reaction networks under isobaric and isothermal conditions is considered. With a given detailed kinetic mechanism and measured data of the key species over a finite time horizon, the complexity reduction is formulated in the form of a mixed-integer quadratic optimization problem where the objective function is derived from the parametric sensitivity matrix. The proposed method sequentially eliminates reactions from the mechanism and simultaneously tunes the remaining parameters until the pre-specified tolerance limit in the species concentration space is reached. The computational efficiency and numerical stability of the optimization are improved by a pre-reduction step followed by suitable scaling and initial conditioning of the Hessian involved. The proposed complexity reduction method is illustrated using three well-known case studies taken from the reaction kinetics literature.

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1. Introduction

The mathematical models of reaction kinetic systems are most often too large and detailed for dynamic analysis or parameter estimation purposes as they are usually constructed based on detailed kinetic studies. Moreover, advanced control design often requires the significant simplification of dynamical models to be able to compute the feedback action in real time [1, 2]. There are a number of important and extensively studied areas where there are detailed models of chemically reacting systems available. These include biochemical systems, such as signal transduction pathway modeling and reacting flow or catalytic reaction systems. These models are used for both model analysis (stability analysis and the investigation of strange nonlinear dynamic properties, such as oscillations or chaotic behavior), and for dynamic predictions (simulation). Because of the huge number of species and/or chemical reactions present in the detailed reaction kinetic mechanism of these systems, the need has arisen for developing simplified or reduced mechanisms that can accurately describe the dynamics of the system under some restricted circumstances (e.g. in isobaric or isothermal conditions).

The complexity of reaction kinetic models is determined by the number of species (reacting chemical components), and by the number of chemical reactions that are taking place among them. The complexity of the functional form of the reaction rate expression plays an important role, too. Then the aim of complexity reduction is to obtain a reduced or simplified mechanism of the system such that the reduced model-predicted dynamic behavior of at least the key important species is close to the original one. In addition, the physical meaning of the variables in the simplified model should be preferably conserved, and the characteristic model structure should also remain the same.

There are three main categories of commonly applied approaches for obtaining simplified kinetic representations: (i) the use of engineering model simplification transformations, such as quasi-steady state or quasi-equilibrium assumptions, (ii) the use of general nonlinear model reduction techniques applied to reaction kinetic models, (iii) the use of optimization methods for reducing the number of reacting species and reactions.

Engineering model reduction transformations. This is a simple and traditional method [3] that uses the quasi-steady state, the quasi-equilibrium and the variable lumping transformation [4] for obtaining a reduced model. Unfortunately, the reaction kinetic form of the model cannot be always preserved, and the simplified model may have rather different qualitative dynamic properties than the original one; for example may lose its structural stability property.

General model reduction techniques. If one considers the concentrations of the key important species as output variables, then the reaction kinetic model can be written in the form of a nonlinear input-affine state-space model, for which recent extensions to balanced truncation are available for the reduction [5]. This approach, however, applies a nonlinear coordinate transformation and thus both the physical meaning of the variables and the characteristic kinetic structure may be lost.

An alternative way of general model reduction techniques without the need for nonlinear coordinate transformation is the singular perturbation method. Anderson et al. [6] propose a model reduction algorithm that can be used to uncover the structure of the underlying biological system while avoiding any coordinate transformations and ensuring that the state vector in the reduced model is a strict subset of the one in the full model. The approach is similar to singular perturbation but does not try to identify fast or slow states; in fact, it collapses (lumps) states based on the worst-case error.

The related method of invariant grids [7] can also be used for obtaining reduced models of reaction kinetic systems that are based on the construction of low-dimensional manifolds of reduced description for equations of chemical kinetics from the standpoint of invariant manifolds.

Optimization-based kinetic model reduction. The general formulation of a complexity reduction problem for reaction kinetic systems leads to a mixed integer nonlinear program (MILNP) problem, see e.g. [8], that presents computational complexity challenges in realistic problem sizes. Similarly to the case of the related parameter estimation problem, one has to use efficient and reliable global optimization algorithms (see e.g. in [9]) to solve the general model reduction problem. Therefore, the specialties of the system and/or the complexity reduction problem can be used to develop efficient solution heuristics. For example, there are combined approaches (see e.g. [10]) that

apply engineering model reduction (variable lumping) in order to improve the computational efficiency of the MINLP solution. The inherent relationship between model reduction and model parameter estimation has also been realized recently (see e.g. [11]), where the need to re-estimate the parameters of the reduced model has arisen.

The *model reduction methods applied to biochemical reaction systems* exhibit a few important specialties compared to the general case [12]. These reactions take place in a liquid phase under almost constant temperature; therefore isobaric and isothermal conditions are assumed, which imply constant reaction rate coefficients. At the same time, one should assume complex nonlinear dependence of the reaction rate on the species concentration; therefore the mass action law [13] is not necessarily applicable here. In the general case when both the structure and the parameters of the reaction kinetic model are to be determined from a detailed mechanism and measured data, an MINLP [14] can be formulated that is difficult to solve in the general case.

The need for kinetic model reduction is traditionally strong in the area of *reacting flow systems (e.g. flames and combustion)*, where the detailed chemical mechanisms contain hundreds to thousands of species and reactions. An MINLP is obtained if one has a detailed reaction mechanism obeying the mass action law on a finite number of control points, and the task is to determine an approximate simpler kinetic scheme under isobaric and adiabatic circumstances that ensure that the production rates are within pre-specified limits from the production rates of the full mechanism [15].

Model reduction of reaction kinetic networks. The simplest models within the class of reaction kinetic systems form the subclass of reaction kinetic networks that obey the mass action law [16, 17, 18]. This sub-class is also called chemical reaction networks (CRNs). Here one assumes constant reaction rate coefficients and polynomial dependence of the reaction rate on the species concentrations that corresponds to closed, isothermal and isobaric conditions. The applicability of this model class is surprisingly wide: besides the description of purely chemical mechanisms, CRNs can be effectively used to model processes of living (i.e. cell) environments [19], compartmental models [20] or general nonnegative systems with possible application domains completely outside of (bio)chemistry [21, 16].

In complex chemically reacting systems there are usually multiple pathways that contribute to the dynamic evolution of a particular species concen-

tration. Then the model reduction task involves a step to identify the dominant pathways, which can be performed by using a combination of graph-theoretical and optimization techniques [22].

An early approach to obtain CRNs with reduced complexity was based on principal component analysis of the parametric sensitivity matrix of the detailed kinetic model [23]. An improved version using also concentration sensitivities was developed for the case of gas phase reactions [24]. Finally, a sophisticated combined method for constructing the minimal suitable mechanism based on combined species and reaction selective inclusion and elimination has been proposed recently [25].

A systematic model reduction method that combines the sensitivity and principal component analysis methods with variable lumping is proposed in [26]. A simultaneous adjustment of the structure of CRN and its parameters such that the qualitative dynamical properties of the system are preserved during the reduction is the basis of the complexity reduction method presented in [27] in the application area of biochemical networks.

Motivation and aim. The above literature review clearly shows that there are numerous methods available to reduce the complexity of CRNs that all use the specialties of the problem and the model to propose a feasible solution to the inherently computationally challenging problem. However, there are certain important features of the model reduction task that received little attention but they significantly influence the mathematical problem to be solved and the properties of the solutions. Firstly, measured data are usually not available about all of the species but only about a small subset of them (the key species). Secondly, the reaction kinetic parameters, most notably the reaction rate coefficients can only be determined with an approximately 10 % of accuracy even in the best cases, and the estimated value is strongly model structure dependent. This implies that the value of these parameters is not precise, therefore the re-estimation of them can significantly improve the fit between the output of the original detailed and the reduced model.

Therefore, the overall aim of our work was to propose a robust, numerically stable yet feasible method for reducing the complexity, i.e. the number of reactions of a CRN, that is also able to re-estimate the reaction rate coefficients and produce a sub-set of the original detailed reaction kinetic scheme as a result, but with suitably adjusted coefficients.

Instead of the general MINLP formulation of the problem, we construct a convex mixed integer quadratic problem (MIQP) formulation for which

efficient solvers exist. The effect of the problem and model parameters, as well as the tuning parameters of the proposed algorithm is also investigated on the solution procedure and on the solution properties.

2. Problem formulation

2.1. The initial value problem corresponding to chemical reaction network dynamics

In this paper, we consider deterministic chemical reaction networks (CRNs) with mass action kinetics assuming constant temperature and perfect mixing of the materials [28, 13]. From a mathematical point of view, the species concentrations under these assumptions can be described by initial value problems of parametric ordinary differential equations (ODEs)

$$\begin{aligned}\dot{x}(t) &= f(x(t), k), & t \in [t_0, t_f], & \quad (1) \\ x(t_0) &= x_0, & & \quad (2)\end{aligned}$$

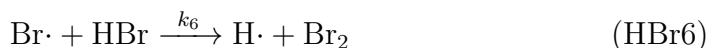
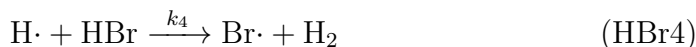
where the right-hand side function $f : \mathbb{R}^n \times \mathbb{R}^m \rightarrow \mathbb{R}^n$ in Eq. (1) can be easily constructed from the list and parameters of chemical reactions in the CRN (see the following subsection).

First, we explain the variables occurring in Eqs. (1) and (2): t is the independent time variable; t_0 and t_f are the initial and final times, respectively; $x(t) \in \mathbb{R}^n$ is the concentration vector of the n chemical species X_1, \dots, X_n at time t , where x_i corresponds to the concentration of the species X_i , $i = 1, \dots, n$; $k \in \mathbb{R}^m$ is the vector of kinetic parameters corresponding to m reactions; $x_0 = (x_{0,1}, \dots, x_{0,n})^T \in \mathbb{R}^n$ in Eq. (2) is the vector of the corresponding initial values; and $f(x(t), k)$ in the right hand-side of Eq. (1) collects the change rates of the species' concentrations.

Note that $x(t)$ implicitly depends on the initial values x_0 and the kinetic parameters k . To stress these dependencies we may also use the notation $x(t, k, x_0)$ or only $x(t, k)$, especially when we are interested in the parametric sensitivities $\partial x(t, k) / \partial k$.

2.2. Representation of chemical reaction network by chemical reactions

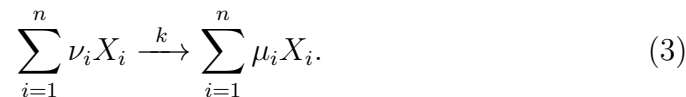
As an introductory example we consider the hydrogen-bromine chemical reaction network according to Snow [29]. Its reactions take place in the gas phase at a temperature of about 1000 K and a pressure of about 1 bar. The chemical reactions are listed in Eqs. (HBr1)–(HBr6).



In Eqs. (HBr1)–(HBr6), the involved chemical species comprise Br_2 (bromine molecule), $\text{Br}\cdot$ (bromine radical), H_2 (hydrogen molecule), $\text{H}\cdot$ (hydrogen radical), HBr (hydrogen bromide) and a so-called *third body*, also referred to as *inert component*¹, arbitrarily denoted by the symbol M . The third body M is a kind of catalyst which does not react with the other chemical species. Its only relevance is to adsorb or transfer kinetic energy from the reactant species, e.g. to split a bromine molecule into its corresponding radicals (Eq. (HBr1)). In the paper of Snow [29], nitrogen (N_2) was the third body, but any other inert gas would do as well.

2.3. Constructing the ODE from chemical reactions

Ordinary differential equations can be easily constructed from the CRN’s chemical reactions. Starting from the chemical reactions, we first define the reaction rates as follows. For a general equation with n species X_1, \dots, X_n and associated stoichiometric coefficients² ν_1, \dots, ν_n (reactants) and μ_1, \dots, μ_n (products):



¹Usually, chemists use the term “third body” while chemical engineers employ the term “inert component”. Since the third body/inert component is only used for the transfer of kinetic energy, it can be either a pure chemical component or a mixture of components.

²Stoichiometric coefficients denote the multiplicity of chemical species in the reactants and products of a chemical reaction. For example, within the reactants of the reaction equation (HBr2), $\text{Br}\cdot$ and M have the stoichiometric coefficients 2 and 1, respectively.

