

The effect of conservation on the dynamics of chemical reaction networks

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Abstract: Component mass conservation gives a linear first integral to the dynamic reaction kinetic equations and greatly influences the set of admissible reactions. Therefore, mass conservation can be related to the deficiency of the reaction network and thus to its dynamic properties. In particular, it is shown that a mass conserving CRN without isomers and with a full rank complex composition matrix has zero deficiency. The concepts and results are illustrated on the example of the original and the lumped version of Michaelis-Menten kinetics.

Keywords: Process control; Chemical variables control; Modelling; Graph theoretic models; Structural stability;

1. INTRODUCTION

It is well-known that kinetic systems form a wide class of nonlinear models with good dynamical descriptive properties [3]. Therefore (bio)chemical reaction networks (CRNs) are often used to model complex biological mechanisms [11], or even to describe dynamical systems in application fields seemingly far from chemistry such as mechanical or electrical systems [12]. The increasing and extended interest towards this field is shown by the fact that numerous surveys and tutorials have been published even in journals where the primary scope is not chemistry [1, 2, 13].

The classical chemical theory of deterministic CRNs obeying the mass action law (MAL CRNs) assumes closed isotherm and isobaric conditions, where the total mass is conserved. This mass conservation applies also for the set of species that participate in any chemical reaction. It is intuitively clear, that a MAL CRN system with these mass conservations should not produce any “exotic” nonlinear behavior, but will be globally stable within each stoichiometric compatibility class.

The mathematical generalization of MAL CRN systems, however, does not require conservation assumptions, that allows the description of various nonlinear behaviour like multiplicities, limit cycles or even chaotic phenomena. Naturally, this generalization makes the MAL CRN system class to be a wide class of smooth positive nonlinear systems.

The aim of this paper is to investigate the dynamic consequences of conservations on the qualitative properties of MAL CRN dynamics.

2. BASIC NOTIONS

Consider a CRN that obeys the mass action law. The structure of the CRN is uniquely given in terms of its Kirchhoff matrix A_k and its complex composition matrix $Y \in \mathbb{Z}_{+0}^{n \times m}$ with non-negative integer elements, the columns of which describe the composition of its complexes C_i , $i = 1, \dots, m$ over its species X_j , $j = 1, \dots, n$. The Kirchhoff matrix $A_k \in \mathbb{R}^{m \times m}$ describes the structure of chemical reactions $C_i \mapsto C_j$ with the reaction rate coefficient $k_{ij} > 0$.

The following general assumptions are considered throughout this paper.

- (G1) There is no isolated (i.e. unconnected) complex in the CRN.
- (G2) There is no inert (i.e. non-reacting) specie in the system.
- (G3) Y is of full rank.

Assumption (G3) implies that

- the columns of Y are linearly independent in the $n \geq m$ case
- the rows of Y are linearly independent in the $n \leq m$ case

Both the reaction graph determined by the matrix A_k and the properties of Y influence the structural dynamical properties of a CRN. Let us introduce the following notations.

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$$[Y]_{ij} = \alpha_{ij} \quad , \quad [A_k]_{ij} = \begin{cases} -\sum_{l=1}^m k_{il} & \text{if } i = j \\ k_{ji} & \text{if } i \neq j \end{cases} \quad (1)$$

With the above matrices the time evolution of the specie concentrations $x = [x_1, \dots, x_n]^T$ is described by the following set of ODEs:

$$\frac{dx}{dt} = Y A_k \varphi(x) \quad , \quad \varphi_i(x) = \prod_{j=1}^m x_j^{\alpha_{ij}} \quad (2)$$

2.1 The reaction graph

The vertexes V of the reaction graph $G = (V, E)$ correspond to the complexes, and the edges E to the reactions. Two complexes C_k and C_l are connected by a directed edge $C_k C_l$, if a reaction in the form of $C_k \mapsto C_l$ exists. Edge weights can be associated to the edges that are the reaction rate constants $k_{kl} > 0$, thus the reaction graph is a weighted directed graph.

Note that the Kirchhoff matrix A_k of a CRN uniquely determines its reaction graph and vice versa. However, the Kirchhoff matrix of the reaction graph does not uniquely determine the reaction kinetic system itself, since the information on the composition of the complexes is missing from the graph: it is contained in the complex composition matrix Y .

