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MULTISTATIONARITY IN EARTH'S PRE-INDUSTRIAL CARBON CYCLE MODELS

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ABSTRACT

Chemical reaction networks (CRNs) provide a language for representing systems of interacting entities. In this paper, the pre-industrial carbon cycle models of Schmitz (2002) and Anderies et al. (2013) are viewed and analyzed as CRNs. In this framework, we assess the models' capacity for multiple steady states or multistationarity via Chemical Reaction Network Theory – an approach that associates the topological structure of the CRN to the dynamical behavior of the network. Using the computational approach of Feliu & Wiuf (2013), this paper shows that the CRN representation of the pre-industrial model of Schmitz is injective, which is sufficient to conclude that the system cannot admit multiple steady states. On the other hand, the multistationarity of the pre-industrial model of Anderies et al. is shown using the criterion for the uniqueness of complex balancing equilibrium of Müller & Regensburger (2012).

Keywords: Chemical reaction networks, pre-industrial carbon cycle model, multistationarity

INTRODUCTION

A chemical reaction network (CRN) represents a universe whose evolution is determined by the transformation of its elements into other elements (Veloz & Razeto-Barry, 2017). In biochemistry-related areas such as systems biology, bioinformatics, enzyme kinetics, gene regulatory networks and many others, chemical reaction networks provide a language for systemic modelling (Johnston, 2011; Veloz & Razeto-Barry, 2017). The study of CRNs gave rise to a significant body of theoretical work, notably the so-called Chemical Reaction Network Theory (CRNT). The field had its foundations from the works of Feinberg, (1972), Horn(1972) and Horn & Jackson (1972). The focus of CRNT is to draw the connection between the topological structure of a network's reaction graph and the *qualitative properties* of the network. By qualitative properties we mean properties of dynamical systems with a common underlying structure (Feliu & Wiuf, 2013).

In this paper, we pay attention to a particular qualitative property, namely the capacity of a network to admit multiple steady states, or *multistationarity*. More precisely, this paper aims to investigate the multistationarity of two models of global carbon cycle at pre-industrial state by associating a CRN to each model and by subsequently applying known results in CRNT. The models of interest are those derived from the global carbon cycle representations of Schmitz (2002) and Anderies et al. (2013).

Fortun et al. (2017b) showed the existence of steady states and the parametrization of the set of positive equilibria of a power-law system approximation of pre-industrial carbon cycle model of Schmitz (2002). In this paper, this finding is enhanced by establishing the non-multistationarity of system. This is accomplished by showing that its corresponding CRN representation has the injectivity property, which is a sufficient condition for the absence of multiple positive equilibria. We apply the computational method of Feliu&Wiuf (2013) in determining injectivity of the CRN.

The multistationarity of the power-law system approximation of the pre-industrial carbon cycle model of Anderies et al. (2013) was observed by Fortun et al. (2017a). Here, this finding is verified by considering a different but dynamically equivalent CRN representation for the model. The new CRN representation turns out to be a good candidate for applying the criterion for the uniqueness of complex balancing equilibrium of Müller & Regensburger (2012).

PRE-INDUSTRIAL CARBON CYCLE MODELS

The first model is derived from the carbon cycle box model of Schmitz (2002). The model is an isothermal (i.e., with fixed temperature) simplification of the global carbon cycle. In the pre-industrial condition, Schmitz's model involves six carbon pools whose masses are denoted by M_i. The digraph shown in Figure 1 depicts the interaction among the different pools. The arrows represent the carbon fluxes or the transfer of carbon mass from one pool to another.

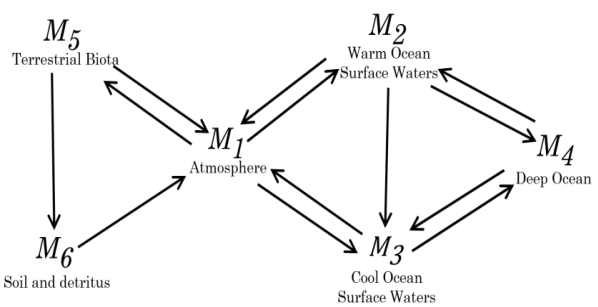

Figure 1. Digraph corresponding to the pre-industrial carbon cycle model of Schmitz (2002).

Furthermore, the rates of transfer of carbon mass from one pool to another are all power-law functions with a single exception – the rate of transfer from atmosphere to terrestrial biota. Fortun et al. (2017b) constructed a power-law approximation of the exception using a standard method from Biochemical Systems Theory (BST) to obtain a Generalized Mass Action (GMA) system, i.e. a system where each flux is approximated separately with a power-law term (Voit, 2000). The resulting ODE system, called **SM-PRI-GA**, is given by

$$\begin{aligned}
\dot{M}_1 &= k_{21}M_2^{9.4} + k_{31}M_3^{10.2} + k_{51}M_5 \\
&\quad + k_{61}M_6 - k_{21}M_1 - k_{13}M_1 - k_{15}M_1^{0.36} \\
\dot{M}_2 &= k_{12}M_1 + k_{42}M_4 - k_{23}M_2 \\
&\quad - k_{24}M_2 - k_{21}M_2^{9.4} \\
\dot{M}_3 &= k_{13}M_1 + k_{23}M_2 + k_{43}M_4 \\
&\quad - k_{34}M_3 - k_{31}M_3^{10.2} \\
\dot{M}_4 &= k_{24}M_2 + k_{34}M_3 - k_{42}M_4 - k_{43}M_4 \\
\dot{M}_5 &= k_{15}M_1^{0.36} - k_{51}M_5 - k_{56}M_5 \\
\dot{M}_6 &= k_{56}M_5 - k_{61}M_6
\end{aligned} \tag{1}$$

The second model is the pre-industrial carbon cycle representation of Anderies et al. (2013). Unlike the model of Schmitz, this model takes into account the impact of temperature in the system, thereby forming a feedback system. The model also considers only the basic interactions in three pools (land, atmosphere, and ocean) that are most significant at a global scale. Pictorially, the system is depicted using the biochemical map in Figure 2. The map consists of nodes that represent carbon pools, solid arrows that indicate transfer of carbon, and dashed arrows that indicate if a pool affects or modulates a process.

