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Complex Balanced Equilibria of Weakly Reversible Power Law Kinetic Systems

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Abstract

In this paper, we use the concept of kinetic reactant deficiency to determine the existence of complex balanced equilibria of power law kinetic systems. We previously introduced a class of power law kinetic systems whose kinetic order vectors (which we call "interactions") are reactant-determined (i.e. reactions with the same reactant complex have identical vectors) and are linear independent per linkage class, denoted by PL-TIK systems. A subset of PL-TIK systems was found to admit a complex balanced equilibrium. In this work, we prove that zero kinetic reactant deficiency systems are precisely the PL-TIK systems. Our main result is the existence of complex balanced equilibria for weakly reversible systems with zero kinetic reactant deficiency (for any rate constant), hence, generalizing the previous study.

1 Introduction

This paper deals with weakly reversible power law kinetic (PLK) systems and appropriate conditions to admit complex balanced equilibria. We say that a kinetic system is complex balanced if it contains a complex balanced steady state. At this state, for each complex, formation and degradation are at equilibrium. The concept first appeared in the works of Horn, Jackson and Feinberg [9, 13, 14]. One of their early major results was to show that any weakly reversible, zero deficiency CRN with mass action kinetics has a complex balanced equilibrium for any set of rate constants [10].

In [18], we discovered that a subclass of weakly reversible PL-TIK systems do admit a complex balanced equilibrium, without regard to the deficiency of a system. PL-TIK systems are power law kinetic systems whose reactions with the same reactant complexes have the same kinetic order vectors (called interactions), which are linear independent per linkage class.

The novelty of this present paper is the generalization of this result to the whole class of PL-TIK systems (see Theorem 6). More interestingly, this result is established by defining a parameter called the kinetic reactant deficiency (see Definition 10) which measures the degree of the kinetic interactions. This new parameter is defined analogously as that of the kinetic deficiency of Müller-Regensburger [16, 17] which is necessarily limited to cycle-terminal networks. In Proposition 2, it is shown that PL-TIK systems are precisely those networks with kinetic reactant deficiency equal to 0. We can also consider our main result (the Zero Kinetic Reactant Deficiency Theorem) as a “Weak Reversibility Theorem” in the sense posed in our previous work [18]. That is, a weakly reversible zero kinetic reactant deficiency system has a positive equilibrium. This result is regardless of the network deficiency of the system.

The paper is organized as follows. Fundamentals of chemical reaction networks and kinetics needed for the later sections are provided in Section 2. The PLK systems with reactant determined kinetics and their subclasses such as PL-TIK systems are discussed in Sections 3.1 and 3.2. The concept of reactant deficiency is introduced at the beginning of Section 3.3 and it is shown in Section 3.4 how PL-RDK systems with zero kinetic reactant deficiency can admit a positive equilibrium. A parametrization tool of the positive equilibria is also developed in Section 3.5. The main result of the paper which is the Zero Kinetic Reactant Deficiency Theorem is proved in Section 4. Our results are also illustrated through the multisite phosphorylation system and an SIR epidemic network. Lastly, we conclude and provide future perspectives in Section 5.

2 Preliminaries to chemical reaction network theory

In a chemical reaction, a **species** is represented by a variable. We denote the nonempty finite set of distinct species by $\mathscr{S} = \{X_1, X_2, ..., X_m\}$ with cardinality of $\mathscr{S}$ equals m. A **complex** is a linear combination of the species with nonnegative integer coefficients. We denote the nonempty finite set of complexes by $\mathscr{C} = \{C_1, C_2, ..., C_n\}$ where the cardinality of $\mathscr{C}$ is equal to n. A **reaction** is an ordered pair of distinct complexes. Thus, if we denote this nonempty finite set of reactions by $\mathscr{R}$, we have $\mathscr{R} \subset \mathscr{C} \times \mathscr{C}$. Let r be the cardinality of $\mathscr{R}$. Consider the reaction

$$\alpha X_1 + \beta X_2 \to \gamma X_3,$$

X_1, X_2 and X_3 are the species. $\alpha X_1 + \beta X_2$ and γX_3 are the complexes. In particular, $\alpha X_1 + \beta X_2$ is called the **reactant** (or **source**) **complex** and γX_3 the **product complex**. The nonnegative coefficients α, β and γ are called **stoichiometric coefficients**. Under power law kinetics (PLK), the rate at which the reaction occurs is given by

$$\mathbf{K} = k X_1^a X_2^b$$

with rate constant $k > 0$ and $a, b \in \mathbb{R}$. We call a and b as kinetic orders. Thus, the reaction rate is a monomial in the reactant concentrations X_1 and X_2 with the exponents a and b. Assuming mass action kinetics (MAK), (a subset of PLK), we have $a = \alpha$ and $b = \beta$, that is, the stoichiometric coefficients of the reactant complexes are the kinetic orders. Within a network involving additional species and reactions, the above reaction contributes to the dynamics of the species concentrations as

$$\dot{X} = \begin{bmatrix} \dot{X}_1 \\ \dot{X}_2 \\ \dot{X}_3 \\ \vdots \end{bmatrix} = k X_1^a X_2^b \begin{pmatrix} -\alpha \\ -\beta \\ \gamma \\ \vdots \end{pmatrix} + \dots$$

2.1 Chemical reaction networks as directed graphs

Chemical reaction networks (CRNs) can be represented as a directed graph or reaction graph with the rate constants as we will show in our first example.

Example 1. *Consider the chemical reaction network (CRN) below [12].*

$$E_1 + A \underset{k_{21}}{\overset{k_{12}}{\longleftrightarrow}} AE_1 \xrightarrow{k_{23}} E_1 + A_P$$
$$E_2 + A_P \underset{k_{54}}{\overset{k_{45}}{\leftrightarrow}} A_P E_2 \xrightarrow{k_{56}} E_2 + A$$

The vertices or nodes are the complexes and the reactions are the edges. Here, we have $m = 6$ *(species),* $n = 6$ *(complexes),* $n_r = 4$ *(reactant complexes) and* $r = 6$ *(reactions). We can write*

$$\begin{aligned}
&\mathscr{S} = \{X_1, X_2, X_3, X_4, X_5, X_6\} = \{E_1, A, AE_1, A_P, E_2, A_PE_2\}\\
&\mathscr{C} = \{C_1, C_2, C_3, C_4, C_5, C_6\} = \{E_1 + A, AE_1, E_1 + A_P, E_2 + A_P, A_PE_2, E_2 + A\}\,.
\end{aligned}$$

On the other hand, the set of reaction $\mathscr{R}$ *consists of the following:*

$$\begin{aligned}
&R_1 : E_1 + A \to AE_1\\
&R_2 : AE_1 \to E_1 + A\\
&R_3 : AE_1 \to E_1 + A_P\\
&R_4 : E_2 + A_P \to A_PE_2\\
&R_5 : A_PE_2 \to E_2 + A_P\\
&R_6 : A_PE_2 \to E_2 + A.
\end{aligned}$$

In a CRN, 0 is called the zero complex symbolizing an “outside” reactor. $0 \to X$ and $X \to 0$ are called inflow reaction and outflow reaction for any complex X.

The **linkage classes** of a CRN are the subgraphs of a reaction graph where for any complexes C_i, C_j of the subgraph, there is a path between them. Thus, the number of linkage classes, denoted as l, of Example 1 is two ($l = 2$). The linkage classes are:

$$\begin{aligned}
&\mathscr{L}_1 = \{R_1, R_2, R_3\}\\
&\mathscr{L}_2 = \{R_4, R_5, R_6\}\,.
\end{aligned}$$

A subset of a linkage class where any two vertices are connected by a directed path in each direction is said to be a **strong linkage class**. Considering Example 1, there are four strong linkage classes whose number is denoted by sl. We also identify the **terminal strong linkage classes**, the number denoted as t, to be the strong linkage classes where there is no reaction from a complex in the strong linkage class to a complex outside the same strong linkage class. The terminal strong linkage classes can be of two kinds: cycles (not necessarily simple) and singletons (which we call “terminal points”). In Example 1, we have $t = 2$ where both are terminal points.

