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Positive equilibria of weakly reversible power law kinetic systems with linear independent interactions

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Abstract In this paper, we extend our study 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. In particular, we consider PL-TLK systems, i.e. such whose T-matrix (the matrix with the interactions as columns indexed by the reactant complexes), when augmented with the rows of characteristic vectors of the linkage classes, has maximal column rank. Our main result states that any weakly reversible PL-TLK system has a complex balanced equilibrium. On the one hand, we consider this result as a "Higher Deficiency Theorem" for such systems since in our previous work, we derived analogues of the Deficiency Zero and the Deficiency One Theorems for mass action kinetics (MAK) systems for them, thus covering the "Low Deficiency" case. On the other hand, our result can also be viewed as a "Weak Reversibility Theorem" (WRT) in the sense that the statement "any weakly reversible system with a kinetics from the given set has a positive equilibrium" holds. According to the work of Deng et al. and more recently of Boros, such a WRT holds for MAK systems. However, we show that a WRT does not hold for two proper MAK supersets: the set PL-NIK of non-inhibitory power law kinetics (i.e. all kinetic orders are non-negative) and the set

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PL-FSK of factor span surjective power law kinetics (i.e. different reactants imply different interactions).

Keywords Chemical reaction networks · Power law kinetics · Linear independent interactions · Complex balanced equilibria · Zero kinetic deficiency · Weak Reversibility Theorem

List of symbols

$\widehat{T}$	Augmented T matrix
δ	Deficiency of a CRN
ψ_K	Factor map of a kinetics K
I_a	Incidence matrix of a CRN
A_k	k-Laplacian matrix
$\widetilde{\delta}$	Kinetic deficiency
$\widetilde{S}$	Kinetic flux subspace
F	Kinetic order matrix
$\widetilde{S}_{MR}$	Kinetic order subspace
$\widetilde{s}$	Kinetic rank
$\widetilde{q}$	Kinetic reactant rank
$\widetilde{S}_R$	Kinetic reactant flux subspace
$\widetilde{R}$	Kinetic reactant subspace
K	Kinetics of a CRN
Y	Molecularity map/matrix of complexes
π	Product map
$\Delta(\mathscr{N})$	Rank difference
δ_ρ	Reactant deficiency
ρ	Reactant map
Y_{res}	Reactant matrix
R	Reactant subspace
$\widetilde{\mathscr{N}}$	Reactant network of kinetic complexes
$E_+(\mathscr{N}, K)$	Set of positive equilibria of a system
$Z_+(\mathscr{N}, K)$	Set of complex balanced equilibria of a system
N	Stoichiometric matrix
S	Stoichiometric subspace of a CRN
$\tau(\mathscr{N})$	Terminality of a CRN
T	T matrix

Abbreviations

BST	Biochemical systems theory
CBK	Complex balanced kinetics
CKS	Chemical kinetic system
CRN	Chemical reaction network
CRNT	Chemical reaction network theory

GMAK	Generalized mass action kinetics
GCRN	Generalized chemical reaction network
ILC	Independent linkage classes
KDZT	Kinetic Deficiency Zero Theorem
LCELT	Linkage Class Equilibria Lifting Theorem
MAK	Mass action kinetics
ODE	Ordinary differential equation
PLK	Power-law kinetics
PL-FSK	Power-law factor span surjective kinetics
PL-ILK	Inflow-excluded linkage class linear independent kinetics
PL-IRK	Inflow-excluded reactant set linear independent kinetics
PL-LLK	Linkage class linear independent kinetics
PL-NIK	Power law non-inhibitory kinetics
PL-RDK	Power-law reactant-determined kinetics
PL-RLK	Reactant set linear independent kinetics
PL-TIK	$\widehat{T}$-rank maximal PL-ILK kinetics
PL-TLK	$\widehat{T}$-rank maximal PL-LLK kinetics
RDK	Reactant-determined kinetic orders
RSS	Reactant-determined stoichiometric subspace
SFRF	Species formation rate function
WRT	Weak Reversibility Theorem

1 Introduction

In this paper we extend our study of power law inflow-excluded linear independent kinetics (PL-ILK) and its subsets that were introduced in [18] (see Fig. 2 for an overview). We refer to these kinetics sets from now on as the "family of power law kinetics with linear independent interactions" for the following reason: in most biochemical modeling frameworks (e.g. Biochemical Systems Theory), a kinetic order specifies the type (activating/inhibiting) and strength of the bilateral interaction between network nodes. The kinetic order vector (a row in the kinetic order matrix or a column in the T matrix) collects the information of the interactions involved in a reaction. Hence the linear independence of these vectors can be viewed as linear independence of interactions. PL-ILK and its relevant subsets express different forms of this linear independence of interactions.

PL-LLK consists of power law kinetics whose interactions per linkage class are linearly independent. Its subset PL-TLK was characterized in [18] as those with the property that the augmented T matrix, i.e. the T matrix augmented by the rows of characteristic vectors of the linkage classes, had maximal column rank. Since PL-LLK and PL-TLK are empty on networks with inflow reactions, the sets PL-ILK and PL-TIK were introduced on such networks after excluding the zero vector (of the zero reactant complex) in the T matrix, they had the analogous properties of PL-LLK and PL-TLK. On networks without inflow, they were by definition equal to PL-LLK and PL-TLK. The main results for PL-TIK systems in [18], which are reviewed and refined in Sect. 3, were a "Lifting Theorem" for linkage class equilibria and analogues of the

Deficiency Zero Theorem (DZT) and Deficiency One Theorem (DOT) for mass action kinetics (MAK) systems. We combine these analogues to a "Low Deficiency Theorem" in Sect. 3. Several models of complex biological systems displaying PL-TIK kinetics were also documented in the Supplementary Material of [18].

In this paper, we show (in Theorem 7 of Sect. 4) that on networks without inflow reactions, any weakly reversible PL-TIK system has a positive complex balanced equilibrium, thus extending the existence statement of the Low Deficiency Theorem to higher deficiency systems. On networks with inflow reactions, we identify subsets of PL-TIK systems with the same property. For such systems, if the network has independent linkage classes, then the parametrization statement of the Low Deficiency Theorem is also valid. Significantly for the theory of Generalized Mass Action Kinetics (GMAK) systems of Müller and Regensburger [17], our result provides the first examples of such systems with zero kinetic deficiency on networks with positive deficiency (see Sect. 4 for definitions and details).

Our main results can also be viewed from the perspective of the following problem for subsets of power law kinetics: "If $\mathscr{N}$ is any weakly reversible CRN, given a subset $\mathscr{K}^*$ of $\mathcal{PLK}(\mathscr{N})$, does every chemical kinetic system $(\mathscr{N}, K)$ with $K \in \mathscr{K}^*$ have a positive equilibrium?" If the answer is "Yes", then we say that $\mathscr{K}^*$ has a Weak Reversibility Theorem (WRT). To our knowledge, there are currently two WRT's documented in the CRNT literature for power law kinetics: for mass action kinetics (assuming the correctness of the proof by Deng et al. [6] or of Boros [5]) and for power law kinetics with reactant-determined interactions and zero kinetic deficiency [1]. Our result is hence a special case of the latter WRT. Given this very short list, the next question is of course: for which other kinetics subsets do WRT's exist? Of particular interest are those which are proper supersets of mass action kinetics. We show in Sect. 5 that there is no WRT for the supersets of non-inhibitory power law kinetics (PL-NIK) and the superset of factor span surjective power law kinetics (PL-FSK).

We provide in Sect. 2 a summary of fundamental concepts on chemical reaction networks and kinetics needed in the later sections. Brief summaries of the results on GMAK systems and S-systems are provided in Sects. 4.2 and 5.1, respectively. In Sect. 6, we provide a summary of our results and an outlook for further research.

2 Fundamental concepts of chemical reaction networks and kinetics

In this section, we collect the fundamental concepts and results about chemical reaction networks (CRNs) and chemical kinetic systems (CKS) needed for our study. One can look at [1–3,18] for details of the concepts presented here.

2.1 Basic properties of chemical reaction networks

We expound first on the notion that a CRN is a digraph with a vertex-labelling, i.e., its stoichiometry.

Definition 1 A **chemical reaction network (CRN)** is a digraph $(\mathscr{C}, \mathscr{R})$ where each vertex has positive degree and stoichiometry, i.e., there is a finite set $\mathscr{S}$ (whose ele-

ments are called **species**) such that $\mathscr{C}$ is a subset of $\mathbb{R}^{\mathscr{S}}_{\geq}$. Each vertex is called a **complex** and its coordinates in $\mathbb{R}^{\mathscr{S}}_{\geq}$ are called **stoichiometric coefficients**. The arcs are called **reactions**.

We denote the number of species with m, the number of complexes with n, and the number of reactions with r.

The concept of stoichiometry allows the embedding of the graph's vertices in the real vector space $\mathbb{R}^{\mathscr{S}}_{\geq}$, called **species composition space** (or simply, **species space**). The elements of this space are viewed as (chemical) compositions, i.e., the coordinate values are concentrations of the different (chemical) species. We denote a CRN as a triple $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ to indicate the pair $((\mathscr{C}, \mathscr{R}), \mathscr{S})$. They are equivalent (see [8]) provided $\mathscr{S} = \bigcup_{y \in \mathscr{C}} \operatorname{supp} y$, i.e., each species appears in at least one complex.

Definition 2 A complex is called **monospecies** if it consists of only one species, i.e. of the form nX_i, n a non-negative integer and X_i a species. It is called **monomolecular** if $n = 1$, and is identified with the **zero complex** for $n = 0$.

The zero complex represents the "outside" of the system studied, from which chemicals can flow into the system at a constant rate and to which they can flow out at a linear rate (proportional to the concentration of the species). In biological systems, the "outside" also stands for the degradation of a species. An **inflow reaction** is a reaction with reactant "0" and an **outflow reaction** is a reaction with a monomolecular complex as reactant and the zero complex as product, respectively.