Table 1: Reaction rates and rate coefficients of Hydrogen-Bromine reaction

Reaction	Reaction rate	Rate coefficient
(HBr1)	$r_1 = k_1 [\text{Br}_2] [\text{M}]$	$k_1 = 6.26 \cdot 10^5 \frac{\text{cm}^3}{\text{mol s}}$
(HBr2)	$r_2 = k_2 [\text{Br}\cdot]^2 [\text{M}]$	$k_2 = 1.56 \cdot 10^{15} \frac{\text{cm}^6}{\text{mol}^2 \text{s}}$
(HBr3)	$r_3 = k_3 [\text{Br}\cdot] [\text{H}_2]$	$k_3 = 2.61 \cdot 10^9 \frac{\text{cm}^3}{\text{mol s}}$
(HBr4)	$r_4 = k_4 [\text{H}\cdot] [\text{HBr}]$	$k_4 = 1.39 \cdot 10^{13} \frac{\text{cm}^3}{\text{mol s}}$
(HBr5)	$r_5 = k_5 [\text{H}\cdot] [\text{Br}_2]$	$k_5 = 1.17 \cdot 10^{14} \frac{\text{cm}^3}{\text{mol s}}$
(HBr6)	$r_6 = k_6 [\text{Br}\cdot] [\text{HBr}]$	$k_6 = 1.31 \cdot 10^4 \frac{\text{cm}^3}{\text{mol s}}$

Assuming that the system obeys the mass action law, the corresponding reaction rate r is given by

$$r = k \cdot \prod_{i=1}^n [X_i]^{\nu_i},$$

where $[X_i]$ denotes the concentration of species X_i , and $k > 0$ is the reaction rate coefficient. It is important to note that reaction rates depend on the reactants but not on the products.

For example, the reaction rate of the chemical equation (HBr1) is given by

$$r_1 = k_1 [\text{Br}_2] [\text{M}].$$

Here, k_1 is the reaction rate coefficient while $[\text{Br}_2]$ and $[\text{M}]$ are the concentrations of Br_2 and M , respectively³. Obviously, Br_2 and M constitute the reactants of the chemical equation (HBr1). It is important to note that the expressions for the reaction rates are linear in the reaction rate coefficients. We show all reaction rates of the chemical reaction network (HBr1)–(HBr6) in Table 1.

To derive the differential equations describing the time evolution of chemical species concentrations, we will apply the classical description using the stoichiometric matrix [7]. According to this notation, considering n species

³In chemistry, concentrations are commonly denoted by enclosing rectangular brackets.

and k reactions, the species concentrations can be described as

$$\frac{d[X]}{dt} = N \cdot r, \quad (4)$$

where $[X] \in \mathbb{R}^n$ is the species concentration vector, $r \in \mathbb{R}^k$ is the vector of reaction rates and $N \in \mathbb{R}^{n \times k}$ is the stoichiometric matrix, the columns and rows of which correspond to reactions and species, respectively. N_{ij} is a real (most often integer) number denoting how many atoms/molecules of species X_i are produced or consumed in the j th reaction (where a positive value corresponds to overall production and a negative value to overall consumption). For example, in reaction (HBr2), the participating species are Br·, M, and Br₂. One molecule of Br₂ is produced, two Br· radicals are consumed, while formally one catalyst molecule M is both consumed and produced (therefore, the overall production/consumption corresponding to M is zero). Thus, using $X = (\text{Br}_2, \text{Br}\cdot, \text{H}_2, \text{H}\cdot, \text{HBr}, \text{M})^T$, the second column of the stoichiometric matrix for the reactions (HBr1)–(HBr6) is given by $(1, -2, 0, 0, 0, 0)^T$.

Applying the above notation and rules, the stoichiometric matrix for the reaction system (HBr1)–(HBr6) can be written as

$$N = \begin{pmatrix} -1 & 1 & 0 & 0 & -1 & 1 \\ 2 & -2 & -1 & 1 & 1 & -1 \\ 0 & 0 & -1 & 1 & 0 & 0 \\ 0 & 0 & 1 & -1 & -1 & 1 \\ 0 & 0 & 1 & -1 & 1 & -1 \\ 0 & 0 & 0 & 0 & 0 & 0 \end{pmatrix}. \quad (5)$$

Using N and the reaction rates in Table 1, we can easily write the ordinary

differential equations of the hydrogen-bromine CRN shown in Eqs. (6)–(11).

$$\frac{d[\text{Br}_2]}{dt} = -r_1 + r_2 - r_5 + r_6 \quad (6)$$

$$\frac{d[\text{Br}\cdot]}{dt} = 2r_1 - 2r_2 - r_3 + r_4 + r_5 - r_6 \quad (7)$$

$$\frac{d[\text{H}_2]}{dt} = -r_3 + r_4 \quad (8)$$

$$\frac{d[\text{H}\cdot]}{dt} = r_3 - r_4 - r_5 + r_6 \quad (9)$$

$$\frac{d[\text{HBr}]}{dt} = r_3 - r_4 + r_5 - r_6 \quad (10)$$

$$\frac{d[\text{M}]}{dt} = 0 \quad (11)$$

2.4. Initial Values

After the construction of the ODEs, we only have to specify the initial values at the initial time t_0 . For the hydrogen-bromine CRN we take the values of Turányi et al. [23]:

$$\begin{aligned} [\text{Br}_2](t_0) &= 1 \cdot 10^{-8} \frac{\text{mol}}{\text{cm}^3}, \\ [\text{Br}\cdot](t_0) &= 0, \\ [\text{H}_2](t_0) &= 1 \cdot 10^{-8} \frac{\text{mol}}{\text{cm}^3}, \\ [\text{H}\cdot](t_0) &= 0, \\ [\text{HBr}](t_0) &= 0, \\ [\text{M}](t_0) &= 1 \cdot 10^{-5} \frac{\text{mol}}{\text{cm}^3}. \end{aligned} \quad (12)$$

2.5. Notational conventions

In the general case, if X_1, \dots, X_n are the chemical species,

$$(x_1, \dots, x_n)^T = ([X_1], \dots, [X_n])^T \quad (13)$$

is the *state vector*. The reaction rate coefficients k_1, \dots, k_m of a CRN with m reactions are collected in the *parameter vector*

$$k = (k_1, \dots, k_m)^T \in \mathbb{R}^m. \quad (14)$$

Then, the notation is consistent with Eqs. (1) and (2). In particular, the hydrogen-bromine system is

$$\dot{x}_1 = -k_1 x_1 x_6 + k_2 x_2^2 x_6 - k_5 x_1 x_4 + k_6 x_2 x_5, \quad (15)$$

$$\dot{x}_2 = 2k_1 x_1 x_6 - 2k_2 x_2^2 x_6 - k_3 x_2 x_3 + k_4 x_4 x_5 + k_5 x_1 x_4 - k_6 x_2 x_5, \quad (16)$$

$$\dot{x}_3 = -k_3 x_2 x_3 + k_4 x_4 x_5, \quad (17)$$

$$\dot{x}_4 = k_3 x_2 x_3 - k_4 x_4 x_5 - k_5 x_1 x_4 + k_6 x_2 x_5, \quad (18)$$

$$\dot{x}_5 = k_3 x_2 x_3 - k_4 x_4 x_5 + k_5 x_1 x_4 - k_6 x_2 x_5, \quad (19)$$

$$\dot{x}_6 = 0, \quad (20)$$

which is obviously linear in the reaction rate coefficients $k_i, i = 1, 2, \dots, 6$.

3. Model Reduction

3.1. Objective

Suppose that in a chemical reaction network we are only interested in variables corresponding to a few species. The concentrations of these species can be relevant because for example they are the measurable system output. Thus we want to reduce the network such that their concentrations remain unchanged. These species are named *important* in the following and we collect the indices of the associated variables into the set

$$\mathcal{I} := \{i_1, i_2, \dots, i_{n_{\mathcal{I}}}\}, \quad (21)$$

where $i_j \in \{1, 2, \dots, n\}$, $j = 1, 2, \dots, n_{\mathcal{I}}$ and $n_{\mathcal{I}}$ is the number of important species.

Additionally, we only care about the trajectories of the important species within a limited time horizon $[t_0, t_f]$. Then, the objective of the model reduction is to

1. reduce the number of reactions, i.e. set the corresponding rate coefficient k_i to zero, while keeping the concentration functions of the important species essentially unchanged on the time horizon $[t_0, t_f]$,
2. simultaneously adjust the remaining rate coefficients to improve the fit of the important species.

3.2. The reduced model and its error

Due to the similar structure of the CRNs, where the reduced model is structurally a subset of the original one, the reduced model is totally specified by the reduced rate coefficient vector $\tilde{k} \in \mathbb{R}^m$. Reaction l is not present in the reduced CRN, iff $\tilde{k}_l = 0$ holds. The states $\tilde{x}(t)$ of the reduced model drop simply out as the solution of the initial value problem

$$\dot{\tilde{x}} = f(\tilde{x}, \tilde{k}), \quad \tilde{x}(t_0) = x_0, \quad (22)$$

where f and x_0 are the same as in Eqs. (1) and (2).

Of course, the *error* of the reduced model needs to be measured. This measure has to rely on the states $\tilde{x}(t)$ of the reduced model as well as on the states $x(t)$ of the original model, and it can be quantified by means of some functional $\Phi(\tilde{x}, x)$. We choose the least-square functional

$$\Phi(\tilde{x}, x) := \sum_{l=0}^N \sum_{i \in \mathcal{I}} w_{il}^2 (\tilde{x}_i(t_l) - x_i(t_l))^2, \quad (23)$$

where $t_0 < t_1 < \dots < t_N$ are selected time points, and w_{il} , $i \in \mathcal{I}$, $0 \leq l \leq N$ are some weights, e.g. to take into account the magnitude of $x_i(t_l)$. Actually, the same objective function for model reduction was used by Androulakis [8].

3.3. A straightforward MINLP

Note that $\tilde{x}(\cdot)$ and $x(\cdot)$ in Eq. (23) are totally determined by means of the corresponding parameter vectors \tilde{k} and k , respectively. Hence, the nonlinear function

$$\phi(\tilde{k}, k) := \Phi(\tilde{x}(\cdot, \tilde{k}), x(\cdot, k)), \quad (24)$$

is well defined since, for each $t \in [t_0, t_f]$, $\tilde{x}(t, \tilde{k})$ and $x(t, k)$ are uniquely determined by means of the corresponding initial value problems in Eqs. (1), (2) and Eq. (22).

As already mentioned in the preceding subsection, the number of non-zeros in \tilde{k} equals the number of reactions present in the reduced model. Let NNZ denote the function which returns the number of non-zeros of a real vector, i.e.

$$\text{NNZ} : \mathbb{R}^m \rightarrow \{0, 1, \dots, m\}, \quad \text{NNZ}(v) = \#\{i : v_i \neq 0\} \quad (v \in \mathbb{R}^m). \quad (25)$$

Obviously, the first objective of the model reduction is to find a reduced parameter vector $\tilde{k} \in \mathbb{R}^m$ which minimizes $\text{NNZ}(\tilde{k})$, such that the model

error $\phi(\tilde{k}, k)$ is small, say $\phi(\tilde{k}, k) < \delta$, where $\delta > 0$ is the user-specified error tolerance.

In terms of mathematical optimization, according to Androulakis [8], we want to solve the mixed-integer nonlinear program (MINLP)

$$\min_{\tilde{k} \in [\underline{k}, \bar{k}]} \text{NNZ}(\tilde{k}) \quad (26)$$

$$\text{s.t. } \phi(\tilde{k}, k) \leq \delta. \quad (27)$$

where k is fixed to the original values, and $\underline{k}, \bar{k} \in \mathbb{R}^m$ ($0 \leq \underline{k} \leq \bar{k}$) are the lower and upper bounds on \tilde{k} . The simplicity of the formulation is appealing. We have a simple linear objective function in Eq. (26) subject to a single nonlinear and nonconvex constraint in Eq. (27). In general, to find the global optimum of this MINLP, a global numerical MINLP solver has to be applied for the solution. In this context, the key problem is the evaluation of the constraint in Eq. (27) which requires the integration of the initial value problem (22). This may be very time consuming, especially when the MINLP solver additionally requires first- and second derivatives.

The situation would be much better, if we could approximate the non-convex MINLP by an optimization problem class, which can be solved more easily. This is exactly what we will do in the following: we will approximate the MINLP by a finite sequence of maximal m convex mixed-integer quadratic programs, which can be solved much faster.

At first, we consider the parametric MINLP

$$\left\{ \begin{array}{l} \min_{\tilde{k} \in [\underline{k}, \bar{k}]} \phi(\tilde{k}, k) \\ \text{s.t. } \text{NNZ}(\tilde{k}) \leq \tilde{m}. \end{array} \right\}, \quad (\text{MINLP}(\tilde{m}))$$

which depends on the integer parameter $\tilde{m} \in \{1, 2, \dots, m\}$. We realize that by solving $\text{MINLP}(\tilde{m})$ for $\tilde{m} = 1, 2, \dots, m$, the associated objective function value is monotonically decreasing. Let $\tilde{k}(\tilde{m})$ denote the optimal solution of $\text{MINLP}(\tilde{m})$. Then, for the smallest \tilde{m} which satisfies $\phi(\tilde{k}(\tilde{m}), k) \leq \delta$, the corresponding solution $\tilde{k}(\tilde{m})$ is identical to the solution of MINLP (26), (27).

The benefit of the reformulation is that, if we could approximate the non-convex objective function $\phi(\tilde{k}, k)$ in $\text{MINLP}(\tilde{m})$ by a convex quadratic objective function, we would significantly reduce the computational complexity.

