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On Brusselator and Oregonator as chemical reaction networks: A graph approach

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Abstract—This paper shows graph similarities between Brusselator and Oregonator reaction mechanisms, using the jacobian matrix in convex coordinates as an adjacency matrix which defines a weighted directed pseudograph. A linear transformation is defined for the task of mapping the weights of the three dimensional system onto a two dimensional one where the Oregonator's pseudograph is isomorphic to Brusselator's.

Keywords: Brusselator, Oregonator, Chemical Reaction Networks, Graph theory.

I. INTRODUCTION

The Belousov-Zhabotinsky (BZ) reaction, namely the decomposition of organic acid by bromate ions in acid solutions containing metallic catalyst, is by far the most investigated oscillatory chemical reaction, capable of display interesting complex behavior like mixed mode oscillations or, for specific regions of reactant concentrations, chaos.

The first reaction mechanism that showed sustained oscillations, as in the BZ reaction, was the Brusselator (Prigogine and Lefever, 1968). The Brusselator is formed by 6 chemical species and 4 elementary reactions. Later on, in 1972, a second reaction mechanism (called FKN mechanism because researchers names Field, Koros and Noyes) with more than 10 elementary reactions was proposed to explain the observed dynamical behavior in the BZ reaction showing a good qualitative agreement (Noyes *et al.*, 1972). In 1974, the same research group reduce the FKN mechanism to a 5 elementary reactions and 7 chemical species preserving the richness of dynamical behavior (Field and Noyes, 1974). This mechanism was named Oregonator. After these efforts, in 2001, a reaction mechanism with more than 40 elementary reactions of the BZ reaction was reported (Hegedus *et al.*, 2001).

Along decades both mechanisms (Brusselator and Oregonator) has been subject of rigorous mathematical studies (sensitivity analysis, bifurcation scenarios, chemical chaos, conditions for synchronization, etc. (Epstein and Pojman, 1998)), but a question remains unanswered: What mathematical property do Brusselator and Oregonator share that make them display sustained oscillations as in the BZ

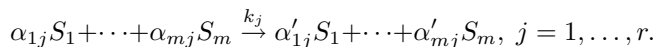
reaction? We address this question from a graph theoretic point of view.

In the next section we define concepts from the chemical engineering literature. Section III is devoted to explain well documented approaches intended to classify chemical reaction networks (CRN) and justify our motivation to clarify the (mathematical) relation between the Brusselator and Oregonator reaction mechanism. In section IV by means of graph theory and the Stoichiometric Network Analysis (SNA) we show the existence of an isomorphism between Oregonator and Brusselator pseudographs. Some conclusions are drawn in section V.

II. CHEMICAL REACTION BACKGROUND

II-A. Definitions of chemical reaction systems

Consider a chemical reaction system of r reactions and m reacting chemical species represented by:



where $\alpha_{ij} \in \mathbb{R}$. Chemical species are represented by S_i , $i = 1, \dots, s$. The variable denoting chemical concentration for a chemical specie is $x_i \in \bar{\mathbb{R}}_+$ where $\bar{\mathbb{R}}_+ \triangleq \{\mathbf{z} \in \mathbb{R} \mid z_i \geq 0, l = 1, \dots, n\}$ and $\mathbb{R}_+ \triangleq \{\mathbf{z} \in \mathbb{R} \mid z_i > 0, l = 1, \dots, n\}$. The rate constant, $k_j \in \mathbb{R}_+$, $j = 1, \dots, r$, encode external factors influencing the velocity of j -th reaction and the concentrations of chemical species which are constant throughout the reaction. The *stoichiometric coefficient*, $n_{ij} = \alpha'_{ij} - \alpha_{ij}$, is the net amount of i -th chemical specie which is consumed (or produced) in the j -th reaction. These stoichiometric coefficients are arranged in the *stoichiometric matrix* $N \in \mathbb{R}^{s \times r}$. The monomials of the *reaction rates*, $v_j(k_j, x) = k_j \prod_{i=1}^m x_i^{\kappa_{ij}}$ are formed according to the mass action rate law, where the *kinetic exponents* κ_{ij} encode the molecularity of the i -th specie in the j -th reaction. These kinetic exponents are arranged in the *kinetic matrix*, $\kappa \in \bar{\mathbb{R}}_+^{s \times r}$. The ODEs corresponding to a reaction network are defined as

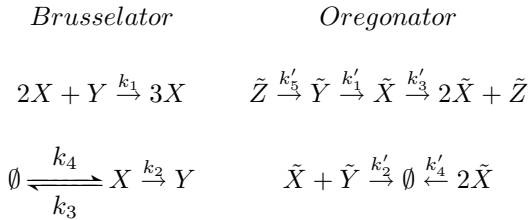
$$\dot{x} = N \cdot v(k, x), \quad x(0) \geq 0 \quad (1)$$

In general, N does not have maximal row rank. For $d = \text{rank}(N)$, there exist $s - d$ conservation relations

$$W^T \cdot x = c \quad (2)$$

with $W^T \cdot N = 0$ for a $W \in \mathbb{R}^{s \times (s-d)}$, where $c \in \mathbb{R}_+$.

