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Analysis of Equilibria Properties of Chemical Reaction Networks with Independent Decompositions for Classes of Kinetics

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Abstract

This paper implements the use of existing decompositions in literature to analyze equilibria properties of chemical reaction networks endowed with classes of kinetics including power-law, poly-PL (i.e., nonnegative linear combination of power-law functions) and quotients of poly-PL functions. In particular, we develop a program where reactions of a network are assigned to subnetworks and determine the independence of the resulting decomposition. Independent decompositions are useful in the sense that with this property, the intersection of the sets of equilibria of the corresponding subsystems is equal to the set of equilibria of the whole system.

1 Introduction

A chemical reaction network (CRN) is composed of reactions which can be seen as interactions among species existing within the system. A CRN endowed with a chemical kinetics is called a chemical kinetic system. This system has a corresponding set of ordinary differential equations, which describes its dynamics over time. On the other hand, Biochemical Systems Theory (BST) is a mathematical and computational approach used

to analyze systems. It was proposed by M. Savageau in the late 1960's. He identified that power-law representation is a valid description of processes in biochemistry. The representation is both general and simple, which turned out to be rich enough to capture typical nonlinearities [22].

Hernandez et al. [11] introduced the Multistationarity Algorithm, a general computational method to determine if a CRN endowed with power-law kinetics has capacity for multistationarity, i.e., whether the system can admit multiple equilibria for particular set of rate constants. This was an extension of the work of H. Ji and M. Feinberg [14], which considers mass actions systems that are actually power-law systems too.

Evolutionary game theory (EGT) considers how groups change their strategy over time based on payoff functions [20]. Veloz et al. illustrated how to model the EGT systems using reaction networks [21]. The applications of EGT is evident in chemistry [15, 17], which were beyond its biological origins. Poly-PL kinetic systems are CRNs endowed with non-negative linear combinations of power-law functions. Poly-PL functions appears in games in EGT. Magpantay et al. [16] then introduced a Multistationarity Algorithm for poly-PL kinetic systems by transforming such systems to power-law systems and then applying the method of Hernandez et al. This method accommodates a larger class of kinetic systems containing the power-laws.

Poly-PL quotient kinetics [10] are rational kinetics that include the Hill-type kinetics which has importance in enzymology, and more generally in biochemistry. In a nutshell, one can convert poly-PL quotient kinetics to poly-PL kinetics and then to power-law [10]. Hence, we emphasize the importance of power-law kinetics (a generalization of mass action) in solving problems of equilibria properties such as multistationarity in kinetic systems.

M. Feinberg established the essential relationship between independent decompositions and the set of positive equilibria of a network in 1987, which we call the Feinberg Decomposition Theorem (FDT) [4]. Moreover, a corresponding relationship between incidence-independent, weakly reversible decompositions and complex-balanced equilibria of a weakly reversible network was provided by Fariñas et al. [3].

This work integrates results of decomposition theory and multistationarity algorithms for systems, which are either power-law, poly-PL, or poly-PL quotient with underlying CRN having independent (known) decompositions. We also provide a general computer

program which is flexible for identifying whether the CRN has independent and incidence-independent decomposition by assigning subnetwork number to each reaction.

The paper is organized as follows: Section 2 provides the fundamentals of chemical reaction networks and chemical kinetic systems. It also presents relevant results from decomposition theory of CRNs and deficiency theorems. Section 3 provides further discussion on some known decompositions in literature. Section 4 gives steps in dealing with multistationarity of power-law, poly-PL, or poly-PL quotient kinetic systems with independent decompositions. Summary and outlook constitute Section 5. Finally, Appendix B provides a program that determines whether the a particular decomposition of a CRN is independent or incidence-independent.

2 Preliminaries

We recall some fundamental notions about chemical reaction networks and chemical kinetic systems [2,5]. In addition, we also present important results on the decomposition theory, which was introduced by Feinberg in [4].

2.1 Fundamentals of chemical reaction networks

Definition 2.1. *A* **chemical reaction network** *(CRN) $\mathscr{N} = (\mathscr{S}, \mathscr{C}, \mathscr{R})$ of nonempty finite sets $\mathscr{S}$, $\mathscr{C} \subseteq \mathbb{R}^{\mathscr{S}}_{\geq 0}$, and $\mathscr{R} \subset \mathscr{C} \times \mathscr{C}$, of m species, n complexes, and r reactions, respectively, such that*

i. $(C_i, C_i) \notin \mathscr{R}$ for each $C_i \in \mathscr{C}$, and

ii. for each $C_i \in \mathscr{C}$, there exists $C_j \in \mathscr{C}$ such that $(C_i, C_j) \in \mathscr{R}$ or $(C_j, C_i) \in \mathscr{R}$.

We can view $\mathscr{C}$ as a subset of $\mathbb{R}^m_{\geq 0}$. The ordered pair (C_i, C_j) corresponds to the familiar notation $C_i \to C_j$.

Definition 2.2. *The* **molecularity matrix**, *denoted by Y, is an $m \times n$ matrix such that Y_{ij} is the stoichiometric coefficient of species X_i in complex C_j. The* **incidence matrix**, *denoted by I_a, is an $n \times r$ matrix such that*

$$(I_a)_{ij} = \begin{cases} -1 & \text{if } C_i \text{ is in the reactant complex of reaction } R_j, \\ 1 & \text{if } C_i \text{ is in the product complex of reaction } R_j, \\ 0 & \text{otherwise.} \end{cases}$$

The **stoichiometric matrix**, *denoted by N, is the $m \times r$ matrix given by $N = YI_a$.*

We denote the standard basis for $\mathbb{R}^{\mathscr{I}}$ by $\left\{\omega_i \in \mathbb{R}^{\mathscr{I}} \mid i \in \mathscr{I}\right\}$.

Definition 2.3. *Let $\mathscr{N} = (\mathscr{S}, \mathscr{C}, \mathscr{R})$ be a CRN. The* **incidence map** *$I_a : \mathbb{R}^{\mathscr{R}} \to \mathbb{R}^{\mathscr{C}}$ is the linear map such that for each reaction $r : C_i \to C_j \in \mathscr{R}$, the basis vector ω_r to the vector $\omega_{C_j} - \omega_{C_i} \in \mathscr{C}$.*

Definition 2.4. *The* **reaction vectors** *for a given reaction network $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ are the elements of the set $\{C_j - C_i \in \mathbb{R}^m | \, (C_i, C_j) \in \mathscr{R}\}$.*

Definition 2.5. *The* **stoichiometric subspace** *of a reaction network $(\mathscr{S}, \mathscr{C}, \mathscr{R})$, denoted by S, is the linear subspace of $\mathbb{R}^m$ given by $S = span\,\{C_j - C_i \in \mathbb{R}^m | \, (C_i, C_j) \in \mathscr{R}\}$. The* **rank** *of the network, denoted by s, is given by $s = \dim S$. The set $(x + S) \cap \mathbb{R}^m_{\geq 0}$ is said to be a* **stoichiometric compatibility class** *of $x \in \mathbb{R}^m_{\geq 0}$.*

Definition 2.6. *Two vectors $x, x^* \in \mathbb{R}^m$ are* **stoichiometrically compatible** *if $x - x^*$ is an element of the stoichiometric subspace S.*

We can view complexes as vertices and reactions as edges. With this, CRNs can be seen as graphs. At this point, if we are talking about geometric properties, **vertices** are complexes and **edges** are reactions. If there is a path between two vertices C_i and C_j, then they are said to be **connected**. If there is a directed path from vertex C_i to vertex C_j and vice versa, then they are said to be **strongly connected**. If any two vertices of a subgraph are **(strongly) connected**, then the subgraph is said to be a **(strongly) connected component**. The **(strong) linkage classes** of a CRN are the (strong) connected components of the graph. The maximal strongly connected subgraphs where there are no edges from a complex in the subgraph to a complex outside the subgraph is said to be the **terminal strong linkage classes**. We denote the number of linkage classes and the number of strong linkage classes by l and sl, respectively. A CRN is said to be **weakly reversible** if $sl = l$.