As in the previous model, a GMA system approximation of the model of Anderies et al. is computed (Fortun et al., 2017a) and the resulting system, named as **AN-PRI-GA**, is as follows:

$$\begin{aligned}
\dot{A}_1 &= a_1A_1^{p_1}A_2^{q_1} - a_2A_1^{p_2}A_2^{q_2} \\
\dot{A}_2 &= a_2A_1^{p_2}A_2^{q_2} - a_1A_1^{p_1}A_2^{q_1} \\
\dot{A}_3 &= a_mA_2 - a_m\beta A_3
\end{aligned} \tag{2}$$

where

$$p_1 = -1.89423, \quad p_2 = -0.270554,$$
$$q_1 = 0.42569 \text{ and } \quad q_2 = 0.438628.$$

CHEMICAL REACTION NETWORK (CRN)

In this section, we shall translate the models presented in the previous section as chemical reaction networks with power-law rate functions. Our aim is to determine the capacity for multistationarity of each system through these CRN representations. We first require some notations and terminologies.

We adopt the following notation used by Feinberg (1979) and (Müller & Regensburger, 2012). Denote the set of real numbers by $\mathbb{R}$, the non-negative real numbers by $\mathbb{R}_{\geq}$ and the positive real numbers by $\mathbb{R}_{>}$. Objects in the reaction systems are viewed as members of vector spaces. Suppose $\mathcal{I}$ is a finite (index)

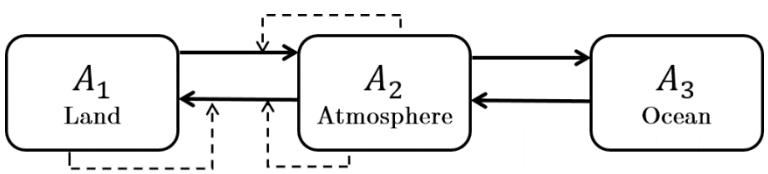

Figure 2. Biochemical map of the pre-industrial carbon cycle model of Anderies et al. (2013).

set. By $\mathbb{R}^{\mathcal{I}}$ we mean the usual vector space of real-valued functions indexed by $\mathcal{I}$. For $x \in \mathbb{R}^{\mathcal{I}}$, the i^{th} coordinate is denoted by x_i. Addition, subtraction, and scalar multiplication in $\mathbb{R}^{\mathcal{I}}$ are defined in the usual way. The sets $\mathbb{R}^{\mathcal{I}}_{\geq}$ and $\mathbb{R}^{\mathcal{I}}_{>}$ are called the **non-negative** and **positive orthants** of $\mathbb{R}^{\mathcal{I}}$, respectively. We define the standard basis $\{\omega_i\}_{i\in\mathcal{I}}$ by the characteristic function

$$(\omega_i)(j) = \begin{cases} 1 & \text{if } i = j, \\ 0 & \text{if } i \neq j, \end{cases}$$

for all $j \in \mathcal{I}$. If $x \in \mathbb{R}^{\mathcal{I}}_{>}$ and $y \in \mathbb{R}^{\mathcal{I}}$, we define $x^y \in \mathbb{R}_{>}$ by

$$x^y = \prod_{i\in\mathcal{I}} x_i^{y_i}. \tag{3}$$

The vector $\log x \in \mathbb{R}^{\mathcal{I}}$, where $x \in \mathbb{R}^{\mathcal{I}}_{>}$ is given by

$$(\log x)_i = \log x_i \text{, for all } i \in \mathcal{I}.$$

By the **support** of $x \in \mathbb{R}^{\mathcal{I}}$, denoted by x, we mean the subset of $\mathcal{I}$ assigned with non-zero values by x. That is,

$$\operatorname{supp} x := \{i \in \mathcal{I} | x_i \neq 0\}.$$

We now formally define a chemical reaction network (CRN).

Definition 1 (Feinberg, 1979). A **chemical reaction network** is a triple $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ of three non-empty finite sets:

1. a set **species** $\mathcal{S} = \{X_1, X_2, \ldots, X_m\}$,
2. a set $\mathcal{C}$ of **complexes**, which are non-negative integer linear combination of the species, and
3. a set $\mathcal{R} \subseteq \mathcal{C} \times \mathcal{C}$ of **reactions** such that
   a. $(i, i) \notin \mathcal{R}$ for all $i \in \mathcal{C}$, and
   b. for each $i \in \mathcal{C}$, there exists a $j \in \mathcal{C}$ such that $(i, j) \in \mathcal{R}$ or $(j, i) \in \mathcal{R}$.

We reserve m to denote the number of species, n to denote the number of complexes, and r to denote the number of reactions in a CRN.

If $(i, j) \in \mathcal{R}$, we say that i reacts to j. The usual notation in chemistry to denote this relation is $i \to j$. In this paper, the notations $i \to j$ and (i, j) are used interchangeably. Moreover, if $i \to j \in \mathcal{R}$, we say that i is the **reactant complex** and j is the **product complex** of the reaction.

Arceo et al. (2015) proposed CRNT approaches in studying GMA systems. To analyze the dynamic behavior of a GMA system through CRNT, it requires translating the GMA system into a CRN whose evolution is governed by power-law rate functions. In this way, the two systems (the GMA system and its associated CRN) are dynamically equivalent, i.e., they have the same ordinary differential equations. The CRN representation needed is referred to as the *total CRN representation* of the GMA system (Arceo et al., 2015). The procedure to obtain the representation is presented below as a definition.

Definition 2. The **total CRN representation of a GMA** system is a network of reactions based from its biochemical map. This is constructed as follows:

1. To characterize an independent variable X_i, add the inflow $0 \to X_i$ to the reaction network.
2. For each efflux coming out of X_i (indicated by an outlofw arrow), add the outflow reaction $X_i \to 0$.
3. For each interaction $X_i \to X_j$, with a regulatory arrow from each element $\{X_k\}$, associate the reaction $X_i + \sum X_k \to X_j + \sum X_k$.