Obviously, the key contributions of non-convexity in Eq. (23) are due to terms of type

$$(\tilde{x}_i(t_l) - x_i(t_l))^2. \quad (28)$$

Since $\tilde{x}_i(t_0) = x_i(t_0) = x_0$ and Eqs. (1) and (22), we have the identity

$$(\tilde{x}_i(t_l) - x_i(t_l))^2 = \left(\int_{t_0}^{t_l} [f_i(\tilde{x}(t), \tilde{k}) - f_i(x(t), k)] dt \right)^2. \quad (29)$$

We consider only the integrand of (29) and add the zero term $(-f_i(x(t), \tilde{k}) + f_i(x(t), \tilde{k}))$ to obtain

$$f_i(\tilde{x}(t), \tilde{k}) - f_i(x(t), k) = \underbrace{f_i(\tilde{x}(t), \tilde{k}) - f_i(x(t), \tilde{k})}_{=: A_i(\tilde{x}(t), x(t), \tilde{k})} + \underbrace{f_i(x(t), \tilde{k}) - f_i(x(t), k)}_{=: B_i(x(t), \tilde{k}, k)}. \quad (30)$$

Note that, since $f(x, k)$ in Eq. (1) depends only linearly on k , we have

$$f_i(x(t), k) = \sum_{j=1}^m b_{ij}(x(t)) k_j, \quad (31)$$

where

$$b_{ij}(x) := \frac{\partial f_i}{\partial k_j}(x, k) \quad (32)$$

is independent of k . Hence we have the identity

$$B_i(x(t), \tilde{k}, k) = \sum_{j=1}^m b_{ij}(x(t)) (\tilde{k}_j - k_j), \quad (33)$$

which is linear in k . We emphasize that Eq. (33) is an exact identity. On the other hand, if we assume that \tilde{x} is close to $x(t)$, we have by means of the continuity of f that

$$A_i(\tilde{x}(t), x(t), \tilde{k}) \approx 0. \quad (34)$$

Surely we may assume that $\tilde{x}_i(t) \approx x_i(i)$ for $i \in \mathcal{I}$, i.e. the important species are not affected too much by the reduction. However, there is in general no justification why for non-important species ($i \notin \mathcal{I}$) $\tilde{x}_i(t)$ should be close to $x_i(t)$. Then, equation (34) is no longer valid and the reduction algorithm may fail. One solution of the preceding problem is to enlarge the set \mathcal{I} by the indices of species which are indeed not important, but indispensable for

a correct simulation of the important species. Turányi [30] calls these kind of species *necessary species* and further proposes an algorithm to identify them.

Loosely speaking, these necessary species have a strong influence on the term $A_i(\tilde{x}(t), x(t), \tilde{k})$ in Eq. (30). However, we found a way to deal implicitly with necessary species without applying Turányi's algorithm. If a species x_l is necessary for some index $l \notin \mathcal{I}$, then in general for some $i \in \mathcal{I}$ the absolute value of the sensitivity

$$\frac{\partial f_i(x(t), k)}{\partial x_l} \quad (35)$$

is relatively high. The corresponding change of f_i might be approximated to first-order by

$$\frac{\partial f_i(x(t), k)}{\partial x_l} (\tilde{x}_l(t) - x_l(t)).$$

But $(\tilde{x}_l(t) - x_l(t))$ may be approximated by first-order Taylor series expansion:

$$(\tilde{x}_l(t) - x_l(t)) \approx \frac{\partial x_l(t)}{\partial k} (\tilde{k} - k).$$

On the other hand, if a species $x_l(t)$ is not necessary at all, then the absolute of the corresponding sensitivities in Eq. (35) is relatively small for all $i \in \mathcal{I}$. This motivates us to approximate $A_i(\tilde{x}(t), x(t), \tilde{k})$ in Eq. (30) by the linearization in $(\tilde{k} - k)$

$$A_i(\tilde{x}(t), x(t), \tilde{k}) \approx \sum_{j=1}^m \underbrace{\frac{\partial f_i(x(t), k)}{\partial x} \frac{\partial x(t)}{\partial k_j}}_{=: \tilde{a}_{ij}(t)} (\tilde{k}_j - k_j). \quad (36)$$

We are aware, that this is an heuristic approach and some problems may arise when $(\tilde{k} - k)$ is so large that the linearization is not valid anymore. However, since we are always able to compare the reduced model with the original one, we may ignore this possible complications. Finally we collect the two alternative approximations in Eqs. (34) and (36) and approximate the term $A_i(\tilde{x}(t), x(t), \tilde{k})$ in Eq. (30) by

$$G_i(\tilde{x}(t), x(t), \tilde{k}) \approx \sum_{j=1}^m \sigma \tilde{a}_{ij}(t) (\tilde{k}_j - k_j), \quad \sigma \in \{0, 1\}, \quad (37)$$

to yield

$$f_i(\tilde{x}(t), \tilde{k}) - f_i(x(t), k) \approx \sum_{j=1}^m \underbrace{(\sigma \tilde{a}_{ij}(t) + b_{ij}(t))}_{=: \tilde{g}_{ij}(t)} (\tilde{k}_j - k_j), \quad (38)$$

where $\sigma = 0$ means that we are relying on Eq. (34), while $\sigma = 1$ refers to Eq. (36). In general, both choices of σ are possible and may be used for the subsequently introduced reduction method. However, if the partial Jacobian $(\partial f_i / \partial k_j)$, $i \in \mathcal{I}$, $j \in \{1, \dots, m\}$, is very sparse, the choice $\sigma = 0$ may produce only poor approximations of $(f_i(\tilde{x}(t), \tilde{k}) - f_i(x(t), k))$, so that then $\sigma = 1$ should be chosen.

Inserting Eqs. (29) and (38) into Eq. (23) finally yields the approximate objective functional

$$\begin{aligned} \tilde{\phi}(\tilde{k}, k) &:= \sum_{l=1}^N \sum_{i \in \mathcal{I}} w_{il}^2 \left(\int_{t_0}^{t_l} \sum_{j=1}^m \tilde{g}_{ij}(t) (\tilde{k}_j - k_j) dt \right)^2 \\ &= \sum_{l=1}^N \sum_{i \in \mathcal{I}} \left(w_{il} \int_{t_0}^{t_l} \sum_{j=1}^m \tilde{g}_{ij}(t) (\tilde{k}_j - k_j) dt \right)^2 \\ &= \sum_{l=1}^N \sum_{i \in \mathcal{I}} \left(\sum_{j=1}^m \left(w_{il} \underbrace{\int_{t_0}^{t_l} \tilde{g}_{ij}(t) dt}_{=: \tilde{c}_{ilj}} \right) (\tilde{k}_j - k_j) \right)^2 \\ &= \sum_{l=1}^N \sum_{i \in \mathcal{I}} \left(w_{il} \sum_{j=1}^m \tilde{c}_{ilj} (\tilde{k}_j - k_j) \right)^2. \end{aligned} \quad (39)$$

Setting $\tilde{C}_{il} := (\tilde{c}_{il1}, \dots, \tilde{c}_{ilm})$, we have

$$\begin{aligned} \tilde{\phi}(\tilde{k}, k) &= \sum_{l=1}^N \sum_{i \in \mathcal{I}} \left(w_{il} \tilde{C}_{il} (\tilde{k} - k) \right)^2 \\ &= \sum_{l=1}^N \sum_{i \in \mathcal{I}} (\tilde{k} - k)^T \left(w_{il} \tilde{C}_{il} \right)^T \left(w_{il} \tilde{C}_{il} \right) (\tilde{k} - k) \\ &= (\tilde{k} - k)^T \left(\sum_{l=1}^N \sum_{i \in \mathcal{I}} \left(w_{il} \tilde{C}_{il} \right)^T \left(w_{il} \tilde{C}_{il} \right) \right) (\tilde{k} - k), \end{aligned} \quad (40)$$

which is obviously quadratic in $\tilde{k} - k$ and therewith quadratic in \tilde{k} . We may further compute the integrals by trapezoidal sums, say on the interval $[t_{l-1}, t_l]$ ($1 \leq l \leq N$):

$$\int_{t_{l-1}}^{t_l} \tilde{g}_{ij}(t) dt = \frac{\tilde{g}_{ij}(t_{l-1}) + \tilde{g}_{ij}(t_l)}{2} (t_l - t_{l-1}), \quad (41)$$

where the “=” shall be interpreted from a numerical point of view, i.e. we assume that the grid $t_0 < t_1 < \dots < t_N$ is sufficiently fine to accurately compute the integrals in Eq. (41). Hence, we have

$$\tilde{c}_{i\bar{l}j} = \frac{1}{2} \sum_{l=1}^{\bar{l}} (\tilde{g}_{ij}(t_l) + \tilde{g}_{ij}(t_{l-1})) (t_l - t_{l-1}), \quad (42)$$

and setting for notational convenience

$$\tilde{G}_i(t) := (\tilde{g}_{i1}(t), \dots, \tilde{g}_{im}(t)) \quad (43)$$

yields

$$\tilde{C}_{i\bar{l}} = \frac{1}{2} \sum_{l=1}^{\bar{l}} (\tilde{G}_i(t_l) + \tilde{G}_i(t_{l-1})) (t_l - t_{l-1}), \quad (44)$$

and

$$\begin{aligned} \tilde{\phi}(\tilde{k}, k) &= (\tilde{k} - k)^T \left[\sum_{\bar{l}=1}^N \sum_{i \in \mathcal{I}} \left(\frac{w_{i\bar{l}}}{2} \sum_{l=1}^{\bar{l}} (\tilde{G}_i(t_l) + \tilde{G}_i(t_{l-1})) (t_l - t_{l-1}) \right)^T \right. \\ &\quad \left. \left(\frac{w_{i\bar{l}}}{2} \sum_{l=1}^{\bar{l}} (\tilde{G}_i(t_l) + \tilde{G}_i(t_{l-1})) (t_l - t_{l-1}) \right) \right] (\tilde{k} - k) \\ &= (\tilde{k} - k)^T \underbrace{\left(\sum_{j=0}^N \sum_{i \in \mathcal{I}} (w_{i\bar{l}}^* \tilde{G}_i(t_l))^T (w_{i\bar{l}}^* \tilde{G}_i(t_l)) \right)}_{=: H} (\tilde{k} - k), \quad (45) \end{aligned}$$

where $w_{i\bar{l}}^*$, $i \in \mathcal{I}$, $0 \leq l \leq N$ are weighting factors, depending on the original weights $w_{i\bar{l}}$ and the length of the intervals $[t_{l-1}, t_l]$. The $m \times m$ -matrix H in (45) is positive semidefinite by construction.

3.4. Relationship to sensitivity analysis

We expand the definition of \tilde{G}_i in Eq. (45):

$$\tilde{G}_i(t) = \sigma \frac{\partial f_i(x(t), k)}{\partial x} \frac{\partial x(t)}{\partial k} + \frac{\partial f_i(x(t), k)}{\partial k}, \quad \sigma \in \{0, 1\}. \quad (46)$$

Now we see how to relate the factor $\sigma \in \{0, 1\}$ to the sensitivity of the change rate f_i with respect to k : for $\sigma = 0$ the function $G_i(t)$ is identical to the *partial* derivative of f_i with respect to k ; for $\sigma = 1$, $G_i(t)$ can be identified with the *total* derivative of f_i with respect to k . In both cases we have to compute the partial derivatives $\partial f_i / \partial k$, by either by symbolic or algorithmic differentiation. Furthermore, for the choice $\sigma = 1$, $G_i(t)$ depends on the parametric sensitivities $\partial x(t) / \partial k$. Hence, then the computation of H requires a sensitivity analysis of the CRN with the original parameter vector k . In general, these sensitivities should be computed by an efficient numerical integrator with sensitivity analysis capabilities, e.g. [31].

3.5. From MINLP to MIQP

In the following, we substitute in the MINLP sequence (MINLP(\tilde{m})) the original objective function $\phi(\tilde{k}, k)$ by the convex and quadratic approximation $\tilde{\phi}(\tilde{k}, k)$ to yield the MIQP

$$\left\{ \begin{array}{l} \min_{\tilde{k} \in [\underline{k}, \bar{k}]} (\tilde{k} - k)^T H (\tilde{k} - k) \\ \text{s.t. } \text{NNZ}(\tilde{k}) \leq \tilde{m}. \end{array} \right\}, \quad (\text{MIQP}(\tilde{m}))$$

which depends on the integer parameter \tilde{m} . However, for practical reasons, we eliminate the NNZ-operator in MIQP(\tilde{m}) by means of a reformulation using the binary variable vector $y \in \{0, 1\}^m$ which will satisfy

$$\sum_{i=1}^m y_i = \text{NNZ}(\tilde{k}).$$

Therefore, we set up the equivalent MIQP

$$\min_{\tilde{k}, y} \frac{1}{2} (\tilde{k} - k)^T H (\tilde{k} - k) \quad (47)$$

$$\text{s.t. } y_i \in \{0, 1\}, \quad i = 1, \dots, m \quad (48)$$

$$\tilde{k}_i \geq 0, \quad i = 1, \dots, m \quad (49)$$

$$\tilde{k}_i - \bar{k}_i y_i \leq 0, \quad i = 1, \dots, m \quad (50)$$

$$\tilde{k}_i - \underline{k}_i y_i \geq 0, \quad i = 1, \dots, m \quad (51)$$

$$\sum_{i=1}^m y_i \leq \tilde{m}. \quad (52)$$

Note that the objective function in Eq. (47), if we recall the construction of H and Eq. (46), can be interpreted as minimizing the weighted quadratic deviation of the change rates. In particular, we do *not* directly minimize the deviation in the species concentration but the deviation of their time derivatives. The same idea has been successfully applied in the incremental identification of kinetic models for homogeneous reaction systems [32].