Two useful maps are associated with each reaction:

Definition 3 The **reactant map** $\rho : \mathscr{R} \to \mathscr{C}$ maps a reaction to its reactant complex while the **product map** $\pi : \mathscr{R} \to \mathscr{C}$ maps it to its product complex. We denote $|\rho(\mathscr{R})|$ with n_r, i.e., the number of reactant complexes.

The concept of connectivity in digraphs also applied to CRNs but with different terminologies. A connected component in a CRN is usually called a **linkage class**. A **strong linkage class** is a subset of a linkage class where any two elements are connected by a directed path in each direction. A **terminal strong linkage class** is a strong linkage class such that there is no reaction from a complex in the strong linkage class to a complex not in the strong linkage class.

We denote the number of linkage classes with l, those of the strong linkage class with sl, and the number of terminal strong linkage classes with t. Clearly $sl \geq t \geq l$.

Definition 4 A chemical reaction network is called **weakly reversible** if $sl = l$ and **t-minimal** if $t = l$.

The terminal strong linkage classes can be of two kinds: cycles (not necessarily simple) and singletons (which we call "terminal points"). We have the following useful classification of CRNs according to the types of their terminal strong linkage classes.

Definition 5 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 $n - n_r < t$.

Remark 1 We denote by t_c the number of cycle-terminal classes and t_p the number of point-terminal classes. Then $t = t_c + t_p$. Note also that $n - n_r = t_p = t - t_c$. A CRN is cycle-terminal if $t_p = 0$ (i.e. $n = n_r$), point-terminal if $t_c = 0$ (i.e. $t = n - n_r$) and point- and cycle-terminal otherwise (i.e. $t_p > 0$ and $t_c > 0$ or equivalently, $t > n - n_r$).

Each linkage class $\mathscr{L}^i$ forms a subnetwork and we designate the number of complexes and reactions in $\mathscr{L}^i$ with n^i and r^i, respectively, $i = 1, \ldots, l$. Let

$$e^1, e^2, \ldots, e^l \in \{0, 1\}^n$$

be the characteristic vectors of the sets $\mathscr{C}^1, \mathscr{C}^2, \ldots, \mathscr{C}^l$, respectively, where $\mathscr{C}^i$ is the set of complexes in linkage class $\mathscr{L}^i$.

We recall several matrices associated to CRNs which are relevant to our study.

Definition 6 The **incidence matrix** I_a is an $n \times r$ matrix where each row corresponds to a complex and each column to a reaction, satisfying

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

If the CRN also has an arc labeling, i.e., a map $k : \mathscr{R} \to \mathbb{R}_>$, then we can associate to it a k-Laplacian matrix as follows:

Definition 7 The **k-Laplacian matrix** of an arc 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 stoichiometry information of a CRN is given through the **matrix of complexes** Y. More precisely, if the complexes are $y_1, \ldots, y_n$ and we let the i-th coordinate of y_j its stoichiometric coefficient with respect to the species X_i then Y is defined as follows:

Definition 8 The **matrix of complexes** Y is the $m \times n$ matrix whose $(i, j)_{th}$ element is the stoichiometric coefficient of y_j with respect to X_i.

Two other matrices play important roles in the Linear Geometry of species (composition) space:

Definition 9 The **stoichiometric matrix** N is the $m \times r$ matrix defined by $N = Y I_a$. Its image Im N is called the **stoichiometric subspace** S, whose dimension s is called the rank of the network. Clearly S is generated by the reaction vectors.

The cosets with respect to the stoichiometric subspace form the basis for the concept of stoichiometric classes:

Definition 10 For $x \in \mathbb{R}^m_{\geq}$, the set $(x + S) \cap \mathbb{R}^m_{\geq 0}$ is called a **stoichiometric class**.

Definition 11 The **reactant matrix** Y_{res} is the $m \times n_r$ matrix Y without the columns of the terminal points. Its columns are the reactant complexes $\rho(R_1), \rho(R_2), \ldots, \rho(R_r)$. Its image Im Y_{res} is called the **reactant subspace** R, whose dimension q is called the **reactant rank** of the CRN. Clearly R is generated by the reactant complexes.

Arceo et al. [1] conducted an initial systematic study of the reactant subspace R's connection to kinetic behavior and identified the set of RSS networks as particularly interesting.

Definition 12 A CRN has the **reactant-determined stoichiometric subspace (RSS) property** (or type RSS) if S is contained in R.

For each CRN, a non-negative integer called deficiency can be computed. This number is of particular interest to CRNT enthusiasts because of its relevance to the dynamic behavior of the system.

Definition 13 The **deficiency** of a chemical reaction network is the integer $\delta = n - l - s$.

We can define the deficiency not only for the whole network, but also for each linkage class $\mathscr{L}^i$. Considering the stoichiometric matrix N in block form, i.e., $N = \left[N^1, \ldots, N^l\right]$, we let $s^i = \text{rank } N^i$.

Definition 14 The **deficiency of linkage class** $\mathscr{L}^i$ (denoted by δ^i) is defined by the formula $\delta^i = n^i - 1 - s^i$.

An essential measure of the linear independence of reactant complexes is given in the following definition introduced by Arceo et al. [1].

Definition 15 The **reactant deficiency** of a network is given by $\delta_\rho := n_r - q$, i.e., the difference between the number of reactant complexes and the reactant rank q.

Remark 2 Theorem 1 of [1] summarizes the relationship between deficiency and reactant deficiency of a CRN. In particular, for cycle terminal networks, $0 \leq \delta_\rho - \delta \leq \ell$.

A network property of considerable importance in our further discussion is that of independence of linkage classes (ILC).

Definition 16 A CRN $\mathscr{N}$ with the property $\delta = \delta^1 + \delta^2 + \cdots + \delta^l$ is called a network with **independent linkage classes**, ILC or ILC-network. Otherwise, if $\delta \neq \delta^1 + \delta^2 + \cdots + \delta^l$, it is called a network with **dependent linkage classes** or DLC-network.

2.2 Fundamentals of chemical kinetic systems

Definition 17 A **kinetics** K for a reaction network $(\mathscr{S}, \mathscr{C}, \mathscr{R})$ is an assignment to each reaction $j \in \mathscr{R}$ of a rate function $K_j : \Omega_K \to \mathbb{R}_{\geq 0}$ where Ω_K is a set such that $\mathbb{R}^m_{>0} \subseteq \Omega_K \subseteq \mathbb{R}^m_{\geq 0}$, $c \wedge d \in \Omega_K$, and

$$K_j(c) \geq 0, \quad \forall c \in \Omega_K.$$

A kinetics for a network $\mathscr{N}$ is denoted by $K = (K_1, K_2, \ldots, K_r) : \Omega_K \to \mathbb{R}^{\mathscr{R}}_{\geq 0}$. The pair $(\mathscr{N}, K)$ is called a **chemical kinetic system** (CKS).

We focus on the kind of kinetics relevant to our context:

Definition 18 A **chemical kinetics** is a kinetics K satisfying the positivity condition: for each reaction $j : y \to y'$, $K_j(c) > 0$ if and only if supp $y \subset$ supp c.

Definition 19 The **species formation rate function** (SFRF) of a CKS is the vector field $f(x) = NK(x) = \sum_{y \to y'} K_{y \to y'}(x)(y' - y)$.

$$dx/dt = f(x)$$

is the ODE or dynamical system of the CKS. A zero of f is an element c of $\mathbb{R}^{\mathscr{S}}$ such that $f(c) = 0$. A zero of f is an **equilibrium** or **steady state** of the ODE system. For a differentiable f, a steady state c is called **non-degenerate** if the $\ker(J_c(f)) \cap S = \{0\}$, where $J_c(f)$ is the Jacobian matrix of f at c.

Definition 20 A **positive equilibrium** x is an element of $\mathbb{R}^m_>$ for which $f(x) = 0$. The **set of positive equilibria** of a chemical kinetic system is denoted by $E_+(\mathscr{N}, K)$.

Definition 21 A positive vector c in $\mathbb{R}^{\mathscr{S}}$ is called **complex balanced** (CB) if $K(x)$ is contained in $\ker I_a$. Further, if c is a positive equilibrium then we call it a complex balanced equilibrium. We denote by Z_+ the **set of complex balanced equilibria** of a system.

Proposition 1 [13] *If a chemical kinetic system has complex balanced equilibria, then the underlying CRN is weakly reversible.*

Proposition 2 [7] *If a chemical kinetic system has deficiency* 0*, then its equilibria are all complex balanced.*

Linkage classes partition both the set of complexes and the set of reactions, the linear maps Y, I_a and N can be decomposed by restricting their domains to the complexes or reactions in a linkage class. Hence we can write $Y = \left[Y^1, \ldots, Y^l\right]$, $I_a = \left[I_a^1, \ldots, I_a^l\right]$ and $N = \left[N^1, \ldots, N^l\right]$.

We can use the partition of the reaction set into subsets $\mathscr{R}^i$ for each linkage class to obtain the corresponding decomposition $K = \left[K^1, \ldots, K^l\right]$, with $K^i : \mathbb{R}^{\mathscr{S}} \to \mathbb{R}^{\mathscr{R}}$. We then define a linkage class decomposition for SFRF $f = f^1 + f^2 + \cdots + f^l$ with $f^i = N^i K^i$.

Given this decomposition of the SFRF with respect to the linkage classes, we can consider the sets of positive equilibria $E_+(\mathscr{N}^i, K^i)$ of the f^i and their relationships to the positive equilibria of the whole system. Clearly, for any network and any kinetics, the intersection $\cap_i E_+(\mathscr{L}^i, K^i)$ is contained in $E_+(\mathscr{N}, K)$. The following theorem demonstrates the impact of the structural property of ILC on the kinetic behavior of the system:

Theorem 1 (Feinberg's Decomposition Theorem [9]) *Let $\mathscr{N}$ be a network with ILC, and K a chemical kinetics on $\mathscr{N}$. Then $E_+(\mathscr{N}, K) = \cap_i E_+(\mathscr{N}^i, K^i)$. In particular, $E_+(\mathscr{N}, K) \neq \emptyset$ implies $E_+(\mathscr{N}^i, K^i) \neq \emptyset$ for each linkage class L^i.*

In general, $E_+(\mathscr{N}^i, K^i) \neq \emptyset$ for each linkage class L^i does not imply the existence of a positive equilibrium for the whole system, even under ILC. Hence identifying kinetics sets with this property is an interesting research area. One large kinetic sets are the so-called power-law kinetics [14].