Example 1. Consider the biochemical map of SM-PRI-GA in Figure 1 (the digraph is its biochemical map) and AN-PRI-GA in Figure 2. Since there are no assumed independent variables in each system and there are no outflows (or effluxes), we need only to consider the third condition in the preceding

definition. For SM-PRI-GA, its total CRN representation is given by where

$$\begin{aligned}\mathcal{S} = \mathcal{C} = \quad & \{M_1, M_2, M_3, M_4, M_5, M_6\},\\ \mathcal{R} = \quad & \{M_1 \to M_2, M_1 \to M_3, M_1 \to M_5,\\ & M_2 \to M_1, M_2 \to M_3, M_2 \to M_4,\\ & M_3 \to M_1, M_3 \to M_4, M_4 \to M_2,\\ & M_4 \to M_3, M_5 \to M_1, M_5 \to M_6,\\ & M_6 \to M_1\}.\end{aligned}$$

Hence, $m = n = 6$ and $r = 13$. In the case of AN-PRI-GA, the CRN representation of the system is given $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ by where

$$\begin{aligned}\mathcal{S} = \quad & \{A_1, A_2, A_3\},\\ \mathcal{C} = \quad & \{A_1 + 2A_2, 2A_1 + A_2, A_1 + A_2, 2A_2, A_2, A_3\},\\ \mathcal{R} = \quad & \{A_1 + 2A_2 \to 2A_1 + A_2, A_1 + A_2 \to 2A_2,\\ & A_2 \to A_3, A_3 \to A_2\}.\end{aligned}$$

In this case, $m = 3, n = 6$ and $r = 4$.

A CRN may be viewed as a digraph with its complexes as vertices and its reactions as arcs. This description is called the **reaction graph** of the CRN.

Example 2. The reaction graph for the CRN representation of SM-PRI-GA is precisely shown in Figure 1. On the other hand, the following reaction graph corresponds to the CRN representation of AN-PRI-GA.

$$\begin{gathered}A_1 + 2A_2 \to 2A_1 + A_2\\ A_1 + A_2 \to 2A_2\\ A_2 \rightleftarrows A_3\end{gathered}$$

The reaction graph of SM-PRI-GA is made of one connected piece containing all the complexes. On the other hand, the reaction graph of AN-PRI-GA is composed of three separate pieces; the first piece contains the linked complexes $A_1 + 2A_2$ and $2A_1 + A_2$, the second piece contains the linked complexes $A_1 + A_2$ and $2A_2$, and the third piece contains the connected complexes A_2 and A_3. These pieces comprised of mutually linked complexes are called the **linkage classes** of the CRN. We denote the number of a CRN's linkage classes by ℓ.

We say that two complexes are *strongly connected* if there is a directed path from one to the other and vice versa. If every pair of complexes in each linkage class of CRN is strongly connected, then we say that the network is **weakly reversible**. Observe that the CRN representation for SM-PRI-GA is weakly reversible but the CRN representation for AN-PRI-GA is not weakly reversible.

Many features of CRNs can be examined by working in terms of finite dimensional spaces $\mathbb{R}^{\mathcal{S}}$, $\mathbb{R}^{\mathcal{C}}$ and $\mathbb{R}^{\mathcal{R}}$, which are referred to as **species space**, **complex space** and **reaction space**, respectively. Since these are vector spaces of real-valued functions, the set $\{\omega_i\}_{i\in\mathcal{I}}$ forms a basis of $\mathbb{R}^{\mathcal{I}}$ where $\mathcal{I} = \mathcal{S}, \mathcal{C}$ or $\mathcal{R}$. We collect some linear algebraic notions related to the study of CRNs.

In a CRN, each complex is associated with a complex vector in .

Definition 3. The **complex vector** of $y \in \mathcal{C}$ is defined as

$$\sum_{i\in\mathcal{S}} y_i\omega_i \in \mathbb{R}^{\mathcal{S}},$$

where y_i is the stoichiometric coefficient of $i \in \mathcal{S}$.

The set of complexes for the two CRNs of interest are expressed as set of complex vectors as follows:

SM-PRI-GA:

$$\mathcal{C} = \{M_1, M_2, M_3, M_4, M_5, M_6\}$$

$$\left\{\begin{bmatrix}1\\0\\0\\0\\0\\0\end{bmatrix}, \begin{bmatrix}0\\1\\0\\0\\0\\0\end{bmatrix}, \begin{bmatrix}0\\0\\1\\0\\0\\0\end{bmatrix}, \begin{bmatrix}0\\0\\0\\1\\0\\0\end{bmatrix}, \begin{bmatrix}0\\0\\0\\0\\1\\0\end{bmatrix}, \begin{bmatrix}0\\0\\0\\0\\0\\1\end{bmatrix}\right\}.$$

=

AN-PRI-GA:

$$\mathcal{C} = \{A_1 + 2A_2, 2A_1 + A_2, A_1 + A_2, 2A_2, A_2, A_3\}$$
$$= \left\{\begin{bmatrix}1\\2\\0\end{bmatrix}, \begin{bmatrix}2\\1\\0\end{bmatrix}, \begin{bmatrix}1\\1\\0\end{bmatrix}, \begin{bmatrix}0\\2\\0\end{bmatrix}, \begin{bmatrix}0\\1\\0\end{bmatrix}, \begin{bmatrix}0\\0\\1\end{bmatrix}\right\}.$$

For every reaction, we associate a reaction vector, which is obtained by subtracting the reactant complex from the product complex. By the rank of a CRN, we mean the maximallinearly independent reaction vectors that the CRN contains.

Definition 4. For a reaction $y \to y'$, the associated **reaction vector** is $y - y' \in \mathbb{R}^{\mathcal{S}}$. The **stoichiometric subspace** S of the CRN is the linear subspace of $\mathbb{R}^{\mathcal{S}}$ defined by

$$S \coloneqq \text{span}\{y' - y \in \mathbb{R}^{\mathcal{S}} \,|\, y \to y' \in \mathcal{R}\}.$$

The **rank** of the CRN, denoted by s, is defined as $s = \dim S$.

One can verify that the ranks of the CRN representation of SM-PRI-GA andAN- PRI-GA are 5 and 2, respectively.

A non-negative integer, called *deficiency*, can be associated to each CRN. The earliest results in CRNT were centered about the classification of reaction networks by means of this index.

Definition 5. The **deficiency** of a CRN is the integer $\delta = n - \ell - s$.

The deficiency is not a measure of a network's size. In fact, a very large or complex network can have a low deficiency(Shinar & Feinberg, 2012). Instead, the deficiency measuresthe amount of linear independence among the reactions of the network. The higher the deficiency, the lower the extent of linear independence of the reactions(Shinar & Feinberg, 2011). The deficiencies of the CRNs of SM-PRI-GA and AN-PRI-GA are shown computed below.

SM-PRI-GA:

$$\delta = n - \ell - s = 6 - 1 - 5 = 0.$$

AN-PRI-GA:

$$\delta = n - \ell - s = 6 - 3 - 2 = 1.$$

For later reference, we define three maps relevant in the study of CRNs: incidence map,map of complexes, and stoichiometric map.

Definition 6. Let $(\mathcal{S}, \mathcal{C}, \mathcal{R})$ be a CRN.