3.6. Comparison with PCA-based methods

Turányi proposes in [30] a reduction method based on the Principal Component Analysis (PCA) [23] of the sensitivities of the reaction rates with respect to the parameters

$$(\tilde{F}(t))_{ij} = \frac{\partial \log(f_i)}{\partial \log(k_j)}(x(t), k) = \frac{\partial f_i}{\partial k_j}(x(t), k) \cdot \frac{k_j}{x_i(t)}. \quad (53)$$

The objective function used by PCA in a particular case can be related to ours. For $b_{ij}(t)$ in Eq. (33) we have the identity $b_{ij}(t) = \frac{\partial f_i}{\partial k_j}(x(t), k)$, and consequently, if we use the notation $\tilde{F}_i = (\tilde{F}_{i1}, \tilde{F}_{i2}, \dots, \tilde{F}_{im})$ and if σ and the weights w_{il}^* in Eq. (45) are set to

$$\sigma = 0, \quad w_{il}^* = \frac{1}{x_i(t_l)}, \quad i \in \mathcal{I}, \quad l = 0, \dots, N,$$

then we have the identity

$$\sum_{l=0}^N \sum_{i \in \mathcal{I}} \tilde{F}_i(t_l)^T \tilde{F}_i(t_l) = H. \quad (54)$$

This directly relates Turányi’s method to our MIQP approach. However, PCA-based model reduction is not able to eliminate reactions and simultaneously adjust the remaining rate coefficients. Therefore, we expect that the MIQP approach is able to further reduce the number of reactions compared to PCA-based reduction. Indeed this hypothesis is confirmed in Section 5, where we compare the reduced models of both approaches.

4. Implementation Issues

4.1. Scaling, regularization and pre-reduction

In order to have a robust and numerically efficient method, one should pay attention to the implementation issues, that is the subject of this section. First we have found that a direct optimization of the MIQP (47)–(52) may result in non-acceptable results, due to numerical ill-conditioning. To avoid this problems one can apply scaling, regularization and pre-reduction to significantly improve the solution quality.

To force the optimized parameters \hat{k} to be in the same order of magnitude, a *scaling* of H with the diagonal matrix $D := \text{diag}(k)$ is performed, i.e. we employ the matrix

$$H_s := D^T H D. \quad (55)$$

Formally, this leads to scaling the original parameter vector k to

$$k = (1, 1, \dots, 1)^T. \quad (56)$$

Hence, from now on, we assume without loss of generality the validity of Eq. (56).

Obviously, the matrix H_s is (at least) positive semidefinite by construction. However, using finite-precision arithmetic, H_s may become indefinite. Indeed, this is the case for many case studies. To circumvent optimization with an indefinite Hessian, we compute the minimal eigenvalue $\lambda_{\min}(H_s)$ of H_s and use the *regularization*

$$H_r = H_s + \gamma I, \quad \gamma = |\min(\lambda_{\min}(H_s), 0)|, \quad (57)$$

where I is the m -dimensional unit matrix. However, the minimal eigenvalue is computed numerically and due to unreliabilities in this computation, H_r may still be indefinite, or at least the numerical MIQP solver claims H_r to be indefinite. In order to help the above detailed regularization and to facilitate

the subsequent optimization, a *pre-reduction* step is also performed. There we reduce the dimension of the parameter vector \tilde{k} by at least $m_{\text{pre-reduce}}$ reactions. The key point of the pre-reduction is to successively drop the parameters which, if only they are individually set to zero, have the least influence on the objective function. The corresponding algorithm is shown in Table 2.

Table 2: Heuristic pre-reduction algorithm to determine the set \mathcal{J} of important reactions

<pre> $\mathcal{J} := \{1, 2, \dots, m\}$ for $l = 1, \dots, m$ do if $\lambda_{\min}(H_{\mathcal{J}}) \geq 0$ and $\#\mathcal{J} \leq m - m_{\text{pre-reduce}}$ then break else $j = \arg \min_{j \in \mathcal{J}} \{\Delta k(j)^T H_{\mathcal{J}} \Delta k(j) : \Delta k_i(j) = -\delta_{ij} k_i \quad (i \in \mathcal{J})\}$^a $\mathcal{J} = \mathcal{J} \setminus \{j\}$ end if end for return \mathcal{J} </pre>
<p>^aHere, δ_{ij} denotes the Kronecker symbol, i.e. $\delta_{ij} = 0$, iff $i \neq j$ and $\delta_{ij} = 1$, iff $i = j$. In detail, $\Delta k(j)$ is a $\#\mathcal{J}$-dimensional vector with only one non-zero entry at the position of index j.</p>

The algorithm produces a set of parameter indices \mathcal{J} which is of cardinality $n_{\mathcal{J}} = \#\mathcal{J}$ less or equal than m , such that

$$\mathbb{R}^{n_{\mathcal{J}} \times n_{\mathcal{J}}} \ni H_{\mathcal{J}} := (H_r)_{ij}, \quad i, j \in \mathcal{J} \quad (58)$$

is positive semidefinite. The corresponding parameter vectors and binary variable vector are denoted by $\tilde{k}_{\mathcal{J}}, k_{\mathcal{J}}$ and $y_{\mathcal{J}}$, respectively. Then, the pre-reduced set of reactions is used as an initial CRN in the model reduction, i.e. H, \tilde{k}, k and y in MIQP (47)–(52) are replaced by $H_{\mathcal{J}}, \tilde{k}_{\mathcal{J}}, k_{\mathcal{J}}$ and $y_{\mathcal{J}}$, respectively.

4.2. Termination condition

The model reduction was formulated as a finite sequence of MIQPs in Eqs. (47)–(52) where in each iteration step we specify the maximum number of existing reactions \tilde{m} , $\tilde{m} = 1, 2, \dots, m$. This MIQP sequence is derived from the original sequence $\text{MINLP}(\tilde{m})$, where for each \tilde{m} the goal is to find a

reduced parameter vector \tilde{k} such that the original objective function $\phi(\tilde{k}, k)$ is small. This original objective function is substituted by the quadratic approximation $\tilde{\phi}(\tilde{k}, k)$ (see Eq. (45)). At first sight, it might be straightforward to terminate the iteration based on the original objective function in Eq. (24). However, relying on the original objective is not necessary at all. Any other measurement for the model error can be used as well. In general, the termination condition can be any user-specified condition. This condition might even test sophisticated features of the reduced model like stability, weak reversibility, etc.

In the simplest particular case the termination condition can be defined such that the average relative deviation for all the important species should be smaller than a given limit, let say 5%:

$$\phi_{\text{model_error}}(\tilde{k}, k) < \delta := 0.05, \quad (59)$$

where we decided to measure the model error by means of the function

$$\phi_{\text{model_error}}(\tilde{k}, k) = \frac{1}{Nn_{\mathcal{I}}} \sum_{l=1}^N \sum_{i \in \mathcal{I}} \left(\frac{|\tilde{x}_i(t_l) - x_i(t_l)|}{\tilde{w}_{il}} \right). \quad (60)$$

A natural choice for the weighting factors \tilde{w}_{il} in Eq. (60) can be $\tilde{w}_{il} = x_i(t_l)$, however if the concentration of an important species approaches zero the well known problem of the relative deviation occurs: the denominator approaches zero causing high relative deviation despite of small absolute deviation. This can be handled by choosing $\tilde{w}_{il} = \max\{Tol_i, x_i(t_l)\}$, where the tolerance value Tol_i is arbitrarily chosen to be

$$Tol_i = 10^{-4} \max_l x_i(t_l).$$

This gives relatively smaller weights to those points where the species concentration is less than 0.01%-of the maximum.

Note that though the approximate objective function $\tilde{\phi}(\tilde{k}, k)$ of the MIQPs (47)–(52) is monotonically increasing as the maximum number of non-zero reaction coefficients decreases, this is not necessarily valid either for the original objective function $\phi(\tilde{k}, k)$ in Eq. (24), or for the model error function $\phi_{\text{model_error}}$ in Eq. (60). Instead, there is only some correlation instead of direct causality between the objective function of the MIQPs and the model error.

4.3. Computational Environment

For the computational tasks performed, different software programs were used for general computations, numerical sensitivity analysis and optimization.

General computations: IVP, eigenvalues, etc.

Apart from numerical sensitivity analysis and optimization, all computations were performed in MATLAB 7.12 (Windows 32bit). For the solution of initial value problems (IVPs) of type (1)–(2), the built-in `od15s` initial value problem solver was employed, with non-standard absolute and relative tolerances. Further, we used the built-in `eig` function to compute the minimal eigenvalue $\lambda_{\min}(H)$.

At this point we shall give a warning to those readers who want to reproduce our results. To the authors' best knowledge, since version 5.3, MATLAB uses the LAPACK QZ-algorithm [33] for the computation of the eigenvalues. In particular, the accuracy of the computed eigenvalues is limited. We found that, if we deal with non-trivial matrices with a high condition number, the minimal eigenvalue computed by different MATLAB versions may differ by more than 100 %. Since the minimal eigenvalue affects the regularization in the reduction algorithm, we have the strange effect that the outcome of the algorithm is affected by the used MATLAB version. However, the robustness of the algorithm is not affected at all, only the number of eliminated reactions may be concerned to some extent. The idea to employ the minimal eigenvalue for the regularization is to provide a minimal intrusive regularization. To overcome the problems with different MATLAB versions one could either hand-code the QZ-algorithm provide another heuristic choice of their regularization parameter γ in Eq. (57). For example, we could set γ to an arbitrarily small value, and the following pre-reduction will hopefully make the Hessian positive definite. If the MIQP solver still claims H_r to be indefinite we would just increase γ , e.g. by doubling its value, and then let the MIQP solver try again. Anyway, in the numerical experiments, the pre-reduction step seemed to be much more important than the regularization, so we did no further investigations with respect to this issue.

Numerical Sensitivity Analysis

For the numerical sensitivity analysis, required for computation of $\tilde{G}_i(t_l)$ in Eq. (46) we used the JADE environment [34]. JADE combines automatic

differentiation by means of the derivative code compiler `dcc` [35] and the numerical sensitivity solver NIXE [31] to generate accurate sensitivities.

Numerical optimization

The solutions of the MIQP (47)–(52) were performed in the AMPL mathematical programming environment [36] using version 11.0 of the CPLEX MIQP solver [37]. The best reduction results are achieved if the MIQP is solved with high accuracy. Therefore, we changed the default CPLEX MIQP solver parameters as follows: convergence tolerance for barrier algorithm `comptol=1e-12`; tolerance for optimality of reduced costs `optimality=1e-9`; amount by which an integer variable can differ from the nearest integer and still be considered feasible `integrality=1e-9`. Any other parameter keeps its default value.

4.4. Tuning knobs

Of course, the proposed reduction methods require some tuning factors which can be divided into two groups: the parameters of the numerical solvers and the parameters of the model reduction method itself.

The first class comprises the absolute and relative tolerance of the numerical integration routines for the solution of the IVP, as well as the parameters for the CPLEX numerical MIQP solver. However, these parameters may strongly depend on the numerical solvers and we do not discuss them in detail.

The second class comprises the number N of the grid points, as well as the location the grid points, t_0, t_1, \dots, t_N and the associated weights w_{il} , $i \in \mathcal{I}$, $l = 0, \dots, N$ in Eq. (23). Further the choice of $\sigma = 0$ or $\sigma = 1$ in Eq. (38) may affect the solution. And last but not least the specification of the number of pre-reduced reactions $m_{\text{pre-reduce}}$ is an important tuning factor.

5. Case Studies

The use of the proposed method has been illustrated on three case studies taken from the literature.

5.1. Reduction of hydrogen-bromine reaction network

The hydrogen-bromine reaction is a well-known reaction mechanism in the literature [29, 23]. Because of the small size of this system it is easy to interpret the main idea of the method. The detailed description of the model equations (6-11) can be found in Subsection 2.2.

Initialization

The species in the reaction networks are Br_2 , HBr , H_2 , $\text{Br}\cdot$, $\text{H}\cdot$ and M from which the molecules, namely Br_2 , HBr and H_2 were selected as *important*. The rate constants corresponding to the reactions can be found in Table 3. The initial concentrations of species were taken from Turányi et al. [23]: $[\text{Br}_2]_0 = [\text{H}_2]_0 = 10^{-8} \text{ mol/cm}^3$, $[\text{M}]_0 = 10^{-5} \text{ mol/cm}^3$, the initial concentrations of the other species were considered to be zero. The time interval for model reduction is $[0, 1]$ second.