Definition 2.7. *For a CRN, the* **deficiency** *is given by $\delta = n - l - s$ where n is the number of complexes, l is the number of linkage classes, and s is the dimension of the stoichiometric subspace S.*

Example 2.8. *Consider the CRN with the following reactions.*

$$R_1 : X_1 \to 0$$

$$R_2 : X_2 \to X_3$$

$$R_3 : X_3 \to X_4$$

$$R_4 : 0 \to X_2$$

$$R_5 : X_1 + X_2 \to X_1$$

The molecularity, incidence, and stoichiometric matrices are given in the following equation.

$$\begin{aligned} N &= YI_a \\ &= \begin{bmatrix} 1 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 & 0 & 1 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \end{bmatrix} \begin{bmatrix} -1 & 0 & 0 & 0 & 1 \\ 1 & 0 & 0 & -1 & 0 \\ 0 & -1 & 0 & 1 & 0 \\ 0 & 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & -1 \end{bmatrix} \\ &= \begin{bmatrix} -1 & 0 & 0 & 0 & 0 \\ 0 & -1 & 0 & 1 & -1 \\ 0 & 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 \end{bmatrix} \end{aligned}$$

In addition, the number of complexes is $n = 6$ and there is only one linkage class, i.e., $l = 1$. Also, the rank of the network is $s = 4$. Thus, the deficiency of the CRN is $\delta = n - l - s = 6 - 1 - 4 = 1$.

2.2 Fundamentals of chemical kinetic systems

Definition 2.9. *A* **kinetics** *K for a reaction network $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ is an assignment to each reaction $r : y \to y' \in \mathscr{R}$ of a rate function $K_r : \Omega_K \to \mathbb{R}_{\geq 0}$ such that $\mathbb{R}^m_{>0} \subseteq \Omega_K \subseteq \mathbb{R}^m_{\geq 0}$, $c \wedge d \in \Omega_K$ if $c, d \in \Omega_K$, and $K_r(c) \geq 0$ for each $c \in \Omega_K$. Furthermore, it satisfies the positivity property: supp $y \subset$ supp c if and only if $K_r(c) > 0$. The system $(\mathscr{S}, \mathscr{C}, \mathscr{R}, K)$ is called a* **chemical kinetic system**.

Definition 2.10. *The* **species formation rate function** *(SFRF) of a chemical kinetic system is given by $f(x) = NK(x) = \sum_{C_i \to C_j \in \mathscr{R}} K_{C_i \to C_j}(x)(C_j - C_i)$.*

The ordinary differential equation (ODE) or dynamical system of a chemical kinetics system is $\dfrac{dx}{dt} = f(x)$. An **equilibrium** or **steady state** is a zero of f.

Definition 2.11. *The* **set of positive equilibria** *of a CKS* $(\mathscr{S}, \mathscr{C}, \mathscr{R}, K)$ *is given by*

$$E_+(\mathscr{S}, \mathscr{C}, \mathscr{R}, K) = \{x \in \mathbb{R}^m_{>0} | f(x) = 0\}.$$

A CRN is said to admit **multiple (positive) equilibria** if there exist positive rate constants such that the ODE system admits more than one stoichiometrically compatible equilibria.

Analogously, the **set of complex balanced equilibria** [13] is given by

$$Z_+(\mathscr{N}, K) = \{x \in \mathbb{R}^m_{>0} | I_a \cdot K(x) = 0\} \subseteq E_+(\mathscr{N}, K).$$

A positive vector $c \in \mathbb{R}^m$ is complex balanced if $K(c)$ is contained in Ker I_a, and a chemical kinetic system is complex balanced if it has a complex balanced equilibrium.

2.2.1 Power–law kinetic systems

Definition 2.12. *A kinetics* K *is a* **power-law kinetics** *(PLK) if* $K_i(x) = k_i x^{F_i}$ *for* $i = 1, ..., r$ *where* $k_i \in \mathbb{R}_{>0}$ *and* $F_{ij} \in \mathbb{R}$. *The power-law kinetics is defined by an* $r \times m$ *matrix* F, *called the* **kinetic order matrix** *and a vector* $k \in \mathbb{R}^r$, *called the* **rate vector**.

If the kinetic order matrix is the transpose of the molecularity matrix, then the system becomes the well-known **mass action kinetics (MAK)**.

Definition 2.13. *A PLK system has* **reactant-determined kinetics** *(of type PL-RDK) if for any two reactions* i, j *with identical reactant complexes, the corresponding rows of kinetic orders in* F *are identical, i.e.,* $F_{ik} = F_{jk}$ *for* $k = 1, 2, ..., m$. *A PLK system has* **non-reactant-determined kinetics** *(of type PL-NDK) if there exist two reactions with the same reactant complexes whose corresponding rows in* F *are not identical.*

Example 2.14. *Consider the CRN* $\mathscr{N}$ *in Example 2.8.*

$$R_1 : X_1 \to 0$$
$$R_2 : X_2 \to X_3$$
$$R_3 : X_3 \to X_4$$
$$R_4 : 0 \to X_2$$
$$R_5 : X_1 + X_2 \to X_1$$

We endow the CRN with the following kinetics.

$$K(X) = \begin{bmatrix} k_1 {X_1}^{-0.2} \\ k_2 {X_2}^{1.3} \\ k_3 {X_3}^{0.5} \\ k_4 V \\ k_5 {X_1}^{-0.1} {X_2}^{2.7} \end{bmatrix}$$

$(\mathscr{N}, K)$ *is a power-law kinetic system. In particular, it is a PL-RDK system.*

2.2.2 Poly-PL kinetic systems

Definition 2.15. *A kinetics* $K : \mathbb{R}^m_{>0} \to \mathbb{R}^r$ *is a* **poly-PL kinetics** *if*

$$K_i(x) = k_i \left(a_{i,1} x^{F_{i,1}} + \ldots + a_{i,j} x^{F_{i,j}} \right)$$

where $1 \leq i \leq r$ *with* $k_i > 0$, $F_{i,j}, a_{i,j} \in \mathbb{R}^m$ *and* $1 \leq j \leq h_i$ *(where* h_i *is the number of terms for the i-th reaction). It is defined by* $r \times m$ *matrices* $F_{i,k} = [F_{ij}]$*, called the* **kinetic order matrices***, vectors* $k = [k_i]$ *called the* **rate vector** *and* $a_{i,j} \in \mathbb{R}^r_{>0}$ *called the* **poly-rate vectors**.