2.2 The deficiency of a CRN

The stoichiometric subspace First we define the set of *reaction vectors* as: $\mathcal{R} = \{\rho^{(l,k)} = \eta^{(l)} - \eta^{(k)} \mid C_k C_l \in E \text{ in } G\}$, where $\eta^{(i)}$ denotes the i th column of Y .

The deficiency is an integer number which depends on the properties of matrix Y , and on the structure of the reaction graph G . The *deficiency* δ is defined as:

$$\delta = m - \ell - s \quad (3)$$

where m is the number of complexes and ℓ is the number of connected components in the reaction graph, while s is the dimension of the stoichiometric sub-space, i.e. $s = \text{rank}(\mathcal{R})$.

The deficiency zero theorem An important structural property of CRNs is (weak) reversibility. A CRN is called weakly reversible if whenever there exists a directed path from complex C_i to C_j in the reaction graph, then there exists a directed path from C_j to C_i . The main result of the well-known deficiency zero theorem is the parameter-independent robust stability of weakly reversible deficiency zero CRNs. The exact form of the theorem is taken from [6].

Deficiency Zero Theorem. For any reaction network of deficiency zero the following statements hold true:

- (1) If the network is not weakly reversible then, for arbitrary kinetics (not necessarily mass action), the differential equations for the corresponding reaction system cannot admit a positive steady state (i.e. a steady state in \mathbb{R}_+^n).

- (2) If the network is not weakly reversible then, for arbitrary kinetics (not necessarily mass action), the differential equations of the corresponding reaction system cannot admit a cyclic composition trajectory along which all species concentrations are positive.
- (3) If the network is weakly reversible then, for mass action kinetics (but regardless of the positive values the reaction rate coefficients take), the differential equations of the corresponding reaction system have the following properties: There exists within each positive stoichiometric compatibility class precisely one steady state; that steady state is asymptotically stable; and there is no nontrivial cyclic composition trajectory along which all species concentrations are positive.

2.3 Conservation equations

Mass conservative chemical reactions Let us assume that the given set of chemical reactions is *physically plausible*, i.e. each reaction obeys the mass conservation. This means, that for each reaction $C_l \mapsto C_p$, the following equality holds

$$\sum_{i=1}^n \alpha_{il} \mathcal{M}_i = \sum_{i=1}^n \alpha_{ip} \mathcal{M}_i = c_s, \quad (4)$$

where $\mathcal{M}_i > 0$ is the molecular weight of the component X_i , l and p are column indexes in Y and $c_s > 0$ is a constant weighted column-sum. Let us form a row vector $M \in \mathbb{R}^n$ from the molecular weights, then the above equation can be written as

$$M \cdot \eta^{(l)} = M \cdot \eta^{(p)} = c_s, \quad \text{or} \quad M \cdot \rho^{(l,p)} = 0 \quad (5)$$

where $\rho^{(l,p)}$ is the corresponding reaction vector. A set of reactions with the above property will be called **mass conservative reaction set**.

The zero complex is a special complex that is used to describe the environment with infinite source and sink capacity for all components. The zero complex \emptyset is described algebraically by a zero column vector in Y , i.e. $\eta^{(0)} = \underline{0}_n^T \in \mathbb{R}^n$. Eq. (4) shows that **a reaction in the form of $C_i \mapsto \emptyset$ or $\emptyset \mapsto C_i$ cannot be part of a mass conservative reaction set**.

Conservation in the specie concentration space The column conservation property of A_k can be expressed algebraically as $\underline{1}_m \cdot A_k = \underline{0}_m$, where $\underline{1}_m$ is the m -elements row vector with identically 1 entries. In addition, equation (4) states that the weighted column-sum of any column in Y is the same (c_s), where the weights are the molecular weights \mathcal{M}_i . Therefore, we can form a weighted column-summation vector w such that

$$w \cdot Y = \underline{1}_m \Rightarrow w \cdot Y \cdot A_k = \underline{0}_m \quad (6)$$

with $w = [\frac{\mathcal{M}_1}{c_s}, \dots, \frac{\mathcal{M}_m}{c_s}]$, that is the weighted mass conservation property in the specie concentration space.