Table 3: Rate coefficients of the original and the reduced models of the Hydrogen-Bromine reaction network

Rate Coefficients	Original	(1*)	(2a*)	(2b*)
k_1	$6.260 \cdot 10^5$	1.000	0.9937	1
k_2	$1.560 \cdot 10^{15}$	1.000	1.0066	1
k_3	$2.610 \cdot 10^9$	1.000	0.8542	1
k_4	$1.390 \cdot 10^{13}$	1.000	0.0	0
k_5	$1.170 \cdot 10^{14}$	1.000	1.0236	1
k_6	$1.310 \cdot 10^4$	0.0	0.0	0

In the second column are the rate coefficients of the original model, in the third column (1) are the relative rate coefficients of the reduced-by-one model, while in the last two columns (2a and 2b) are the rate coefficients for the reduced-by-two models.

*The rate constants are in the table for the reduced networks in relative units, i.e. the ratio of the estimated and the original value. For example, a value of 1.0 means that the rate coefficient did not change.

Computation of matrix H

The matrix H is computed with the assumption of the validity of Eq. (34) i.e. $\sigma = 0$ in Eq. (38). To solve the IVP (1)–(2) the Matlab `ode15s` solver was used with $AbsTol = 10^{-19}$ and $RelTol = 10^{-13}$ absolute and relative tolerance settings. For the computation of the Hessian, $N = 100$ equidistantly sampled time points in the time interval were chosen:

$$t_l = \frac{l}{N}, \quad l = 1, \dots, N.$$

The weighting factors w_{il} in Eq. (23) were set to

$$w_{il} = \frac{1}{N \cdot \max(10^{-12}, x_i(t_l))}, \quad i \in \mathcal{I}, \quad l = 1, \dots, N,$$

to reflect the relative error, where the “max”-term was introduced to avoid division by zero. Actually, apart from the “max”-term, these weights equally reflect the relative error of the important species, an approach also followed by Androulakis [8].

Table 4: Important species concentration at the final time ($t_f = 1$ s) in the original model and in the reduced models.

Species	Original conc.	Relative deviation		
		(1)	(2a)	(2b)
[Br ₂]	$1.2876 \cdot 10^{-9}$	$2.2481 \cdot 10^{-5}$	0.3730	0.5140
[H ₂]	$1.6504 \cdot 10^{-9}$	$1.9882 \cdot 10^{-5}$	0.3359	0.4652
[HBr]	$1.6699 \cdot 10^{-8}$	$-3.9301 \cdot 10^{-6}$	-0.0664	-0.0919

Results

One can see the solution of the original system of equations (6)–(11) for the important species together with the solutions of the reduced systems in Figure 1. The corresponding rate coefficient values can be found in Table 3. In the first step the algorithm omits the k_6 parameter which corresponds to the 6th reaction, while the other parameter values are not changed in the first 4 digits. The resulted trajectories perfectly fit to the original solution.

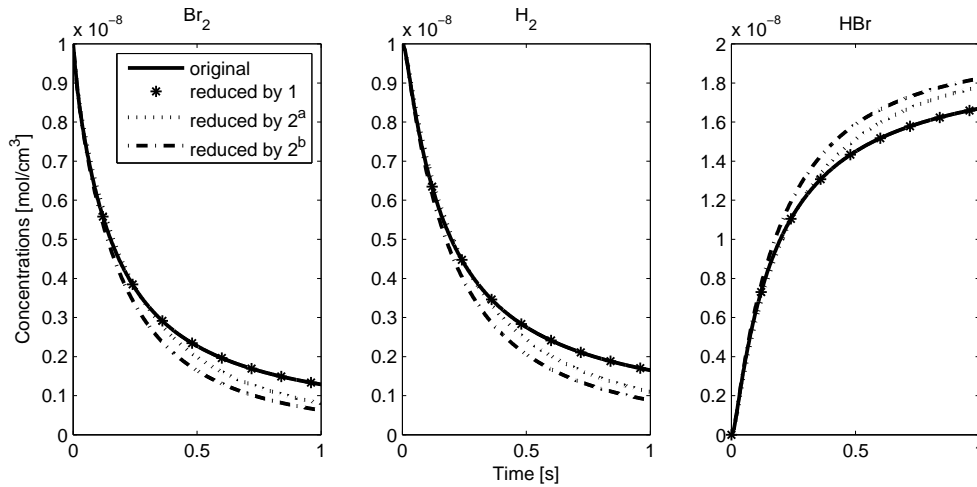


Figure 1: The concentrations of each important species in the original system and in the reduced systems.

If we further omit one more reaction the algorithm neglects the 4th and 6th rate coefficients. Using the \underline{k} and \bar{k} constraints in Eqs. (50) and (51) one can easily decide to let the algorithm estimate the value of non-zero parameters or not. If we want to identify the negligible parameters but want to keep the original values of the non-zero parameters then $\underline{k}_i = \bar{k}_i = 1$ should be defined. Figure 1 shows the result marked with dotted line when $\underline{k}_i = 0.1$ and $\bar{k}_i = 10$ and marked with dash-dotted line when $\underline{k}_i = \bar{k}_i = 1$ was chosen. The corresponding parameters are given in Table 3, in the columns (2^a) and (2^b) respectively.

The relative deviation of the concentration at the final time point (RD) for each important species

$$RD_i = \frac{\tilde{x}_i(t_f) - x_i(t_f)}{x_i(t_f)}, \quad i \in \mathcal{I} \quad (61)$$

can be found in Table 4, where \tilde{x}_i is the concentration of the i -th important species in the reduced system and x_i is the corresponding concentration in the original system. If only less than 5% difference is acceptable then it is clear that only the 6th reaction can be omitted from the network.

5.2. Reduction of formaldehyde oxidation reaction network

Formaldehyde oxidation in the presence of carbon-monoxide is a medium-size reaction network which consists of 25 reactions listed with the corresponding rate coefficients in Table 6. The detailed reaction network was published by Vardanyan [38] and used for model reduction by Turányi [23]. In this section the model reduction of this reaction system on two different time horizons is shown.

The species in the network are HCO, O₂, HO₂, CO, CH₂O, H₂O₂, M which is a kind of catalyst, OH, H₂O, CO₂, H, H₂, O, and finally *Destruction* which is a *sink* for reaction (6) and (7). From this list of species, 9 species (HCO, HO₂, H₂O₂, OH, H₂O, CO₂, H, H₂, O) were chosen as important. The initial conditions for the reaction network are $[O_2]_0 = 1.27 \cdot 10^{18} \text{ cm}^{-3}$, $[CO]_0 = 2.83 \cdot 10^{18} \text{ cm}^{-3}$, $[CH_2O]_0 = 6.77 \cdot 10^{16} \text{ cm}^{-3}$, $[M]_0 = 7.09 \cdot 10^{18} \text{ cm}^{-3}$ and zero for the other species, the same as in [23].

Two different time horizons were chosen for model reduction, the shorter is $[0, 5 \cdot 10^{-3}]$ seconds the same as presented in [23] while the longer $[0, 0.1]$ seconds shows much more colorful dynamic behavior. In both cases the sensitivity part was included in the computation, i.e. $\sigma = 1$ in Eq. (38). For

the solution of IVP (1)–(2), an absolute tolerance of $AbsTol = 10^{-14}$ and a relative tolerance of $RelTol = 10^{-10}$ were set.

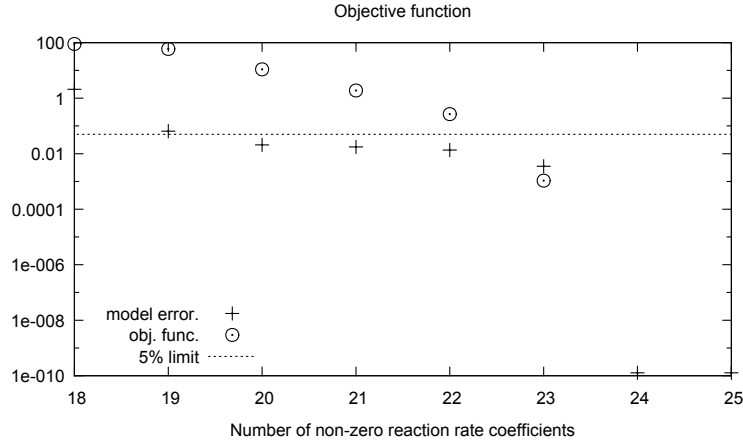


Figure 2: Model error and objective function against the number of non-zero reaction coefficients in case of the formaldehyde reaction network in the longer time horizon

5.2.1. Model reduction in longer time horizon

In this time horizon $N = 1500$ equidistant time points were selected and the weighting factors in Eq. (23) are

$$w_{il} = \frac{\nu}{N \cdot \max(10^{-2}, x_i(t_l))}, \quad \nu = 10^{-10},$$

where the choice of $\nu = 10^{-10}$ in the numerator is introduced to avoid large eigenvalues of H . The choice $\nu = 1$ would result in a mathematically equivalent optimization problem. However, according to our experiences, the MIQP solver of CPLEX has computational difficulties with large eigenvalues which is the only reason for our particular choice of ν . In other respects, again apart from the “max”-term to avoid by-zero division, these weights equally reflect the relative error of the important species, an approach also followed by Androulakis [8].

The solution of the sequence of MIQPs resulted in the set of objective function values as a function of maximal number of non-zero reaction coefficients $\tilde{k}(m)$. The objective function (47), the model error (60) together with the 5% limit can be seen in Figure 2. One can conclude that on the specified

level of acceptance the reaction network can be reduced by 5 reactions. We have depicted the important concentration trajectories which belong to the original reaction network together with the trajectories of the reduced models in Figure 3. The reduced model is in good agreement with the original one. The corresponding estimated parameter values can be found in Table 6. in column A5.

Table 5: Relative deviation of the important species in the reduced models and in the reference paper.

Important species	Relative deviation in concentration		
	A5	B12	Turányi [23]
HCO	0	0.008	0.023
HO ₂	0.054	0.006	0.024
H ₂ O ₂	0.001	0.031	0.019
OH	0.036	0.009	0.023
H ₂ O	0.006	0.016	0.016
CO ₂	0.004	0.029	0.017
H	0.042	0.031	0.036
H ₂	0.001	0.004	0.01
O	0.001	0.009	0.004

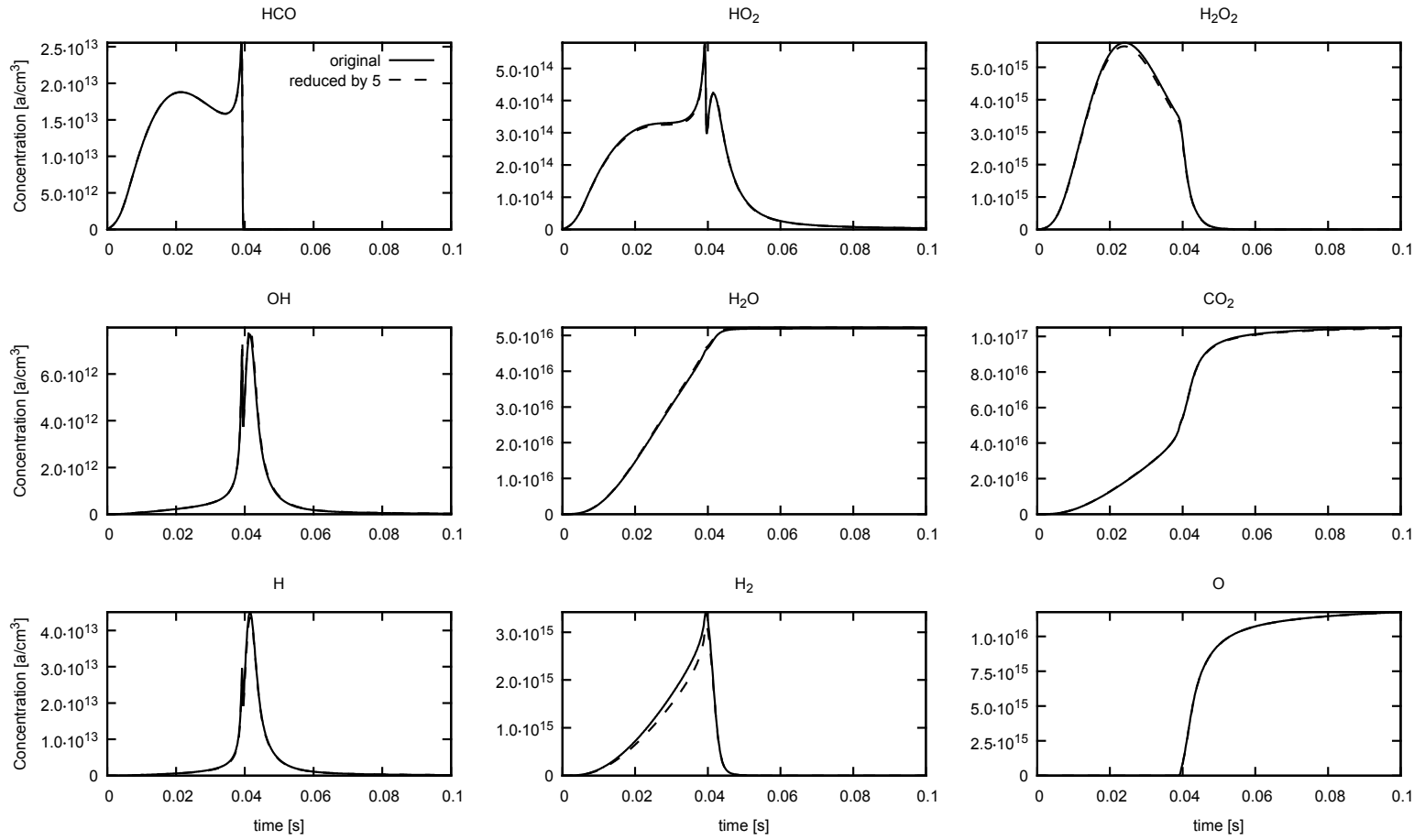


Figure 3: The concentrations of each important species in the original system and in the reduced systems in the longer time horizon.