From the definition, poly-PL kinetics (PYK) consists of non-negative linear combinations of power-law functions. In particular, power-law kinetics can be seen as "mono-PL kinetics with coefficient 1". For more details of the poly-PL kinetics, one may refer to [16, 20].

2.2.3 STAR–MSC transformation

The **S-invariant termwise addition of reactions via maximal stoichiometric coefficients (STAR-MSC)** method is based on the idea of using the maximal stoichiometric coefficient (MSC) among the complexes in the CRN to construct reactions whose reactant complexes and product complexes are different from existing ones. We translate the reactants and products uniformly to create $h-1$ replicas of the original network. Hence, its transform $\mathscr{N}^*$ becomes the union of the replicas and the original CRN [16].

All vectors $x = (x_1, \ldots, x_m)$ are positive. Let $M = 1 + \max\{y_i | y \in \mathscr{C}\}$, where the second summand is the maximal stoichiometric coefficient, which is a positive integer. For every positive integer z, let z be identified with the vector $(z, z, \ldots, z)$ in $\mathbb{R}^m$. For each complex $y \in \mathscr{C}$, form the $(h-1)$ complexes $y + M, y + 2M, \ldots, y + (h-1)M$.

2.3 Two deficiency theorems

We now state the Deficiency Zero and Deficiency One Theorems primarily from the works of Feinberg [4–6]. These theorems are useful in determining properties of equilibria of systems with underlying CRNs of deficiency zero or one. As we may observe, the structural property of weak or non-weak reversibility of a CRN plays an important role in such equilibria properties of the corresponding kinetic system.

Theorem 2.16. *(Deficiency Zero Theorem) For any CRN of deficiency zero, the following statements hold:*

i. If the network is not weakly reversible, then for arbitrary kinetics, the differential equations for the corresponding reaction system cannot admit a positive equilibrium.

ii. If the network is not weakly reversible, then for arbitrary kinetics, the differential equations for the corresponding reaction system cannot admit a cyclic composition trajectory containing a positive composition.

iii. If the network is weakly reversible, then for any mass action kinetics (regardless of the positive values the rate constants take), the differential equations have these properties:
There exists within each positive stoichiometric compatibility class precisely one equilibrium; that equilibrium is asymptotically stable; and there cannot exist a nontrivial cyclic composition trajectory along which all species concentrations are positive.

Theorem 2.17. *(Deficiency One Theorem) Consider a mass action system. Let δ be the deficiency of the network and let δ_θ be the deficiency of the θth linkage class, each containing just one terminal strong linkage class. Suppose that both of the following conditions hold:*

i. $\delta_\theta \leq 1$ for each linkage class and

ii. the sum of the deficiencies of all the individual linkage classes equals the deficiency of the whole network.

Then, no matter what positive values the rate constants take, the corresponding differential equations can admit no more than one equilibrium within a positive stoichiometric compatibility class. If the network is weakly reversible, the differential equations for the system admit precisely one equilibrium in each positive stoichiometric compatibility class.

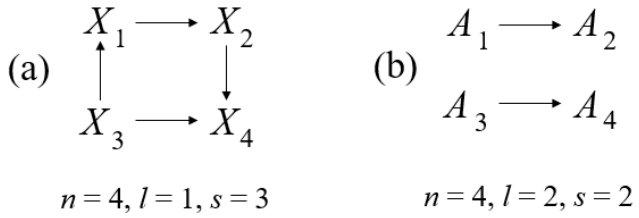

Figure 1. Examples of CRNs of deficiency zero

Example 2.18. *The CRN in Figure 1 (a) has deficiency zero and is weakly reversible. Endowed with mass action kinetics and regardless of the positive values the rate constant take, there exists within each positive stoichiometric class precisely one equilibrium. On the other hand, the CRN in Figure 1 (b) has deficiency zero and is not weakly reversible. Hence, endowed with any kinetics, the corresponding differential equations cannot admit a positive equilibrium.*

2.4 Review of decomposition theory

Definition 2.19. *A* ***decomposition*** *of $\mathscr{N}$ is a set of subnetworks $\{\mathscr{N}_1, \mathscr{N}_2, ..., \mathscr{N}_k\}$ of $\mathscr{N}$ induced by a partition $\{\mathscr{R}_1, \mathscr{R}_2, ..., \mathscr{R}_k\}$ of its reaction set $\mathscr{R}$.*

We denote a decomposition by $\mathscr{N} = \mathscr{N}_1 \cup \mathscr{N}_2 \cup ... \cup \mathscr{N}_k$ since $\mathscr{N}$ is a union of the subnetworks in the sense of [8]. It also follows immediately that, for the corresponding stoichiometric subspaces, $S = S_1 + S_2 + ... + S_k$.

The following important concept of independent decomposition was introduced by Feinberg in [4].

Definition 2.20. *A network decomposition $\mathscr{N} = \mathscr{N}_1 \cup \mathscr{N}_2 \cup ... \cup \mathscr{N}_k$ is* ***independent*** *if its stoichiometric subspace is a direct sum of the subnetwork stoichiometric subspaces.*

It was shown that for an independent decomposition, $\delta \leq \delta_1 + \delta_2 ... + \delta_k$ [7].

Definition 2.21. *A decomposition of CRN $\mathscr{N}$ is* ***incidence-independent*** *if the incidence map I_a of $\mathscr{N}$ is the direct sum of the incidence maps of the subnetworks. It is* ***bi-independent*** *if it is both independent and incidence-independent.*

We can also show incidence-independence by satisfying the equation

$$n - l = \sum (n_i - l_i),$$

where n_i is the number of complexes and l_i is the number of linkage classes, in each subnetwork i.

In [3], it was shown that for any incidence-independent decomposition,

$$\delta \geq \delta_1 + \delta_2 ... + \delta_k.$$

Example 2.22. *Consider a specific case of a generalization of a subnetwork of a CRN of a global carbon cycle model by Schmitz [7, 12, 18]. Let $\mathscr{N} = \mathscr{N}_1 \cup \mathscr{N}_2$ where $\mathscr{N}_1$ and $\mathscr{N}_2$ are given as follows.*

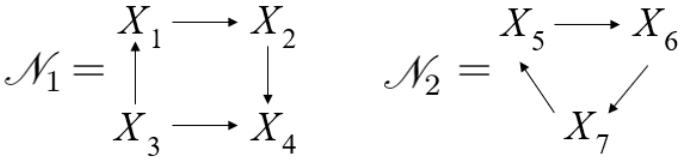

Figure 2. Subnetworks in Example 2.22

We can easy see from Table 2.1 that the dimension of the stoichiometric subspace of the whole network equals that of the sum of the respective stoichiometric subspaces of the subnetworks, i.e., $s = 5 = 3 + 2 = s_1 + s_2$. Thus, the corresponding decomposition is independent. In addition, $n - l = 5 = 3 + 2 = (n_1 - l_1) + (n_2 - l_2)$. Hence, the corresponding decomposition is incidence-independent. Therefore, the decomposition is bi-independent.