A *reaction mechanism* is “a detailed description of the pathway leading from the reactants to the products, including as complete a characterization as possible of the composition, structure and other properties of reaction intermediates and transition states (Temkin *et al.*, 1996)”. Because some chemical species are present in excess, do not vary on time for practical purposes. These are named *external species* (Eiswirth *et al.*, 1991); those who do vary on time are called *internal species*. A *chemical reaction network* (CRN) is constructed using *pseudoreactions*, i.e. those remaining in the reaction mechanism by setting a \emptyset for every external specie, leaving the internal ones intact. The linear combination of internal species before and after the chemical arrow in a CRN are named *complexes* (Feinberg, 1987).



The associated CRNs for the Brusselator and Oregonator are depicted above where the internal species for the former are denoted by X and Y , meanwhile for the latter are \tilde{X} , \tilde{Y} and \tilde{Z} . The stoichiometric matrices corresponding to the networks above are:

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

$$\tilde{N} = \begin{bmatrix} 1 & -1 & 1 & -2 & 0 \\ -1 & -1 & 0 & 0 & 1 \\ 0 & 0 & 1 & 0 & -1 \end{bmatrix}$$

Note that neither of them is rank deficiency, thus no conservation relations are needed. The monomial vectors of reaction rates are

$$v(\mathbf{k}, \mathbf{x}) = \begin{bmatrix} k_1 x_1^2 x_2 \\ k_2 x_1 \\ k_3 x_1 \\ k_4 \end{bmatrix}, \quad \tilde{v}(\mathbf{k}', \tilde{\mathbf{x}}) = \begin{bmatrix} k'_1 \tilde{x}_2 \\ k'_2 \tilde{x}_1 \tilde{x}_2 \\ k'_3 \tilde{x}_1 \\ k'_4 \tilde{x}_1^2 \\ k'_5 \tilde{x}_3 \end{bmatrix}$$

II-B. Stoichiometric network analysis

Stoichiometric Network Analysis (SNA) relies on a decomposition of the entire CRN in subnetworks. These subnetworks are the minimal sets of reactions for which the corresponding chemical reaction system will admit steady states.

The key feature of SNA theory is to observe the dynamics of the system in the reaction rate space, rather than in the species concentration space. This approach enables to draw some conclusions about the chemical reaction network dynamics without specifying the concentration values or kinetic parameters at the steady state.

For a chosen set of parameters k , any steady state of the system must satisfy the condition

$$N \cdot v^*(k, x) = 0 \quad (3)$$

where all the stationary reaction rates belong to the intersection of the $\ker(N)$ with \mathbb{R}_+^r , forming a convex polyhedral cone, K_v (Clarke, 1980). The unique and minimal set of generating vectors spanning K_v are called *extreme currents*, E'_i s. The extreme currents along this work were calculated with the program routine FluxAnalyzer (Klamt, 2002).

$$K_v = \{v \in \bar{\mathbb{R}}_+^r \mid N \cdot v = 0, v \geq 0\} \quad (4)$$

$$= \{\ker(N) \cap \bar{\mathbb{R}}_+^r\} \quad (5)$$

$$= \left\{ \sum_{i=1}^f j_i E_i > 0, \forall i \right\} \quad (6)$$

The non-negative entries of the extreme currents denote subnetworks for which a steady state exists (Clarke, 1980). The parameters $j > 0$, are called *convex parameters* and quantify the influence of an extreme current on full network dynamics. The reaction rates can be expressed as a linear combination of convex parameters as follows:

$$v(j) = \sum_{i=1}^f j_i E_i \quad (7)$$

The jacobian matrix, after a map transformation (Clarke, 1980), and the use of eq. 7, can be expressed as

$$\text{Jac}(v) = N \text{diag}(v) \kappa^T \text{diag}(h_i) \quad (8)$$

$$\Rightarrow \text{Jac}(j) = N \text{diag}\left(\sum_{i=1}^f j_i E_i\right) \kappa^T \text{diag}(h_i) \quad (9)$$

where $h_i = x_{i,ss}^{-1}$, $i = 1, \dots, s$ is the inverse steady state concentrations.