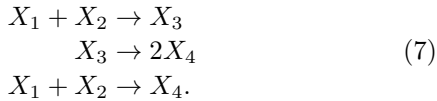
3. THE EFFECT OF THE CONSERVATION EQUATIONS ON THE STRUCTURAL PROPERTIES OF A CRN

The conservation equations (4) or (5) show that they put an algebraic constraint on the columns of the complex

composition matrix Y . At the same time, they partition the set of reactions that is reflected in the linkage classes of the CRN. Therefore, two different cases will be considered: first reaction graphs forming a single linkage class (i.e. connected component) is investigated, thereafter the multiple connected component case is discussed. The effect of conservation equations on the deficiency of the CRN will be investigated, because it may have a determining effect on its dynamic properties.

3.1 The mass conservation relation between complexes

Based on the above, we say that two complexes C_i and C_j in a CRN are in a *mass conserving relation* if there exists an (elementwise) strictly positive vector M such that $M\eta^{(i)} = M\eta^{(j)}$. Clearly, any reaction $C_i \rightarrow C_j$ obeys the mass conservation if and only if C_i and C_j are in a mass conserving relation, and this property only depends on the i th and j th columns of the complex composition matrix Y . Naturally, it is not enough for a CRN to be mass-conserving that the reacting complex-pairs are individually in a mass conserving relation. E.g. the following simple CRN consists of reacting complex-pairs in mass conserving relations, although the entire network is not mass conserving:



Therefore, it is possible only in certain cases to decide whether a CRN violates mass conservation by inspecting the reactions individually (see the examples later).

With a fixed M , the mass conserving relation is clearly symmetric and transitive (and it is also reflexive, if we consider complexes trivially reacting to themselves). Obviously, an entire CRN is mass-conservative if and only if all reacting complex pairs are in mass conserving relations with one common positive M .

Note that our chemically motivated notion of mass conservation is not equivalent to the definition that is often used in chemical reaction network theory. According to the latter, a CRN is sometimes called mass-conservative if and only if there exists a strictly positive vector in the kernel of $(Y \cdot A_k)^T$ [7]. Consider the simple network in Eq. (7) where all the rate coefficients are 1 for simplicity. Then, the Y and A_k matrices of the network are the following:

$$Y = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 2 & 1 \end{bmatrix}, \quad A_k = \begin{bmatrix} -2 & 0 & 0 & 0 \\ 1 & -1 & 0 & 0 \\ 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 0 \end{bmatrix} \quad (8)$$

It can be checked that the positive vector

$$[0.7693 \ 0.0265 \ 1.0611 \ 0.5306]^T$$

is in the kernel of $(Y \cdot A_k)^T$ but the CRN is not mass conserving according to our definition.

3.2 The single connected component case

Assume we have a CRN with a mass conservative reaction set (implying the absence of the zero complex). Recalling that isolated complexes are not allowed, with m complexes we should have at least $r_m = m - 1$ reactions in the

single connected component (i.e. $\ell = 1$) case. Moreover, the constant $c_s > 0$ in Eq. (5) is the same for all reactions, and the Kirchhoff matrix A_k consists of a single column-conservation block in this case.

A simple example A simple reaction graph with $n = 3$ species (A, B, C) and $m = 3$ complexes is shown in Fig. 1. The minimum set of reactions with reaction vectors

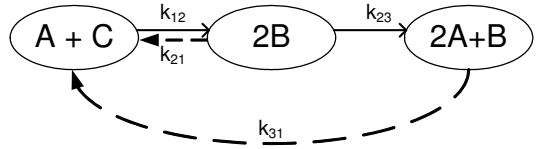


Fig. 1. The structure graph of the simple example of a single linkage class

$$\rho^{(1,2)} = \begin{bmatrix} 1 \\ -2 \\ 1 \end{bmatrix}, \quad \rho^{(2,3)} = \begin{bmatrix} -2 \\ 1 \\ 0 \end{bmatrix} \quad (9)$$

is denoted by continuous edge lines in the figure.

The maximum number of complexes in a single connected component with a mass conservative reaction set can be determined by the defining equation (5) $M \cdot \eta^{(j)} = c_s$, $j = 1, \dots, m$ where $\eta^{(j)} \in \mathbb{Z}_{+0}^n$ is the column of the matrix Y corresponding to the complex C_j , and $M^T \in \mathbb{R}^n$ is the vector of the molecular weights with positive elements. There are two possible cases to consider.