We now define important CRN classes. A CRN is **weakly reversible** if $sl = l$, i.e. every linkage class is a strong linkage class. A CRN is **t-minimal** if $t = l$. Let n_r be the number of reactant complexes of a CRN. Then $n - n_r$ is the number of terminal points. A CRN is called **cycle-terminal** if and only if $n - n_r = 0$, i.e., each complex is a reactant complex. It is called **point-terminal** if and only if $n - n_r = t$ and **point- and cycle-terminal** if $n - n_r < t$.

Clearly, the CRN in Example 1 is not weakly reversible since $4 = sl \neq l = 2$. However, this paper focuses on weakly reversible networks.

The dynamics of the CRN of Example 1 can be written as

$$\dot{X} = \begin{bmatrix} \dot{[E_1]} \\ \dot{[A]} \\ \dot{[AE_1]} \\ \dot{[A_P]} \\ \dot{[E_2]} \\ \dot{[A_PE_2]} \end{bmatrix} = \begin{array}{c} \begin{array}{cccccc} R_1 & R_2 & R_3 & R_4 & R_5 & R_6 \end{array} \\ \begin{bmatrix} -1 & 1 & 1 & 0 & 0 & 0 \\ -1 & 1 & 0 & 0 & 0 & 1 \\ 1 & -1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & -1 & 1 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 \\ 0 & 0 & 0 & 1 & -1 & -1 \end{bmatrix} \end{array} \begin{bmatrix} k_{12}[E_1]^{f_{11}}[A]^{f_{12}} \\ k_{21}[AE_1]^{f_{23}} \\ k_{23}[AE_1]^{f_{33}} \\ k_{45}[E_2]^{f_{44}}[A_P]^{f_{45}} \\ k_{54}[A_PE_2]^{f_{56}} \\ k_{56}[A_PE_2]^{f_{66}} \end{bmatrix} = NK(X).$$

Here, N is called the stoichiometric matrix and $K(X)$ is called the kinetic vector. In this paper, we are interested with kinetic vectors under **power law kinetics**. They have the form

$$K_i(x) = k_i \Pi_{j=1}^{m} x^{F_{ij}} \quad \forall i \in \overline{1,r}$$

with $k_i \in \mathbb{R}_+$ and $F_{ij} \in \mathbb{R}$. Power law kinetics is defined by an $r \times m$ matrix $F = [F_{ij}]$, called the **kinetic order matrix**, and vector $k \in \mathbb{R}^r$, called the **rate vector**. In our running example, the kinetic order matrix is

$$F = \begin{array}{c} \begin{array}{cccccc} E_1 & A & AE_1 & A_P & E_2 & A_PE_2 \end{array} \\ \begin{bmatrix} f_{11} & f_{12} & 0 & 0 & 0 & 0 \\ 0 & 0 & f_{23} & 0 & 0 & 0 \\ 0 & 0 & f_{33} & 0 & 0 & 0 \\ 0 & 0 & 0 & f_{44} & f_{45} & 0 \\ 0 & 0 & 0 & 0 & 0 & f_{56} \\ 0 & 0 & 0 & 0 & 0 & f_{66} \end{bmatrix} \end{array} \begin{array}{c} \\ R_1 \\ R_2 \\ R_3 \\ R_4 \\ R_5 \\ R_6 \end{array}. \tag{2.1}$$

A particular example of power law kinetics is the well-known mass action kinetics (MAK) where the kinetic order matrix consists of stoichiometric coefficients of the reactants. If Example 1 is under MAK, the kinetic system will be an enzymatic cycle (1-site phosphorylation system) where E_1, E_2, A and A_P are the substrate, product, kinase and phosphotase, respectively. With MAK assumption, the kinetic order matrix is

$$F = \begin{array}{cccccc|c} E_1 & A & AE_1 & A_P & E_2 & A_PE_2 & \\ \hline 1 & 1 & 0 & 0 & 0 & 0 & R_1 \\ 0 & 0 & 1 & 0 & 0 & 0 & R_2 \\ 0 & 0 & 1 & 0 & 0 & 0 & R_3 \\ 0 & 0 & 0 & 1 & 1 & 0 & R_4 \\ 0 & 0 & 0 & 0 & 0 & 1 & R_5 \\ 0 & 0 & 0 & 0 & 0 & 1 & R_6 \end{array} . \tag{2.2}$$

We further decompose the stoichiometric matrix N. Writing the stoichiometric complexes as column vectors of the (molecularity) matrix Y, we have

$$Y = \begin{array}{cccccc|c} C_1 & C_2 & C_3 & C_4 & C_5 & C_6 & \\ \hline 1 & 0 & 1 & 0 & 0 & 0 & E_1 \\ 1 & 0 & 0 & 0 & 0 & 1 & A \\ 0 & 1 & 0 & 0 & 0 & 0 & AE_1 \\ 0 & 0 & 1 & 1 & 0 & 0 & A_P \\ 0 & 0 & 0 & 1 & 0 & 1 & E_2 \\ 0 & 0 & 0 & 0 & 1 & 0 & A_PE_2 \end{array} .$$

Considering the directed graph of our CRN, the incidence matrix

$$(I_a)_{(i,j)} = \begin{cases} -1, \text{if } i \text{ is the reactant complex of reaction } j \in \mathscr{R}, \\ 1, \text{if } i \text{ is the product complex of reaction } j \in \mathscr{R}, \\ 0, \text{otherwise} \end{cases}$$

will be

$$I_a = \begin{array}{cccccc|c} R_1 & R_2 & R_3 & R_4 & R_5 & R_6 & \\ \hline -1 & 1 & 0 & 0 & 0 & 0 & C_1 \\ 1 & -1 & -1 & 0 & 0 & 0 & C_2 \\ 0 & 0 & 1 & 0 & 0 & 0 & C_3 \\ 0 & 0 & 0 & -1 & 1 & 0 & C_4 \\ 0 & 0 & 0 & 1 & -1 & -1 & C_5 \\ 0 & 0 & 0 & 0 & 0 & 1 & C_6 \end{array} .$$

It is important to note that stoichiometric matrix $N = YI_a$. The stoichiometric map $N : \mathbb{R}^r \to \mathbb{R}^m$ is defined as the composition $Y \circ I_a$.

2.2 Dynamically equivalent CRNs

It is noteworthy to discuss here that it is possible that different chemical reaction networks with the same set of kinetics could generate the same set of ordinary differential equations, i.e. they can be dynamically equivalent. G. Farkas [8] introduced the idea of dynamic equivalence in the kinetic lumping schemes for MAK systems while G. Craciun and C. Pantea [7] were among the first to establish its mathematical foundations.

We will present in Example 2 below a dynamically equivalent CRN with that of Example 1. Dynamic equivalence is useful for qualitative mathematical analysis of chemical kinetic systems. For instance, original CRNs might not satisfy certain characteristics (e.g. weak reversibility) but one can formulate a suitable dynamically equivalent CRN such that mathematical conclusions hold true. The coincidence of the ODE systems ensures the correctness of these conclusions for the original system though they are purely mathematical constructs which might not be biologically or chemically feasible as we will see in the following example.