Table 2.1. Network Numbers for Example 2.22

	$\mathscr{N}$	$\mathscr{N}_1$	$\mathscr{N}_2$
n	7	4	3
l	2	1	1
s	5	3	2

Feinberg established the following basic relation between an independent decomposition and the set of positive equilibria of a kinetics on the network:

Theorem 2.23. *(Feinberg Decomposition Theorem [4]) Let $P(\mathscr{R}) = \{\mathscr{R}_1, \mathscr{R}_2, ..., \mathscr{R}_k\}$ be a partition of a CRN $\mathscr{N}$ and let K be a kinetics on $\mathscr{N}$. If $\mathscr{N} = \mathscr{N}_1 \cup \mathscr{N}_2 \cup ... \cup \mathscr{N}_k$ is the network decomposition of $P(\mathscr{R})$ and $E_+(\mathscr{N}_i, K_i) = \left\{x \in \mathbb{R}^{\mathscr{S}}_{>0} | N_i K_i(x) = 0\right\}$ then*

$$E_+(\mathscr{N}_1, K_1) \cap E_+(\mathscr{N}_2, K_2) \cap ... \cap E_+(\mathscr{N}_k, K_k) \subseteq E_+(\mathscr{N}, K).$$

If the network decomposition is independent, then equality holds.

Analogously, Farinas et al. introduced their results for incidence-independent decompositions and complex balanced equilibria [3]:

Theorem 2.24. *(Theorem 4 [3]) Let $\mathscr{N} = (\mathscr{S}, \mathscr{C}, \mathscr{R})$ be a a CRN and $\mathscr{N}_i = (\mathscr{S}_i, \mathscr{C}_i, \mathscr{R}_i)$ for $i = 1, 2, ..., k$ be the subnetworks of a decomposition. Let K be any kinetics, and $Z_+(\mathscr{N}, K)$ and $Z_+(\mathscr{N}_i, K_i)$ be the sets of complex balanced equilibria of $\mathscr{N}$ and $\mathscr{N}_i$, respectively. Then*

i. $Z_+(\mathscr{N}_1, K_1) \cap Z_+(\mathscr{N}_2, K_2) \cap ... \cap Z_+(\mathscr{N}_k, K_k) \subseteq Z_+(\mathscr{N}, K)$.
If the decomposition is incidence independent, then

ii. $Z_+(\mathscr{N}, K) = Z_+(\mathscr{N}_1, K_1) \cap Z_+(\mathscr{N}_2, K_2) \cap ... \cap Z_+(\mathscr{N}_k, K_k)$, *and*

iii. $Z_+(\mathscr{N}, K) \neq \varnothing$ *implies* $Z_+(\mathscr{N}_i, K_i) \neq \varnothing$ *for each* $i = 1, ..., k$.

We will discuss some applications of the Feinberg Decomposition Theory for CRNs along with deficiency theorems in Section 4.

3 Some important decompositions of CRNs in literature

We now consider some various decompositions available in literature.

Linkage class decomposition partitions a network into its linkage classes. It is a basic decomposition of a CRN. It is special in the sense that corresponding partition of the reaction set also induces a partition on the set of complexes.

Example 3.1. *Consider the following CRN.*

$$R_1 : 0 \to X_1 + X_2$$
$$R_2 : X_1 + X_2 \to X_1$$
$$R_3 : X_2 \to X_2 + X_3$$

There are two linkage classes as depicted in Figure 3 that induce the linkage class decomposition of the CRN.

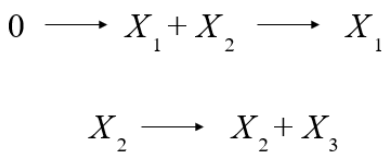

Figure 3. Linkage classes in Example 3.1

Definition 3.2. *[3] A decomposition $\mathscr{N} = \mathscr{N}_1 \cup \mathscr{N}_2 \cup ... \cup \mathscr{N}_k$ with $\mathscr{N}_i = (\mathscr{S}_i, \mathscr{C}_i, \mathscr{R}_i)$ is a* $\mathscr{C}$***-decomposition*** *if for each pair of distinct i and j, $\mathscr{C}_i$ and $\mathscr{C}_j$ are disjoint.*

In [3], it was shown that $\mathscr{C}$-decompositions form a subset of incidence-independent decompositions.

Before we formally discuss another set of decompositions, we review some concepts and properties underlying the multistationarity algorithms in the context of decomposition theory [11, 14].

Definition 3.3. *A subset $\mathscr{O}$ of $\mathscr{R}$ is said to be an* **orientation** *if for every reaction $y \to y' \in \mathscr{R}$, either $y \to y' \in \mathscr{O}$ or $y' \to y \in \mathscr{O}$, but not both.*

For an orientation $\mathscr{O}$, we define a linear map $L_{\mathscr{O}} : \mathbb{R}^{\mathscr{O}} \to S$ such that

$$L_{\mathscr{O}}(\alpha) = \sum_{y \to y' \in \mathscr{O}} \alpha_{y \to y'} (y' - y).$$

Each orientation $\mathscr{O}$ defines a partition of $\mathscr{N}$ into $\mathscr{O}$ and its complement $\mathscr{O}'$, which generates the following decomposition:

Definition 3.4. *For an orientation $\mathscr{O}$ on $\mathscr{N}$, the* $\mathscr{O}$***-decomposition*** *of $\mathscr{N}$ consists of the subnetworks $\mathscr{N}_{\mathscr{O}}$ and $\mathscr{N}_{\mathscr{O}'}$, i.e., $\mathscr{N} = \mathscr{N}_{\mathscr{O}} \cup \mathscr{N}_{\mathscr{O}'}$.*

We now review the important concept of "equivalence classes" from [14]. Let $\{v^l\}_{l=1}^d$ be a basis for $KerL_{\mathscr{O}}$. If for $y \to y' \in \mathscr{O}$, $v^l_{y\to y'} = 0$ for all $1 \le l \le d$ then the reaction $y \to y'$ belongs to the zeroth equivalence class P_0. For $y \to y', \overline{y} \to \overline{y}' \in \mathscr{O}\backslash P_0$, if there exists $\alpha \neq 0$ such that $v^l_{y\to y'} = \alpha v^l_{\overline{y}\to\overline{y}'}$ for all $1 \le l \le d$, then the two reactions are in the same equivalence class denoted by P_i, $i \neq 0$.

The central concept of "fundamental classes" is actually the basis of the Higher Deficiency Algorithm of Ji and Feinberg and the Multistationarity Algorithm by Hernandez et al. The reactions $y \to y'$ and $\overline{y} \to \overline{y}'$ in $\mathscr{R}$ belong to the same **fundamental class** if at least one of the following is satisfied [14].

i. $y \to y'$ and $\overline{y} \to \overline{y}'$ are the same reaction.

ii. $y \to y'$ and $\overline{y} \to \overline{y}'$ are reversible pair.

iii. Either $y \to y'$ or $y' \to y$, and either $\overline{y} \to \overline{y}'$ or $\overline{y}' \to \overline{y}$ are in the same equivalence class on $\mathscr{O}$.

It is worth mentioning that he orientation $\mathscr{O}$ is partitioned into equivalence classes while the reaction set $\mathscr{R}$ is partitioned into fundamental classes.