(i) $m \leq n$

As Y is of full rank, the complexes form a linearly independent set of column vectors, and there is infinitely many such molecular weight vectors M that satisfies Eq.(5). (In the case of $m = n$ and fixed c_s one has a unique solution M).

(ii) $m > n$

Then, with c_s and M fixed, we can have maximum n different and linearly independent complexes, since the linear set of equations

$$M \cdot Y^* = [c_s, c_s, \dots, c_s] \quad (10)$$

would uniquely determine M from a given $Y^* \in \mathbb{Z}_+^{n \times n}$, where we have collected the set of linearly independent complex vectors to the matrix Y^* .

We shall now show that we can not have more complexes corresponding to a column of $\eta^{(j)}$, $j > n$ from the rest of Y that is both linearly dependent of the columns of Y^* ($\eta^{(1)}, \dots, \eta^{(n)}$) and satisfies $M \cdot \eta^{(j)} = c_s$. Let us assume that this dependent column of Y is in the form of a linear combination

$$\eta^{(j)} = \varphi_1 \eta^{(1)} + \dots + \varphi_n \eta^{(n)} \quad (11)$$

If we multiply both sides by the row vector M , the equation

$$c_s = c_s(\varphi_1 + \dots + \varphi_n) \implies \varphi_1 + \dots + \varphi_n = 1 \quad (12)$$

is obtained. But the coefficients in the linear combination (11) are uniquely determined, therefore they can satisfy the additional constraint (12) originating from the mass conservation only in a very special fortunate case when $\mathcal{M}_i = \mathcal{M}_k$ for some (i, k) specie

pair. The corresponding species X_i and X_k are then called *isomers* in the chemical terminology.

An example of isomers Let us have only two species X_1 and X_2 in a CRN, and let $\mathcal{M}_1 = \mathcal{M}_2 = 1$ with $c_s = 2$. Then the columns of the complex composition matrix with three complexes $2X_1, 2X_2, X_1 + X_2$

$$Y = \begin{bmatrix} 2 & 0 & 1 \\ 0 & 2 & 1 \end{bmatrix}$$

satisfy both Eq. (11) and the additional constraint (12) when $3 = m > n = 2$.

Deficiency Now we only need to consider the $n \geq m$ case. Because of the full rank property of Y the columns of it are linearly independent and span a maximum m dimensional stoichiometric subspace, i.e. $s = \text{rank}(\mathcal{R}) \leq m$. At the same time we have $s \geq m - 1$ because of the minimum number of reactions.

If $r \geq m$ then the conservation equations (5) put an additional linear relationship to the reaction vectors, therefore $s = m - 1$, otherwise $s = r_m = m - 1$. Therefore, in both cases we have $\delta = m - \ell - s = m - 1 - m + 1 = 0$.

Simple example continued Fig. 1 shows that $m = n = 3$ in this case. If one chooses the molecular weight of specie A to be 1, then the molecular weight vector is $M = [1 \ 2 \ 3]$, and $c_s = 4$. The reaction vectors in Eq. (9) span the stoichiometric sub-space, therefore $s = 2$ and $\delta = 0$.

Is is easy to see that the dimension of the stoichiometric sub-space will not increase if one adds any further reaction to the CRN. For example, the reaction vectors of two reactions denoted by dashed lines in Fig. 1 can be expressed as $\rho^{(2,1)} = -\rho^{(1,2)}$, and $\rho^{(3,1)} = -(\rho^{(1,2)} + \rho^{(2,3)})$.

3.3 Multiple connected component cases

Assume a mass action law CRN with only mass conservative reactions that has ℓ linkage classes, i.e. ℓ connected components in its reaction graph. Then the set of complexes are partitioned according to these linkage classes, where the partitions have m_j , $j = 1, \dots, \ell$ members, respectively, where $m = m_1 + \dots + m_\ell$.