Example 2. *Below is an example of a weakly reversible network (here, $sl = l = 1$) which is dynamically equivalent to our CRN in Example 1, given that they have the same kinetic order matrix F in Equation 2.1:*

$$\begin{tikzcd}
E_1 + E_2 + A \arrow[r, leftrightarrow, "k_{12}", "k_{21}"'] & AE_1 + E_2 \arrow[d, "k_{23}"] \\
A_P E_2 + E_1 \arrow[u, "k_{56}"] \arrow[r, leftrightarrow, "k_{43}", "k_{34}"'] & E_1 + E_2 + A_P
\end{tikzcd}$$

Remark 1. The CRN above can be obtained by a mathematical technique introduced by M. Johnston in [15]. The power law kinetic system is a mathematical construct that, via dynamic equivalence, facilitates the qualitative analysis of the original biochemical system.

2.3 Deficiency, reactant deficiency and kinetic deficiency of a chemical kinetic system

The linear subspace of $\mathbb{R}^m$ defined by $\operatorname{Im} N$ is called the **stoichiometric subspace**, denoted as S. Let $s = \dim S$. The **deficiency** δ is defined as $\delta = n - l - s$. This non-negative integer is, as Shinar and Feinberg pointed out in [20], essentially a measure of the linear dependency of the network's reactions. In the running example, the deficiency of the network is two. It is one of the important parameters in CRNT to establish claims regarding the existence, multiplicity, finiteness and parametrization of the **set of positive steady states**, denoted as E_+. It is defined as $E_+(\mathscr{N}, K) = \left\{x \in \mathbb{R}^m_+ \middle| NK(X) = 0\right\}$.

Furthermore, considering the linkage classes of the network, we can write

$$N = [N_1, N_2, \cdots, N_l] \text{ and } K(X) = [K_1(X), K_2(X), \cdots, K_l(X)]^\top$$

in block forms where l is the number of linkage class. Let s_i be the dimension of the image of N_i and n_i be the number of complexes in linkage class $\mathscr{L}_i$. We can define the **linkage class deficiency** of $\mathscr{L}_i$ as $\delta_i = n_i - 1 - s_i$ and the **set of positive steady states for linkage class** $\mathscr{L}_i$ as $E_+(\mathscr{L}_i, K) = \left\{x \in \mathbb{R}^m_+ \middle| N_i K_i(X) = 0\right\}$.

Arceo et al. [2] introduced the reactant deficiency of a CRN. It is an essential measure of the linear independence of reactant complexes as shown by the definition below.

Definition 1. The **reactant deficiency** of a network is given by $\delta_\rho := n_r - q$ where n_r the number of reactant complexes and q is the rank of matrix Y_{res}, i.e., the $m \times n_r$ matrix Y without the columns of the terminal points. The columns of Y_{res} are the reactant complexes $\rho(R_1)$, $\rho(R_2)$, ..., $\rho(R_r)$ where $\rho : \mathscr{R} \to \mathscr{C}$ maps a reaction $r : y \to y'$ to its reactant complex y.

Müller and Regensburger [16, 17] also introduced a parameter for a reaction network, known as the kinetic deficiency of a generalized chemical reaction network (GCRN). The brief definition is given below.

Definition 2. A **generalized chemical reaction network** (**GCRN**) $(G, y, \widetilde{y})$ is given by a digraph $G = (V, E)$ without self-loops, and two functions

$$y : V \to \mathbb{R}^m \text{ and } \widetilde{y} : V_s \to \mathbb{R}^m$$

assigning to each vertex a (stoichiometric) complex and to each source a kinetic complex.

In the above definition, $V = \{1, \ldots, n\}$ is a finite set of vertices and $E \subseteq V \times V$ is a finite set of edges. An edge $e = (i, j) \in E$ is denoted by $i \to j$ to emphasize that it is directed from the source i to a target j. Moreover, the set V_s is the set of source vertices, that is,

$$V_s = \{i | i \to j \in E\}.$$

Definition 3. Let $\mathscr{N}$ be a cycle-terminal network with n complexes and l linkage classes. The **kinetic order subspace** $\widetilde{S}_{MR}$ is the span $\{\widetilde{y}(y') - \widetilde{y}(y) | y \to y'\}$, where $\widetilde{y}$ is the **kinetic complexes map**. If $\widetilde{s} = \dim \widetilde{S}_{MR}$, then the **kinetic deficiency** is defined as $\widetilde{\delta} = n - l - \widetilde{s}$.

In Proposition 3, we are going to relate the reactant deficiency and kinetic deficiency to our kinetic reactant deficiency to be introduced in Section 3.3.

3 The kinetic reactant deficiency for power law kinetic systems

3.1 Power law reactant-determined kinetics

In [3], the set of power law kinetics with reactant-determined kinetic orders of a network $\mathscr{N}$ (PL-RDK system) is introduced. It is defined as follows:

Definition 4. 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 $k = 1, ..., m$.

In our Example 1, if $f_{23} = f_{33}$ and $f_{56} = f_{66}$ in Equation 2.1, then the given kinetics is of type PL-RDK. An equivalent formulation for the dynamics of a PL-RDK system can be written using the factor map and the $k-$ Laplacian matrix defined below (Arceo et al. [3]).

Definition 5. The **factor map** $\psi_K : \mathbb{R}^m \to \mathbb{R}^n$ is defined as

$$(\psi_K)_c(x) = \begin{cases} (x^F)_i, \text{if } c \text{ is a reactant complex of reaction } i, \\ 0, \text{otherwise.} \end{cases}$$

Definition 6. The **k- Laplacian matrix** of a CRN is an $n \times n$ matrix such that

$$(A_k)_{ij} = \begin{cases} k_{ji}, \text{if } i \neq j, \\ k_{jj} - \sum_{x=1}^{n} k_{jx}, \text{if } i = j. \end{cases}$$

where k_{ji} is the label (often called the rate constant) associated to the reaction from C_j to C_i.

The set of positive steady states E_+ of a PL-RDK system can be defined using A_k and ψ_K. We have the following decomposition:

$$E_+(\mathscr{N}, K) = \left\{ x \in \mathbb{R}^m_+ \middle| Y A_k \psi_K(x) = 0 \right\}.$$

The set of positive steady states for the linkage classes can also be redefined using the block forms of A_k and ψ_K. Another set of power law kinetics of special interest for us is the set of factor span surjective systems PL-FSK($\mathscr{N}$). We use the following characterization which was derived in [1] as our working definition:

Definition 7. A PL-RDK kinetics is **factor span surjective** if and only if all rows with different reactant complexes in the kinetic order matrix F are pairwise different (i.e., $\rho(r) \neq \rho(r')$ implies $F_{r,\cdot} \neq F_{r',\cdot}$).

3.2 The T-matrix and the PL-TIK systems

Müller and Regensburger [17] introduced the $m \times n$ matrix $\widetilde{Y}$ for cycle terminal networks (that is, every complex is a reactant complex). But, we generalize this concept into arbitrary networks and define it as follows.

$$(\widetilde{Y})_{ij} = \begin{cases} F_{ki}, \text{if } j \text{ is a reactant complex of reaction } k, \\ 0, \text{otherwise} \end{cases}$$

where F is the kinetic order matrix.

In 2017, Talabis et al. [22] defined the T-matrix and the augmented T-matrix ($\widehat{T}$) as follows:

Definition 8. The $m \times n_r$ **T-matrix** is the truncated $\widetilde{Y}$ where the non-reactant columns are deleted and n_r is the number of reactant complexes. The T-matrix defines a map $T : \mathbb{R}^{\rho(\mathscr{R})} \to \mathbb{R}^{\mathscr{S}}$. The **kinetic reactant subspace** $\widetilde{R}$ is the image of T. Its dimension is called the **kinetic reactant rank** $\widetilde{q}$.