1. The **incidence map** $I_a : \mathbb{R}^{\mathcal{R}} \to \mathbb{R}^{\mathcal{C}}$ is the linear map defined by

   $I_a \omega_R \coloneqq \omega_{y'} - \omega_y$ for all $R = (y, y') \in \mathcal{R}$.

   Its matrix representation is the $n \times r$ matrix, called **incidence matrix**, is given by

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

2. The **map of complexes** $Y : \mathbb{R}^{\mathcal{C}} \to \mathbb{R}^{\mathcal{S}}$ is the linear map defined by

   $$Y\omega_y \coloneqq y, \text{for all } y \in \mathcal{C}.$$

   Its matrix representation is the $m \times n$ matrix, called the **matrix of complexes** Y, whose $(i,j)^{\text{th}}$ entry is the stoichiometric coefficient of the i^{th} species in the j^{th} complex.

3. The **stoichiometric map** $N : \mathbb{R}^{\mathcal{R}} \to \mathbb{R}^{\mathcal{S}}$ is defined as $N = Y \circ I_a$. Its matrix representation, called the **stoichiometric matrix**, is the $m \times r$ matrix whose j^{th} column is the

reaction vector $y'_j - y_j$ of the reaction $R_j = (y_j, y'_j) \in \mathcal{R}$ for $j = 1, \ldots, r$.

Remark 1. Since the columns of N are precisely the reaction vectors, clearly $\mathrm{Im} N = S$.

To capture the evolution of a CRN, a system ordinary differential equations (ODEs) is specified. In this representation, the state of the system is described by the concentrations of the species, which are specified through a vector of composition $c \in \mathbb{R}^{\mathcal{S}}_{>}$, where each coordinate denotes the concentration of species $i \in S$. In order to write the ODEs, it is necessary to know the rate of occurrence of each of the chemical reactions in the network. It is generally assumed that the rate of each reaction depends in its own way on the (instantaneous) composition of species. That is, there exists a nonnegative real-valued **rate function** $K_{y \to y'}$ such that $K_{y \to y'}(c)$ is the instantaneous occurrence rate of reaction $y \to y'$ when the composition is c. A **kinetics** for a CRN is an assignment of such a rate function to each reaction in the network. This is defined formally as follows.

Definition 7. A **kinetics** of a CRN $\mathcal{N} = (\mathcal{S}, \mathcal{C}, \mathcal{R})$ is an assignment of a rate function $K_{ij} : \mathbb{R}^{\mathcal{S}}_{\geq} \to \mathbb{R}_{\geq}$ to each reaction $(i, j) \in \mathcal{R}$, and

$$K_{ij}(c) > 0 \text{ for all } c \in \mathbb{R}^{\mathcal{S}}_{>} \text{ if and only if } \operatorname{supp} i \subset \operatorname{supp} c.$$

A kinetics for a network $\mathcal{N}$ is denoted by $K = [K_1, K_2, \ldots, K_r]^{\mathsf{T}}$. The pair $(\mathcal{N}, K)$ is called the **chemical kinetic system** (CKS).

We denote the set of all kinetics on a CRN $\mathcal{N}$ by $\mathcal{K}(\mathcal{N})$.

In light of the GMA system approximation of the pre-industrial carbon cycle models, we focus our discussion on power-law kinetic systems. Power-law kinetics is determined by **arate vector** $k \in \mathbb{R}^{\mathcal{R}}_{>}$ whose elements are the rate constants for each reaction, and an $r \times m$ matrix F, called the **kinetic order matrix**, where F_{ij} is the kinetic order of the j^{th} species concentration in the i^{th} reaction.

Definition 8. A kinetics $K : \mathbb{R}^{\mathcal{S}}_{>} \to \mathbb{R}^{\mathcal{R}}$ is a **power-law kinetics** (PLK) if

$$K_{ij}(c) = k_{ij} x^{(F_{i,\cdot})^{\mathsf{T}}} \text{ for all } (i, j) \in \mathcal{R},$$

where $k_{ij} \in \mathbb{R}_{>}$ and $F_{ij} \in \mathbb{R}$.

In the definition $F_{i,\cdot}$ pertains to the row of the kinetic order matrix corresponding to the reaction $i \in \mathcal{R}$. By Equation (3),

$$x^{(F_{i,\cdot})^{\mathsf{T}}} = \prod_{s \in \mathcal{S}} x_s^{(F_{i,\cdot})_s^{\mathsf{T}}} \in \mathbb{R}_{>}.$$

Example 3. Let $F_{\mathcal{G}}$ and $F_{\mathcal{N}}$ denote the kinetic order matrices of the CRN representation of SM-PRI-GA and AN-PRI-GA, respectively. These matrices are given below.

$$F_{\mathcal{G}} = \begin{array}{c} \begin{matrix} M_1 & M_2 & M_3 & M_4 & M_5 & M_6 \end{matrix} \\ \left[\begin{array}{cccccc} 1 & 0 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 & 0 \\ 0.36 & 0 & 0 & 0 & 0 & 0 \\ 0 & 9.4 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 10.2 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 \end{array}\right] \end{array} \begin{array}{l} M_1 \to M_2 \\ M_1 \to M_3 \\ M_1 \to M_5 \\ M_2 \to M_1 \\ M_2 \to M_3 \\ M_2 \to M_4 \\ M_3 \to M_1 \\ M_3 \to M_4 \\ M_4 \to M_2 \\ M_4 \to M_3 \\ M_5 \to M_1 \\ M_5 \to M_6 \\ M_6 \to M_1 \end{array}$$

and

$$F_{\mathcal{N}} = \begin{array}{c} \begin{matrix} A_1 & A_2 & A_3 \end{matrix} \\ \left[\begin{array}{ccc} -1.894 & 0.426 & 0 \\ -0.271 & 0.439 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{array}\right] \end{array} \begin{array}{l} A_1 + 2A_2 \to 2A_1 + A_2 \\ A_1 + A_2 \to 2A_2 \\ A_2 \to A_3 \\ A_3 \to A_2 \end{array}.$$

The respective kinetics $K_{\mathcal{G}}$ and $K_{\mathcal{N}}$ of the two systems are as follows:

$$K_{\mathcal{G}} = \begin{bmatrix} k_{12}M_1 \\ k_{13}M_1 \\ k_{15}M_1^{0.36} \\ k_{21}M_2^{9.4} \\ k_{23}M_2 \\ k_{24}M_2 \\ k_{31}M_3^{10.2} \\ k_{34}M_3 \\ k_{42}M_4 \\ k_{43}M_4 \\ k_{51}M_5 \\ k_{56}M_5 \\ k_{61}M_6 \end{bmatrix}$$

and

$$K_{\mathcal{N}} = \begin{bmatrix} k_{12}A_1^{-1.894}A_2^{0.426} \\ k_{34}A_1^{-0.271}A_2^{0.439} \\ k_{56}A_2 \\ k_{65}A_3 \end{bmatrix}.$$

Arceo et al. (2017)identified some of subsets PLK systems and presented them through a kinetics landscape. One class of power-law kinetics they identified is the set of power-law kinetics with reactant-determined kinetic order (PL-RDK). These are kinetic systems with power-law rate functions whose kinetic orders are identical for all branching reactions (i.e.,reactions with similar reactant complex).

