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REMARKS ON CRITERIA FOR THE EXISTENCE OF A POSITIVE EQUILIBRIUM IN REACTION NETWORKS†

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Abstract. It is interesting to know the behavior of a network from its structure. One interesting topic is to find a relation between the existence of a positive equilibrium of the reaction network and its structure. One approach to study this topic is using the concept of deficiency. Another is using some conditions on nodes, which can apply to large-size networks compared to deficiency. In this work, we show the relation between deficiency and the conditions.

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1. Introduction

Many systems including biological and chemical systems are studied by their mathematical models using differential equations. To construct such a model, we need to know some quantitative information like the type of reactions and the values of the parameters involved in each reaction. However, it is not easy to have the information. Thus it is important to find some relation between the functionality of a network and the network structure.

The existence of a positive equilibrium of the reaction network was studied by its structure using the concept of network deficiency ([3],[4]). Other structure conditions based on the injectivity property have been presented in recent papers ([1],[2]) to determine whether networks have the capacity for more than one steady state. It is not easy to apply the concept of deficiency to large-size networks. So the author used another conditions (P1)–(P2) on nodes ([6]) instead of deficiency to obtain the same result as using the concept of zero deficiency. (P1)–(P2) are easy to apply to large-size networks compared to deficiency.

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In this paper, we present the connection between zero deficiency and the conditions (P1)–(P2). Deficiency and (P1)–(P2) are defined in Section 2. We define a network of interest and some notations, which will allow us to show the relation mathematically. In Sections 3, we show that (P1)–(P2) implies zero deficiency but the converse is not true.

2. Preliminaries

In this section, some notations and a network of interest are defined. And we also introduce Lemma 1 and Lemma 2 to show that we can use (P1)–(P2) to obtain the same result as using deficiency.

Definition 1. *A chemical reaction network consists of three finite sets:*

i) a set $\mathcal{S}$ of elements called the species of the network.

ii) a set $\mathcal{C}$ of functions in $\overline{\mathbb{P}}^{\mathcal{S}}$ called the complexes of the network.

iii) a relation $\mathcal{R} \subset \mathcal{C} \times \mathcal{C}$ having the following properties:

a) $(y, y) \notin \mathcal{R}$ for all $y \in \mathcal{C}$.

b) For each $y \in \mathcal{C}$, there exists $y' \in \mathcal{C}$ such that $(y, y') \in \mathcal{R}$ or $(y', y) \in \mathcal{R}$.

Here $\overline{\mathbb{P}}$ means the set of nonnegative real numbers, $\mathbb{P} = \overline{\mathbb{P}} - \{0\}$, and $\overline{\mathbb{P}}^{\mathcal{S}}$ the vector space of nonnegative real-valued functions with the domain $\mathcal{S}$. The element $(y, y') \in \mathcal{R}$ denotes a reaction $y \to y'$ called a directed arrow from y to y'.

Using Definition 1, we can assign each network to a directed graph with complexes and reactions as nodes and directed arrows, respectively. Throughout this work, a network means a chemical reaction network or its directed graph if there is no specific comment about the network.

A network is weakly reversible if each directed arrow is contained in a directed arrow circle. The network in Fig.1 is not weakly reversible because there is no directed arrow circle containing A→2B.

For species A, B and positive real numbers r_a, r_b, the complex $r_aA+r_bB \in \overline{\mathbb{P}}^{\mathcal{S}}$ means $(r_aA + r_bB)(A) = r_a$, $(r_aA + r_bB)(B) = r_b$ and $(r_aA + r_bB)(s) = 0$ if $s \notin \{A, B\}$. For simplicity, we will assume $y(y^s) = 1$ for all complexes y and species y^s with $y(y^s) > 0$ without loss of generality.

The differential equation corresponding to a chemical reaction network $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ with a kinetics $\mathcal{K}$ can be written as the vector form $\frac{dc}{dt} = \sum_{\mathcal{R}} \mathcal{K}_{y\to y'}(c)\,(y' - y), c \in \overline{\mathbb{P}}^{\mathcal{S}}$ where $\mathcal{K}_{y\to y'} : \overline{\mathbb{P}}^{\mathcal{S}} \to \overline{\mathbb{P}}$ and $\mathcal{K}_{y\to y'}(c)$ is the kinetics of the reaction $y \to y'$ at c. And c^* is called a positive equilibrium if $0 = \sum_{\mathcal{R}} \mathcal{K}_{y\to y'}(c^*)\,(y' - y)$.