III. TWO PREVIOUS APPROACHES

Next, we discuss two most accepted approaches.

1. The Chemical Reaction Network Theory (CNRT) is a formalism based on a non-negative integer called *deficiency*, δ , of a CRN (Feinberg, 1987; Feinberg and Ellison, 2000). This integer relates the structure of the network with the existence of (multiple) equilibria for the corresponding system of ODEs as in (1). The dynamical information the deficiency provided, can be summarized as follows¹:

¹ δ is independent of parameter values.

- If $\delta = 0$, then, regardless of the (positive) rate constants, the set of ODE's derived from the network and endowed with mass action kinetics, *cannot* admit multiple steady states or sustained oscillations.
- If $\delta = 1$, and the network satisfies some additional weak conditions, then the Deficiency One Theory (DOT) (Feinberg, 1987; Feinberg and Ellison, 2000) can decide whether the network can or cannot admit multiple steady states.
- If $\delta > 1$, under some conditions, the Advanced Deficiency Theory (ADT) along with its algorithm (Feinberg, 1987; Feinberg and Ellison, 2000), can be applied to decided about multistationarity of the network.

The mathematical definition of the deficiency is:

$$\delta = n - l - \text{rank}(N) \quad (10)$$

where n is the number of complexes (including the zero complex, \emptyset) and l the number of *linkage classes*. As noted before, the complexes of a network are the objects that appear before and after the reaction arrows, and each one of them must appear only once in the network. Thus the set of complexes for the Brusselator network is, $\{\emptyset, X, Y, 2X + Y, 3X\}$, then $n = 5$. For the Oregonator network the set of complexes is $\{\emptyset, \tilde{X}, \tilde{Y}, \tilde{Z}, 2\tilde{X}, 2\tilde{X} + \tilde{Z}, \tilde{X} + \tilde{Y}\}$, therefore $\tilde{n} = 7$.

A *linkage class*, l , is a group of complexes that are connected by reaction arrows, i.e. the number of separate "pieces" of which the network is composed. For example, the Brusselator network is composed by two linkage classes, the sets of complexes $L_1 = \{2X + Y, 3X\}$ and $L_2 = \{\emptyset, X, Y\}$, thus $l = 2$. Doing the same with the Oregonator network we have that $\tilde{l} = 2$.

Therefore, their deficiencies are $\delta = 5 - 2 - 2 = 1$ for the Brusselator, and $\tilde{\delta} = 7 - 2 - 3 = 2$, for the Oregonator. Moreover, using the CRNT Toolbox (Feinberg and Ellison, 2000) both DOT and ADT, conclude the same for both networks, i.e. "Taken with mass action kinetics, the network CANNOT admit multiple steady states or a degenerate steady state NO MATTER WHAT (POSITIVE) VALUES THE RATE CONSTANTS MIGHT HAVE ". Note that multistationarity does not preclude the possibility for oscillations to appear (Toth, 1999).

2. SNA can be used to identify those extreme currents cycles leading to instability. A classification of chemical oscillators based on certain characteristics of these cycles has been reported to be fruitful (Eiswirth *et al.*, 1991; Clarke, 1980). To perform this task is necessary to draw the entire *network diagram*, D_N , where the chemical species are connected by arrows denoting reactions. The total number of feathers of an arrow equals the stoichiometric number of that

specie as reactant and the total number of barbs equals the stoichiometric number of a specie as product in the corresponding reaction. Using those subnetworks defined by the extreme currents, a *current diagram* D_C , is drawn in the same fashion. This D_C requires that the sum over all feathers equals the sum over all barbs for every species in the diagram (see Fig. 1).

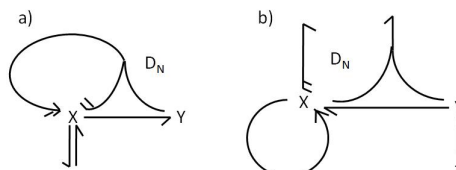


Fig. 1. Network diagrams. a) Brusselator, b) Oregonator.

The current cycles are classified depending upon if the kinetic order (number of feathers) of the exit reaction (κ_{exit}) from the cycle is lower than, equal to, or higher than the kinetic order of the cycle (κ_{cycle}). Fig. 2 graphically summarize these concepts.

- if $\kappa_{exit} > \kappa_{cycle}$ then the current is a *weak current cycle*, which is always stable.
- if $\kappa_{exit} = \kappa_{cycle}$ the current cycle is termed *critical current cycle* (CCC), which can lead to instability (and possibly to oscillations) depending in other features of the network.
- if $\kappa_{exit} < \kappa_{cycle}$ the network has a *strong cycle* (SC) and therefore a source of instability.