Definition 3.5. *The* **fundamental decomposition** *or* **$\mathscr{F}$-decomposition** *of $\mathscr{N}$ is the decomposition generated by the partition of $\mathscr{R}$ into fundamental classes.*

Theorem 3.6. *[12] Let $\mathscr{N}_{\mathscr{O}}$ be the subnetwork of $\mathscr{N}$ defined by the orientation $\mathscr{O}$ being a subset of $\mathscr{R}$. Then the following holds:*

i. The $\mathscr{P}$-decomposition of $\mathscr{N}_{\mathscr{O}}$ is independent if and only if the $\mathscr{F}$-decomposition of $\mathscr{N}$ is independent.

ii. The $\mathscr{P}$-decomposition of $\mathscr{N}_{\mathscr{O}}$ is incidence-independent if and only if the $\mathscr{F}$-decomposition of $\mathscr{N}$ is incidence-independent.

iii. The $\mathscr{P}$-decomposition of $\mathscr{N}_{\mathscr{O}}$ is bi-independent if and only if the $\mathscr{F}$-decomposition of $\mathscr{N}$ is bi-independent.

Example 3.7. *Consider the network given in Example 3.1. We can verify that $KerL_{\mathscr{O}}$ is trivial, i.e., with the zero vector alone as element. The fundamental (network) decomposition yields the only subnetwork as the network itself.*

4 Analysis for various kinetic systems

In this section, we employed steps for the computation of analysis of equilibria properties of kinetic systems using established results integrated with the program that we developed in Appendix B. Basically, if the given has poly-PL kinetics, then one may transform it to power-law [16].

The initial part of the program uses the work given in [19]. We also mention that we created a program in [9] for particular fundamental decomposition. On the other hand, our current work is flexible in the sense that it does not consider the fundamental decomposition alone. The following is the standard procedure for the program.

PROCEDURE analysis

INPUT1: reaction set and assignment of each reaction to a subnetwork

OUTPUT1: subnetworks defined by partitioning the reaction set

OUTPUT2: determine if the network is independent or not

4.1 Analysis for power–law kinetic systems

We make use of the following steps:

1. Use a known decomposition (e.g., decompositions from Section 3) and determine if the CRN is independent under this decomposition.
2. If the CRN has an independent decomposition, then choose among the obtained subnetworks of the original network under the decomposition.
3. Check the properties of the subnetwork using deficiency theorems or multistationarity algorithm.

Example 4.1. *Consider the following CRN of Anderies et al.'s carbon cycle model in the pre-industrial state [1, 7].*

$$R_1 : A_1 + 2A_2 \to 2A_1 + A_2$$
$$R_2 : A_1 + A_2 \to 2A_2$$
$$R_3 : A_2 \to A_3$$
$$R_4 : A_3 \to A_2$$

Let us check the independence of the linkage class decomposition using the program.

```
model.id = 'anderies';
model.name = 'anderies';
model.species = struct('id', {'A1' 'A2' 'A3'});
model.reaction(1) = struct('id', 'A1+2A2->2A1+A2', 'reactant', struct('
    species', {'A1' 'A2'}, 'stoichiometry', {1 2}), 'product', struct('
    species', {'A1' 'A2'}, 'stoichiometry', {2 1}), 'reversible', false,
        'subnetwork', 1);
model.reaction(2) = struct('id', 'A1+A2->2A2', 'reactant', struct('
    species', {'A1' 'A2'}, 'stoichiometry', {1 1}), 'product', struct('
    species', {'A2'}, 'stoichiometry', {2}), 'reversible', false,  '
    subnetwork', 2);
model.reaction(3) = struct('id', 'A2<->A3', 'reactant', struct('species
    ', {'A2'}, 'stoichiometry', {1}), 'product', struct('species', {'A3
    '}, 'stoichiometry', {1}), 'reversible', true,    'subnetwork', 3);
INDEPENDENT(model)
```

Then the following output is obtained.

```
CONCLUSION1: The decomposition is NOT INDEPENDENT.
CONCLUSION2: The decomposition is INCIDENCE-INDEPENDENT.
CONCLUSION3: The decomposition is NOT BI-INDEPENDENT.
```

Since the linkage class decomposition is not independent, we try the fundamental decomposition on the other hand.

```
model.id = 'anderies';
model.name = 'anderies';
model.species = struct('id', {'A1' 'A2' 'A3'});
model.reaction(1) = struct('id', 'A1+2A2->2A1+A2', 'reactant', struct('
    species', {'A1' 'A2'}, 'stoichiometry', {1 2}), 'product', struct('
    species', {'A1' 'A2'}, 'stoichiometry', {2 1}), 'reversible', false,
        'subnetwork', 1);
model.reaction(2) = struct('id', 'A1+A2->2A2', 'reactant', struct('
    species', {'A1' 'A2'}, 'stoichiometry', {1 1}), 'product', struct('
    species', {'A2'}, 'stoichiometry', {2}), 'reversible', false,  '
    subnetwork', 1);
model.reaction(3) = struct('id', 'A2<->A3', 'reactant', struct('species
    ', {'A2'}, 'stoichiometry', {1}), 'product', struct('species', {'A3
    '}, 'stoichiometry', {1}), 'reversible', true,    'subnetwork', 2);
INDEPENDENT(model)
```

Then the following output is obtained.

```
CONCLUSION1: The decomposition is INDEPENDENT.
CONCLUSION2: The decomposition is INCIDENCE-INDEPENDENT.
CONCLUSION3: The decomposition is BI-INDEPENDENT.
```

One may analyze the CRN using the fundamental decomposition.

Let us endow the network with mass action kinetics. Under the decomposition, we have the following subnetworks: $\{R_1, R_2\}$ *and* $\{R_3, R_4\}$*. We choose the subnetwork* $\{R_3, R_4\}$*. Note that it has deficiency zero. In addition, the network is reversible and hence, weakly reversible. By the third item in the Deficiency Zero Theorem (DZT), the subnetwork with mass action kinetics does not have the capacity for multistationarity. Finally, by the Feinberg Decomposition Theorem, the whole CRN with mass action kinetics does not have the capacity for multistationarity, too. We refer to the DZT for full information of the*

properties.

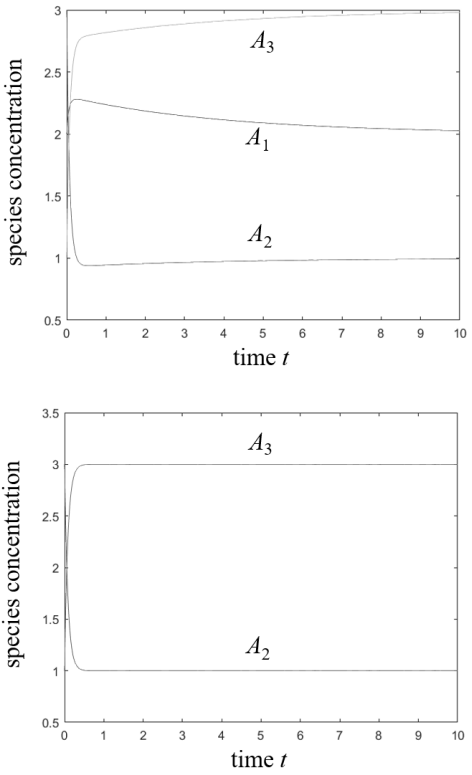

Figure 4. A comparison of a graph for the dynamics of each of the network (above) and the subnetwork $\{R_3, R_4\}$ (below)