Definition 22 A kinetics $K : \mathbb{R}^m_> \to \mathbb{R}^r$ is a **power-law kinetics** (**PLK**) if

$$K_i(x) = k_i x^{F_i} \quad \forall i \in \{1, \ldots, r\}$$

with $k_i, F_{ij} \in \mathbb{R}_+$. 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**.

Arceo et al. [2] presented a kinetics landscape with algebraic properties which include power-law systems. The SFRF of a **PLK** system can be written as

$$f(x) = \sum_{i \in \mathscr{R}} k_i \prod_{i=1}^{r} x_j^{F_{ij}} \cdot N_{.,i} \quad \text{for } x \in \mathbb{R}^m_>.$$

where $N_{.,i}$ is the i^{th} column of stoichiometric matrix N.

An example of PLK is the well-known Mass Action Kinetics (MAK) where the kinetic order matrix is the transpose of the molecularity matrix [4,8]. Hence, we can write the SFRF of a MAK as:

$$f(x) = \sum_{(i,j) \in \mathscr{R}} k_i \prod_{i=1}^{r} x_j^{Y_{ji}} \cdot N_{.,i} \quad \text{for } x \in \mathbb{R}^m_>$$

In [3], two supersets of MAK namely, $\mathcal{PL} - \mathcal{RDK}(\mathscr{N})$ and $\mathcal{PL} - \mathcal{NIK}(\mathscr{N})$, were defined as follows.

Definition 23 A power law kinetics is in $\mathcal{PL}$–$\mathcal{NIK}(\mathscr{N})$ (or **has non-inhibitory kinetics**) if

(i) the kinetic order matrix F is non-negative and
(ii) a kinetic order $F_{r,s} > 0$ iff the species s is an element of supp $\rho(r)$.

Definition 24 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 $k = 1, \ldots, m$.

Definition 25 The **factor map** $\psi_K : \mathbb{R}^m \to \mathbb{R}^n$ is defined as

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

Another set of power-law kinetics of special interest for us is the set of factor span surjective systems $\mathcal{PL} - \mathcal{FSK}(\mathscr{N})$. We use the following characterization which was derived in [2] as our working definition:

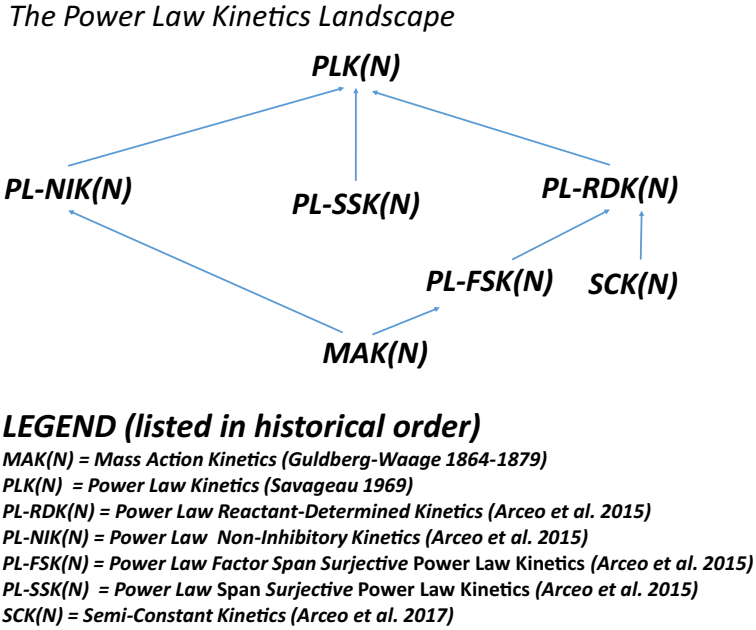

Fig. 1 The power-law kinetics landscape

Definition 26 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 $F_{r,\cdot} \neq F_{r',\cdot}$).

The SFRF of a PL-RDK kinetics has the following decomposition:

$$f = Y \cdot A_k \cdot \psi_K$$

The Power-Law Kinetics Landscape in Fig. 1 provides an overview of kinetics subsets studied so far in CRNT.

3 Power-law kinetic systems with linear independent interactions

In this section, we discuss $\mathcal{PL} - \mathcal{RDK}(\mathcal{N})$ and its subsets, in particular, those power-law kinetics systems with linear independent interactions (i.e., $\mathcal{PL} - \mathcal{ILK}(\mathcal{N})$) presented in [18]. We start by defining the T-matrix of a kinetic system. In Sect. 3.1, we focus on networks without inflow reactions (i.e., $\mathcal{PL} - \mathcal{LLK}(\mathcal{N})$). In Sect. 3.2, we extend the study to networks with inflow reactions (i.e., $\mathcal{PL} - \mathcal{ILK}(\mathcal{N})$) and its relation to other kinetic systems. We recall the Low Deficiency Theorems for PL-TIK systems and extend the results of Theorem 4 of [18] to complex balanced equilibria.

Müller and Regensburger [17] introduced the $m \times n$ matrix $\widetilde{Y}$ defined as:

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

where F is the kinetic order matrix in Definition 22. This matrix $\widetilde{Y}$ is a generalization of that defined in [17].

Talabis et al. [18] defined the T-matrix and the augmented T-matrix ($\widehat{T}$) as follows:

Definition 27 The $m \times n_r$ **T-matrix** is the truncated $\widetilde{Y}$ where the non-reactant columns are deleted. 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** $\widetilde{q}$.

Definition 28 The block matrix $\widehat{T} \in \mathbb{R}^{(m+l)\times n_r}$ is defined as

$$\widehat{T} = \begin{bmatrix} T \\ L_{pr}^{\top} \end{bmatrix},$$

where $L_{pr}^{\top}$ is the truncated matrix L (i.e., non-reactant rows are left out).

3.1 Power law kinetics with linear independent interactions on networks without inflows

We are now in the position to review the classes of PL-RDK without inflow reactions presented in [18].

Definition 29 A PL-RDK kinetics is **linkage class linear independent** (of type **PL-LLK**) if the columns of T corresponding to each linkage class are linearly independent.

Definition 30 A PL-LLK kinetics is $\widehat{T}$-rank maximal (to type **PL-TLK**) if the column rank of $\widehat{T}$ is maximal.

Definition 31 A PL-RDK kinetics is **reactant set linear independent** (of type **PL-RLK**) if it satisfies the following equivalent conditions:

(i) the columns of the T matrix are linearly independent;
(ii) the map T is injective (hence a bijection $\mathbb{R}^{\rho(\mathscr{R})} \to \widetilde{R}$); and
(iii) $\widetilde{q} = n_r$.

Remark 3 By the preceding definitions, $\mathcal{PL} - \mathcal{RLK}(\mathscr{N}) \subseteq \mathcal{PL} - \mathcal{TLK}(\mathscr{N})$. However, it can be shown that $\mathcal{MAK} - \mathcal{RLK}(\mathscr{N}) \subset \mathcal{MAK} - \mathcal{TLK}(\mathscr{N})$ as illustrated in the succeeding example.

Example 1 Since MAK-RLK is equivalent to the network having zero reactant deficiency, we search among weakly reversible networks with zero deficiency and positive reactant deficiency. The network

$$R_1, R_2 :: A \leftrightarrow A + B$$

$R_3, R_4 :: 2A \leftrightarrow 2B$

has $\delta = 4 - 2 - 2 = 0$ and $\delta_\rho = 4 - 2 = 2$ (and hence, non-MAK-RLK). Its augmented T $(= Y_{res})$ matrix is:

$$\widehat{T} = \begin{array}{c} \begin{matrix} A & A+B & 2A & 2B \end{matrix} \\ \begin{bmatrix} 1 & 1 & 2 & 0 \\ 0 & 1 & 0 & 2 \\ 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 \end{bmatrix} \end{array} \begin{matrix} A \\ B \\ L_1 \\ L_2 \end{matrix} .$$

Since its determinant $= 1$, then it has maximal column rank, i.e. the network is MAK-TLK.

The following proposition characterizes the networks for which PL-RLK systems exist:

Proposition 3 *$\mathcal{PL} - \mathcal{RLK}(\mathcal{N}) \neq \emptyset$ iff $\mathcal{N}$ has no inflow reactions and $n_r \leq m$.*

Proof To prove ($\Rightarrow$), observe that a T matrix with all columns linearly independent cannot be constructed if a zero column (generated by an inflow reaction) exists or the number of columns is greater than the maximal rank m. To show ($\Leftarrow$), if y_j is one of the nonzero reactant complexes, set $T_{ij} = 1$, if $i = j$ and 0 otherwise, for $i = 1, \ldots, m$ and $j = 1, \ldots, n_r$. Clearly, all n_r columns are linearly independent and the constructed system is PL-RLK.

Outflow reactions may exist, since they are typically linear, i.e. have kinetic order row $= (1, \ldots, 1)$. This has the following consequence for cycle terminal networks:

Corollary 1 *A cycle terminal network $\mathcal{N}$ for which $\mathcal{PL} - \mathcal{RLK}(\mathcal{N}) \neq \emptyset$ does not contain the zero complex.*

Proof If the zero complex is in the network, then Proposition 3 implies that it must be a terminal point.

Remark 4 For a particular PL-RDK system, we have a stronger necessary condition for it to be in PL-RLK.

The following proposition shows the connection of $\mathcal{PL} - \mathcal{RLK}(\mathcal{N})$ to the reactant deficiency theory in Sect. 2. It is also a nice example of network structure kinetic behavior relationship.

Proposition 4 *A network has zero reactant deficiency iff any MAK system is reactant set linear independent.*

Proof For a MAK system, T is the restriction of Y to $\mathbb{R}^{\rho(\mathscr{R})}$ and $\widetilde{R} = R$. Hence, after Definition 31 (iii), the RLK property is equivalent to $q = n_r$.