Determination of the molecular weights As chemical reactions connect only complexes within the same linkage class L_j , the conservation equation $M \cdot \eta^{(i)} = c_s^{(j)}$ is valid only if the corresponding complex C_i is in L_j , and the constant $c_s^{(j)}$ may be different for different linkage classes. However, for any reaction vector $\rho^{(i,p)}$ the conservation equation has the same form $M \cdot \rho^{(i,p)} = 0$. This enables to compute the molecular weight vector M that is joint for the entire CRN as follows.

Let us form the reaction matrix R from the reaction vectors $\rho^{(i,p)}, C_i C_p \in E$ of the reaction graph G . The rank of this matrix is equal to the dimension of the stoichiometric sub-space, i.e. $n \geq s = \text{rank}(R)$. At the same time, the reaction vectors are formed as differences

of the component vectors $\rho^{(i,p)} = \eta^{(i)} - \eta^{(p)}$, thus the rank of R is is constrained by $n \geq \text{rank}(Y) \geq \text{rank}(R)$. Now we can form the matrix R^* from a set of s linearly independent reaction vectors, that gives rise to the linkage class independent form of the conservation equations

$$M \cdot R^* = [0, 0, \dots, 0] \quad (13)$$

The elements $\mathcal{M}_i > 0$ of the molecular weight vector can be determined from the above equation by fixing $n - s - 1$ molecular weights \mathcal{M}_i (such that $\mathcal{M}_i \neq \mathcal{M}_p$ for $i \neq p$) that we could uniquely determine the rest from Eq. (13).

Then for each linkage class L_j we can compute the constant $c_s^{(j)}$ by finding a complex $\eta^{(i)}$ from this class and computing $M \cdot \eta^{(i)} = c_s^{(j)}$.

The maximal dimension of the stoichiometric sub-space Because of the above linkage class independent form of the conservation equations (13), and the given constant positive nature of the component weight vector $M \in \mathbb{R}_+^n$, the maximal number of the linearly independent reaction vectors is $n - 1$. This implies that the maximal dimension of the stoichiometric sub-space $s_m = n - 1$.

The maximal set of the linearly independent reaction vectors can also be partitioned according to the linkage class they belong to, as no reaction is taking place between complexes in different linkage classes. Let the number of such reactions belonging to the linkage class L_j be denoted by $r_j \geq 1$, such that $r_1 + \dots + r_\ell = s \leq n - 1$. Here we have accounted for the fact that the stoichiometric subspace may not be maximal.

The number of complexes in a linkage class induced by the set of linearly independent reaction vectors can be determined from the fact, that at least $m_j = r_j + 1$ linearly independent column vectors η^i corresponding to complexes C_i are needed to generate this set and to form a connected component with r_j edges. On the other hand, if we added new different complexes within this linkage class then the number of linearly independent reaction vectors would increase, therefore we could only add new reactions between the existing complexes to keep this situation. Finally we conclude that r_j linearly independent reaction vector induces $m_j = r_j + 1$ linearly independent complexes.

The overall number of complexes can be computed as

$$m = \sum_{j=1}^{\ell} m_j = \sum_{j=1}^{\ell} (r_j + 1) = s + \ell \quad (14)$$

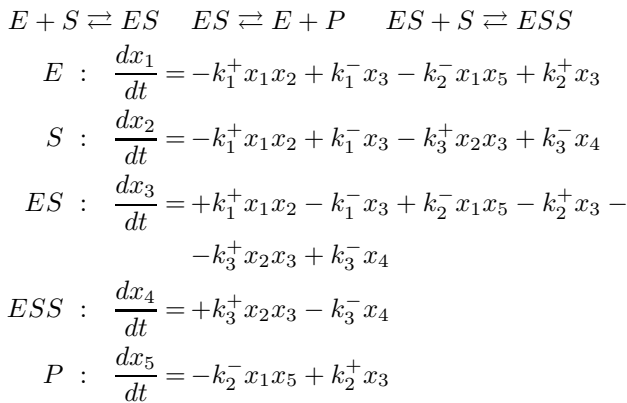
The deficiency Now we can assemble the above results to determine the deficiency of the CRN with only mass conservative reactions that has ℓ linkage classes. This is computed by the definition as $\delta = m - s - \ell = s + \ell - s - \ell = 0$ using Eq. (14).