In particular, we consider a set of ODEs for the network for illustration.

$$A_1{}' = 0.5A_1{A_2}^2 - 0.5A_1A_2$$

$$A_2{}' = 0.5A_1A_2 - 0.5A_1{A_2}^2 - 9A_2 + 3A_3$$

$$A_3{}' = 9A_2 - 3A_3$$

In addition, for the subnetwork $\{R_3, R_4\}$*, we have the following:*

$$A_2{}' = -9A_2 + 3A_3$$

$$A_3{}' = 9A_2 - 3A_3$$

We refer to Figure 4 and verify that $(A_1, A_2, A_3) = (2, 1, 3)$ *is an equilibrium for the network and* $(A_2, A_3) = (1, 3)$ *is an equilibrium for the chosen subnetwork (without species* A_1*).*

Example 4.2. *Consider the power-law kinetic system in Example 2.14.*

$$\begin{array}{ll} R_1 : X_1 \to 0 & k_1 {X_1}^{-0.2} \\ R_2 : X_2 \to X_3 & k_2 {X_2}^{1.3} \\ R_3 : X_3 \to X_4 & k_3 {X_3}^{0.5} \\ R_4 : 0 \to X_2 & k_4 V \\ R_5 : X_1 + X_2 \to X_1 & k_5 {X_1}^{-0.1} {X_2}^{2.7} \end{array}$$

We can verify from our MATLAB program that the following fundamental decomposition is independent:

$$\{\{R_1, R_2, R_3\}, \{R_4, R_5\}\}.$$

We choose the smaller subnetwork $\{R_4, R_5\}$ *with defciency zero. From the Deficiency Zero Theorem, the differential equations for the system cannot admit a positive equilibrium. By the Feinberg Decomposition Theorem, the whole system also has no capacity to admit a positive equilibrium.*

4.2 Analysis for poly-PL kinetic systems

We provide the following steps:

1. Use a known decomposition (e.g., decompositions from Section 3) and determine if the CRN is independent under this decomposition.

2. If the CRN has an independent decomposition, then choose among the obtained subnetworks of the original network under the decomposition.

3. Transform the subnetwork endowed with poly-PL to power-law kinetics using the STAR-MSC method.

4. Check the properties of the subnetwork using deficiency theorems or multistationarity algorithm.

Example 4.3. *Consider the following CRN (with poly-PL kinetics):*

$$R_1 : A_1 \to A_1 + A_2 \qquad (k_1 \left[A_1A_2 + 3A_1^2\right])$$

$$R_2 : A_1 + A_2 \to A_1 + 2A_2 \qquad (k_2 \left[A_1^{0.5}A_2 + A_2^2\right])$$

$$R_3 : A_3 \to A_4 \qquad (k_3 \left[A_3^2 + A_4^{0.3}\right])$$

$$R_4 : A_4 \to A_3 \qquad (k_4 \left[A_3^{-0.1} + A_4^{-3}\right])$$

$$R_5 : A_4 \to A_3 + A_4 \qquad (k_5 \left[5A_3^{0.4}A_4 + 2A_3^2\right])$$

$$R_6 : A_3 + A_4 \to A_4 \qquad (k_6 \left[A_3A_2^{0.2} + 2A_4^2\right])$$

Let us check the independence of the linkage class decomposition using the program.

```
model.id = 'sample';
model.name = 'sample';
model.species = struct('id', {'A1', 'A2', 'A3' 'A4'});
model.reaction(1) = struct('id', 'A1->A1+A2', 'reactant', struct('
    species', {'A1'}, 'stoichiometry', {1}), 'product', struct('species',
     {'A1' 'A2'}, 'stoichiometry', {1 1}), 'reversible', false,  '
    subnetwork', 1);
model.reaction(2) = struct('id', 'A1+A2->A1+2A2', 'reactant', struct('
    species', {'A1' 'A2'}, 'stoichiometry', {1 1}), 'product', struct('
    species', {'A1' 'A2'}, 'stoichiometry', {1 2}), 'reversible', false,
    'subnetwork', 1);
model.reaction(3) = struct('id', 'A3<->A4', 'reactant', struct('species
    ', {'A3'}, 'stoichiometry', {1}), 'product', struct('species', {'A4
    '}, 'stoichiometry', {1}), 'reversible', true, 'subnetwork', 2);
model.reaction(4) = struct('id', 'A4<->A3+A4', 'reactant', struct('
    species', {'A4'}, 'stoichiometry', {1}), 'product', struct('species',
     {'A3' 'A4'}, 'stoichiometry', {1 1}), 'reversible', true,  '
    subnetwork', 2);
INDEPENDENT(model)
```

Then the following output is obtained.

```
CONCLUSION1: The decomposition is INDEPENDENT.
CONCLUSION2: The decomposition is INCIDENCE-INDEPENDENT.
CONCLUSION3: The decomposition is BI-INDEPENDENT.
```

We analyze using the network using the linkage class decomposition. Under the decomposition, we have the following subnetworks: $\{R_1, R_2\}$ *and* $\{R_3, R_4, R_5, R_6\}$*. We choose the subnetwork* $\{R_1, R_2\}$*. Hence, we consider the following:*

$$R_1 : A_1 \to A_1 + A_2 \qquad (k_1 \left[A_1A_2 + 3A_1^2\right])$$

$$R_2 : A_1 + A_2 \to A_1 + 2A_2 \qquad (k_2 \left[A_1^{0.5}A_2 + A_2^2\right])$$

We use the STAR-MSC transformation to convert the poly-PL (sub)system given above to power-law. Hence we have the following transformed network together with the matrix used to determine positive dependency in the multistationarity algorithm (MSA) for poly-PL

kinetic systems [16]:

$$\begin{array}{ll} R_1 : A_1 \to A_1 + A_2 & \begin{pmatrix} -1 \\ 1 \\ 0 \\ 0 \end{pmatrix} \\ R_2 : A_1 + A_2 \to A_1 + 2A_2 & \\ R_3 : 3A_1 + 2A_2 \to 3A_1 + 3A_2 & \\ R_4 : 3A_1 + 3A_2 \to 3A_1 + 4A_2 & \end{array}$$

Therefore, the subsystem with underlying subnetwork does not have the capacity for multistationarity. By the Feinberg Decomposition Theorem, the whole system does not also have the capacity for multistationarity.

4.3 Analysis for poly-PL quotients kinetic systems

In [10], quotients of poly-PL functions were considered as kinetics. In these class of kinetics, each reaction of a CRN is assigned to a rational function where both the numerator and the denominator are poly-PL in form. In particular, equilibria properties of Hill-type kinetic systems were considered. The following is an example of a CRN endowed with quotients of poly-PL functions.

Example 4.4. *We consider an example in [10], which was based on [16]. Consider the following CRN:*

$$R_1 : 5X + Y \to X + 3Y$$
$$R_2 : X + 3Y \to 5X + Y$$

but endowed with the following kinetics:

$$K(X,Y) = \begin{bmatrix} k_1 \dfrac{\alpha_1 X + \alpha_2 Y + \alpha_3 XY + \alpha_4 X^2}{X} \\ k_2 \dfrac{\beta_1 X + \beta_2 Y + \beta_3 XY + \beta_4 X^2}{X^2 Y} \end{bmatrix}.$$

Transformation of a poly-PL quotient kinetics was employed in [10] to a poly-PL kinetics. To integrate the methods of [10, 12, 16] with the program, we consider Figure 5.