Definition 9. 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 are identical, i.e., $F_{ik} = F_{jk}$ for $k = 1, \ldots, m$. Otherwise, a PLK system has **non-reactant-determined kinetics** (of type **PL-NDK**) if there exist two reactions with the same reactant complexes whose corresponding rows of kinetic orders in F are not identical.

The kinetic order matrix for SM-PRI-GA (in Example 3) reveals that the system is of typePL-NDK. On the other hand, the AN-PRI-GA system is of type PL-RDK.

Once a kinetics is associated with a CRN, we can determine the rate at which the concentration of each species evolves at composition c. The rate of formation of the species and the ODEs that govern the species concentration can be specified according to the following definition.

Definition 10. The **species formation rate function (SFRF)** of a chemical kinetic system (CKS) is the vector field

$$f(c) = NK(c) = \sum_{y \to y' \in \mathcal{R}} K_{y \to y'}(c)(y' - y). \quad (4)$$

The equation $\dot{c} = f(c)$ is the **ODE** or **dynamical system** of the CKS.

Remark 2. Using the above formula, one may verify that the ODE systems correspondingto the CRN representations of SM-PRI-GA and AN-PRI-GA are indeed identical to the ODEsystems in Section 2.

Definition 11. A **positive equilibrium** or **steady state** is an element of $\mathbb{R}^{\mathcal{S}}_{>}$ for which $f(c) = 0$. The set of positive equilibria of a chemical kinetic system is denoted by $E_+(\mathcal{N}, K)$.

Definition 12. Two elements $c', c \in \mathbb{R}^{\mathcal{S}}$ are s**toichiometrically compatible** if $c' - c$ is contained in S. The intersection of the coset $c + S$ with $\mathbb{R}^{\mathcal{S}}_{>}$ is called a **stoichiometric compatibility class**.

Since the trajectory of the chemical system is contained in the stoichiometric compatibility class of its initial point (Feinberg, 1979), all

questions relating to existence and numberof steady states are relative to a stoichiometric compatibility class. In particular, a chemical kinetic system is **multistationary** (or has the capability for multiple steady states) ifthere is at least one stoichiometric compatibility class with two distinct steady states. Onthe other hand, the system is **monostationary** if it has at most one steady state for allstoichiometric compatibility classes.

Definition 13 (Wiuf&Feliu, 2013). Let $\mathcal{N}$ be a CRN with associated stoichiometric matrix N. The CRN $\mathcal{N}$ is **multistationary** or has that capacity for multiple steady states if there exists a kinetics $K \in \mathcal{K}(\mathcal{N})$ and distinct stoichiometrically compatible vectors $a, b \in \mathbb{R}^{\mathcal{S}}_{>}$ such that

$$NK(a) = NK(b) = 0.$$

Finally, we discuss the notion of *complex balancing* in chemical kinetics, which was first introduced by Horn & Jackson (1972). Analogous to the species formation rate function, there is a function called *complex formation rate function*, which takes as an argument a concentration vector in the species space. However, unlike the SFRF, the complex formation rate function returns a vector in $\mathbb{R}^{\mathcal{C}}$.

Definition 14. The **complex formation rate function** $g : \mathbb{R}^{\mathcal{S}}_{>} \to \mathbb{R}^{\mathcal{C}}$ of a chemical kinetic system is given by

$$g(c) = I_a K(c) = \sum_{y \to y' \in \mathcal{R}} K_{y \to y'}(c)(\omega_{y'} - \omega_y). \quad (5)$$

The counterpart of a steady state in the complex space is a concentration $c \in \mathbb{R}^{\mathcal{S}}_{>}$ such that $g(c) = 0$. This has a natural interpretation: Observe from Equation (5) that the function g gives the difference between the production and degradation of each complex. Thus, complex balancing occurs when $g(c) = 0$.

Remark 3. In view of Definitions 6, 10 and 14, it is clear that

$$f(c) = Yg(c).$$

Hence, if $c \in \mathbb{R}^{\mathcal{S}}_{>}$ is complex balanced, then is a steady state (the linearity of Y implies $Y(0) = 0$). However, the converse does not necessarily hold (i.e., when Ker Y is nontrivial).

Definition 15. A CKS $(\mathcal{N}, K)$ is called **complex balanced** if it has a complex balanced steady state. The set of positive complex balanced steady states of the CKS is denoted by $Z_+(\mathcal{N}, K)$.

INJECTIVE REACTION NETWORKS

We discuss the notion of an injective network.

Definition 16. (Wiuf & Feliu, 2013). Let $\mathcal{N}$ be a CRN with associated stoichiometric matrix N. We say that $\mathcal{N}$ is injective if for any distinct stoichiometrically compatible vectors $a, b \in \mathbb{R}^{\mathcal{S}}_{>}$ we have

$$NK(a) \neq NK(b) \text{ for all } K \in \mathcal{K}(\mathcal{N}).$$

From Definitions 13 and 16, we find that if $\mathcal{N}$ is injective, then $\mathcal{N}$ does not have the capacity for multiple steady states. Hence, to determine the multistationarity of the SM-PRI-GA and AN-PRI-GA, one can initially verify the injectivity of their corresponding CRN representations. If the network is injective, we can immediately conclude the monostationarity of the system. However, if the network is not injective, multistationarity of the system does not automatically follow.

Characterization

We use the simple characterization of injective power-law kinetic systems provided by Wiuf & Feliu (2013).

Definition 17.(Feliu & Wiuf, 2013). Amatrix with entries is called **sign-non-singular** if the determinant of Y is a nonzero homogeneous polynomial in y_*, with all coefficients being positive or all being negative. For the matrices considered here, Y is sign-non-singular if its determinant has constant nonzero sign for *positive* values of y_*.