3.2 Power law kinetics with linear independent interactions on networks with inflows

We now extend the kinetic systems presented in Sect. 3.1 to networks with inflow reactions by excluding the 0 complex column of T-matrix.

Definition 32 A PL-RDK kinetics is **inflow-excluded linkage class linear independent** (of type **PL-ILK**) if the non-inflow columns (i.e., columns of the complexes associated to non-inflow reactions) of T corresponding to each linkage class are linearly independent.

Definition 33 A PL-RDK kinetics is **inflow-excluded reactant set linear independent** (of type **PL-IRK**) if the non-inflow columns (i.e., columns of the complexes associated to non-inflow reactions) of T are linearly independent.

Definition 34 A PL-ILK kinetics is $\widehat{T}$-rank maximal (to type **PL-TIK**) if its column rank is maximal.

The following set inclusions hold true:

1. $\mathcal{PL} - \mathcal{ILK}(\mathscr{N}) \supseteq \mathcal{PL} - \mathcal{LLK}(\mathscr{N})$;
2. $\mathcal{PL} - \mathcal{TIK}(\mathscr{N}) \supseteq \mathcal{PL} - \mathcal{TLK}(\mathscr{N})$; and
3. $\mathcal{PL} - \mathcal{IRK}(\mathscr{N}) \supseteq \mathcal{PL} - \mathcal{RLK}(\mathscr{N})$.

In addition, if the network has one linkage class, we have the following equalities:

1. $\mathcal{PL} - \mathcal{TIK}(\mathscr{N}) = \mathcal{PL} - \mathcal{IRK}(\mathscr{N})$; and
2. $\mathcal{PL} - \mathcal{TLK}(\mathscr{N}) = \mathcal{PL} - \mathcal{RLK}(\mathscr{N})$.

Remark 5 For CRNs without inflows, we have: $\mathcal{PL} - \mathcal{ILK}(\mathscr{N}) = \mathcal{PL} - \mathcal{LLK}(\mathscr{N})$ and $\mathcal{PL} - \mathcal{IRK}(\mathscr{N}) = \mathcal{PL} - \mathcal{RLK}(\mathscr{N})$. On the other hand, if there are inflows, $\mathcal{PL} - \mathcal{LLK}(\mathscr{N}) = \mathcal{PL} - \mathcal{RLK}(\mathscr{N}) = \emptyset$.

By definition of T-matrix, we see that $\mathcal{PL} - \mathcal{FSK}(\mathscr{N})$ contains $\mathcal{PL} - \mathcal{IRK}(\mathscr{N})$ and $\mathcal{PL} - \mathcal{RLK}(\mathscr{N})$. On the other hand, for the remaining subsets of $\mathcal{PL} - \mathcal{ILK}(\mathscr{N})$, only the linkage classes are factor span surjective. Figure 2 illustrates the connections between the presented classes of PL-RDK systems.

3.3 Equilibria lifting for PL-TIK systems

One of the main objects of study in CRNT is the relationship between positive equilibria sets of linkage classes and the positive equilibria set of the whole network. Feinberg [10] introduced the "Linkage Class Equilibria Lifting Theorem" (LCELT) for MAK:

Theorem 2 (LCELT-MAK [10]) *For any MAK system with independent linkage class decomposition, i.e.,* $\delta = \delta_1 + \delta_2 + \cdots + \delta_l$, $E_+(\mathscr{L}_i, K) \neq \emptyset$ *for each linkage class implies* $E_+(\mathscr{N}, K) \neq \emptyset$.

Considering the kinetics described in Sect. 3.2, we extend the "Linkage Class Equilibria Lifting Theorem" (LCELT) for PL-TIK system (Theorem 4) of Talabis et al. [18] to complex balanced equilibria.

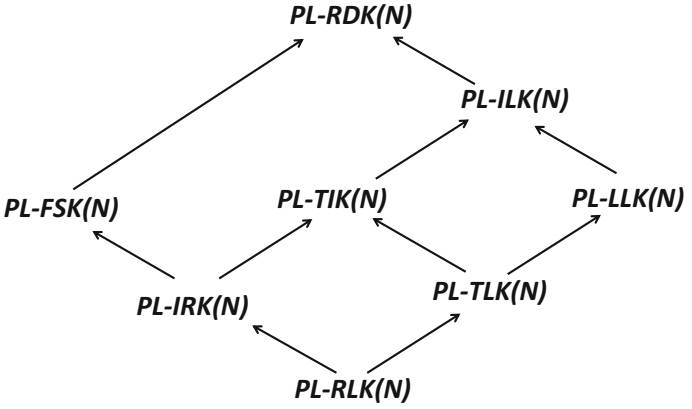

Fig. 2 PL-ILK and related kinetics sets [18]

Theorem 3 (LCELT-PLTIK [18]) *Let* $(\mathscr{N}, K)$ *be a PL-TIK system.*

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

Proof For (ii), the proof is the same with Theorem 4 in [18] after replacing E_+ by Z_+ and expressions involving $Y A_k v^r = 0$ with $A_k v^r = 0$.

Example 2 The following example demonstrates that even for MAK systems, the previous theorem can provide novel results not within the scope of Feinberg's Equilibria Lifting Theorem for MAK systems with independent linkage classes [10]. It also provides a non-weakly reversible example for MAK-TLK systems which are not MAK-RLK.

The CRN C_R is given by:

$$R_1, R_2 : A \leftrightarrow B$$
$$R_3 : A + B \rightarrow 2A$$
$$R_4 : A + B \rightarrow 2B.$$

The augmented Y_{res} matrix is given by

$$\widehat{T} = \begin{array}{c} \begin{matrix} B & A & A+B \end{matrix} \\ \begin{bmatrix} 0 & 1 & p \\ 1 & 0 & q \\ 1 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix} \end{array} \begin{matrix} A \\ B \\ L_1 \\ L_2 \end{matrix}$$

With the first column eliminated and with $p = q = 1$, the matrix above has maximal column-rank. This is now a MAK-TLK system, which is not MAK-RLK (reactant deficiency = 1).

Observe that the network deficiency of C_R is equal to two ($> 1+0$), hence, we have the dependent linkage class case. Note however, that the linkage classes as subnetworks are dynamically equivalent, since their ODE systems are both $\dot{A} = B - A = -\dot{B}$. Since the weakly reversible, zero-deficiency first linkage class has a unique equilibrium in each stoichiometric class, this is also true for the (non-weakly reversible) second linkage class.

LCELT-PLTIK leads to the conclusion that the whole network C_R has a positive equilibrium. Using CRNToolbox, we obtain the following conclusion from the Ji-Feinberg High Deficiency Algorithm (HDA) for C_R: "taken with mass action kinetics, the network CANNOT admit multiple positive steady states or a degenerate positive steady state no matter what (positive) values the rate constants might have". Hence we can conclude that the network has a unique, non-degenerate positive equilibrium in each stoichiometric class.

3.4 The Low Deficiency Theorem for PL-TIK systems

In this section, we summarize the Deficiency Zero and Deficiency One Theorems for PL-TIK systems presented in [18] and call it as "Low Deficiency Theorem for PL-TIK systems". We first introduce some useful concepts.

Definition 35 [18] 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 $\mathbf{Q} \cap \mathbb{R}^m_{>} \neq \emptyset$.

We also recall the kinetic flux subspace $\widetilde{S}$ of a PL-RDK system on an RSS network introduced by Arceo et al. [1].

Definition 36 For a PL-RDK system on an RSS network, the **kinetic flux subspace** $\widetilde{S}$ is the subspace $T(Y_{res}^{-1}(S))$ of $\widetilde{R}$. $\widetilde{s} = \dim \widetilde{S}$ is called the **kinetic rank**.

Remark 6 As shown in [1], for a PL-RDK on a cycle-terminal network, the kinetic flux subspace coincides with the kinetic order subspace $\widetilde{S}_{MR}$ introduced by Müller and Regensburger in [17]. Thus, for weakly reversible networks, $\widetilde{S}_{MR} = \widetilde{S}_R = \widetilde{S}$.

Let $\mathscr{C}_r$ denote the set of reactant complexes and $\mathscr{C}'$ the set of complexes in the terminal strong linkage class.

Suppose $\mathscr{C}'' = \mathscr{C} \setminus \mathscr{C}'$. 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

$$A_k = \begin{bmatrix} A'_k & * \\ 0 & A''_k \end{bmatrix} \in \mathbb{R}^{(n'+n'') \times (n'+n'')}$$

$$\psi_K = \begin{bmatrix} \psi'_K \\ \psi''_K \end{bmatrix} : \mathbb{R}^m \to \mathbb{R}^{(n'+n'')}$$

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

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

The following result is a direct consequence of Feinberg's Decomposition Theorem (Theorem 1), Theorem 3 and Theorems 5–7 of [18].

Theorem 4 (Low Deficiency Theorem for PL-TIK systems [18]) *Let* $(\mathscr{N}, K)$ *be a t-minimal PL-TIK system where each linkage class has deficiency* 0 *or* 1. *Then*

(I) *If* $\mathscr{N}$ *is weakly reversible then*
  (A) $E_+(\mathscr{N}, K) \neq \emptyset$;
  (B) $E_+(\mathscr{N}, K) = \left\{x \in \mathbb{R}^{\mathscr{S}}_{\geq} \,\middle|\, \log(x) - \log(x^*) \in (\widetilde{S}_R)^{\perp}\right\}$ *provided that* $x^* \in E_+(\mathscr{N}, K)$ *and* $\mathscr{N}$ *has independent linkage class decomposition;*

(II) *If* $\mathscr{N}$ *is non-weakly reversible then*
  (A) $E_+(\mathscr{N}, K) \neq \emptyset$ *if*
    (i) *each linkage class* $\mathcal{L}^i$ *with* $\delta = 0$ *is strongly connected; and*
    (ii) *each non-strongly connected linkage class* $\mathcal{L}^i$ *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) $E_+(\mathscr{N}, K) = \left\{x \in \mathbb{R}^{\mathscr{S}}_{\geq} \,\middle|\, \log(x) - \log(x^*) \in (\widetilde{S}_R)^{\perp}\right\}$ *provided that* $x^* \in E_+(\mathscr{N}, K)$ *and* $\mathscr{N}$ *has independent linkage class decomposition;*

(III) *if* $\mathscr{N}$ *has independent linkage class decomposition and* $E_+(\mathscr{N}, K) \neq \emptyset$, *then* $|E_+(\mathscr{N}, K) \cap \boldsymbol{Q}| = 1$ *for each positive kinetic reactant flux class* $\boldsymbol{Q}$.