Define the $n_r \times l$ matrix $L = [e_1, e_2, ..., e_l]$ where e^i is a characteristic vector for linkage class $\mathscr{L}^i$. The block matrix $\widehat{T} \in \mathbb{R}^{(m+l) \times n_r}$ is defined as

$$\widehat{T} = \begin{bmatrix} T \\ L^\top \end{bmatrix}.$$

In Example 2 with kinetic order matrix F in Equation 2.1, which is of type PL-RDK (if $f_{23} = f_{33}$ and $f_{56} = f_{66}$), the T-matrix and the augmented T-matrix will be

$$T = \begin{array}{ccccc} E_1+E_2+A & AE_1+E_2 & E_1+E_2+A_P & A_PE_2+E_1 & \\ f_{11} & 0 & 0 & 0 & E_1 \\ f_{12} & 0 & 0 & 0 & A \\ 0 & f_{23} & 0 & 0 & AE_1 \\ 0 & 0 & f_{44} & 0 & A_P \\ 0 & 0 & f_{45} & 0 & E_2 \\ 0 & 0 & 0 & f_{56} & A_PE_2 \end{array} \quad \text{and}$$

$$\widehat{T} = \left[\begin{array}{cccc} f_{11} & 0 & 0 & 0 \\ f_{12} & 0 & 0 & 0 \\ 0 & f_{23} & 0 & 0 \\ 0 & 0 & f_{44} & 0 \\ 0 & 0 & f_{45} & 0 \\ 0 & 0 & 0 & f_{56} \\ 1 & 1 & 1 & 1 \end{array}\right] \begin{array}{c} E_1 \\ A \\ AE_1 \\ A_P \\ E_2 \\ A_PE_2 \\ \mathscr{L}_1 \end{array} . \tag{3.1}$$

Observe that all complexes are reactant complexes. In [22], Talabis et al. defined the PL-TIK systems, a subclass of PL-RDK systems.

Definition 9. A PL-RDK kinetics is **$\widehat{T}$-rank maximal** (to type **PL-TIK**) if its column rank is maximal.

Remark 2. PL-TIK systems are PLK systems whose reactions with the same reactant complexes have the same kinetic order vectors (called interactions), which are linear independent per linkage class.

Observe that the rank of $\widehat{T}$ above is 4 (if $f_{ij} \neq 0$) which is equal to the number of columns of $\widehat{T}$. By definition, the kinetic system is PL-TIK, that is, $\widehat{T}$-rank maximal.

3.3 The kinetic reactant deficiency

We introduce now a novel concept called kinetic reactant deficiency which we will use in our quest for complex balanced equilbrium of PL-RDK systems.

Definition 10. Let $\mathscr{N}$ be a network with n_r reactant complexes and K a PL-RDK kinetics with T-matrix T. If $\widehat{q} = \text{rank}(\widehat{T})$, then the **kinetic reactant deficiency** $\widehat{\delta}$ is defined as

$$\widehat{\delta} = n_r - \widehat{q}.$$

The kinetic reactant deficiency of a kinetic system is an integer index that assumes non-negative values. The kinetic reactant deficiency measures the degree of the kinetic interactions of the PL-RDK system. The higher the kinetic reactant deficiency, the lower the extent of linear independence of kinetic orders (kinetic interaction).

If the system is a MAK system, the kinetic reactant deficiency is simply the reactant deficiency of the underlying CRN (s. [2]). One readily observes the analogy to the concept of "kinetic deficiency" introduced by Müller and Regensburger [17]. However, a distinct advantage of the new construct is that it is defined for an arbitrary CRN, whereas the Müller-Regensburger construct is restricted to cycle terminal networks.

As a consequence of Rank-Nullity Theorem and Definition 10, we have the following result.

Proposition 1. *Let* $(\mathscr{N}, K)$ *a PL-RDK system with T-matrix* T *and kinetic reactant deficiency* $\widehat{\delta}$*. Then*

$$\widehat{\delta} = \dim\ker(\widehat{T}).$$

As a direct consequence of Proposition 1, we have the following result.

Proposition 2. $(\mathscr{N}, K)$ *is PL-TIK system iff* $\widehat{\delta} = 0$*.*

Proof. Note that $\widehat{\delta} = 0$ is equivalent to $\dim\ker(\widehat{T}) = 0$. Thus, the columns of $\widehat{T}$ are linearly independent. Hence, the rank of $\widehat{T}$ is equal to the number of columns of $\widehat{T}$. By definition, the kinetic system is PL-TIK, that is, $\widehat{T}$-rank maximal. ■

This result permits us to rewrite the known properties of PL-TIK systems and their equilibria previously done in [18, 22]. We discuss them next.

3.4 Equilibria of PL-RDK systems with zero kinetic reactant deficiency

In [14], Horn and Jackson introduced a subset of E_+ called the set of complex balanced of equilibria denoted as Z_+. A kinetic system is complex balanced at a state (i.e. a species composition) if for each complex, formation and degradation are at equilibrium.

Definition 11. A positive vector c in $\mathbb{R}^m$ is called **complex balanced** (CB) if $K(c)$ is contained in $\ker I_a$. A CKS is called **complex balanced** if it has complex balanced equilibria. The set of complex balanced equilibria of a chemical kinetic system is denoted by $Z_+(\mathscr{N}, K)$. Thus,

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

Remark 3. If $(\mathscr{N}, K)$ is a PL-RDK system then it can be shown that $Z_+(\mathscr{N}, K) = \left\{x \in \mathbb{R}^m_+ \middle| A_k \cdot \psi_K(x) = 0\right\}$.

Due to Proposition 2 and Theorem 3 in [18] (Theorem 4 in [22]), we have the following results:

Theorem 1. *Let* $(\mathscr{N}, K)$ *be a PL-RDK system with* $\widehat{\delta} = 0$.

(i) $E_+(\mathscr{L}_i, K) \neq \emptyset$ *for each linkage class* $\mathscr{L}_i$ *implies* $E_+(\mathscr{N}, K) \neq \emptyset$.

(ii) $Z_+(\mathscr{L}_i, K) \neq \emptyset$ *for each linkage class* $\mathscr{L}_i$ *implies* $Z_+(\mathscr{N}, K) \neq \emptyset$.

Definition 12. The **restricted incidence matrix** $I_{a,R}$ is the truncated I_a, that is, the columns for non-reactant complexes are deleted. For weakly reversible system, $I_{a,R} = I_a$. The **kinetic reactant flux subspace** $\widetilde{S}_R$ is the subspace $T(\mathrm{Im}(I_{a,R}))$ of the kinetic reactant space $\widetilde{R}$. For $q \in \mathbb{R}^m_{\geq}$, the set $(q + \widetilde{S}_R) \cap \mathbb{R}^m_{\geq}$ is called the **kinetic reactant flux class**. A kinetic reactant flux class $\mathbf{Q}$ is said to be positive if $\mathbf{Q} \cap \mathbb{R}^m_{>} \neq \emptyset$.

Let $\mathscr{C}_r$ denote the set of reactant complexes and $\mathscr{C}'$ the set of complexes in the terminal strong linkage class. Suppose $\mathscr{C}'' = \mathscr{C} \backslash \mathscr{C}'$. Let $n_r = |\mathscr{C}_r|$, $n' = |\mathscr{C}'|$, and $n'' = |\mathscr{C}''|$. Consider $A_k \in \mathbb{R}^{n \times n}$, $\psi_K : \mathbb{R}^m \to \mathbb{R}^n$ and a vector $h \in \mathbb{R}^n$ in the block forms

$$A_k = \begin{bmatrix} A'_k & * \\ 0 & A''_k \end{bmatrix} \in \mathbb{R}^{(n'+n'') \times (n'+n'')}, \quad \psi_K = \begin{bmatrix} \psi'_K \\ \psi''_K \end{bmatrix} : \mathbb{R}^m \to \mathbb{R}^{(n'+n'')}$$

$$\text{and } h = \begin{bmatrix} h' \\ h'' \end{bmatrix} \in \mathbb{R}^{(n'+n'')}$$

Let $h \in \ker Y \cap \mathrm{Im}\, A_k$. Denote as $\mathbf{H}''$ the product of $(A''_k)^{-1}$ and h''. Analogously, we can define $(\mathbf{H}'')^i$ for each linkage class $\mathscr{L}_i$.