5 Summary and outlook

We summarize our results and provide some direction for future research.

1. We illustrated how known decompositions can be used to infer properties of equilibria of a kinetic system from its subsystem(s) with underlying reaction network.

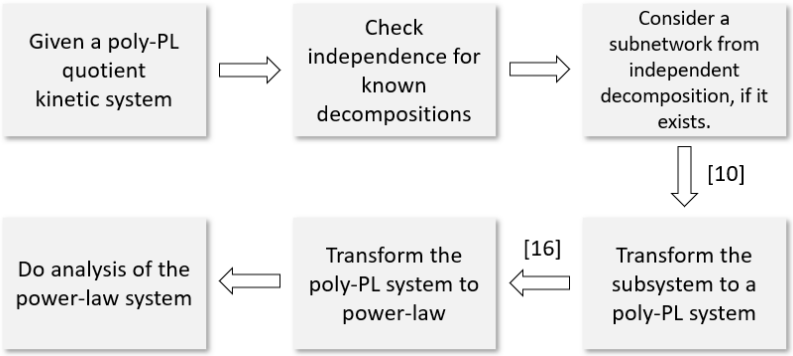

Figure 5. An integrated method in Section 4.3

2. We provided some steps that one can follow to analyze properties of equilibria of power-law and poly-PL kinetic systems.

3. We created a program that gives independence properties of CRNs given a particular assignment of numbers to reactions that corresponds to a decomposition.

4. One can consider more types of decompositions which can be integrated in the methods.

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A Nomenclature

A.1 List of abbreviations

Abbreviation	Meaning
CKS	chemical kinetic system
CRN	chemical reaction network
HDA	higher deficiency algorithm
MSA	multistationarity algorithm
PLK	power-law kinetics
PL-NDK	power-law non-reactant-determined kinetics
PL-RDK	power-law reactant-determined kinetics
SFRF	species formation rate function

A.2 List of important symbols

Meaning	Symbol
deficiency	δ
dimension of the stoichiometric subspace	s
incidence map	I_a
molecularity matrix	Y
number of complexes	n
number of linkage classes	l
orientation	$\mathscr{O}$
stoichiometric matrix	N
stoichiometric subspace	S