5.2.2. Model reduction in shorter time horizon

The model reduction on a shorter time horizon using PCA was presented in [23]. The author concluded that the minimal reaction network which can successfully describe the original dynamics of the important species consists of 13 reactions.

For the computation of matrix H , 100 equally distributed time points along the interval were selected. The weighting factors in Eq. (23) are

$$w_{il} = \frac{\tilde{w}_i}{N \cdot \max(1, x_i(t_l))},$$

where $\tilde{w}_i = 10$ for $i \in \{3, 8, 9\}$ and $\tilde{w}_i = 1$ for the other species. Again, apart from the “max”-term to avoid division by zero and apart from the important species x_3, x_8, x_9 , these weights equally reflect the relative error of the important species, an approach also followed by Androulakis [8]. The increase of the weights for x_3, x_8, x_9 are just a result of some heuristic tuning to achieve a better reduction.

One can find the model error as a function of the number of non-zero rate coefficients in Figure 4 according to which the model can be reduced to 12 reactions while the average relative deviations of the important species are around 1%. The estimated parameter values are given in Table 6, column B12. If we compare the two last columns of the table we find that the proposed method found the same unnecessary parameters as presented in [23] except for the 13th parameter. The relative deviations for the concentrations are depicted in Table 5 from which it can be clearly seen that the simultaneous estimation of the parameters resulted in a better fit than only omitting the unnecessary reactions using the PCA (see Figure 5).

Table 6: Rate coefficients of the Formaldehyde case study

Reactions	Original	A5	B12	[23]
	coeff.	[0, 0.1 s]	[0, 5 · 10 ⁻³ s]	
(1) HCO + O ₂ → HO ₂ + CO	1.00 · 10 ⁻¹³	0.999	1.0051	1
(2) HO ₂ + CH ₂ O → H ₂ O ₂ + HCO	5.70 · 10 ⁻¹⁴	0.9993	1.0012	1
(3) H ₂ O ₂ + M → 2 OH + M	6.66 · 10 ⁻¹⁸	1.0065	0.9925	1
(4) OH + CH ₂ O → H ₂ O + HCO	1.60 · 10 ⁻¹⁰	1.0019	1.012	1
(5) OH + H ₂ O ₂ → H ₂ O + HO ₂	5.10 · 10 ⁻¹²	2.0844	0	0
(6) H ₂ O ₂ → Destruction	1.05 · 10 ²	1.0011	0.808	1
(7) HO ₂ → Destruction	1.05 · 10 ¹	1.2011	0	0
(8) 2 HO ₂ → H ₂ O ₂ + O ₂	3.00 · 10 ⁻¹²	1.0174	1.0398	1
(9) OH + CO → CO ₂ + H	3.30 · 10 ⁻¹³	0.943	0.7241	1
(10) HO ₂ + CO → CO ₂ + OH	1.20 · 10 ⁻¹⁵	1.0316	0.9909	1
(11) H + CH ₂ O → H ₂ + HCO	2.70 · 10 ⁻¹²	0.9493	0.9923	1
(12) H + O ₂ → OH + O	5.51 · 10 ⁻¹⁴	1.0217	0.9354	1
(13) H + O ₂ + M → HO ₂ + M	1.00 · 10 ⁻³²	1.0173	0	1
(14) HO ₂ + M → H + O ₂ + M	4.70 · 10 ⁻¹⁹	0	0	0
(15) O + H ₂ → OH + H	3.02 · 10 ⁻¹³	1.009	0*	0
(16) O + CH ₂ O → OH + HCO	1.00 · 10 ⁻¹⁰	0.9986	0.9341	1
(17) H + H ₂ O ₂ → HO ₂ + H ₂	1.30 · 10 ⁻¹²	0	0	0
(18) H + H ₂ O ₂ → H ₂ O + OH	5.90 · 10 ⁻¹²	1.1459	0	0
(19) O + H ₂ O ₂ → OH + HO ₂	1.00 · 10 ⁻¹³	1.0472	0	0
(20) HCO → H + CO	4.60 · 10 ⁻¹²	0	0	0
(21) OH + H ₂ → H ₂ O + H	1.00 · 10 ⁻¹¹	0*	0*	0
(22) CH ₂ O + O ₂ → HCO + HO ₂	2.90 · 10 ⁻²⁰	0.9934	0.9967	1
(23) H + HO ₂ → 2 OH	5.00 · 10 ⁻¹²	0	0	0
(24) H + HO ₂ → H ₂ O + O	5.00 · 10 ⁻¹¹	0.9852	0	0
(25) H + HO ₂ → H ₂ + O ₂	4.50 · 10 ⁻¹¹	0.9559	0	0

Rate coefficients of the original system and the relative rate coefficients in the reduced systems. In the A5 case the system was reduced by 5 reactions. In the B12 case the reduced system contains 12 reactions in the shorter time horizon. Reactions denoted by (*) were pre-reduced.

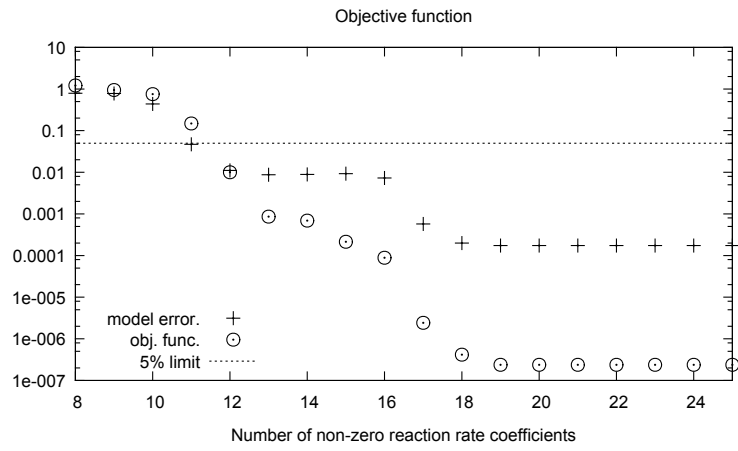


Figure 4: Objective function and model error versus the number of non-zero reaction coefficients in the shorter time horizon.

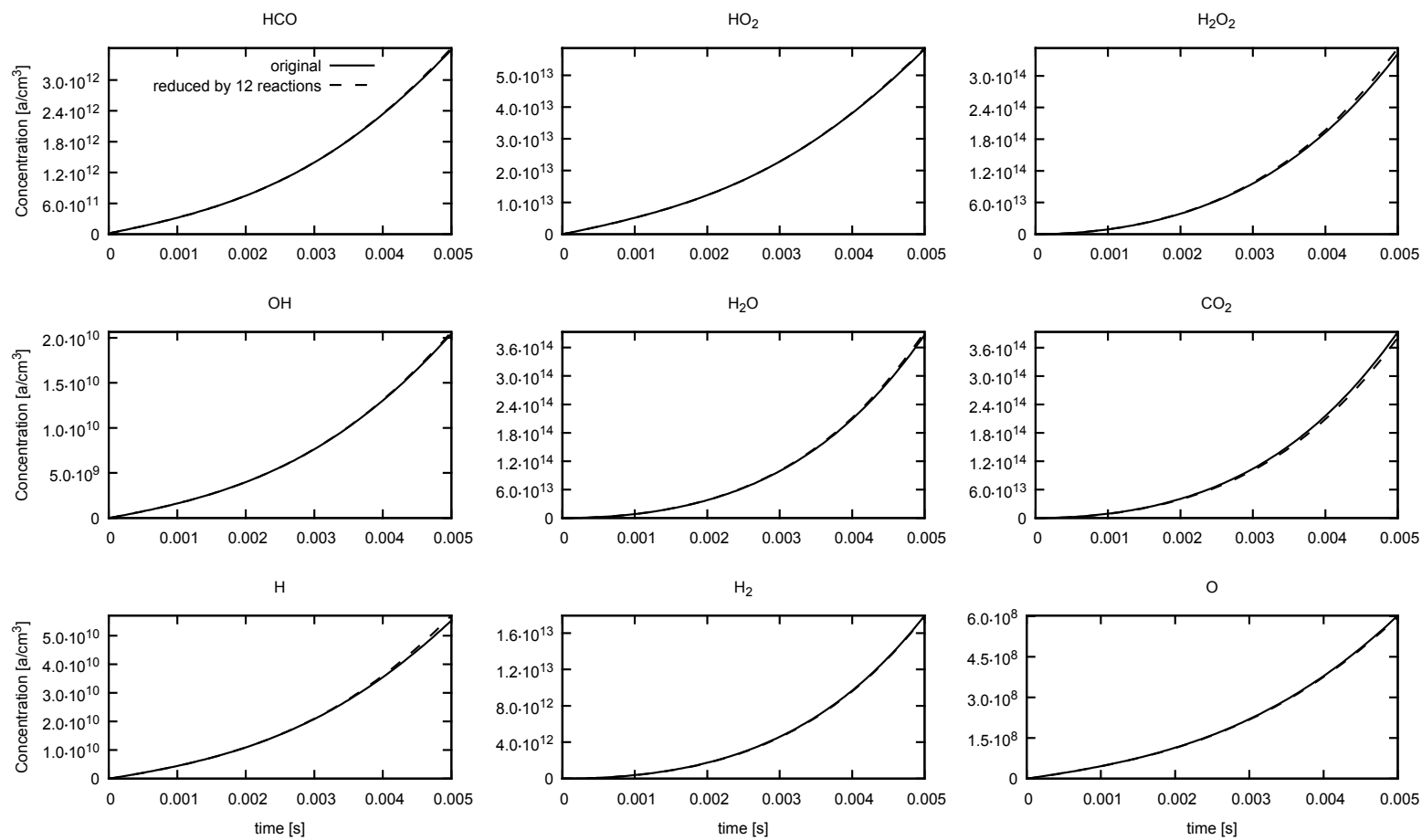


Figure 5: The concentrations of each important species in the original system and in the reduced systems in the shorter time horizon.

5.3. Reduction of the alkane pyrolysis reaction network

The alkane pyrolysis is a large reaction network consisting of 98 reactions and 32 species. The reactions and the corresponding rate coefficients can be found in Table 7. The reduction of this network using Principal Component Analysis was presented in [30]. The author could reduce the original 98 reactions to 38 reactions, while the concentrations of the important species did not change more than 1%. As the author remarked the reaction network has no formation steps for five species, which resulted in that reactions 6, 74, 76, 78, 82, 86, 87, 96 and 98 can be omitted because the corresponding rates are zero. These reactions are marked with a hash (#) symbol in Table 7.

5.3.1. Initialization

During the model reduction the same initial conditions, time horizon and selected important species were used as presented in [30] to produce comparable results. The following species were chosen as important: C_3H_8 , H_2 , CH_4 , C_3H_6 , C_2H_6 , C_2H_4 . The time horizon is $[0, 100]$ seconds along which the H matrix was computed from 1000 equidistant time points using sensitivity information, i.e. $\sigma = 1$ in Eq. (38). The initial conditions are $1.912 \cdot 10^{-3} \text{ mol/dm}^3$ for the propane (C_3H_8) and zero for all the other species. The weighting factors in Eq. (23) are

$$w_{il} = \left(1 - \frac{\delta_{N0} + \delta_{Nl}}{2}\right) \frac{\tilde{w}_i}{N \cdot \max(1, x_i(t_l))}, \quad i \in \mathcal{I}, \quad l = 0, \dots, N$$

where $\tilde{w}_i = 5 \cdot 10^{-4}$ for $i = 5$ and $\tilde{w}_i = 5 \cdot 10^{-3}$ for the other species. Here the factor $(1 - (\delta_{N0} + \delta_{Nl})/2)$ equals 1, for $l = 1, \dots, N - 1$ and $1/2$ for $l = 0$ or $l = N$, where δ is the Kronecker symbol. In this way, the sum over l in Eq. (23) becomes a trapezoidal sum.