Theorem 2. *Let* $(\mathscr{N}, K)$ *be a t-minimal PL-RDK system with* $\widehat{\delta} = 0$ *and where each linkage class has* $\delta = 0$ *or* $= 1$.

(I) If $\mathscr{N}$ *is weakly reversible then*

  (A) $E_+(\mathscr{N}, K) \neq \emptyset$*;*

  (B) $E_+(\mathscr{N}, K) = \left\{ x \in \mathbb{R}^m_{\geq} \middle| \log(x) - \log(x^*) \in (\widetilde{S}_R)^{\perp} \right\}$ *provided that* $x^* \in E_+(\mathscr{N}, K)$ *and* $\delta = \delta_1 + \delta_2 + \ldots + \delta_l$*;*

(II) If $\mathscr{N}$ *is non-weakly reversible then*

  (A) $E_+(\mathscr{N}, K) \neq \emptyset$ *if*

    (i) each linkage class $\mathscr{L}^i$ *with* $\delta = 0$ *is strongly connected; and*

    (ii) each non-strongly connected linkage class $\mathscr{L}^i$ *has* $\delta = 1$ *and contains a terminal strong linkage class which satisfies* $(\boldsymbol{H}'')^i \in \mathbb{R}^{(n^i)''}_{+} \cup \mathbb{R}^{(n^i)''}_{-}$*;*

(B) $E_+(\mathscr{N},K) = \left\{x \in \mathbb{R}^m_{\geq} \middle| \log(x) - \log(x^*) \in (\widetilde{S}_R)^\perp\right\}$ *provided that* $x^* \in E_+(\mathscr{N},K)$ *and* $\delta = \delta_1 + \delta_2 + \ldots + \delta_l$;

(III) if $\delta = \delta_1 + \delta_2 + \ldots + \delta_l$ *and* $E_+(\mathscr{N},K) \neq \emptyset$, *then* $|E_+(\mathscr{N},K) \cap \boldsymbol{Q}| = 1$ *for each positive kinetic reactant flux class* $\boldsymbol{Q}$.

Theorem 3. *Let* $(\mathscr{N},K)$ *be a weakly reversible PL-RDK system with* $\widehat{\delta} = 0$ *and linkage classes* $\mathscr{L}_1, ..., \mathscr{L}_l$.

(i) If $\mathscr{N}$ *has no inflow reaction, then* $Z_+(\mathscr{N},K)$ *is non-empty and the system's kinetic deficiency is zero.*

(ii) If $\mathscr{N}$ *has an inflow reaction and the linkage class* $\mathscr{L}_1$ *containing the zero complex has* $\widetilde{\delta} = 0$, *then* $Z_+(\mathscr{N},K)$ *is non-empty and the system's kinetic deficiency is zero. If its* $\widetilde{\delta} = 1$, *then for the rate constants which satisfy the Müller and Regensburger criterion for complex balancing,* $Z_+(\mathscr{N},K)$ *is non-empty.*

(iii) For systems satisfying (i) and (ii) , the set of positive equilibria $E_+(\mathscr{N},K)$ *contains the parametrized set*

$$\left\{x \in \mathbb{R}^m_{>} \middle| \log(x) - \log(x^*) \in (\widetilde{S}_R)^\perp\right\} = \bigcap E^i_+.$$

If $\delta = \delta_1 + \delta_2 + \ldots + \delta_l$, *then the sets are equal.*

In [18], we showed that if the kinetics on a CRN $\mathscr{N}$ is factor span surjective, i.e. contained in PL-FSK, then its set of kinetic complexes $\widetilde{C}$ forms a reaction network $\widetilde{\mathscr{N}}$, i.e. a digraph where the embedding of the complexes is not necessarily contained in $\mathbb{Z}^m_{\geq}$. Many concepts and results for CRNs hold for reaction networks. In particular, we consider the reactant deficiency of $\widetilde{\mathscr{N}}$ and its relationship to $\widehat{\delta}$, which is expressed in the following Proposition:

Proposition 3. *Let* $(\mathscr{N},K)$ *be a PL-FSK system and* $\widetilde{\mathscr{N}}$ *its reaction network of kinetic complexes. Then*

$$\delta_\rho(\widetilde{\mathscr{N}}) \geq \widehat{\delta}.$$

Proof. Let the columns of $T = (a_i)$ and (a_i, h_i) the corresponding element of $\widehat{T}$. If $\sum z_i(a_i, h_i) = 0$ in $\mathbb{R}^m \times \mathbb{R}^l$, then $\sum a_i z_i = 0$ in $\mathbb{R}^m$, hence if the columns of T are linearly independent, then $z_i = 0$. Hence $\operatorname{rank} T \leq \operatorname{rank} \widehat{T}$. Since the reaction network of kinetic complexes has the same number of reactants as the CRN, then $\delta_\rho(\widetilde{\mathscr{N}}) \geq \widehat{\delta}$. ■

Remark 4. If $\mathscr{N}$ is cycle terminal, as shown in [18], then $\delta_\rho(\widetilde{\mathscr{N}}) \geq \delta(\widetilde{\mathscr{N}}) = \widetilde{\delta}$, the kinetic deficiency of $\mathscr{N}$. In particular, for any factor span surjective kinetics on a cycle terminal network, $\delta_\rho(\widetilde{\mathscr{N}}) = 0$ implies that both $\widetilde{\delta}$ and $\widehat{\delta} = 0$.

3.5 Tools for the parametrization of positive equilibria

To examine the finiteness and uniqueness of positive equilibria, we adapt the techniques used in [6]. In particular, the following proposition and corollaries make claims similar to Boros' Proposition 4.3 and its consequences [6].

Proposition 4. *Let* $(\mathscr{N}, K)$ *be a weakly reversible PL-RDK system with T-matrix* T *and* $\widehat{\delta} = 0$. *Let* $P_1 : \mathbb{R}^m \times \mathbb{R}^l \to \mathbb{R}^m$ *be the first projection map, i.e.,* $Pr_1(v) = v^1$ *for* $v = \begin{bmatrix} v^1 \\ v^2 \end{bmatrix} \in \mathbb{R}^m \times \mathbb{R}^l$. *Then* $P_1|_{\ker \widehat{T}^\top}$ *is a bijection between* $\ker \widehat{T}^\top$ *and* $(\widetilde{S}_R)^\perp$ *where* $(\widetilde{S}_R)$ *is the space generated by* TI_a.

Proof. We want to show $P_1|_{\ker \widehat{T}^\top}$ is both surjective and injective. Let $w \in (\widetilde{S}_R)^\perp$. By definition of $\widetilde{S}_R$, since $\mathscr{N}$ is weakly reversible, each column of $T(I_a)$ corresponds to a reaction (i, j) in such a way that the corresponding column is $T_{\cdot,j} - T_{\cdot,i}$. Thus, we have

$$\langle T_{\cdot,j} - T_{\cdot,i}, w \rangle = 0, \quad \forall (i,j) \in \mathscr{R}_R.$$

Hence, $\langle T_{\cdot,j}, w \rangle = \langle T_{\cdot,i}, w \rangle$. Clearly, $\langle T_{\cdot,i}, w \rangle$ depends only on the linkage class $\mathscr{L}^i$ of complex $C_i \in \mathscr{C}$. Let $\xi_r = \langle T_{\cdot,i}, w \rangle$ for the linkage class $\mathscr{L}^r$.