B The program

We provide a MATLAB program that determines the independence of a particular decomposition of a CRN by assigning a number from 1 to k to each reaction, where k is the number of subnetworks. We use the preliminary steps of the program of Soranzo and Altafini [19]. We should install the free software ERNEST in our MATLAB environment. The script was named INDEPENDENT.m.

```
function [ret] = INDEPENDENT(model)
species = {model.species.id};
n = numel(species); % number of species
reactions = {model.reaction.id};
subnetworks = {model.reaction.subnetwork};
subnetworks2 = [model.reaction.subnetwork];
subnetworks3 = unique(subnetworks2);
subn = numel(subnetworks3);
reactant_complexes = []; % matrix of reactant complexes (species x irrev
    . reactions)
product_complexes = []; % matrix of product complexes (species x irrev.
    reactions)
S = []; % stoichiometric matrix (species x irrev. reactions)
sum = 0;
sum2 = 0;
StoichMatrixForm = [];
sr_edges = cell(0, 4);

[Lia,Locb] = ismember(subnetworks2, subnetworks3);
IdentifyLocb = Locb;
IdentifyUniqLocb = unique(IdentifyLocb(~isnan(IdentifyLocb)));
histIdentifyLocb=histc(IdentifyLocb,IdentifyUniqLocb);
UniqueReactionRow = IdentifyUniqLocb(histIdentifyLocb >=1);
[URsizeRow,URsizeCol] = size((UniqueReactionRow).');

for k=1:URsizeRow
    record=find(ismember(IdentifyLocb,UniqueReactionRow(k)));
    [URsizeRecordRow,URsizeRecordCol] = size(record);
    fprintf('SUBNETWORK %d has the following reaction(s):',
        UniqueReactionRow(k))
    fprintf('\n')
    for i=1:URsizeRecordCol
        disp(model.reaction(record(i)).id);

    if isfield(model.reaction(record(i)), 'modifier') && ~isempty(model.
        reaction(record(i)).modifier)
        warning(['Reaction ' num2str(record(i)) ' contains modifiers,
            which will be ignored. Specify all species in a reaction as
            reactants or products.'])
    end
    reactant_complexes(:, end+1) = zeros(n, 1);
    for j = 1:numel(model.reaction(record(i)).reactant)
        reactant_complexes(find(strcmp(model.reaction(record(i)).
            reactant(j).species, species), 1), end) = model.reaction(
            record(i)).reactant(j).stoichiometry;
    end
    product_complexes(:, end+1) = zeros(n, 1);
```

```
    for j = 1:numel(model.reaction(record(i)).product)
        product_complexes(find(strcmp(model.reaction(record(i)).product(
            j).species, species), 1), end) = model.reaction(record(i)).
            product(j).stoichiometry;
    end
    S(:, end + 1) = product_complexes(:, end) - reactant_complexes(:,
        end);
    if model.reaction(record(i)).reversible
        reactant_complexes(:, end+1) = product_complexes(:, end);
        product_complexes(:, end+1) = reactant_complexes(:, end-1);
        S(:, end + 1) = -S(:, end);
    end
    if numel(model.reaction(record(i)).reactant) > 0 && numel(model.
        reaction(record(i)).product) > 0
        label = [num2str(model.reaction(record(i)).reactant(1).
            stoichiometry) ' ' model.reaction(record(i)).reactant(1).
            species];
        for j = 2:numel(model.reaction(record(i)).reactant)
            label = [label ' + ' num2str(model.reaction(record(i)).
                reactant(j).stoichiometry) ' ' model.reaction(record(i)).
                reactant(j).species];
        end
        for j = 1:numel(model.reaction(record(i)).reactant)
            sr_edges(end+1, :) = {model.reaction(record(i)).reactant(j).
                species, reactions{record(i)}, label, model.reaction(
                record(i)).reactant(j).stoichiometry};
        end
        label = [num2str(model.reaction(record(i)).product(1).
            stoichiometry) ' ' model.reaction(record(i)).product(1).
            species];
        for j = 2:numel(model.reaction(record(i)).product)
            label = [label ' + ' num2str(model.reaction(record(i)).
                product(j).stoichiometry) ' ' model.reaction(record(i)).
                product(j).species];
        end
        for j = 1:numel(model.reaction(record(i)).product)
            sr_edges(end+1, :) = {model.reaction(record(i)).product(j).
                species, reactions{record(i)}, label, model.reaction(
                record(i)).product(j).stoichiometry};
        end

end
clear label
[Y, ind, ind2] = unique([reactant_complexes product_complexes]', 'rows')
    ; % ind2(i) is the index in Y of the reactant complex in reaction i,
    ind(i + r) is the index in Y of the product complex in reaction i

Y = Y'; % complexes matrix (species x complexes)

m = size(Y, 2); % number of complexes

reacts_to = false(m, m); % matrix (complexes x complexes) for the
    reacts_to relation: reacts_to(i, j) = true iff i->j
r = size(reactant_complexes, 2); % number of irrev. reactions
reacts_in = zeros(m, r); % matrix (complexes x irrev. reactions) for the
     reacts_in relation: (reacts_in(i, r) = -1 && reacts_in(j, r) = 1)
    iff i->j
```

```
for i = 1:r
    reacts_to(ind2(i), ind2(i + r)) = true;
    reacts_in(ind2(i), i) = -1;
    reacts_in(ind2(i + r), i) = 1;%incidence
end

is_reversible = isequal(reacts_to, reacts_to'); %test for reversibility

complexes_ugraph_cc = connected_components(umultigraph(reacts_to |
   reacts_to')); % linkage classes

l = max(complexes_ugraph_cc); % number of linkage classes

if is_reversible
    complexes_graph_scc = complexes_ugraph_cc;
else
    complexes_graph_scc = strongly_connected_components(multigraph(
       reacts_to)); % strong-linkage classes
end
n_slc = max(complexes_graph_scc); % number of strong-linkage classes
is_weakly_reversible = n_slc == l; % the reaction network is weakly
   reversible if and only if each linkage class is a strong-linkage
   class
s = rank(S); % reaction network rank

rr = numel(reactions); % number of reactions (counting reversible
   reactions as one)

end

fprintf('The stoichiometric subspace of SUBNETWORK %d is:',
   UniqueReactionRow(k))
S

fprintf('The rank of SUBNETWORK %d is:', UniqueReactionRow(k))
s = rank(S)

fprintf('The value of (n-l) for the SUBNETWORK %d is:',
   UniqueReactionRow(k))
diff=m-l

S = [];
reactant_complexes = [];
product_complexes = [];

sum = sum + s;
sum2 = sum2 + diff;
end

fprintf('The SUM of the RANKS of the SUBNETWORKS is:')
fprintf('\n')
sum

fprintf('The SUM of the values of of (n-l) of the SUBNETWORKS is:')
fprintf('\n')
sum2

S=[];
```

```
for i = 1:numel(reactions)
    if isfield(model.reaction(i), 'modifier') && ~isempty(model.reaction
       (i).modifier)
        warning(['Reaction ' num2str(i) ' contains modifiers, which will
             be ignored. Specify all species in a reaction as reactants
            or products.'])
    end
    reactant_complexes(:, end+1) = zeros(n, 1);
    for j = 1:numel(model.reaction(i).reactant)
        reactant_complexes(find(strcmp(model.reaction(i).reactant(j).
           species, species), 1), end) = model.reaction(i).reactant(j).
           stoichiometry;
    end
    product_complexes(:, end+1) = zeros(n, 1);
    for j = 1:numel(model.reaction(i).product)
        product_complexes(find(strcmp(model.reaction(i).product(j).
           species, species), 1), end) = model.reaction(i).product(j).
           stoichiometry;
    end

    S(:, end + 1) = product_complexes(:, end) - reactant_complexes(:,
       end);
    if model.reaction(i).reversible
        reactant_complexes(:, end+1) = product_complexes(:, end);
        product_complexes(:, end+1) = reactant_complexes(:, end-1);
        S(:, end + 1) = -S(:, end);
    end

    if numel(model.reaction(i).reactant) > 0 && numel(model.reaction(i).
       product) > 0
        label = [num2str(model.reaction(i).reactant(1).stoichiometry) '
           ' model.reaction(i).reactant(1).species];
        for j = 2:numel(model.reaction(i).reactant)
            label = [label ' + ' num2str(model.reaction(i).reactant(j).
               stoichiometry) ' ' model.reaction(i).reactant(j).species
               ];
        end
        for j = 1:numel(model.reaction(i).reactant)
            sr_edges(end+1, :) = {model.reaction(i).reactant(j).species,
                 reactions{i}, label, model.reaction(i).reactant(j).
               stoichiometry};
        end
        label = [num2str(model.reaction(i).product(1).stoichiometry) ' '
            model.reaction(i).product(1).species];
        for j = 2:numel(model.reaction(i).product)
            label = [label ' + ' num2str(model.reaction(i).product(j).
               stoichiometry) ' ' model.reaction(i).product(j).species];
        end
        for j = 1:numel(model.reaction(i).product)
            sr_edges(end+1, :) = {model.reaction(i).product(j).species,
               reactions{i}, label, model.reaction(i).product(j).
               stoichiometry};
        end
    end
end

fprintf('The stoichiometric subspace of the WHOLE NETWORK is:')
```

```
S
fprintf('The rank of the WHOLE NETWORK is:')
fprintf('\n')
s=rank(S)

clear label
[Y, ind, ind2] = unique([reactant_complexes product_complexes]', 'rows')
   ; % ind2(i) is the index in Y of the reactant complex in reaction i,
   ind(i + r) is the index in Y of the product complex in reaction i
Y = Y'; % complexes matrix (species x complexes)
m = size(Y, 2); % number of complexes
reacts_to = false(m, m); % matrix (complexes x complexes) for the
   reacts_to relation: reacts_to(i, j) = true iff i->j
r = size(reactant_complexes, 2); % number of irrev. reactions
reacts_in = zeros(m, r); % matrix (complexes x irrev. reactions) for the
    reacts_in relation: (reacts_in(i, r) = -1 && reacts_in(j, r) = 1)
   iff i->j

for i = 1:r
    reacts_to(ind2(i), ind2(i + r)) = true;
    reacts_in(ind2(i), i) = -1;
    reacts_in(ind2(i+r), i) = 1;%incidence
end

is_reversible = isequal(reacts_to, reacts_to'); %test for reversibility
complexes_ugraph_cc = connected_components(umultigraph(reacts_to |
   reacts_to')); % linkage classes
l = max(complexes_ugraph_cc); % number of linkage classes
if is_reversible
    complexes_graph_scc = complexes_ugraph_cc;
else
    complexes_graph_scc = strongly_connected_components(multigraph(
       reacts_to)); % strong-linkage classes
end
n_slc = max(complexes_graph_scc); % number of strong-linkage classes
is_weakly_reversible = n_slc == l; % the reaction network is weakly
   reversible if and only if each linkage class is a strong-linkage
   class
s = rank(S); % reaction network rank

fprintf('The value of (n-l) for the WHOLE NETWORK is:')
diff=m-l

if sum==s
   fprintf('CONCLUSION1: The decomposition is INDEPENDENT.')
else
   fprintf('CONCLUSION1: The decomposition is NOT INDEPENDENT.')
end

fprintf('\n')

if sum2==diff
   fprintf('CONCLUSION2: The decomposition is INCIDENCE-INDEPENDENT.')
else
   fprintf('CONCLUSION2: The decomposition is NOT INCIDENCE-INDEPENDENT
      .')
end
```

```
fprintf('\n')

if sum==s & sum2==diff
   fprintf('CONCLUSION3: The decomposition is BI-INDEPENDENT.')
else
   fprintf('CONCLUSION3: The decomposition is NOT BI-INDEPENDENT.')
end

fprintf('\n')

clear all
```