Let m and r denote the number of species and reactions a CRN, respectively and consider symbolic vectos $z = (z_1, \dots, z_n)$ and $k = (k_1, \dots, k_m)$. Define the $m \times m$ matrix M by

$$M \coloneqq N \cdot \mathrm{diag}(z) \cdot F \cdot \mathrm{diag}(k),$$

where N denotes the stoichiometric matrix of the network and F is the kinetic order matrix.

Let $\{\omega^1, \dots, \omega^d\}$ be the basis of the left kernel of N and let $i_1, \dots, i_d$ be the indices of the corresponding d rows of N that are linearly dependent of the remaining s rows. To determine the indices, compute a basis of the left kernel of and perform Gaussian elimination to obtain a new basis $\{\omega^1, \dots, \omega^d\}$. Then i_j can be taken to be the index of the first nonzero entry of ω^j.

Define an $m \times m$ matrix M^* by replacing the i_j-th row of M by ω^j. The matrix M^* has d rows of real entries and s rows whose nonzero entries are polynomials in z_* and k_*.

Theorem 1 (Wiuf & Feliu, 2013). A CRN with power-law kinetics and fixed kinetic orders is injective if and only if M^* is sign-non-singular.

For a comprehensive discussion of the previous result along with its proof, the reader is referred to paper of Wiuf & Feliu (2013). Here, we are particularly interested in the computational approach to determine the multiple steady state capacity of a PLK system arising from the previous theorem. Feliu & Wiuf (2013) discussed the said approach and provided a Maple script, which is based from the following algorithm:

1. Input the stoichiometric matrix N and kinetic order matrix F.
2. Compute the matrix $M = N \cdot \mathrm{diag}(z) \cdot F \cdot \mathrm{diag}(k)$.
3. Calculate a basis $\{\omega^1, \dots, \omega^d\}$ of the left kernel of N. Reduce it by Gaussian elimination.
4. Generate the matrix M^*: For each j find the first nonzero entry i_j of the row vector ω_j and replace the i_j-th row of$M$ by ω_j.
5. Compute the determinant of M^*.
   a. If it is zero, then the CRN is not injective.
   b. If there are nonzero terms in the determinant, extract the signs of the coefficients. If all the signs are the same, the CRN is injective. If the signs are different, then the CRN is not injective.

Injectivity Test of Pre-industrial Carbon Cycle Models

The script was used to determine the injectivity of the CKS associated with SM-PRI-GA and AN-PRI-GA (see Appendix). The calculation reveals that the network of SM-PRI-GA is injective. Hence, it cannot admit multiple positive steady states in any stoichiometric compatibility class. This result supplements the results of Fortun et al. (2017b), which characterized the steady states of SM-PRI-GA through a *Deficiency Zero Theorem*. In the aforementioned paper, no statement was made about the uniqueness of the equilibrium in each stoichiometric class.

Implementation of the algorithm to AN-PRI-GA indicates that the network is not injective. Note, however, that non-injectivity is not a sufficient condition for the existence of multiple steady states in some stoichiometric compatibility classes.Nevertheless, Fortun

et al. (2017a) showed that, indeed, AN-PRI-GA is a system that admits multiple steady states in some stoichiometric compatibility classes using anprocedure called *Deficiency-One Algorithm*. In the following section, this findingis verifiedusing an alternative CRN, which is still dynamically equivalent to AN-PRI-GA.

MULTISTATIONARITY CRITERION FOR GMAK SYSTEMS

In this section, the problem of deciding for the multistationarity capacity of AN-PRI-GA is addressed by considering an alternative CRN representation for the system, which allows for the application of a result of Müller & Regensburger (2012).

Alternative CRN representation of AN-PRI-GA

Recall the CRN representation for AN-PRI-GA:

$$\begin{array}{lllll} R_1: & A_1 + 2A_2 & \rightarrow & 2A_1 + A_2 \\ R_2: & A_1 + A_2 & \rightarrow & 2A_2 \\ R_3, R_4: & A_2 & \rightleftarrows & A_3 \end{array} \quad (6)$$

Talabis et al. (2018b) found the following CRN whose stoichiometric subspace is identical to that of (6):

$$\begin{array}{lllll} R_1, R_2: & A_1 + 2A_2 & \rightleftarrows & 2A_1 + A_2 \\ R_3, R_4: & A_2 & \rightleftarrows & A_3 \end{array} \quad (7)$$

The second reaction of (6) $R_2: A_1 + A_2 \rightarrow 2A_2$ is written as $R_2: 2A_1 + A_2 \rightarrow A_1 + 2A_2$ in (7). Observe that these two reactions point to a similar reaction vector. Since one retains the same kinetic order matrix for both systems, the two induced chemical kinetic systems must be dynamically equivalent.

Interestingly, the new network haszero deficiency. Since the induced CKS belongs toa subset of power-law kinetic system with linearly independent kinetic order vectors calledPL-TIK system by Talabis et al. (2018a), the existence of a steady state is guaranteed by theDeficiency Zero Theorem for PL-TIK systems (Talabis et al., 2018a)[1]. However, the theoremis silent about the capacity of the system to admit multiple steady states in some stoichiometric compatibility classes. To verify the capacity of AN-PRI-GA to support multiple steady states in a positive compatibility class, we appeal to the results of Müller &Regensburger (2012) for Generalized Mass Action Kinetic (GMAK) systems.

Uniqueness of Complex Balancing Equilibria in GMAK systems

The papers of (Müller & Regensburger, 2012, 2014) on GMAK systems marked the emergence of results on power law kinetics in CRNT. GMAK systems essentially correspond toPL-RDK systems, but there are some slight differences; see Section 6 of paper of Talabiset al. (2018a) for a detailed discussion. We recall some relevant notions.

Definition 18. The matrix $\tilde{Y}$ is the $m \times n$ matrix defined as

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

In other words, for a reactant complex, the column of $\tilde{Y}$ is the transpose of the kinetic order matrix row of the complex's reaction, otherwise the column is 0.

Definition 19. The **kinetic order subspace** $\tilde{S}_{MR}$ is defined as

$$\tilde{S}_{MR} = \{\tilde{Y}_{.j} - \tilde{Y}_{.i} \mid (i,j) \in \mathcal{R}\}.$$

[1] To be exact, the existence of the equilibrium is guaranteed by Corollary 6 of Talabis et al. (2018a).