For the solution of IVP (1)–(2), $AbsTol = 10^{-20}$ as absolute tolerance and $RelTol = 10^{-10}$ as relative tolerance were set.

5.3.2. Pre-reduction

The size of the reaction network necessitated the usage of the pre-reduction described in section 4.1. We have found that the optimal number of reactions which should be omitted during the pre-reduction is 57. The corresponding reaction coefficients are marked with a star (*) in Table 7.

5.3.3. Results

In the Figure 6 one can find the objective function and the model error as a function of the number of non-zero reaction coefficients. It suggests that if we accept less than 5 % model error then the model can be reduced to 23 reactions, which is 15 reactions fewer than we find in [30]. This is a remarkable result which shows the advantage of the simultaneous reduction and parameter estimation.

The trajectories of the important species in the reduced model together with the original concentrations are depicted in Figure 7. The fitting of the concentration trajectories is almost perfect for all species.

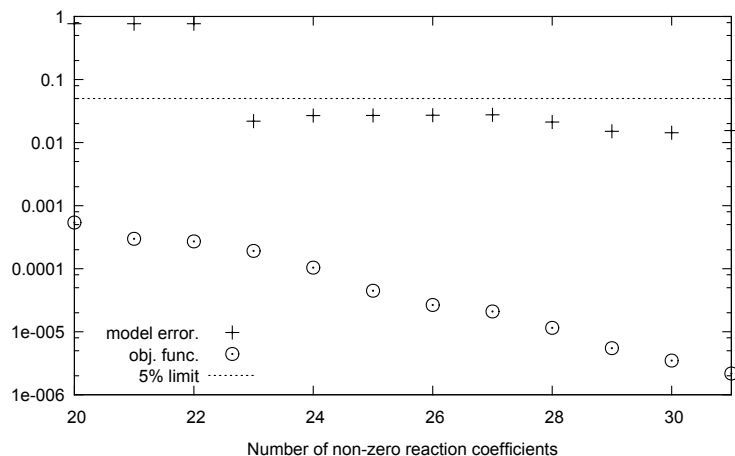


Figure 6: The objective function value versus the number of non-zero reaction coefficients.

Table 7: Rate Coefficients of the alkane pyrolysis case study

	Reactions	Rate coefficients	
		Original	Reduced
(1)	$C_3H_8 \rightarrow CH_3\cdot + C_2H_5\cdot$	$1.3203 \cdot 10^{-06}$	0.9903
(2)	$1-C_4H_8 \rightarrow CH_3\cdot + C_2H_5\cdot$	$1.5304 \cdot 10^{-04}$	0*
(3)	$1-C_5H_{10} \rightarrow C_2H_5\cdot + C_3H_5\cdot$	$7.7239 \cdot 10^{-04}$	0*
(4)	$1-C_6H_{12} \rightarrow 1-C_3H_7\cdot + C_3H_5\cdot$	$2.3342 \cdot 10^{-03}$	0*
(5)	$(C_3H_5)_2 \rightarrow C_3H_5\cdot + C_3H_5\cdot$	$3.1620 \cdot 10^{-02}$	1.0082
(6)#	$1,5\text{-heptadiene} \rightarrow C_3H_5\cdot + C_4H_7\cdot$	$9.7127 \cdot 10^{-01}$	-

	Reactions	Rate coefficients	
		Original	Reduced
(7)	$\text{n-C}_4\text{H}_{10} \rightarrow \text{CH}_3\cdot + 1\text{-C}_3\text{H}_7\cdot$	$3.6312 \cdot 10^{-06}$	0*
(8)	$\text{n-C}_4\text{H}_{10} \rightarrow \text{C}_2\text{H}_5\cdot + \text{C}_2\text{H}_5\cdot$	$2.6527 \cdot 10^{-06}$	0*
(9)	$\text{H}_2 + \text{CH}_3\cdot \rightarrow \text{H}\cdot + \text{CH}_4$	$1.4971 \cdot 10^{+06}$	0*
(10)	$\text{H}_2 + \text{C}_3\text{H}_5\cdot \rightarrow \text{H}\cdot + \text{C}_3\text{H}_6$	$1.6856 \cdot 10^{+05}$	1.138
(11)	$\text{C}_3\text{H}_8 + \text{H}\cdot \rightarrow 1\text{-C}_3\text{H}_7\cdot + \text{H}_2$	$3.1881 \cdot 10^{+08}$	0.5922
(12)	$\text{C}_3\text{H}_8 + \text{CH}_3\cdot \rightarrow 1\text{-C}_3\text{H}_7\cdot + \text{CH}_4$	$8.3505 \cdot 10^{+05}$	0.7493
(13)	$\text{C}_3\text{H}_8 + \text{C}_2\text{H}_5\cdot \rightarrow 1\text{-C}_3\text{H}_7\cdot + \text{C}_2\text{H}_6$	$1.6128 \cdot 10^{+05}$	1.5675
(14)	$\text{C}_3\text{H}_8 + 2\text{-C}_3\text{H}_7\cdot \rightarrow 1\text{-C}_3\text{H}_7\cdot + \text{C}_3\text{H}_8$	$3.5234 \cdot 10^{+04}$	1.7239
(15)	$\text{C}_3\text{H}_8 + 1\text{-C}_3\text{H}_7\cdot \rightarrow 2\text{-C}_3\text{H}_7\cdot + \text{C}_3\text{H}_8$	$8.2443 \cdot 10^{+04}$	0
(16)	$\text{C}_3\text{H}_8 + \text{C}_3\text{H}_5\cdot \rightarrow 1\text{-C}_3\text{H}_7\cdot + \text{C}_3\text{H}_6$	$2.5859 \cdot 10^{+03}$	0.8467
(17)	$\text{C}_3\text{H}_6 + \text{H}\cdot \rightarrow \text{C}_3\text{H}_5\cdot + \text{H}_2$	$1.1565 \cdot 10^{+10}$	0.5149
(18)	$\text{C}_3\text{H}_8 + \text{H}\cdot \rightarrow 2\text{-C}_3\text{H}_7\cdot + \text{H}_2$	$5.4813 \cdot 10^{+08}$	0.5551
(19)	$\text{C}_3\text{H}_8 + \text{CH}_3\cdot \rightarrow 2\text{-C}_3\text{H}_7\cdot + \text{CH}_4$	$9.7586 \cdot 10^{+05}$	1.2128
(20)	$\text{C}_3\text{H}_8 + \text{C}_2\text{H}_5\cdot \rightarrow 2\text{-C}_3\text{H}_7\cdot + \text{C}_2\text{H}_6$	$8.2443 \cdot 10^{+04}$	0
(21)	$\text{C}_3\text{H}_8 + \text{C}_3\text{H}_5\cdot \rightarrow 2\text{-C}_3\text{H}_7\cdot + \text{C}_3\text{H}_6$	$9.7813 \cdot 10^{+03}$	1.0561
(22)	$\text{H}_2 + \text{C}_2\text{H}_5\cdot \rightarrow \text{H}\cdot + \text{C}_2\text{H}_6$	$7.1206 \cdot 10^{+05}$	0*
(23)	$\text{C}_2\text{H}_6 + \text{CH}_3\cdot \rightarrow \text{C}_2\text{H}_5\cdot + \text{CH}_4$	$4.9539 \cdot 10^{+05}$	0*
(24)	$\text{n-C}_4\text{H}_{10} + \text{H}\cdot \rightarrow 1\text{-C}_4\text{H}_9\cdot + \text{H}_2$	$3.1881 \cdot 10^{+08}$	0*
(25)	$\text{n-C}_4\text{H}_{10} + \text{CH}_3\cdot \rightarrow 1\text{-C}_4\text{H}_9\cdot + \text{CH}_4$	$9.8842 \cdot 10^{+05}$	0*
(26)	$\text{n-C}_4\text{H}_{10} + \text{C}_2\text{H}_5\cdot \rightarrow 1\text{-C}_4\text{H}_9\cdot + \text{C}_2\text{H}_6$	$1.6128 \cdot 10^{+05}$	0*
(27)	$\text{n-C}_4\text{H}_{10} + \text{C}_3\text{H}_5\cdot \rightarrow 1\text{-C}_4\text{H}_9\cdot + \text{C}_3\text{H}_6$	$2.5859 \cdot 10^{+03}$	0*
(28)	$\text{C}_3\text{H}_6 + \text{CH}_3\cdot \rightarrow \text{C}_3\text{H}_5\cdot + \text{CH}_4$	$6.9894 \cdot 10^{+05}$	1.7449
(29)	$\text{C}_3\text{H}_6 + \text{C}_2\text{H}_5\cdot \rightarrow \text{C}_3\text{H}_5\cdot + \text{C}_2\text{H}_6$	$2.3810 \cdot 10^{+05}$	0*
(30)	$\text{n-C}_4\text{H}_{10} + \text{H}\cdot \rightarrow 2\text{-C}_4\text{H}_9\cdot + \text{H}_2$	$1.0937 \cdot 10^{+09}$	0*
(31)	$\text{n-C}_4\text{H}_{10} + \text{CH}_3\cdot \rightarrow 2\text{-C}_4\text{H}_9\cdot + \text{CH}_4$	$1.0723 \cdot 10^{+06}$	0*
(32)	$\text{n-C}_4\text{H}_{10} + \text{C}_2\text{H}_5\cdot \rightarrow 2\text{-C}_4\text{H}_9\cdot + \text{C}_2\text{H}_6$	$1.6450 \cdot 10^{+05}$	0*
(33)	$\text{n-C}_4\text{H}_{10} + \text{C}_3\text{H}_5\cdot \rightarrow 2\text{-C}_4\text{H}_9\cdot + \text{C}_3\text{H}_6$	$1.2885 \cdot 10^{+04}$	0*
(34)	$\text{C}_2\text{H}_5\cdot \rightarrow \text{H}\cdot + \text{C}_2\text{H}_4$	$5.7421 \cdot 10^{+02}$	0.9013
(35)	$1\text{-C}_3\text{H}_7\cdot \rightarrow \text{CH}_3\cdot + \text{C}_2\text{H}_4$	$2.5147 \cdot 10^{+04}$	1.4012
(36)	$1\text{-C}_3\text{H}_7\cdot \rightarrow \text{H}\cdot + \text{C}_3\text{H}_6$	$7.3732 \cdot 10^{+02}$	0
(37)	$2\text{-C}_3\text{H}_7\cdot \rightarrow \text{H}\cdot + \text{C}_3\text{H}_6$	$1.2185 \cdot 10^{+03}$	1.0313
(38)	$2\text{-C}_4\text{H}_9\cdot \rightarrow \text{CH}_3\cdot + \text{C}_3\text{H}_6$	$2.5889 \cdot 10^{+05}$	0*
(39)	$2\text{-methyl-1-propyl}\cdot \rightarrow \text{CH}_3\cdot + \text{C}_3\text{H}_6$	$1.6603 \cdot 10^{+05}$	0*
(40)	$3\text{-methyl-1-butyl}\cdot \rightarrow 2\text{-C}_3\text{H}_7\cdot + \text{C}_2\text{H}_4$	$3.8624 \cdot 10^{+05}$	0*
(41)	$4\text{-methyl-2-pentyl}\cdot \rightarrow 2\text{-C}_3\text{H}_7\cdot + \text{C}_3\text{H}_6$	$7.1039 \cdot 10^{+05}$	0*