To prove surjectivity, we want to show that for $w \in (\widetilde{S}_R)^\perp$, there exists $v \in \ker \widehat{T}^\top$ such that $Pr_1(v) = w$. Let $v \in \mathbb{R}^{m+l}$ such that $v = \left[w^\top, -\xi_1, \ldots - \xi_l\right]^\top$. This implies that

$$\widehat{T}^\top v = T^\top w + L_{pr} \begin{bmatrix} -\xi_1 \\ \vdots \\ -\xi_l \end{bmatrix} = 0.$$

Therefore, $v \in \ker \widehat{T}^\top$ and $Pr_1(v) = w$. On the other hand, to prove injectivity, we want to show that if $Pr_1(v_1) = Pr_1(v_2)$, then $v_1 = v_2$. Let $w = Pr_1(v_1) = Pr_1(v_2)$. We can write $v_1 = [w^\top, u_1^\top]^\top$ and $v_2 = [w^\top, u_2^\top]^\top$. Thus, it suffices to show that $u_1 = u_2$. Since $v_1 \in \ker \widehat{T}^\top$,

$$0 = \widehat{T}^\top v_1 = T^\top w + L_{pr} u_1 = \begin{bmatrix} \langle T_{\cdot,1}, w \rangle \\ \vdots \\ \langle T_{\cdot,l}, w \rangle \end{bmatrix} + L_{pr} u_1.$$

Note that $\langle T_{.,i}, w\rangle$ depends on the linkage class of complex C_i. Thus, the equation above can be written as

$$\begin{bmatrix} \xi_1 \\ \vdots \\ \xi_l \end{bmatrix} + L_{pr} u_1 = 0.$$

It implies that $Lu_1 = \begin{bmatrix} -\xi_1 \\ \vdots \\ -\xi_l \end{bmatrix}$. Analogously, $Lu_2 = \begin{bmatrix} -\xi_1 \\ \vdots \\ -\xi_l \end{bmatrix}$. Therefore $Lu_1 = Lu_2$. Since columns of L are linearly independent, L is of full column rank. Thus, $u_1 = u_2$, implying $Pr_1|_{\ker \widehat{T}^\top}$ is injective. ■

The connection presented by Proposition 4 will be the key for Corollaries 1 and 2.

Corollary 1. *Let $(\mathscr{N}, K)$ be a weakly reversible PL-RDK system with T-matrix T and $\widehat{\delta} = 0$. Fix $w \in (\widetilde{S}_R)^\perp$ and $x^* \in \mathbb{R}^m_+$ such that there exists $\gamma^* \in \mathbb{R}^l_+$ such that $\widehat{T}^\top \begin{bmatrix} \log(x^*) \\ -\log(\gamma^*) \end{bmatrix} = w$. Then for $x \in \mathbb{R}^m_+$ the following are equivalent:*

1. *There exists $\gamma \in \mathbb{R}^l_+$ such that $\widehat{T}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix} = w$.*
2. *The vector $\log(x) - \log(x^*) \in (\widetilde{S}_R)^\perp$.*

Proof. The equivalence is an immediate consequence of Proposition 4. ■

Corollary 2. *Let $(\mathscr{N}, K)$ be a weakly reversible PL-RDK system with T-matrix T and $\widehat{\delta} = 0$. Fix $w \in (\widetilde{S}_R)^\perp$. Then for all $q \in \mathbb{R}^m_+$, there exists $(x, \gamma) \in \mathbb{R}^m_+ \times \mathbb{R}^l_+$ such that $x \in (q + \widetilde{S}_R)$ and $\widehat{T}^\top \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix} = w$.*

Proof. The statement is an immediate consequence of Corollary 1 and Lemma 3.3 of [6]. ■

4 The Zero Kinetic Reactant Deficiency Theorem

Our main result (Theorem 6) is the existence of complex balanced equilibria for all weakly reversible PL-RDK systems with zero kinetic reactant deficiency for any choice of rate constants. To prove our main result, we need the following proposition and theorem:

Proposition 5 ([13]). *If $Z_+(\mathscr{N}, K) \neq \emptyset$, then $\mathscr{N}$ is weakly reversible.*

The following theorem, denoted as the "Structure Theorem of the k-Laplacian Kernel (STLK)" in [3] is one of the basis for important results in early CRNT (cf. [10]). For $t \in \mathbb{N}$, $\overline{1,t} := \{1, 2, ..., t\}$.

Theorem 4 (Structure Theorem of the Laplacian Kernel ([10])). *Let* $(\mathscr{C}, \mathscr{R}, k)$ *be a labeled directed graph with* $k : \mathscr{R} \to \mathbb{R}$. *Let* $\mathscr{C}'' = \mathscr{C} \setminus \cup_{k=1}^{t} \mathscr{C}^k$. *Let* A_k *be the Laplacian matrix. Denote by* A_k'' *the submatrix of* A_k *with rows and columns corresponding to* V''. *Then*

(i) A_k'' *is invertible,*

(ii) $\dim \ker A_k = t$, *and*

(iii) there exists a basis $y_1, y_2, ..., y_t \in \mathbb{R}^n_{\geq 0}$ *in* $\ker A_k$ *such that* $supp(y_k) = \mathscr{C}_k \quad \forall k \in \overline{1,t}$ *(i.e.,* $k \in \{1, 2, ..., t\}$*).*

Furthermore, we state here an important result found in [5] that will be useful in proving our prelimary result.

Proposition 6 ([5]). *Let* $l, m \in \mathbb{Z}_+$ *and* $n_1, n_2, \cdots, n_l \in \mathbb{Z}_+$. *Let* $A_j \in \mathbb{R}^{n_j \times m}$ *and* $b_j \in \mathbb{R}^{n_j}$ *(*$j \in \{1, 2, \cdots, l\}$*). Assume that* $\{x \in \mathbb{R}^m | A_j \cdot x = b_j\} \neq \emptyset$ *for all* $j \in \{1, 2, \cdots, l\}$ *and* $\operatorname{Im}\left[A_1^\top, A_2^\top, \cdots, A_l^\top\right] = \operatorname{Im} A_1^\top \oplus \operatorname{Im} A_2^\top \oplus \ldots \oplus \operatorname{Im} A_l^\top$. *Then*

$$\bigcap \{x \in \mathbb{R}^m | A_j \cdot x = b_j\} \neq \emptyset.$$

Theorem 5. *Let* $(\mathscr{N}, K)$ *be a weakly reversible PL-RDK system. Then*

(i) $Z_+(\mathscr{N}, K) = \bigcap Z_+(\mathscr{L}_i, K)$ *for each linkage class* $\mathscr{L}_i$.

(ii) $Z_+(\mathscr{N}, K) \neq \emptyset$ *if and only if* $Z_+(\mathscr{L}_i, K) \neq \emptyset$ *for each linkage class.*

Proof. Suppose $\mathscr{N}$ is weakly reversible. To prove (i), consider A_k and $\psi_K(x)$ in block forms:

$$A_k = \begin{bmatrix} A_{k,1} & & 0 \\ & \ddots & \\ 0 & & A_{k,l} \end{bmatrix} \text{ and } \psi_K(x) = \begin{bmatrix} (\psi_{K,1})(x) \\ \vdots \\ (\psi_{K,l})(x) \end{bmatrix}$$

where $A_{k,i}$ and $\psi_{K,i}(x)$ correspond to linkage class $\mathscr{L}^i$. Thus,

$$\operatorname{Im} A_k = \operatorname{Im} A_{k,1} \oplus \operatorname{Im} A_{k,2} \oplus \ldots \oplus \operatorname{Im} A_{k,l} \tag{4.1}$$

Recall the definition of $Z_+(\mathscr{N}, K) = \left\{x \in \mathbb{R}^m_+ \middle| A_k \cdot \psi_K(x) = 0\right\}$ and $Z_+(\mathscr{L}_i, K) = \left\{x \in \mathbb{R}^m_+ \middle| A_{k,i} \cdot \psi_{K,i}(x) = 0\right\}$. Clearly, $A_k \cdot \psi_K(x) \in \operatorname{Im} A_k$ and $A_{k,i} \cdot \psi_{K,i}(x) \in \operatorname{Im} A_{k,i}$. Hence, Equation 4.1 concludes the proof.