4. CASE STUDY: CONSERVATION IN THE VERSIONS OF THE MICHAELIS-MENTEN REACTION SCHEME

The aim of this section is to show how the model reduction (or simplification) transformation can destroy the conservation properties of an originally physically plausible model, and what are the structural and dynamic consequences of this. The detailed description of the Michaelis-Menten reaction scheme and the applied model reduction transformations can be found in [8].

4.1 The original full scheme

The Michaelis-Menten reaction scheme describes a simple enzyme-kinetic reaction with the following reaction and dynamic model equations



where the concentration state vector x is formed as

$$x_1 = [E], \quad x_2 = [S], \quad x_3 = [ES], \quad x_4 = [ESS], \quad x_5 = [P]$$

from the species E for the enzyme, S for the substrate, P for the product, and ES and ESS being intermediate chemical complexes.

The dynamical behavior of the concentration variables and the reaction graph that consists of two reversible connected components are seen in figure 2, with the following model parameters used for the simulations:

$$k_1^+ = 1, \quad k_1^- = 0.8, \quad k_2^+ = 1.1, \quad k_2^- = 0.75, \quad k_3^+ = 2, \quad k_3^- = 1.8$$

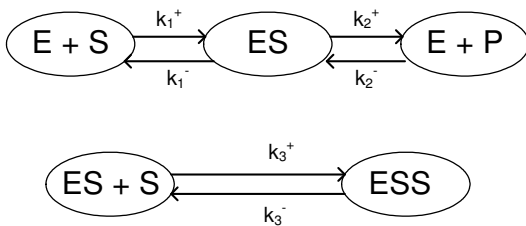


Fig. 2. The structure graph of the Michaelis-Menten reaction scheme

Conservation analysis This CRN clearly obeys the mass conservation. Now we have two "free" molecular weights that we can fix, that are $M_1 = \mathcal{M}_E = 2$ and $M_2 = \mathcal{M}_S = 1$. Then a vector M obeying the mass conservation is

$$M = [2 \ 1 \ 3 \ 4 \ 1]$$

and the constants are $c_s^{(1)} = 3$ and $c_s^{(2)} = 4$.

The *deficiency* is computed from the definition, with $m = 5$, $\ell = 2$ and $s = 3$. Then the deficiency of this reversible model is zero, therefore its equilibrium points are stable because of the deficiency zero theorem.

4.2 The lumped reaction scheme

The two intermediate species ES and ESS with similar dynamics are lumped to form the lumped pseudo-component E_S with concentration $\bar{x}_3 = [E_S]$. Then the equations needed for the transformation are

$$\bar{x}_3 = x_3 + x_4, \quad x_3 = \frac{1}{2}\bar{x}_3, \quad x_4 = \frac{1}{2}\bar{x}_3 \quad (15)$$

and the concentration variable x_4 is left out from the model. The idea behind this transformation is that species concentrations with "similar" dynamics are essentially approximately identical, that is seen from (15).

The reduced kinetic equations are

$$\frac{dx_1}{dt} = -k_1^+ x_1 x_2 + \frac{1}{2}k_1^- \bar{x}_3 + \frac{1}{2}k_2^+ \bar{x}_3 - k_2^- x_1 x_5 \quad (16)$$

$$\frac{dx_2}{dt} = -k_1^+ x_1 x_2 + \frac{1}{2}k_1^- \bar{x}_3 + \frac{1}{2}k_3^- \bar{x}_3 - \frac{1}{2}k_3^+ x_2 \bar{x}_3 \quad (17)$$

$$\frac{d\bar{x}_3}{dt} = k_1^+ x_1 x_2 - \frac{1}{2}k_1^- \bar{x}_3 - \frac{1}{2}k_2^+ \bar{x}_3 + k_2^- x_1 x_5 \quad (18)$$

$$\frac{dx_5}{dt} = \frac{1}{2}k_2^+ \bar{x}_3 - k_2^- x_1 x_5 \quad (19)$$

It is important to note that the number of complexes has also been reduced by one, as both ES and ESS formed complexes that were replaced by a new complex formed by E_S . Thus the new complex composition matrix Y is in the form

$$Y = \begin{bmatrix} 1 & 0 & 0 & 0 \\ 1 & 0 & 0 & 1 \\ 0 & 1 & 0 & 1 \\ 0 & 0 & 1 & 0 \end{bmatrix}$$

and the reaction graph is depicted in Fig. 3

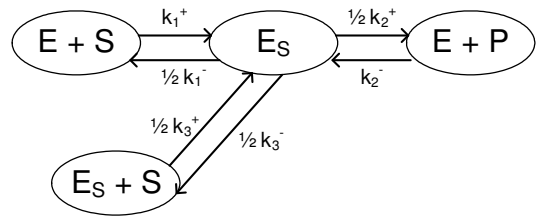
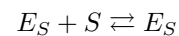