We show in the following example a weakly reversible PL-TIK system with a positive equilibrium.

Running Example-Part 1 *Consider the weakly reversible network:*

$$R_1, R_2 : 2\mathrm{A} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} \mathrm{A} + \mathrm{C}$$

$$R_3, R_4 : \mathrm{A} + \mathrm{C} \underset{k_4}{\overset{k_3}{\rightleftharpoons}} 2\mathrm{C}$$

$$R_5, R_6 : 2\mathrm{B} \underset{k_6}{\overset{k_5}{\rightleftharpoons}} \mathrm{B} + \mathrm{D}$$

$$R_7, R_8 : \mathrm{B} + \mathrm{D} \underset{k_8}{\overset{k_7}{\rightleftharpoons}} 2\mathrm{D}$$

$$R_9, R_{10} : 2\mathrm{A} + 2\mathrm{E} \underset{k_{10}}{\overset{k_9}{\rightleftharpoons}} \mathrm{A} + \mathrm{E}$$

$$R_{11}, R_{12} : 2\mathrm{C} + 2\mathrm{F} \underset{k_{12}}{\overset{k_{11}}{\rightleftharpoons}} \mathrm{C} + \mathrm{F}$$

Suppose the kinetic order matrix is

$$F = \begin{array}{c} \begin{array}{cccccc} A & B & C & D & E & F \end{array} \\ \left[\begin{array}{cccccc} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 1 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 1 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ -1 & 0 & 0 & 0 & 1 & 0 \\ -1 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 1 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 & 0 & -1 \end{array}\right] \end{array} \begin{array}{c} r_1 \\ r_2 \\ r_3 \\ r_4 \\ r_5 \\ r_6 \\ r_7 \\ r_8 \\ r_9 \\ r_{10} \\ r_{11} \\ r_{12} \end{array} .$$

The network properties are presented in Table 1. This is a network with higher deficiency and, by definition, PL-FSK. We can partition the complexes into linkage classes: $\{\{2A, A+C, 2C\}, \{2B, B+D, 2D\}, \{2A+2E, A+E\}, \{2C+2F, C+F\}\}$. *Constructing* $\widehat{T}$ *we have*

$$\widehat{T} = \begin{bmatrix} T \\ L_{pr}^{\top} \end{bmatrix} = \begin{array}{c} \begin{array}{cccccccccc} C_1 & C_2 & C_3 & C_4 & C_5 & C_6 & C_7 & C_8 & C_9 & C_{10} \end{array} \\ \left[\begin{array}{ccc|ccc|cc|cc} \boldsymbol{1} & \boldsymbol{1} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{-1} & \boldsymbol{-1} & \boldsymbol{0} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{1} & \boldsymbol{1} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{1} & \boldsymbol{1} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{1} & \boldsymbol{1} \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{1} & \boldsymbol{1} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{1} & \boldsymbol{-1} & \boldsymbol{0} & \boldsymbol{0} \\ \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{0} & \boldsymbol{1} & \boldsymbol{-1} \\ 1 & 1 & 1 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 1 & 1 & 1 \end{array}\right] \end{array} \begin{array}{c} \boldsymbol{A} \\ \boldsymbol{B} \\ \boldsymbol{C} \\ \boldsymbol{D} \\ \boldsymbol{E} \\ \boldsymbol{F} \\ \mathcal{L}_1 \\ \mathcal{L}_2 \\ \mathcal{L}_3 \\ \mathcal{L}_4 \end{array} .$$

Vertical lines show the block matrices for each linkage class. The bold sub-matrix is the T-matrix of the given system. Since the rank of $\widehat{T}$ *is 10, the kinetic system is PL-TIK. From Table 1, the system is t-minimal* ($t = l$) *with each linkage class having deficiency equal 0 or 1. Thus, by Low Deficiency Theorem for PL-TIK systems,* $E_+ \neq \emptyset$.

4 A Higher Deficiency Theorem for weakly reversible PL-TIK systems

In this section, we state and prove our first main result. Although the conclusions are valid for weakly reversible systems regardless of deficiency value, we prefer to view it as a "Higher Deficiency Theorem" since the cases deficiency $=$ 0 or $=$ 1

Table 1 Network numbers for the Running Example

CRN properties	Value
Species	6
Complexes	10
Reactant complexes	10
Reactions	12
Linkage classes	4
Strong linkage classes	4
Terminal sl-classes	4
δ_1	1
δ_2	1
δ_3	0
δ_4	0
Deficiency	3

are essentially covered by the Low Deficiency Theorem cited in the previous section. The theorem states that all weakly reversible PL-TLK systems (i.e. PL-TIK system on networks without inflow reactions) and many weakly reversible PL-TIK systems on networks with inflow reactions possess a complex-balanced positive equilibrium. For such systems, the theorem also provides a partial parametrization of the set of positive equilibria. The main ingredients of the proof are the validity of key propositions on CRNs for reaction networks in the sense of Gopalkrishnan et al. [12], the results of Müller and Regensburger [17] and the Linkage Class Equilibria Lifting Theorem for PL-TIK (Theorem 3).

We formally introduce a superset of chemical reaction networks which we will call simply "reaction networks". The terminology is due to Gopalkrishnan et al. [12], though our concept is slight more special since we adopt a digraph (and not a "triple") approach.

4.1 Some properties of reaction networks

CRNT researchers sometimes remark in their papers, that some of their results also hold for "real coefficients", i.e. not only for the stoichiometric coefficients, which are non-negative integers. Gopalkrishnan et al. [12] formalized this in the concept of "reaction network", which we introduce in the slightly more special digraph formulation as follows:

Definition 37 A reaction network (RN) is a digraph with a vertex labeling $y : \mathscr{C} \to \mathbb{R}^m$. It is a **chemical reaction network** if $y(\mathscr{C})$ is contained in $Z^m_{\geq}$.

Many concepts and results for CRNs also hold for RNs. In particular, all concepts and results involving only the digraph structure (and not the vertex labeling) are valid, such as those involving connectivity. For example, the concepts involving terminal classes such as cycle or point terminal, the numbers t, t_p and t_c, terminality, and their relationships all hold without any change.

Even those which involve "stoichiometry" are often valid without change, since CRNT uses mostly linear vector spaces over $\mathbb{R}$ (and not modules/semi-modules over $\mathbb{Z}$ or $\mathbb{Z}_{\geq}$) to define and characterize them. In particular, the incidence map $I_a : \mathbb{R}^{\mathscr{R}} \to \mathbb{R}^{\mathscr{C}}$ and the map of complexes $Y : \mathbb{R}^{\mathscr{C}} \to \mathbb{R}^{\mathscr{S}}$ are well defined. Similarly, the stoichiometric subspace S and the reactant subspace R, being real vector spaces generated by the reaction vectors and the reactant complexes, respectively, are also valid concepts as such.

Definition 38 The deficiency of a reaction network is the integer $\delta = n - l - s$.

The following proposition extends the geometric interpretation of deficiency to reaction networks (the proof is identical and extracted from the Appendix of [15]).

Proposition 5 *The deficiency is equal to* $\dim(\ker Y \cap \operatorname{Im} I_a)$.

Proof Basic dimensional consideration implies

$$\dim(\ker(Y I_a)) = \dim(\ker(I_a)) + \dim(\ker(Y) \cap \operatorname{Im}(I_a)).$$

From rank-nullity theorem,

$$\dim(\ker(Y I_a)) = r - \dim(\operatorname{Im}(Y I_a)) = r - s.$$

The rank of I_a corresponds to the number of complexes minus the number of linkage classes, so that

$$\dim(\operatorname{Im}(I_a)) = n - l.$$

It follows that

$$\dim(\ker(I_a)) = r - (n - l) = r + l - n.$$

And, hence, $\delta = \dim(\ker Y \cap \operatorname{Im} I_a) = \dim(\ker(Y I_a)) - \dim(\ker(I_a)) = (r - s) - (r + l - n) = n - l - s$.

Recall the definition of reactant deficiency, δ_ρ. We now extend the fundamental relationship between it and network deficiency, δ, to reaction networks. The following extracts are taken from [1]:

Definition 39 The rank difference $\Delta(\mathscr{N})$ is defined as $s - q$. The **terminality** of a reaction network is the non-negative integer $\tau(\mathscr{N}) := t - l$.

The following result summarizes the relationship between deficiency and reactant deficiency of a reaction network.

Theorem 5 *Let $\mathscr{N}$ be a reaction network with (network) deficiency δ and reactant deficiency δ_ρ. Then*

$$\delta - \delta_\rho = \tau(\mathscr{N}) - t_c - \Delta(\mathscr{N}).$$

In particular,

(i) *if* $\mathscr{N}$ *is cycle terminal, then* $0 \leq \delta_\rho - \delta = l + \Delta(\mathscr{N}) \leq l$;
(ii) *if* $\mathscr{N}$ *is point terminal, then* $\delta - \delta_\rho = \tau(\mathscr{N}) - \Delta(\mathscr{N})$;
(iii) *if* $\mathscr{N}$ *is point and cycle terminal, then* $\delta - \delta_\rho < \tau(\mathscr{N}) - \Delta(\mathscr{N})$.

Proof $\delta - \delta_\rho = n - l - s - n_r + q = n - n_r - l - s + q = \tau(\mathscr{N}) - t_c - \Delta(\mathscr{N})$.