GMAK theory introduced the concept of kinetic deficiency $\tilde{\delta}$, which replaces the rank of the network with the dimension of the kinetic order subspace $\tilde{S}_{MR}$ in the deficiency definition. Their *Kinetic Deficiency Zero Theorem (KDZT)* includes the following statements:

Theorem 2 (Müller &Regensburger, 2012). For a weakly reversible GMAK system $\mathcal{N}$ and its set of complex balanced equilibria $Z_+(\mathcal{N}, K)$.

(i) $\tilde{\delta} = 0$if and only if $\mathcal{N}$ has a complex balanced
(ii) $Z_+(\mathcal{N}, K) = \{x \in \mathbb{R}^{\mathcal{S}}_{>} \mid \log x - \log x^* \in \tilde{S}^{\perp}_{MR}\}$ for any $x^* \in Z_+(\mathcal{N}, K)$

Note that the CKS induced by the new CRN representation for AN-PRI-GA is a GMAK system. Observe that

$$\tilde{Y} = \begin{array}{c} \\ \mathrm{A}_1 \\ \mathrm{A}_2 \\ \mathrm{A}_3 \end{array} \begin{array}{c} \begin{array}{cccc} A_1 + 2A_2 & 2A_1 + A_2 & A_2 & A_3 \end{array} \\ \begin{bmatrix} p_1 & p_2 & 0 & 0 \\ q_1 & q_2 & 1 & 0 \\ 0 & 0 & 0 & 1 \end{bmatrix} \end{array}$$

and

$$I_a = \begin{array}{c} \\ A_1 + 2A_2 \\ 2A_1 + A_2 \\ A_2 \\ A_3 \end{array} \begin{array}{c} \begin{array}{cccc} R_1 & R_2 & R_3 & R_4 \end{array} \\ \begin{bmatrix} -1 & 1 & 0 & 0 \\ 1 & -1 & 0 & 0 \\ 0 & 0 & -1 & 1 \\ 0 & 0 & 1 & -1 \end{bmatrix} \end{array}.$$

Hence,

$$\tilde{Y} \cdot I_a = \begin{array}{c} \\ \mathrm{A}_1 \\ \mathrm{A}_2 \\ \mathrm{A}_3 \end{array} \begin{array}{c} \begin{array}{cccc} R_1 & R_2 & R_3 & R_4 \end{array} \\ \begin{bmatrix} p_2 - p_1 & p_1 - p_2 & 0 & 0 \\ q_2 - q_1 & q_1 - q_2 & -1 & 1 \\ 0 & 0 & 1 & -1 \end{bmatrix} \end{array}.$$

Thus,

$$\tilde{S}_{MR} = Im\left(\tilde{Y} \cdot I_a\right) = \operatorname{span}\left\{\begin{bmatrix} 1 \\ 0 \\ \frac{q_1 - q_2}{p_1 - p_2} \end{bmatrix}, \begin{bmatrix} 0 \\ 1 \\ -1 \end{bmatrix}\right\}$$

The kinetic deficiency is thus

$$\tilde{\delta} = n - l - \dim \tilde{S}_{MR} = 4 - 2 - 2 = 0.$$

By the first statement of Theorem 2, the network is complex balanced. Moreover, it follows from the second statement that for any $x^* \in Z_+(\mathcal{N}, K)$,

$$Z_+(\mathcal{N}, K) = \{x \in \mathbb{R}^{\mathcal{S}}_{>} \mid \log x - \log x^* \in \tilde{S}^{\perp}_{MR}\}$$

where

$$(\tilde{S}_{MR})^{\perp} = \operatorname{span}\left\{\begin{bmatrix} \frac{q_2 - q_1}{p_1 - p_2} \\ 1 \\ 1 \end{bmatrix}\right\} = \operatorname{span}\left\{\begin{bmatrix} -0.0797 \\ 1 \\ 1 \end{bmatrix}\right\}. \quad (8)$$

(Recall that $p_1 = -1.8942$, $p_2 = -0.2706$, $q_1 = 0.4257$, and $q_2 = 0.4386$.)

Note that for zero deficiency networks $E_+(\mathcal{N}, K) = Z_+(\mathcal{N}, K)$; i.e., all steady states are complex balanced (Feinberg, 1972).

Müller & Regensburger (2012) provided a criterion for the uniqueness of complex balancing equilibrium in stoichiometric class in terms of sign vector relationships between S and $\tilde{S}^{\perp}_{MR}$.

Definition 20 (Müller &Regensburger, 2012). The **sign vector** $\operatorname{sign}(x) \in \{-,0,+\}^m$ of a vector $x \in \mathbb{R}^{\mathcal{S}}$ is obtained by applying the sign function component wise; we write

$$\operatorname{sign}(S) = \{\operatorname{sign}(x) \mid x \in S\}$$

for any subset $S \subseteq \mathbb{R}^{\mathcal{S}}$.

Theorem 3 (Müller &Regensburger, 2012). Let S and $\tilde{S}^{\perp}_{MR}$ be subspaces of $\mathbb{R}^{\mathcal{S}}$. Then the following statements are equivalent:

(i) $|\, Z_+(\mathcal{N}, K) \cap \mathcal{P} \,| \leq 1$ for every stoichiometric compatibility class $\mathcal{P}$.
(ii) $\operatorname{sign}(S) \cap \operatorname{sign}\left(\tilde{S}^{\perp}_{MR}\right) = \{0\}$.

Consider the vector

$$\sigma = \begin{bmatrix} -1 \\ 0.5 \\ 0.5 \end{bmatrix} \in S.$$

This is clearly sign compatible with the vector in $\tilde{S}_{MR}^{\perp}$; see Equation (8). By Theorem 3 and the fact that $E_+(\mathcal{N}, K) = Z_+(\mathcal{N}, K)$, the system has the capacity to admitat least two distinct stoichiometrically compatible equilibria. This is consistent with the finding of Fortun et al. (2017a).

SUMMARY

This paper aims to assess the capacity of two pre-industrial carbon cycle models to admit multiple steady states in some positive stoichiometric compatibility classes. Using the algorithm of Feliu & Wiuf (2013),it was shown that the power-law system approximation of the pre-industrial carbon cycle model of Schmitz (2002) or SM-PRI-GA is injective. This implies that the CRN cannot admit multiple steady states in any positive stoichiometric class. This result supplements the characterization of the steady states of SM-PRI-GA provided by Fortun et al. (2017b). Furthermore, a CRN with power-law kinetics corresponding to a power-law system approximation of the pre-industrial carbon cycle model of Anderies et al.(2013) or AN-PRI-GA was obtained from Talabis et al. (2018b). This CRN representationis an alternative to the CRN representation generated by Fortun et al. (2017a). Viewed asa GMAK system with zero deficiency, the GMAK theory of Müller & Regensburger (2012)indicates that the system cannot admit multiple steady states in any positive stoichiometriccompatibility class. This result agrees with the finding in Fortun et al. (2017a).