Let $y \sim y'$ denote $y \to y'$ or $y' \to y$. Then this is an equivalence relation on $\mathcal{C}$ which induces equivalence classes called the linkage of classes of the network. The rank of the network is the rank of the set $\{y - y' | y \to y' \in \mathcal{R}\}$. Deficiency for a chemical reaction network is defined by $n - \ell - r$ where n, ℓ, r are the number of complexes, the number of linkage classes, and the rank of the network, respectively. More details and the proof of Lemma 1 can be found in [3].

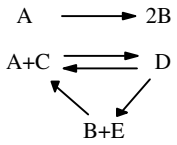

FIGURE 1. A network with five nodes [2].

Lemma 1. *Assume the deficiency of a network is zero. If the network is not weakly reversible, then the differential equation corresponding to the network with an arbitrary kinetics cannot have a positive equilibrium.*

A weakly reversible network is defined graphically with a directed arrow circle. So it is not difficult to check non-weakly reversibility. However, checking zero deficiency is difficult for large-size networks: In oder to calculate deficiency, it is necessary to find a maximal linearly independent subset of the set $\mathcal{S} = \{y - y' | (y, y') \in \mathcal{R}\}$. Since $\mathcal{S}$ has many elements for large-size networks, it is not easy to find such a subset from a large-size set.

To solve this problem, the author defined properties (P1)–(P2) on the set of complexes to obtain the result in Lemma 1 without checking zero deficiency. (P1)–(P2) can be applied to networks with activations and inhibitions. More details and the proof of Lemma 2 can be found in [6].

Definition 2. *Properties (P1) and (P2) on the set $\mathcal{C}$ of a chemical reaction network are defined as follows: For $i = 1, \cdots, \nu$,*

(P1) There exists $\{\mathcal{C}_i | i = 1, \cdots, \nu\}$ such that $\mathcal{C} = \bigcup_{\ell=1}^{\nu} \mathcal{C}_\ell$ and $\mathcal{C}_i \subset \mathcal{C} - \bigcup_{\ell=1}^{i-1} \mathcal{C}_\ell$.

(P2) Each complex y_i in $\mathcal{C}_i$ has a species y_i^s such that $y(y_i^s) = 0$ for all y in $\mathcal{C} - (\{y_i\} \cup (\bigcup_{\ell=1}^{i-1} \mathcal{C}_\ell))$. Here $\bigcup_{\ell=1}^{i-1} \mathcal{C}_\ell (i = 1)$ means the empty set.

In Fig.1, let $\mathcal{C} = \{A + C, B + E, D, A, 2B\}$, $\mathcal{C}_1 = \{A + C, B + E, D\}$, $\mathcal{C}_2 = \{A, 2B\}$, and $\nu = 2$. Then the network satisfies (P1)–(P2). There are a number of networks satisfying (P1)–(P2) in recent papers [5,7]

Lemma 2. *Let a network satisfy (P1) and (P2) in Definition 2. If the differential equation corresponding to the network with a kinetics has a positive equilibrium, then the network is weakly reversible.*

3. The relation between (P1)–(P2) and deficiency

In this section, we show that the properties (P1)–(P2) imply zero deficiency by using Lemma 3 and Lemma 4. But zero deficiency does not imply the properties (P1)–(P2).

Lemma 3. *Let a network satisfy the properties (P1) and (P2) in Definition 2. Then there exist an integer $n > 0$ and a set $\{\hat{\mathcal{C}}_i | i = 1, \cdots, n\}$ satisfying (P1)–(P2) and all complexes of each $\hat{\mathcal{C}}_i$ are contained in a same linkage class.*

Proof. For $\mathcal{C}_i (1 \leq i \leq \nu)$ satisfying (P1)–(P2) we can partition each $\mathcal{C}_i$ into subsets $\mathcal{C}_{i_j} (1 \leq j \leq c_i)$, where the linkage classes containing complexes of $\mathcal{C}_{i_j}$ are the same. Let $\hat{\mathcal{C}}_1 = \mathcal{C}_{1_1}$,$\hat{\mathcal{C}}_2 = \mathcal{C}_{1_2}$,$\cdots$, $\hat{\mathcal{C}}_n = \mathcal{C}_{\nu_{c_\nu}} (n = \sum_{i=1}^{\nu} c_i)$. Then the set $\{\hat{\mathcal{C}}_i | i = 1, \cdots, n\}$ satisfies the properties (P1)–(P2) and all complexes of each $\mathcal{C}_{i_j}$ belong to a same linkage class. □