(i) If $\mathscr{N}$ is cycle terminal, $t_p = n - n_r = 0 \Leftrightarrow t = t_c \Leftrightarrow \tau(\mathscr{N}) - t_c = -l$. Hence, $\delta - \delta_\rho = -l - \Delta(\mathscr{N})$. Since $R = \operatorname{Im} Y$, $q = c \geq s$, and $\Delta(\mathscr{N})$ is negative. Hence $\delta_\rho - \delta = l + \Delta(\mathscr{N}) \leq l$. For the lower bound: $\delta_\rho = n_r - q = n - q \geq n - c = \dim \ker Y \geq \dim(\ker Y \cap \operatorname{Im}\ I_a) = \delta$.
(ii) If $\mathscr{N}$ is point terminal, $t_c = 0$, hence the simpler formula.
(iii) If $\mathscr{N}$ is point and cycle terminal, then $t_c > 0$, which implies the inequality.

4.2 A brief overview of GMAK theory

Generalized mass action kinetics (GMAK) systems were introduced by Müller and Regensburger in two papers [16,17] as a more geometric approach to power law kinetic systems. The basic concepts of GMAK theory are the generalized chemical reaction network (GCRN) and the generalized mass action kinetics (GMAK) system:

Definition 40 A generalized chemical reaction network (**GCRN**) $(G, y, \widetilde{y})$ is given by a digraph $G = (V, E)$ without self-loops, and two functions

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

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,

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

Definition 41 A **generalized mass action system** $(G_k, y, \widetilde{y})$ is a GCRN $(G, y, \widetilde{y})$ where edges $(i, j) \in E$ are labeled with constants $k_{ij} \in \mathbb{R}_>$. Assuming GMAK, the rate of the reaction is determined by the source kinetic complex $\widetilde{y}(i)$ and the positive rate constant k_{ij}:

$$v_{i \to j}(x) = k_{ij} x^{\widetilde{y}(i)}.$$

In [18], it was shown that there is a natural bijection between $\mathcal{PL} - \mathcal{RDK}(\mathscr{N})$ and the GMAK subset $\left\{ (G_k, y, \widetilde{y}) \middle| y \text{ is injective, } \operatorname{Im} y \subset Z^m_{\geq} \text{ and } \widetilde{y}(0) = 0 \right\}$. (The properties are necessary for compatibility with (bio)chemical conventions). The bijection induces an isomorphism of vertex-labeled digraphs between $\mathscr{N}$ and the pair (G, y). $\operatorname{Im} \widetilde{y}$ is called the set of kinetic complexes and clearly, $\operatorname{span}(\operatorname{Im} \widetilde{y})$ is the kinetic reactant

subspace $\widetilde{R}$ of the PL-RDK system. In the following, for simplicity, we shall formulate the results for PL-RDK systems, although they are valid for GMAK systems in general.

For cycle-terminal PL-RDK systems, Müller and Regensburger introduced a kinetic analogue of the network's stoichiometric subspace as follows:

Definition 42 Let $\mathscr{N}$ be a cycle-terminal network with n complexes and l linkage classes and K a PL-RDK kinetics. The kinetic order subspace $\widetilde{S}_{MR}$ of the system $(\mathscr{N}, K)$ is the span $\left\{\widetilde{y}(y') - \widetilde{y}(y) \middle| y \to y'\right\}$, 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 [18], it was shown that for cycle terminal networks, the kinetic reactant flux subspace $\widetilde{S}_R$ coincides with $\widetilde{S}_{MR}$.

The main results of Müller and Regensburger that we will use are parts of Theorem 1 [17].

Theorem 6 [17] *Let $(\mathscr{N}, K)$ be a weakly reversible PL-RDK system with T-matrix T.*

(i) $\widetilde{\delta} = 0$ *iff* $(\mathscr{N}, K)$ *has a complex balanced equilibrium for all rate constants, i.e.* $Z_+(\mathscr{N}, K) \neq \emptyset$.

(ii) *If* $\widetilde{\delta} > 0$, *then* $Z_+(\mathscr{N}, K) \neq \emptyset$ *iff* $(\kappa_k)^C = 1$, *where* $(\kappa_k)_{ij} = K_j/K_i$ *and* K_i, K_j *are tree constants (from the Matrix Tree Theorem) and* C *is an appropriately defined matrix.*

We will not need the technical details of C's definition. The interested reader can find them in [17, pp. 310–311]. We shall call statement (i) the Kinetic Deficiency Zero Theorem (KDZT) and statement (ii) the Müller and Regensburger Criterion for Complex Balancing.

4.3 The reaction network of kinetic complexes $\widetilde{\mathscr{N}}$ of a cycle terminal PL-FSK system $(\mathscr{N}, K)$

Proposition 6 *For a cycle terminal PL-FSK system $(\mathscr{N}, K)$, the digraph $\widetilde{\mathscr{N}} = (\widetilde{\mathscr{C}}, \widetilde{\mathscr{R}})$ together with vertex labeling $i : \widetilde{\mathscr{C}} \to \mathbb{R}^{\mathscr{S}}$ is a CRN. In fact $\widetilde{y}$ extends to a digraph isomorphism $\mathscr{N} \to \widetilde{\mathscr{N}}$.*

The proof is straightforward. As a consequence, we can apply all the concepts and results for reaction networks to the reaction network of kinetic complexes of a cycle terminal PL-FSK system.

Recall that, for any cycle terminal CRN $\mathscr{N}$, Müller and Regensburger [17] defined the kinetic deficiency $\widetilde{\delta}(\mathscr{N}) := n - l - \widetilde{s}$, where $\widetilde{s}$ is dimension of the kinetic order subspace $\widetilde{S}_{MR}$, which in this case also coincides with the kinetic flux subspace $\widetilde{S}$ (see [18] for details). We hence have the following Corollary:

Corollary 2 *If $\delta(\widetilde{\mathscr{N}})$ is the (network) deficiency of $\widetilde{\mathscr{N}}$, then $\widetilde{\delta}(\mathscr{N}) = \delta(\widetilde{\mathscr{N}})$. For the reactant deficiency $\delta_\rho(\widetilde{\mathscr{N}})$, we have $\delta_\rho(\widetilde{\mathscr{N}}) \geq \widetilde{\delta}(\mathscr{N})$.*

Proof Clearly, $\widetilde{S}_{MR}$ is by definition the stoichiometric subspace of $\widetilde{\mathscr{N}}$. In view of the digraph isomorphism $\widetilde{y} : \mathscr{N} \to \widetilde{\mathscr{N}}$, the number of complexes and linkage classes also coincide, so that the first assertion follows. The second assertion follows from the fact that in a cycle terminal reaction network, $\delta_\rho \geq \delta$, as shown in the previous proposition.

4.4 Proof of the Higher Deficiency Theorem

We can now state and prove our first main result:

Theorem 7 *Let $(\mathscr{N}, K)$ be a weakly reversible PL-TIK system with linkage classes $\mathscr{L}_1, \ldots, \mathscr{L}_l$.*

(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*

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

If the network has independent linkages classes, then the sets are equal.

Proof We first note that PL-IRK systems form a subset of PL-FSK, since linear independence of the non-inflow columns of the T-matrix imply in particular that they are different. Since each linkage class $\mathscr{L}_i$ of a weakly reversible PL-TIK system is a weakly reversible PL-IRK system, its reaction network of kinetic complexes $\widetilde{\mathscr{L}}_i$ is well-defined. By definition, $\delta_\rho(\widetilde{\mathscr{L}}_i) = \widetilde{n}_{r,i} - \widetilde{q}_i$, where $\widetilde{n}_{r,i}$ is the number of complexes of linkage class $\mathscr{L}_i$ and $\widetilde{q}_i$ the rank of the reactant subspace of $\widetilde{\mathscr{L}}_i$.

Since for each linkage class $\mathscr{L}_i$ the kinetics is PL-RLK, then $n_r = \widetilde{q}$, and hence $\delta_\rho(\widetilde{\mathscr{L}}_i) = 0$. It follows from Corollary 2 that $\widetilde{\delta}(\widetilde{\mathscr{L}}_i) = 0$. By Theorem 6(i), the system has a complex balanced positive equilibrium (for each set of rate constants). Hence $Z_+(\mathscr{L}_i, K)$ is non-empty. Applying the LCELT-PL-TIK (Theorem 3) delivers the non-emptiness claim for the whole system. Since this is true for any rate constant, Theorem 6(i) shows that the whole system's kinetic deficiency is zero.

For (ii): Since $\widetilde{\delta}_\rho(\mathscr{L}_i) = 1$, its kinetic deficiency $= 0$ or 1. If $\widetilde{\delta}(\mathscr{L}_i) = 0$, then all linkage classes have a complex-balanced equilibrium as in (i) and we have the same conclusion. If $\widetilde{\delta}_\rho(\mathscr{L}_i) = 1$, the existence of a complex-balanced equilibrium is rate-constant dependent. Using Theorem 6(ii), we can conclude that $Z_+(\mathscr{N}, K)$ is non-empty if the Müller and Regensburger criterion is satisfied.

For (iii): By Corollary 4 of [18], for each linkage class $\left\{ x \in \mathbb{R}^{\mathscr{S}}_{>} \,\middle|\, \log(x) - \log(x^*) \in (\widetilde{S}_R)^{\perp} \right\} = \left\{ x \in \mathbb{R}^{\mathscr{S}}_{>} \middle| (\widehat{T}^r)^{\top} \begin{bmatrix} \log(x^*) \\ -\log(\gamma^*) \end{bmatrix} = \log(v^r) \right\}$ where $\left\{ x \in \mathbb{R}^{\mathscr{S}}_{>} \middle| (\widehat{T}^r)^{\top} \right.$

$\begin{bmatrix} \log(x^*) \\ -\log(\gamma^*) \end{bmatrix} = \log(v^r)\Big\}$ is just the truncated $\left\{ z \in \mathbb{R}_+^{m+1} \middle| (\widehat{T}^r)^\top \cdot z = \log(v^r) \right\}$ used in Theorem 4 of [18].