Fig. 3. Reaction graph of the lumped Michaelis-Menten scheme

Conservation analysis This CRN does not obey the mass conservation, that is seen from the presence of the reaction



in the network. The reaction vector $\rho^{(*)} = \eta^{(4)} - \eta^{(2)}$ corresponding to this reaction pair is $\rho^{(*)} = [0 \ 1 \ 0 \ 0]^T$, that contains only a positive element besides of the zero ones, and thus can not fulfil the conservation constraint $M\rho^{(*)} = 0$ for any positive molecular weight vector M .

Deficiency and structural stability Because of the condensation of two complexes, the number of complexes is now $\bar{m} = 4$, and the number of linkage classes is also reduced by one, i.e. $\bar{l} = 1$. The dimension of the stoichiometric space remains $s = 3$, therefore the reduced model is of zero deficiency, and therefore it is globally stable (we remark that the modified CRN consists of only one linkage class).

4.3 A simplified scheme by using quasi steady state for the specie ES

Let us denote the steady state value of specie ES by x_3^* , and let us notice that ES forms a complex in itself. Therefore, the reduced complex composition matrix \bar{Y} becomes

$$\bar{Y} = \begin{bmatrix} 1 & 0 & 1 & 0 & 0 \\ 1 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 & 0 \end{bmatrix}$$

that shows that the zero complex appears in the reaction kinetic system (see 2nd column of \bar{Y}). The reduced kinetic equations are

$$\frac{dx_1}{dt} = -k_1^+ x_1 x_2 + \bar{k}_1^- - k_2^- x_1 x_5 + \bar{k}_2^+ \quad (20)$$

$$\frac{dx_2}{dt} = -k_1^+ x_1 x_2 + \bar{k}_1^- - \bar{k}_3^+ x_2 + k_3^- x_4 \quad (21)$$

$$\frac{dx_4}{dt} = \bar{k}_3^+ x_2 - k_3^- x_4 \quad (22)$$

$$\frac{dx_5}{dt} = -k_2^- x_1 x_5 + \bar{k}_2^+ \quad (23)$$

where the new reaction rate constants are formed as $\bar{k}_i^\pm = k_i^\pm x_3^*$.

The reaction graph of the reduced system is seen in Fig. 4.

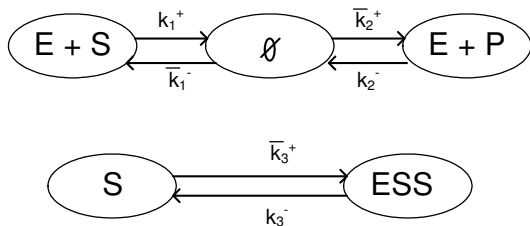


Fig. 4. Reaction graph of the reduced Michaelis-Menten kinetics with ES in quasi steady state

Conservation analysis For the zero complex that appears in the place of ES there is no component mass balance, but the presence of constant positive terms indicate that the systems becomes open.

5. CONCLUSIONS AND FUTURE WORK

In this paper it was shown, that a mass action law CRN with only mass conservative reactions, with a full-rank complex composition matrix Y and without isomers is necessarily of zero deficiency. Therefore, a weakly reversible

conservative CRN having the above mentioned properties possess a unique stable positive equilibrium in each stoichiometric compatibility class.

The mass conservation property can be checked by algebraic methods using only the molecular weights of the components and the complex composition matrix Y , but it has implications on the possible set of complexes and on the chemical reactions that may occur between them, i.e. on the Kirchhoff matrix A_k .

Further analysis is needed to find out how one can recognize the presence of non mass conservative reactions in the network (besides of detecting the zero complex), and – when this fact is not by the intention of modeler – how one can "repair" a non-conservative network when this property is not realistic and/or non-desired.

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