To prove (ii), we let $Z_+(\mathscr{L}_i, K) = \left\{x \in \mathbb{R}^m_+ \middle| A_{k,i} \cdot \psi_{K,i}(x) = 0\right\} \neq \emptyset$ for each linkage class $\mathscr{L}_i$. From the block form of A_k, it follows

$$\operatorname{Im} A_k^\top = \operatorname{Im} A_{k,1}^\top \oplus \operatorname{Im} A_{k,2}^\top \oplus \ldots \oplus \operatorname{Im} A_{k,l}^\top.$$

Using Proposition 6, we have

$$\bigcap Z_+(\mathscr{L}_i, K) = \bigcap \left\{x \in \mathbb{R}^m_+ \middle| A_k \cdot \psi_K(x) = 0\right\} \neq \emptyset. \tag{4.2}$$

Statement (i) together with Equation 4.2 gives (ii). ■

We are now ready to present and prove our main result as follows:

Theorem 6 (Zero Kinetic Reactant Deficiency Theorem)**.** *Let $\mathscr{K}$ a PL-RDK kinetics with T-matrix T on $\mathscr{N}$ and $\widehat{\delta} = 0$.*

(i) $\mathscr{N}$ is weakly reversible if and only if $Z_+(\mathscr{N}, K) \neq \emptyset$.

(ii) if $Z_+(\mathscr{N}, K) \neq \emptyset$ and $x^* \in Z_+(\mathscr{N}, K) \neq \emptyset$ then

$$Z_+(\mathscr{N}, K) = \left\{x \in \mathbb{R}^m_{\geq} \middle| \log(x) - \log(x^*) \in (\widetilde{S}_R)^\perp \right\}.$$

(iii) if $Z_+(\mathscr{N}, K) \neq \emptyset$ then $|Z_+(\mathscr{N}, K) \cap \boldsymbol{Q}| = 1$ for each positive kinetic reactant flux class $\boldsymbol{Q}$.

Proof. For (i): The converse is Proposition 5. For the forward direction, consider a weakly reversible network $\mathscr{N}$. Then, every linkage class is a terminal strong linkage class which means $t_i = 1 = \dim \ker A_{k,i}$ for all $\mathscr{L}_i$.

For any linkage class $\mathscr{L}_i$, by Theorem 4(iii), we can find a $y \in \mathbb{R}^{n,i}_+$ such that $\ker A_{k,i} = \operatorname{span} y$. Because $\psi_{K,i} \in \mathbb{R}^{n,i}_{\geq}$ for all $x \in \mathbb{R}^{m,i}_+$, finding an element in $Z_+(\mathscr{L}_i, K)$ is equivalent to finding some $\gamma \in \mathbb{R}_+$ and $x \in \mathbb{R}^{m,i}_+$ such that $\gamma y = \psi_{K,i}(x)$. Taking the logarithm of $\gamma y = \psi_{K,i}(x)$ coordinate-wise yields $\log(\gamma)\mathbf{1} + \log(y) = T_i^\top$, where $\mathbf{1}$ is the vector in $\mathbb{R}^n$

whose coordinates are all equal to 1. Hence, $x \in E_+(\mathscr{L}_i, K)$ if and only if there exists $\gamma \in \mathbb{R}_+$ such that

$$\log(y) = \widehat{T}_i^\top \cdot \begin{bmatrix} \log(x) \\ -\log(\gamma) \end{bmatrix}. \tag{4.3}$$

Since $\widehat{\delta} = \dim(\ker(\widehat{T})) = 0$, $\widehat{T}^\top$ has full range, $\log(y) \in \operatorname{Im} \widehat{T_i}^\top$. Because log and $-\log$ are bijective, we obtain $Z_+(\mathscr{L}_i, K) \neq \emptyset$. By Theorem 5, $Z_+(\mathscr{N}, K) \neq \emptyset$.

For (ii) and (iii): Assume for the rest of this proof that $Z_+(\mathscr{N}, K) \neq \emptyset$ and fix $x^* \in Z_+(\mathscr{N}, K)$. By Theorem 5, $x^* \in Z_+(\mathscr{L}_i, K)$ for all $i \in 1, 2, .., l$. Thus, by Corollary 1 and Equation 4.3, we have $Z_+(\mathscr{L}_i, K) = \left\{ x \in \mathbb{R}^m_{\geq} \middle| \log(x) - \log(x^*) \in (\widetilde{S}_{R,i})^\perp \right\}$ for each linkage class $\mathscr{L}_i$. Since $\widetilde{S}_R^\perp = (\sum \widetilde{S}_{R,i})^\perp = \cap \widetilde{S}_{R,i}^\perp$, the set

$$\left\{ x \in \mathbb{R}^m_{>} \middle| \log(x) - \log(x^*) \in (\widetilde{S}_R)^\perp \right\} = \cap \left\{ x \in \mathbb{R}^m_{>} \middle| \log(x) - \log(x^*) \in \widetilde{S}_{R,i}^\perp \right\}.$$

Thus, from Theorem 5, $Z_+(\mathscr{N}, K) = \left\{ x \in \mathbb{R}^m_{\geq} \middle| \log(x) - \log(x^*) \in (\widetilde{S}_R)^\perp \right\}$. The last statement follows from Corollary 2. ■

The result is valid for all weakly reversible PL-RDK systems. Theorem 6 extends the existence statement of the Low Deficiency Theorem of [22] to higher deficiency systems and complex balanced systems. On networks with inflow reactions, unlike the Higher Deficiency Theorem of [18], the proof of Theorem 6 does not need the Müller and Regensburger Criterion ([17], Statement(a) of Theorem 1).

Remark 5. To analyze the dynamics of Example 1, we use the translated network in Example 2 with the same kinetic order matrix F (s. Equation 2.1). Given that the system is PL-RDK, we have the augmented matrix $\widehat{T}$ in Equation 3.1 and $\widehat{\delta} = 0$. Since the network in Example 2 is weakly reversible, from Theorem 6, we conclude the existence and parametrization of (complex balanced) equilibria. We can infer that the system in Example 1 has a positive equilibrium.

Remark 6. The forward statement of Theorem 6 can be reformulated as "If $\mathscr{N}$ is weakly reversible and has zero kinetic reactant deficiency, then it has a complex balanced equilibrium for any rate constant". Applying the converse statement of the Müller and Regensburger Criterion implies that the system has zero kinetic deficiency. Hence, PL-TIK is a subset of the PL-RDK kinetics with $\widetilde{\delta} = 0$. It also follows that the existence and parametrization statements of the Deficiency Zero Theorem in [22] are special cases of the results in [17].