Since $\widetilde{S}_R^\perp = (\sum \widetilde{S}_{R,i})^\perp = \cap \widetilde{S}_{R,i}^\perp$, the set $\left\{ x \in \mathbb{R}_>^{\mathscr{S}} \middle| \log(x) - \log(x^*) \in (\widetilde{S}_R)^\perp \right\} = \cap \left\{ x \in \mathbb{R}_>^{\mathscr{S}} \middle| \log(x) - \log(x^*) \in \widetilde{S}_{R,i}^\perp \right\}$. By Theorem 4, each set in the intersection is $E_+(\mathscr{L}_i, K_i)$, and hence the intersection is contained in $E_+(\mathscr{N}, K)$. If the linkage classes are independent, applying Theorem 1 to the decomposition ensures equality of $E_+(\mathscr{N}, K)$ and the parametrized set.

Running Example-Part 2 *In our running example of PL-TIK system, it is clear that the kinetic reactant flux space* $\widetilde{S}_R = \langle C, A, D, B, E, F \rangle$ *has dimension equals 6. Hence,* $\widetilde{\delta}(\mathscr{N}) = n - l - s = 10 - 4 - 6 = 0$ *illustrating our results.*

Example 3 The following system is an example of a PL-TIK system with zero kinetic deficiency on a network with an inflow reaction. Its network deficiency $= 6-2-2 = 2$.

$$R_1, R_2 : \mathrm{A} \underset{k_2}{\overset{k_1}{\rightleftharpoons}} 0$$

$$R_3, R_4 : \mathrm{B} + \mathrm{C} + \mathrm{D} \underset{k_4}{\overset{k_3}{\rightleftharpoons}} 2\mathrm{B} + 2\mathrm{C} + 2\mathrm{D}$$

$$R_5, R_6 : \mathrm{B} + \mathrm{C} + \mathrm{D} \underset{k_6}{\overset{k_5}{\rightleftharpoons}} 3\mathrm{B} + 3\mathrm{C} + 3\mathrm{D}$$

$$R_7, R_8 : \mathrm{B} + \mathrm{C} + \mathrm{D} \underset{k_8}{\overset{k_7}{\rightleftharpoons}} 4\mathrm{B} + 4\mathrm{C} + 4\mathrm{D}$$

Suppose the kinetic order matrix is

$$F = \begin{array}{c} \begin{matrix} A & B & C & D \end{matrix} \\ \left[\begin{array}{cccc} 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & -1 \\ 0 & 1 & -1 & 1 \\ 0 & 1 & 1 & -1 \\ 0 & -1 & 1 & 1 \\ 0 & 1 & 1 & -1 \\ 0 & -2 & 1 & 1 \end{array}\right] \end{array} \begin{matrix} R_1 \\ R_2 \\ R_3 \\ R_4 \\ R_5 \\ R_6 \\ R_7 \\ R_8 \end{matrix}.$$

Table 2 shows the network properties. This is a network with higher deficiency and, by definition, PL-FSK. Constructing $\widehat{T}$ we have

$$\widehat{T} = \begin{bmatrix} T \\ L_{pr}^\top \end{bmatrix} = \begin{array}{c} \begin{matrix} C_1 & C_2 & C_3 & C_4 & C_5 & C_6 \end{matrix} \\ \left[\begin{array}{cc|cccc} 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & -1 & -2 \\ 0 & 0 & 1 & -1 & 1 & 1 \\ 0 & 0 & -1 & 1 & 1 & 1 \\ 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 1 & 1 & 1 \end{array}\right] \end{array} \begin{matrix} A \\ B \\ C \\ D \\ \mathcal{L}_1 \\ \mathcal{L}_2 \end{matrix}.$$

Table 2 Network numbers for Example 3

CRN properties	Value
Species	4
Complexes	6
Reactant complexes	6
Reactions	8
Linkage classes	2
Strong linkage classes	2
Terminal sl-classes	2
δ_1	0
δ_2	2
Deficiency	2

Since the rank of $\widehat{T}$ is 6, the kinetic system is PL-TIK. The first linkage class is a reversible, zero deficiency PL-TIK system and hence, from the Low Deficiency Theorem and Feinberg's classical result, has a complex balanced equilibrium for any rate constant. The second linkage class is a reversible PL-RLK system and by Theorem 7 (i) has a complex balanced equilibrium for any rate constant. From the LCELT-PL-TIK, the whole system has a complex balanced equilibrium for any rate constant and hence zero kinetic deficiency after Müller-Regensburger. Note too that the system has ILC, so the full set of equilibria is described by the parametrized set.

The converse of the last statement in (iii) of the Theorem 7 does not hold in general, as shown by the following computations for our running example.

Running Example-Part 3 *The ODE system of the Running Example will be:*

$$\begin{cases} \dot{A} = -k_1 A + k_2 AC - k_3 AC + k_4 C - k_9 A^{-1} E + k_{10} A^{-1} E^{-1} \\ \dot{B} = -k_5 B + k_6 BD - k_7 BD + k_8 D \\ \dot{C} = k_1 A - k_2 AC + k_3 AC - k_4 C - k_{11} CF + k_{12} CF^{-1} \\ \dot{D} = k_5 B - k_6 BD + k_7 BD - k_8 D \\ \dot{E} = -k_9 A^{-1} E + k_{10} A^{-1} E^{-1} \\ \dot{F} = -k_{11} CF + k_{12} CF^{-1} \end{cases}$$

Solving the equilibrium, we have

$$E_+ = \left\{ \begin{bmatrix} A \\ B \\ C \\ D \\ \sqrt{\frac{k_{10}}{k_9}} \\ \sqrt{\frac{k_{12}}{k_{11}}} \end{bmatrix} \in \mathbb{R}^6_+ \,\middle|\, \begin{matrix} -k_1 A + (k_2 - k_3) AC + k_4 C = 0 \\ -k_5 B + (k_6 - k_7) BD + k_8 D = 0 \end{matrix} \right\}.$$

Clearly, the system above has a solution. And hence, $E_+(\mathscr{N}, K)$ is nonempty. We now compute $E_+(\mathscr{L}_i, K)$ for each linkage class $\mathscr{L}_i$.

For the first linkage class ($\mathscr{L}_1$):

$$E_+^1 = \left\{ \begin{bmatrix} A \\ B \\ C \\ D \\ E \\ F \end{bmatrix} \in \mathbb{R}^6_+ \Big| -k_1 A + (k_2 - k_3)AC + k_4 C = 0 \right\}.$$

For the second linkage class ($\mathscr{L}_2$):

$$E_+^2 = \left\{ \begin{bmatrix} A \\ B \\ C \\ D \\ E \\ F \end{bmatrix} \in \mathbb{R}^6_+ \Big| -k_5 B + (k_6 - k_7)BD + k_8 D = 0 \right\}.$$

For the third and fourth linkage classes ($\mathscr{L}_3$ and $\mathscr{L}_4$):

$$E_+^3 = \left\{ \begin{bmatrix} A \\ B \\ C \\ D \\ \sqrt{\frac{k_{10}}{k_9}} \\ F \end{bmatrix} \in \mathbb{R}^6_+ \right\}, \quad \text{and} \quad E_+^4 = \left\{ \begin{bmatrix} A \\ B \\ C \\ D \\ E \\ \sqrt{\frac{k_{12}}{k_{11}}} \end{bmatrix} \in \mathbb{R}^6_+ \right\}.$$

Hence even the linkage classes are dependent, we see $\bigcap E_+^i = E_+$.

4.5 A significant aspect of the Higher Deficiency Theorem for GMAK theory

To our knowledge, three classes of GMAK systems with zero kinetic deficiency have previously been identified. The first class consists of MAK systems with zero deficiency, since for mass action kinetics, $\widetilde{\delta} = \delta$. Johnston [15] showed that MAK systems with toric equilibria could be translated into GMAK systems whose complex-balanced equilibria bijectively mapped to the toric equilibria. These GMAK systems had both deficiency and kinetic deficiency equal to zero. Fortun et al. [11] derived that zero deficiency, non-defective embedded S-systems were necessarily weakly reversible and has a unique complex-balanced equilibrium (see Sect. 5.1 for background information on S-systems). For those with PL-RDK kinetics, this implies zero kinetic deficiency. Hence, all previously known classes have zero deficiency. Statement (i) of the Theorem 7 provides the first examples of GMAK systems with zero kinetic deficiency on networks with deficiency 1 or higher.

4.6 The Higher Deficiency Theorem at Low Deficiency

In this section, we compare the implications of Theorem 7 for PL-TIK systems on networks with deficiency $= 0$ or $= 1$ with the statements of the Low Deficiency Theorem. The results support our view that Theorem 7 is important mainly for PL-TIK systems with higher deficiency.

We first note that for weakly reversible PL-TLK systems on networks with deficiency $= 1$, Theorem 7 does provide two new results: (i) the existence of complex-balanced equilibria even for network with dependent linkage classes (not covered by the Low Deficiency Theorem) and (ii) the characterization of all positive equilibria as complex balanced in the ILC case (as assumed in the Low Deficiency Theorem). For zero deficiency networks, these results are not new because it is well known that in this case, for any kinetics, all positive equilibria are complex-balanced. Moreover, Theorem 7 provides a relatively straightforward proof of the existence statements compared with that offered in the Low Deficiency Theorem.

On the other hand, besides the existence and parametrization results, the Low Deficiency Theorem provides information on the uniqueness of the positive equilibria relative to the kinetic reactant classes. It also covers non-weakly reversible t-minimal networks satisfying the Boros condition in the deficiency $= 1$ case.

For PL-TIK systems on networks with inflows, Theorem 7 covers only networks with kinetic deficiency 0 in the linkage class containing the zero complex—clearly a much narrower scope than that of the Low Deficiency Theorem.