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APPENDIX

Maple Scripts Used to Check the Injectivity of the CRNs

SM-PRI-GA:

```
with(LinearAlgebra) :
# Enter the stoichiometric matrix
N := Matrix([[-1, 1,-1, 1, 0, 0, 0, 0,-1, 1, 0, 1], [1,-1, 0, 0,-1,-1, 1, 0, 0, 0, 0, 0], [0, 0, 1,-1, 1, 0, 0,-1, 1, 0, 0, 0], [0, 0, 0, 0, 0, 1,-1, 1,-1, 0, 0, 0],
    [0, 0, 0, 0, 0, 0, 0, 0, 1,-1,-1, 0], [0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 1,-1]]) :

# Enter the kinetic order matrix
F := Matrix([[1, 0, 0, 0, 0, 0], [0, 9.4, 0, 0, 0, 0], [1, 0, 0, 0, 0, 0], [0, 0, 10.2, 0, 0, 0], [0, 1, 0, 0, 0, 0], [0, 1, 0, 0, 0, 0], [0, 0, 0, 1, 0, 0], [0, 0, 1, 0, 0, 0], [0, 0, 0,
    1, 0, 0], [0.36, 0, 0, 0, 0, 0], [0, 0, 0, 0, 1, 0], [0, 0, 0, 0, 1, 0], [0, 0, 0, 0, 0, 1]]) :

# Computation of a basis of conservation left kernel of N
X := ReducedRowEchelonForm(Transpose(Matrix(convert(NullSpace(Transpose(N)), list)))) :

# Computation of Mstar
m := Dimension(N)[1] :
r := Dimension(N)[2] :
K := DiagonalMatrix(Vector(m, symbol = k)) :
Z := DiagonalMatrix(Vector(r, symbol = z)) :
M := NZFK :
Mt := M:

s := Rank(N) :
m := Dimension(N)[1] :

if s < m then
  for i from 1 by 1 to Dimension(X)[1] do
    j := 1 :
    while j < m + 1 do
      if X[j] ≠ 0 then Mt[j, 1..-1] := X[i]; j := m + 1;
      else j := j + 1;
      end if:
    end do:
  end do:
end if:

# Computation of the determinant of Mstar
det := expand(Determinant(Mt)) :

# If the determinant is zero, the network is not injective. If the determinant is non-zero, we check the signs
if det = 0 then
    print("The network is not injective; The determinant is identically zero") :
else
    signs := ListTools[MakeUnique](map(sign, [coeffs(det)])) :
    if signs = [1] or signs = [-1] then
      print("The network is injective");
    else print("The network is not injective");
    end if :
end if:
```

"The network is injective" **(1)**

```
> Mt
```

$$\begin{bmatrix} 1 & 1 & 1 & 1 & 1 & 1 \\ z_1 k_1 & (-9.4 z_2 - z_5 - z_6) k_2 & 0. & z_7 k_4 & 0 & 0 \\ z_3 k_1 & z_5 k_2 & (-10.2 z_4 - z_8) k_3 & z_9 k_4 & 0 & 0 \\ 0. & z_6 k_2 & z_8 k_3 & (-z_7 - z_9) k_4 & 0 & 0 \\ 0.36 z_{10} k_1 & 0. & 0. & 0 & (-z_{11} - z_{12}) k_5 & 0 \\ 0. & 0. & 0. & 0 & z_{12} k_5 & -z_{13} k_6 \end{bmatrix} \quad \textbf{(2)}$$

AN-PRI-GA:

```
with(LinearAlgebra) :
# Enter the stoichiometric matrix
N := Matrix([[1,-1, 0, 0], [-1, 1,-1, 1], [0, 0, 1,-1]]) :

# Enter the kinetic order matrix
F := Matrix([[-1.89423, 0.425693, 0], [-0.270554, 0.438628, 0], [0, 1, 0], [0, 0, 1]]) :

# Computation of a basis of conservation left kernel of N
X := ReducedRowEchelonForm(Transpose(Matrix(convert(NullSpace(Transpose(N)), list)))) :

# Computation of Mstar
m := Dimension(N)[1] :
r := Dimension(N)[2] :
K := DiagonalMatrix(Vector(m, symbol = k)) :
Z := DiagonalMatrix(Vector(r, symbol = z)) :
M := NZFK :
Mt := M:

s := Rank(N) :
m := Dimension(N)[1] :

if s < m then
  for i from 1 by 1 to Dimension(X)[1] do
    j := 1 :
    while j < m + 1 do
      if X[j] ≠ 0 then Mt[j, 1..-1] := X[i]; j := m + 1;
      else j := j + 1;
      end if:
    end do:
  end do:
end if:

# Computation of the determinant of Mstar
det := expand(Determinant(Mt)) :

# If the determinant is zero, the network is not injective. If the determinant is non-zero, we check the signs
if det = 0 then
    print("The network is not injective; The determinant is identically zero") :
else
    signs := ListTools[MakeUnique](map(sign, [coeffs(det)])) :
    if signs = [1] or signs = [-1] then
       print("The network is injective");
    else print("The network is not injective");
    end if :
end if:
```

"The network is not injective" (1)

```
> Mt
```

$$\begin{bmatrix} 1 & 1 & 1 \\ \left(1.89423\,z_1 - 0.270554\,z_2\right) k_1 & \left(-0.425693\,z_1 + 0.438628\,z_2 - z_3\right) k_2 & z_4\,k_3 \\ -0. & z_3\,k_2 & -z_4\,k_3 \end{bmatrix} \quad (2)$$

```
> det
```

$$0.425693\,k_2\,z_4\,k_3\,z_1 - 0.438628\,k_2\,z_4\,k_3\,z_2 + 1.89423\,k_1\,k_2\,z_1\,z_3 + 1.89423\,k_1\,k_3\,z_1\,z_4 - 0.270554\,k_1\,k_2\,z_2\,z_3 - 0.270554\,k_1\,k_3\,z_2\,z_4 \quad (3)$$