Example 3. *We consider the example of a multisite phosphorylation system. Phosphorylation is a fundamental biochemical reaction that modulates protein activities in cells. They are encountered in many intracellular processes such as signal transduction, cell-cycle control, or nuclear signal integration. There are several publications dealing with multisite phosphorylation system (Barik et al. [4]; Hermann-Kleiter and Baier [11]; Sadreev et al. [19]; Holstein et al. [12]).*

Holstein et al. [12] describe this systems using networks of phosphorylation and dephosphorylation of a protein at n *sites in a sequential distributive mechanism. The reaction network under mass action is given by*

$R_{1,i} : E_1 + A_{i-1,P} \to A_{i-1,P}E_1$
$R_{2,i} : A_{i-1,P}E_1 \to E_1 + A_{i-1,P}$
$R_{3,i} : A_{i-1,P}E_1 \to E_1 + A_{i,P}$
$R_{4,i} : E_2 + A_{i,P} \to A_{i,P}E_2$
$R_{5,i} : A_{i,P}E_2 \to E_2 + A_{i,P}$
$R_{6,i} : A_{i,P}E_2 \to E_2 + A_{i-1,P}$
for $i = 1, \ldots, n$.

The kinetic order matrix F *of the MAK system above is*

$$F = \begin{array}{c} \\ \\ \\ \\ \\ \\ \\ \\ \end{array}\begin{array}{cccccccc} E_1 & E_2 & \cdots & A_{i-1,P} & A_{i-1,P}E_1 & A_{i,P} & A_{i,P}E_2 & \cdots \\ \end{array}$$

$$F = \left[\begin{array}{cccccccc} \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \\ 1 & 0 & \cdots & 1 & 0 & 0 & 0 & \cdots \\ 0 & 0 & \cdots & 0 & 1 & 0 & 0 & \cdots \\ 0 & 0 & \cdots & 0 & 1 & 0 & 0 & \cdots \\ 0 & 1 & \cdots & 0 & 0 & 1 & 0 & \cdots \\ 0 & 0 & \cdots & 0 & 0 & 0 & 1 & \cdots \\ 0 & 0 & \cdots & 0 & 0 & 0 & 1 & \cdots \\ \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots & \vdots \end{array}\right] \begin{array}{c} \\ R_{1,i} \\ R_{2,i} \\ R_{3,i} \\ R_{4,i} \\ R_{5,i} \\ R_{6,i} \\ \\ \end{array}.$$

Thus, for $n-$ *site phosphorylation system, we have* $2n$ *linkage classes which are non-weakly reversible. Using the same technique as done in Example 2 (see also Remark 1), we construct a dynamically equivalent CRN of multisite phosphorylation system which is a weakly reversible network as follow:*

$$\begin{aligned}
&R_{1,i} : E_1 + E_2 + A_{i-1,P} \rightarrow A_{i-1,P}E_1 + E_2\\
&R_{2,i} : A_{i-1,P}E_1 + E_2 \rightarrow E_1 + E_2 + A_{i-1,P}\\
&R_{3,i} : A_{i-1,P}E_1 + E_2 \rightarrow E_1 + E_2 + A_{i,P}\\
&R_{4,i} : E_1 + E_2 + A_{i,P} \rightarrow A_{i,P}E_2 + E_1\\
&R_{5,i} : A_{i,P}E_2 + E_1 \rightarrow E_1 + E_2 + A_{i,P}\\
&R_{6,i} : A_{i,P}E_2 + E_1 \rightarrow E_1 + E_2 + A_{i-1,P}\\
&\textit{for } i = 1, \ldots, n.
\end{aligned}$$

Here, the kinetic order matrices of the original and translated networks are assumed to be the same, giving us dynamically equivalent systems (they have the same system of ordinary differential equations). The T-matrix of system is

$$T_n = \begin{array}{cc} \begin{array}{cccc} \cdots & A_{n-1}pE_1 & E_2 + A_np & A_{n-1}pE_2 \end{array} & \\ \begin{pmatrix} [T_{n-1}] & 0 & \vdots & 0 \\ 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{pmatrix} & \begin{array}{c} \vdots \\ A_{n-1}pE_1 \\ A_np \\ A_{n-1}pE_2 \end{array} \end{array}.$$

It is proved in [22], that the columns of T_n *are linearly independent, so is* $\widehat{T}$*. Thus,* $\widehat{\delta} = 0$*. Since the network is now weakly reversible, from Theorem 6, we have a complex balanced equilibria (with parametrization).*

Example 4. *One can apply the results of chemical reaction network theory to epidemiological problems, e.g. compartment models in epidemiology. Compartmental modeling is a mathematical framework to simplify the modeling of infectious diseases. The population is partitioned into compartments, with the assumption that every species in a compartment has the same characteristics.*

Consider a simple variation of SIR epidemic model with kinetic orders from $\mathbb{R}$*. We have three state variables (three partitioning of the population):* S*-susceptible individuals,* I*-infected individuals and* R*- recovered individuals. These variables represent the number of people in each compartment at a particular time. The chemical kinetic system will be*

$$\begin{aligned}
&R_1 : \mathrm{I} + \mathrm{S} \rightarrow 2\mathrm{I}\\
&R_2 : 2\mathrm{I} \rightarrow 2\mathrm{R}\\
&R_3 : 2\mathrm{R} \rightarrow 2\mathrm{S}
\end{aligned}$$

$R_4 : 2\mathrm{S} \rightarrow \mathrm{I} + \mathrm{S}$

with kinetic order matrix

$$\begin{array}{cc} & \begin{array}{ccc} S & I & R \end{array} \\ F = & \begin{bmatrix} 1 & 1 & 0 \\ 0 & 2 & 0 \\ 0 & 0 & 2 \\ 0.1 & 0 & 0 \end{bmatrix} \begin{array}{c} R_1 \\ R_2 \\ R_3 \\ R_4 \end{array} \end{array}.$$

The reaction R_1 pertains to the infection flow through the interaction between the susceptible and the infected individuals. R_2 is the recovery flow of the infected. R_3 implies temporal immunity of individuals. And, for the infection via the environment, we represent it as R_4 with kinetic order 0.1*. This is significantly below the kinetic order of R_1 implying the strength of infection via interaction of infected and susceptible over the infection via environmental causes. These SIRS model with both infection via contraction of individuals and via environmental factors (but without lasting resistance to the disease) can be seen in some fungal infection outbreak and flu infection outbreak. Constructing $\widehat{T}$, we have*

$$\begin{array}{cc} & \begin{array}{cccc} I+S & 2I & 2R & 2S \end{array} \\ \widehat{T} = & \begin{bmatrix} 1 & 0 & 0 & 0.1 \\ 1 & 2 & 0 & 0 \\ 0 & 0 & 2 & 0 \\ 1 & 1 & 1 & 1 \end{bmatrix} \begin{array}{c} S \\ I \\ R \\ \mathscr{L}_1 \end{array} \end{array}.$$

Note that the number of reactant complexes n_r is 4 *and $\widehat{q} = \operatorname{rank} \widehat{T} = 4$. Thus, the kinetic reactant deficiency $\widehat{\delta} = 0 = (4 - 4)$. Since $\mathscr{N}$ is weakly reversible, from Theorem 6, we have a complex balanced equilibria (with parametrization) for the "power law" epidemic system.*

5 Conclusions/Outlook

In conclusion, we summarize our main results and outline some perspectives for future research.

1. We introduced the concept of kinetic reactant deficiency, for which we have shown that zero kinetic reactant deficiency systems are precisely the PL-TIK systems introduced in [22].

2. We proved the existence, parametrization and uniqueness of complex balanced equilibria for all weakly reversible reactant-determined systems with zero kinetic reactant deficiency for any choice of rate constants. This is a generalization of the "Weak reversibility" theorem of PL-TLK system presented in [18].
3. We applied the theorem to the CRN representation of a power law approximation of a specific SIRS model and multisite phosphorylation system of Holstein et al. [12] and found that complex balanced steady states exist in these systems.
4. We plan to extend our weak reversibility result to more general kinetics like those which are linear combinations of power laws.

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