5 Weak Reversibility Theorems for power law kinetics subsets

In this section, we consider subsets of power law kinetics which are defined on any weakly reversible network. The subset may be empty on some weakly reversible networks, e.g. the subset $\mathcal{PL} - \mathcal{RLK}(\mathcal{N})$ is empty on any weakly reversible network with $n_r > m$, since the latter property implies linear dependence of some columns (i.e. interactions). Similarly, as previously mentioned. $\mathcal{PL} - \mathcal{LLK}$ is empty on any weakly reversible network with an inflow reaction.

For such a subset K^* of $\mathcal{PLK}(\mathcal{N})$, we introduce the "Weak Reversibility Problem for Power Law Kinetics". It asks the question: "If $\mathcal{N}$ is any weakly reversible CRN, given a subset $\mathscr{K}^*$ of $\mathscr{K}(\mathcal{N})$, does every chemical kinetic system $(\mathcal{N}, K)$ with $K \in \mathscr{K}^*$ have a positive equilibrium?" If the answer is "Yes", then we say that $\mathscr{K}^*$ has a Weak Reversibility Theorem (WRT). We review the known approaches to the problem and existing results and position our first main result in this context. As our third main result, we show that two supersets of mass action kinetics, $\mathcal{PL} - \mathcal{FSK}(\mathcal{N})$ (the set of factor span surjective power law kinetics) and $\mathcal{PL} - \mathcal{NIK}(\mathcal{N})$ (the set of non-inhibitory power law kinetics) do not have a WRT. This of course implies that all supersets of these two sets also do not have a WRT.

We begin with a brief review of some results that we will need from Biochemical Systems Theory (BST) on S-systems.

5.1 A brief review of S-systems

An S-system has the following general form:

$$\dot{X}_i = \alpha_i \prod_{j=1}^{n+m} X_j^{g_{ij}} - \beta_i \prod_{j=1}^{n+m} X_j^{h_{ij}}$$

where g_{ij} are the kinetic orders on the influx terms and h_{ij} are kinetic orders on the efflux terms.

One of the nicest properties of an S-system is that there is an analytic criterion for the existence and uniqueness of positive steady states. This is directly derived by equating the production term to the degradation term (i.e. definition of steady state) for each dependent variable. If all the rate constants are non-zero, one can take the logarithm (componentwise) and obtain a system of linear equations in the logarithms of the original variables. Thus, finding steady states becomes a matter of solving a system of linear equations (in logarithmic space). Details can be found in Voit's book [19, pp. 205–206]. If m_d is the number of dependent variables, the $m_d \times m_d$ matrix of the linear system is the so-called "A-matrix" A_D given by $a_{ij} = g_{ij} - h_{ij}$, where g_{ij}, h_{ij} are the kinetic orders of the i^{th} variable with respect to the j^{th} variable of the production and degradation terms, respectively.

Note that $\det A_D \neq 0$ if and only if there is a unique solution, which when transported to $\mathbb{R}^{\mathscr{S}}$ by exponentiation, gives a unique positive steady state. More precisely:

$$y = {A_D}^{-1} b {A_D}^{-1} A_I y_I,$$

where $b_i = \ln \beta_i - \ln \alpha_i$ for the dependent variables and $(A_I)_{ij} = g_{ij} - h_{ij}$ and $y_I = (\ln X_i)^T$ for the independent variables.

Definition 43 An S-system is non-defective if $\det A_D \neq 0$, otherwise defective. A non-defective S-system is called regular if all rate constants are non-zero.

Arceo et al. [2] introduced the embedded CRN of an S-system, which together with associated kinetics constituted a chemical kinetic system dynamically equivalent to S-system. It was shown in [3] that the total representation of an S-system is open. In [11], it was shown that the same property holds for embedded system. In the same paper, the following equivalence was also derived:

Proposition 7 *Let $(\mathscr{N}, K)$ be a zero deficiency PL-RDK embedded S-System. It is non-defective if and only if its kinetic deficiency $\widetilde{\delta} = 0$.*

5.2 The weak reversibility problem for kinetics subsets

The Weak Reversibility Theorem for $\mathcal{MAK}(\mathscr{N})$ was a long standing conjecture in CRNT. A proof is provided in Deng et al. [6], which however to date is not published in a peer-reviewed journal. A paper of Boros [5] which contains an alternative formulation of the proof, has been submitted for peer review. He has already published a different

proof of the statement for the special case of deficiency = 1 [4]. We hence feel confident now to refer to the Weak Reversibility Theorem for MAK systems (WRT-MAK).

The Kinetic Deficiency Zero Theorem of Müller and Regensburger [17, Theorem 1a)] can be formulated as the Weak Reversibility Theorem for the subset of PL-RDK kinetics with zero kinetic deficiency. Our result on PL-TLK kinetics shows that it is part of this PL-RDK subset and has a WRT.

To our knowledge, besides these two WRT's, no others are known in the CRNT literature. Hence the question "For which other subsets of PLK kinetics is there a WRT?" is wide open for further research.

Remark 7 Formally, the statement "Any weakly reversible, non-defective embedded S-system has a positive equilibrium" is correct. However, we have refrained from declaring a WRT for the subset of non-defective S-system kinetics for two reasons: i) the existence of the positive equilibrium does not depend on the weak reversibility of the network, it is true for all S-system embedded representations and ii) S-system kinetics is defined only for particular networks, i.e. one would probably need to declare it empty for the complementary set. Such a "formal WRT" would not have the same quality as the other WRT's, though it would be the first to be valid for a kinetics set beyond $\mathcal{PL} - \mathcal{RDK}(\mathscr{N})$.

5.3 No WRT for PL-NIK and PL-FSK

A particularly interesting case of the previous question is whether there are supersets of MAK kinetics with a WRT. To avoid trivial answers like $\mathcal{K} = \mathcal{MAK}(\mathscr{N}) \cup (\mathcal{PL} - \mathcal{TIK}(\mathscr{N}) - \mathcal{MAK} - \mathcal{TIK}(\mathscr{N}))$, we introduce the concept of an "intrinsic superset":

Definition 44 A superset of MAK is intrinsic if it is defined by a property which is valid for all MAK systems.

Example 4 The set $\mathcal{PL} - \mathcal{FSK}(\mathscr{N})$ is an intrinsic superset since every MAK kinetics is factor span surjective. Similary, the set $\mathcal{PL} - \mathcal{NIK}(\mathscr{N})$ is also intrinsic, since every MAK kinetics has non-negative kinetic orders (stoichiometric coefficients of the reactant complexes). Clearly the set $\mathscr{K}$ defined above is not intrinsic.

We can now formulate our question more precisely:

Open Question Is there are a proper, intrinsic superset of $\mathcal{MAK}(\mathscr{N})$ with a WRT?

In the rest of this section, we construct a weakly reversible, factor span surjective embedded S-system, which is defective. As reviewed in Sect. 5.2, it follows that for defective S-systems, there are rate constants for which the system does not have a positive equilibrium [19]. Since the system is also non-inhibitory, it also is a counterexample for a WRT in $\mathcal{PL} - \mathcal{NIK}(\mathscr{N})$.

The S-system has 3 dependent variables A, B, C and no independent variables. The ODE system is:

$$\begin{cases} \dot{A} = \alpha_1 B - \beta_1 A \\ \dot{B} = \alpha_2 C^2 - \beta_2 BC \\ \dot{C} = \alpha_3 A^3 - \beta_3 A^2 C \end{cases}$$

Its CRN is: $B \leftrightarrow A + B$, $C \leftrightarrow C + B$, $A \leftrightarrow A + C$. The CRN is clearly weakly reversible, has 3 linkage classes, zero deficiency and reactant deficiency $= 3$. It is non-branching, so any PLK kinetics is PL-RDK, as was shown in [2].

Numbering the reactions in the above graph $r_1, r_2, r_3, r_4, r_5, r_6$ from left to right, we have the kinetic order matrix F and the A-matrix A_D:

$$F = \begin{array}{c} \begin{matrix} A & B & C \end{matrix} \\ \begin{bmatrix} 0 & 1 & 0 \\ 1 & 0 & 0 \\ 0 & 0 & 2 \\ 0 & 1 & 1 \\ 3 & 0 & 0 \\ 2 & 0 & 1 \end{bmatrix} \end{array} \begin{matrix} r_1 \\ r_2 \\ r_3 \\ r_4 \\ r_5 \\ r_6 \end{matrix}$$

$$A_D = \begin{array}{c} \begin{matrix} A & B & C \end{matrix} \\ \begin{bmatrix} -1 & 1 & 0 \\ 0 & -1 & 1 \\ 1 & 0 & -1 \end{bmatrix} \end{array} \begin{matrix} A \\ B \\ C \end{matrix}$$

The S-system is PL-FSK since all rows are pairwise different. Since $\det A_D = -1 + 1 = 0$, it is defective. Observe also that it is PL-LLK, but not PL-TLK. It is also a kinetics which generates a polynomial dynamical system, and hence there is also no WRT for that kinetics subset of $\mathcal{PLK}(\mathcal{N})$.

6 Conclusions/outlook

In conclusion we summarize our results and outline some perspectives for further research.

1. We provided a summary, new examples and some improvements of previous results on power-law kinetic systems with linear independent interactions, including the integration into a "Low Deficiency Theorem for PL-TIK Systems" of the Deficiency Zero and Deficiency One Theorems.
2. We derived a "Higher Deficiency Theorem" for weakly reversible PL-TIK systems and showed in particular that all weakly reversible PL-TLK systems have a complex balanced equilibrium and a such are the first examples of systems with zero kinetic deficiency on networks with deficiency equal to 1 or higher.
3. We introduced the concept of a "Weak Reversibility Theorem" (WRT) for a kinetics subset, provided an overview of WRT's for power law kinetics and positioned our result on PL-TLK kinetics as part of such WRT.

4. We showed that the MAK supersets of PL-NIK (non-inhibitory kinetics) and PL-FSK (factor span-surjective kinetics) do not have WRTs, highlighting the open question of whether a proper, intrinsic superset of MAK kinetics with a WRT exists.

Together with the two open questions regarding kinetics subsets with WRTs, the identification of PL-TIK systems with zero kinetic deficiency on positive deficiency networks with inflows offer interesting research perspectives in our view.

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