	Reactions	Rate coefficients	
		Original	Reduced
(42)	$1\text{-C}_4\text{H}_9\cdot \rightarrow \text{C}_2\text{H}_5\cdot + \text{C}_2\text{H}_4$	$4.9079 \cdot 10^{+05}$	0*
(43)	$1\text{-C}_5\text{H}_{11}\cdot \rightarrow 1\text{-C}_3\text{H}_7\cdot + \text{C}_2\text{H}_4$	$7.9061 \cdot 10^{+05}$	0*
(44)	$2\text{-C}_5\text{H}_{11}\cdot \rightarrow \text{C}_2\text{H}_5\cdot + \text{C}_3\text{H}_6$	$8.1393 \cdot 10^{+04}$	0*
(45)	$2\text{-methyl-1-butyl}\cdot \rightarrow \text{C}_2\text{H}_5\cdot + \text{C}_3\text{H}_6$	$1.5978 \cdot 10^{+05}$	0*
(46)	$\text{H}\cdot + \text{C}_2\text{H}_4 \rightarrow \text{C}_2\text{H}_5\cdot$	$8.0175 \cdot 10^{+09}$	0.4892
(47)	$\text{H}\cdot + \text{C}_3\text{H}_6 \rightarrow 2\text{-C}_3\text{H}_7\cdot$	$3.7913 \cdot 10^{+09}$	0*
(48)	$\text{H}\cdot + \text{C}_3\text{H}_6 \rightarrow 1\text{-C}_3\text{H}_7\cdot$	$1.3296 \cdot 10^{+09}$	0
(49)	$\text{CH}_3\cdot + \text{C}_2\text{H}_4 \rightarrow 1\text{-C}_3\text{H}_7\cdot$	$1.0937 \cdot 10^{+06}$	0*
(50)	$\text{CH}_3\cdot + \text{C}_3\text{H}_6 \rightarrow 2\text{-C}_4\text{H}_9\cdot$	$3.3051 \cdot 10^{+06}$	0*
(51)	$\text{CH}_3\cdot + \text{C}_3\text{H}_6 \rightarrow 2\text{-methyl-1-propyl}\cdot$	$1.1591 \cdot 10^{+06}$	0*
(52)	$\text{C}_2\text{H}_5\cdot + \text{C}_2\text{H}_4 \rightarrow 1\text{-C}_4\text{H}_9\cdot$	$5.8298 \cdot 10^{+05}$	0*
(53)	$\text{C}_2\text{H}_5\cdot + \text{C}_3\text{H}_6 \rightarrow 2\text{-C}_5\text{H}_{11}\cdot$	$3.9122 \cdot 10^{+05}$	0*
(54)	$1\text{-C}_3\text{H}_7\cdot + \text{C}_3\text{H}_6 \rightarrow 2\text{-C}_6\text{H}_{13}\cdot$	$8.4384 \cdot 10^{+05}$	0*
(55)	$2\text{-C}_3\text{H}_7\cdot + \text{C}_2\text{H}_4 \rightarrow 3\text{-methyl-1-butyl}\cdot$	$5.6627 \cdot 10^{+05}$	0*
(56)	$2\text{-C}_3\text{H}_7\cdot + \text{C}_3\text{H}_6 \rightarrow 4\text{-methyl-2-pentyl}\cdot$	$5.6627 \cdot 10^{+05}$	0*
(57)	$\text{C}_2\text{H}_5\cdot + \text{C}_3\text{H}_6 \rightarrow 2\text{-methyl-1-butyl}\cdot$	$1.3720 \cdot 10^{+05}$	0*
(58)	$1\text{-C}_5\text{H}_{11}\cdot \rightarrow 2\text{-C}_5\text{H}_{11}\cdot$	$4.4305 \cdot 10^{+05}$	0*
(59)	$2\text{-C}_5\text{H}_{11}\cdot \rightarrow 1\text{-C}_5\text{H}_{11}\cdot$	$6.8604 \cdot 10^{+04}$	0*
(60)	$1\text{-C}_6\text{H}_{13}\cdot \rightarrow 2\text{-C}_6\text{H}_{13}\cdot$	$1.6935 \cdot 10^{+06}$	0*
(61)	$2\text{-C}_6\text{H}_{13}\cdot \rightarrow 1\text{-C}_6\text{H}_{13}\cdot$	$2.6223 \cdot 10^{+05}$	0*
(62)	$\text{H}\cdot + 2\text{-C}_3\text{H}_7\cdot \rightarrow \text{C}_3\text{H}_8$	$1.0000 \cdot 10^{+11}$	0*
(63)	$\text{CH}_3\cdot + \text{CH}_3\cdot \rightarrow \text{C}_2\text{H}_6$	$2.5119 \cdot 10^{+10}$	0
(64)	$\text{CH}_3\cdot + 1\text{-C}_3\text{H}_7\cdot \rightarrow \text{n-C}_4\text{H}_{10}$	$1.9953 \cdot 10^{+10}$	0*
(65)	$\text{CH}_3\cdot + 2\text{-C}_3\text{H}_7\cdot \rightarrow 2\text{-methylpropane}$	$1.5849 \cdot 10^{+10}$	2.5848
(66)	$\text{CH}_3\cdot + \text{C}_3\text{H}_5\cdot \rightarrow 1\text{-C}_4\text{H}_8$	$1.9953 \cdot 10^{+10}$	1.4427
(67)	$\text{C}_2\text{H}_5\cdot + 2\text{-C}_3\text{H}_7\cdot \rightarrow 2\text{-methylbutane}$	$7.9433 \cdot 10^{+09}$	0*
(68)	$\text{C}_2\text{H}_5\cdot + \text{C}_3\text{H}_5\cdot \rightarrow 1\text{-C}_5\text{H}_{10}$	$1.0000 \cdot 10^{+10}$	1.2315
(69)	$1\text{-C}_3\text{H}_7\cdot + 2\text{-C}_3\text{H}_7\cdot \rightarrow 2\text{-methylpentane}$	$7.9433 \cdot 10^{+09}$	0
(70)	$1\text{-C}_3\text{H}_7\cdot + \text{C}_3\text{H}_5\cdot \rightarrow 1\text{-C}_6\text{H}_{12}$	$1.0000 \cdot 10^{+10}$	0*
(71)	$2\text{-C}_3\text{H}_7\cdot + 2\text{-C}_3\text{H}_7\cdot \rightarrow \text{product}$	$3.1623 \cdot 10^{+09}$	0
(72)	$2\text{-C}_3\text{H}_7\cdot + \text{C}_3\text{H}_5\cdot \rightarrow \text{product}$	$1.0000 \cdot 10^{+10}$	0.9624
(73)	$\text{C}_3\text{H}_5\cdot + \text{C}_3\text{H}_5\cdot \rightarrow (\text{C}_3\text{H}_5)_2$	$6.3096 \cdot 10^{+09}$	1.1095
(74)#	$\text{C}_3\text{H}_5\cdot + \text{C}_4\text{H}_7\cdot \rightarrow 1,5\text{-heptadiene}$	$1.2589 \cdot 10^{+10}$	-
(75)	$\text{CH}_3\cdot + \text{C}_2\text{H}_5\cdot \rightarrow \text{C}_3\text{H}_8$	$1.9953 \cdot 10^{+10}$	0*
(76)#	$\text{CH}_3\cdot + \text{C}_4\text{H}_7\cdot \rightarrow 2\text{-C}_5\text{H}_{10}$	$2.5119 \cdot 10^{+10}$	-

	Reactions	Rate coefficients	
		Original	Reduced
(77)	$C_2H_5\cdot + C_2H_5\cdot \rightarrow n-C_4H_{10}$	$3.9811 \cdot 10^{+09}$	0*
(78)#	$C_2H_5\cdot + C_4H_7\cdot \rightarrow 2-C_6H_{12}$	$1.0000 \cdot 10^{+10}$	-
(79)	$H\cdot + 2-C_3H_7\cdot \rightarrow C_3H_6 + H_2$	$5.0119 \cdot 10^{+10}$	0*
(80)	$CH_3\cdot + 1-C_3H_7\cdot \rightarrow C_3H_6 + CH_4$	$1.2589 \cdot 10^{+09}$	0*
(81)	$CH_3\cdot + 2-C_3H_7\cdot \rightarrow C_3H_6 + CH_4$	$2.5119 \cdot 10^{+09}$	0
(82)#	$CH_3\cdot + C_4H_7\cdot \rightarrow C_4H_6 + CH_4$	$7.9433 \cdot 10^{+09}$	
(83)	$C_2H_5\cdot + 2-C_3H_7\cdot \rightarrow C_3H_6 + C_2H_6$	$1.5849 \cdot 10^{+09}$	0*
(84)	$1-C_3H_7\cdot + 2-C_3H_7\cdot \rightarrow C_3H_6 + C_3H_8$	$1.5849 \cdot 10^{+09}$	0*
(85)	$2-C_3H_7\cdot + 2-C_3H_7\cdot \rightarrow C_3H_6 + C_3H_8$	$1.9953 \cdot 10^{+09}$	0.6416
(86)#	$2-C_3H_7\cdot + C_4H_7\cdot \rightarrow C_4H_6 + C_3H_8$	$5.0119 \cdot 10^{+09}$	-
(87)#	$C_3H_5\cdot + C_4H_7\cdot \rightarrow C_4H_6 + C_3H_6$	$6.3096 \cdot 10^{+09}$	-
(88)	$C_3H_5\cdot + C_2H_5\cdot \rightarrow C_2H_4 + C_3H_6$	$1.2589 \cdot 10^{+09}$	0*
(89)	$C_3H_5\cdot + 1-C_3H_7\cdot \rightarrow C_3H_6 + C_3H_6$	$1.0000 \cdot 10^{+09}$	0*
(90)	$C_3H_5\cdot + 2-C_3H_7\cdot \rightarrow C_3H_6 + C_3H_6$	$1.0000 \cdot 10^{+09}$	0
(91)	$C_2H_5\cdot + 2-C_3H_7\cdot \rightarrow C_3H_8 + C_2H_4$	$1.2589 \cdot 10^{+09}$	0*
(92)	$1-C_3H_7\cdot + 2-C_3H_7\cdot \rightarrow C_3H_8 + C_3H_6$	$1.2589 \cdot 10^{+09}$	0 *
(93)	$CH_3\cdot + C_2H_5\cdot \rightarrow C_2H_4 + CH_4$	$7.9433 \cdot 10^{+08}$	0*
(94)	$C_2H_5\cdot + C_2H_5\cdot \rightarrow C_2H_4 + C_2H_6$	$5.0119 \cdot 10^{+08}$	0*
(95)	$C_2H_5\cdot + 2-C_4H_9\cdot \rightarrow 2-C_4H_8 + C_2H_6$	$1.5849 \cdot 10^{+09}$	0*
(96)#	$C_2H_5\cdot + C_4H_7\cdot \rightarrow C_4H_6 + C_2H_6$	$3.9811 \cdot 10^{+09}$	-
(97)	$C_2H_5\cdot + 2-C_4H_9\cdot \rightarrow n-C_4H_{10} + C_2H_4$	$7.9433 \cdot 10^{+08}$	0*
(98)#	$C_2H_5\cdot + C_4H_7\cdot \rightarrow C_2H_4 + \text{olefin}$	$1.0000 \cdot 10^{+09}$	-

6. Conclusions

A robust numerically stable method for reducing the complexity of large chemical reaction networks is constructed as a sequence of MIQPs where the objective function is derived from the parametric sensitivity matrix. The algorithm uses a given detailed kinetic mechanism and measured data of the key species over a finite time horizon to determine the set of reactions as subsets of the reactions in the detailed mechanism, together with a re-estimated value of the reaction kinetic parameters. The proposed method sequentially eliminates reactions from the mechanism until the pre-specified tolerance limit in the species concentration space is reached.

The computational efficiency and numerical stability of the optimization

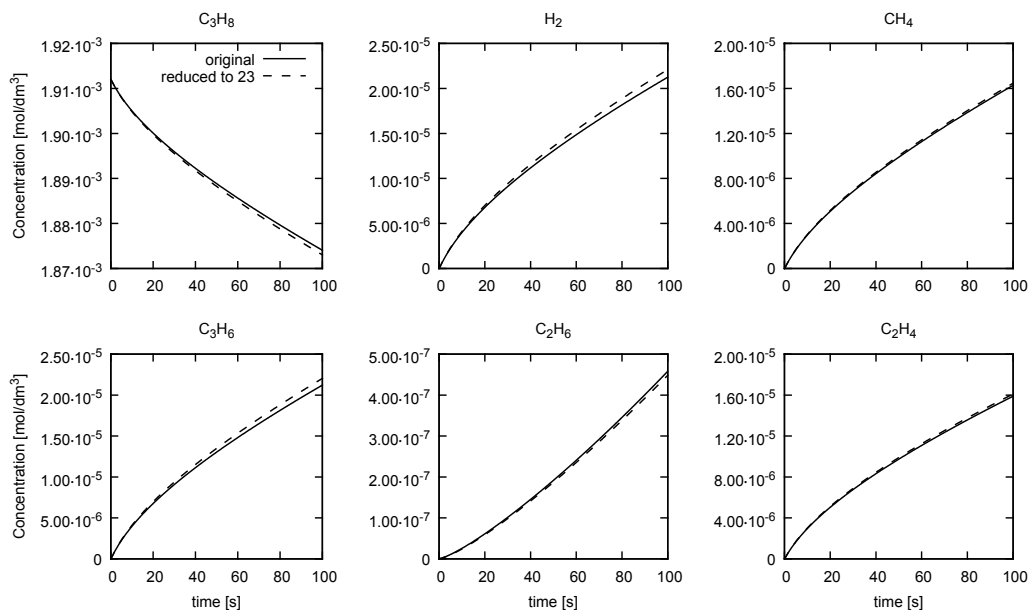


Figure 7: The concentrations of each important species in the original system and in the reduced system.

is improved by applying a pre-reduction step, followed by suitable scaling and initial conditioning of the Hessian involved.

The proposed complexity reduction method is illustrated using two case studies taken from the reaction kinetics literature.

It is expected that the proposed method can be extended to make it suitable for eliminating the non-influential species, i.e. the species that do not change their concentration values over the time interval of interest. This is a possible direction of further work.

A further possible generalization step would be to use the same algorithmic principles applied to general nonlinear models that are linear in their parameters. However, much further work is needed to make this extended algorithm robust and numerically stable by developing suitable pre-reduction, scaling and initial conditioning of the Hessian.

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