From now on we assume that the set $\{\mathcal{C}_i | i = 1, \cdots, \nu\}$ satisfying (P1)–(P2) is $\{\hat{\mathcal{C}}_i | i = 1, \cdots, n\}$ in this paper. We show in Lemma 4 that (P1)–(P2) implies zero deficiency if the number of linkage classes of a network is one.

Lemma 4. *Let a network satisfy the properties (P1) and (P2). If the number of its linkage classes is one, then the deficiency of the network is zero.*

Proof. To find the rank of the set $\Gamma_{\mathcal{R}} = \{y' - y | (y, y') \in \mathcal{R}\}$, construct a subset $\mathcal{R}^0$ of $\mathcal{R}$ by removing one arrow from each circle in the network. Then the ranks of $\Gamma_{\mathcal{R}}$ and $\Gamma_{\mathcal{R}^0}$ are the same. Note that the number of elements of $\Gamma_{\mathcal{R}^0}$ is $n - 1$, where n is the number of complexes.

Letting $\sum_{(y_i, y_j) \in \Gamma_{\mathcal{R}^0}} \alpha_{ij}(y_j - y_i) = 0$ for some constants α_{ij}, we obtain all α_{ij} are zero as follows: This equation can be rewritten as

$$0 = \sum_{(y_i, y_j) \in \Gamma_{\mathcal{R}^0}} \alpha_{ij}(y_j - y_i) = \sum_{y_{1i} \in \mathcal{C}_1} \beta_{1i} y_{1i} + \cdots + \sum_{y_{\nu i} \in \mathcal{C}_\nu} \beta_{\nu i} y_{\nu i}. \tag{1}$$

Since complexes are functions defined in $\overline{\mathbb{P}}^{\mathcal{S}}$, we can consider the right side of the equation (1) a combination of functions in $\overline{\mathbb{P}}^{\mathcal{S}}$. Putting $y_{ji}^s (1 \leq j \leq \nu, y_{ji} \in \mathcal{C}_j)$ in the equation (1) consecutively, we obtain $\beta_{ji} = 0$. Using the definition of $\Gamma_{\mathcal{R}^0}$ and $\beta_{ji} = 0$, we finally obtain $\alpha_{ij} = 0$. Thus $\Gamma_{\mathcal{R}^0}$ is linearly independent. Therefore the rank of the network is the number of elements of $\Gamma_{\mathcal{R}^0}$, which is $n - 1$. This means zero deficiency. □

Using Lemma 4, we show that (P1)–(P2) implies zero deficiency without restriction of the number of linkage classes in the following Theorem.

Theorem 1. *If a network satisfies the properties (P1)–(P2), then the network has zero deficiency.*

Proof. Let $\mathcal{N}$, ℓ, $\mathcal{N}_i(1 \le i \le \ell)$, $\mathcal{R}_i$ and $\Gamma_{\mathcal{R}_i^0}$ be the given network, the number of linkage classes, a network corresponding to each linkage class, the relation of $\mathcal{N}_i$ in Definition 1 and the linearly independent set defined in the proof of Lemma 4, respectively. It follows from Lemma 4 that the ranks of $\cup_{1\le i\le \ell}\Gamma_{\mathcal{R}_i}$ and $\cup_{1\le i\le \ell}\Gamma_{\mathcal{R}_i^0}$ are the same as the rank of the network $\mathcal{N}$. Thus the rank of the network is

$$\sum_{1\le i\le \ell}(n_i - 1) = (\sum_{1\le i\le \ell} n_i) - \ell, \tag{2}$$

where n_i is the number of complexes in the network $\mathcal{N}_i$. Since the networks $\mathcal{N}_i(1 \le i \le \ell)$ are disjoint, $\sum_{1\le i\le \ell} n_i$ is the number of the complexes of $\mathcal{N}$. Therefore the equation (2) implies zero deficiency. □

Remark 1. *The converse of Theorem* 1 *is not true. For example, the network* $A + B \to B + C \to C + A$ *has zero deficiency but does not satisfy (P1)–(P2).*

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