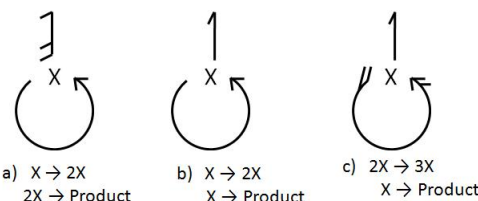


Fig. 2. Simple current cycles. a) weak (2,1; $\kappa_{exit} = 2, \kappa_{cycle} = 1$); b) critical (1,1); and c) strong (1,2).

Based on this classification is possible to categorize oscillatory reactions into two majors classes (Eiswirth *et al.*, 1991):

- Category 1. Networks containing a CCC and a destabilizing exit reaction.
- Category 2. Networks whose instability arises from a SC

Clearly, from Fig. 3, the Brusselator belongs to Category 2. On the other hand, because the Oregonator network contains a CCC and Y is generated in a chain reaction via at least one intermediate, Z , this oscillator belongs to a subdivision of Category 1, the so-called 1B.

As we can see these approaches although well documented do not reveal mathematical properties both Brusselator

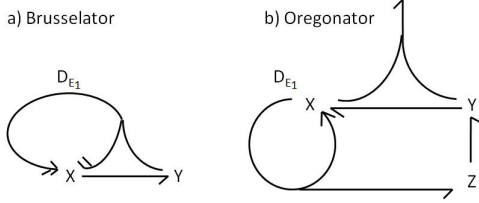


Fig. 3. Extreme current network diagrams

and Oregonator reaction mechanisms share. For example, their deficiencies are $\delta \neq \tilde{\delta}$. On the other hand, the mechanistic classification of current cycles approach also shows that both have unrelated mechanistic structure.

IV. A GRAPH THEORY APPROACH

In this section we propose a graph theoretic approach of CRN based on the information the Jacobian matrix encodes.

IV-A. Brusselator and Oregonator pseudographs

At this point some definitions from graph theory are necessary. A *pseudograph* is a graph that have self-loops and/or multi-arcs (or multi-edges). Because the Jacobian matrix is not symmetric in general, in terms of graph theory this means it defines a *directed graph*, G_D . Formally, G_D is an ordered triple $(V(G_D), A(G_D), \psi_{G_D})$ consisting of a nonempty set $V(G_D)$, of *arcs*, and an *incidence function* ψ_{G_D} that associates with each arc of G_D an ordered pair of (not necessarily distinct) vertices of G_D . If a is an arc and u, v are vertices such that $\psi_{G_D}(a) = (u, v)$, then a is said to join u to v ; u is the tail of a , and v is its head.

How the arcs are oriented is encoded in the adjacency (Jacobian) matrix. For instance, let v_1, v_2, \dots, v_ν be the vertices of a directed graph G_D . Then, the *adjacency matrix* of G_D is the $\nu \times \nu$ matrix $A = [a_{ji}]$ in which a_{ji} is the number of arcs of G_D with tail v_j and head v_i . With each arc of G_D let there be associated a real number w , called its *weight*, i.e. the entries of the Jacobian matrix.

In order to evaluate the equation (8) the extreme currents for every network are needed (see Section II). For the Brusselator we have

$$E_1 = (1, 1, 0, 0)^T \quad (11)$$

$$E_2 = (0, 0, 1, 1)^T \quad (12)$$

and for the Oregonator these are

$$\tilde{E}_1 = (0, 1, 1, 0, 1)^T \quad (13)$$

$$\tilde{E}_2 = (1, 0, 1, 1, 1)^T \quad (14)$$

Note that the steady state space of both chemical reaction networks is spanned by two vectors. Using (10) and (11) without $\text{diag}(h_1, h_2)$, the Jacobian for the Brusselator looks like

$$Jac|_{Brus} = \begin{bmatrix} j_1 - j_2 & j_1 \\ -j_1 & -j_1 \end{bmatrix} \quad (15)$$

In the same way, using (12) and (13), Oregonator's Jacobian is

$$Jac|_{Oreg} = \begin{bmatrix} -3\tilde{j}_2 & \tilde{j}_2 - \tilde{j}_1 & 0 \\ -\tilde{j}_1 & -\tilde{j}_1 - \tilde{j}_2 & \tilde{j}_1 + \tilde{j}_2 \\ \tilde{j}_1 + \tilde{j}_2 & 0 & -\tilde{j}_1 - \tilde{j}_2 \end{bmatrix} \quad (16)$$

Recalling graph definitions above and defining chemical species as vertices, the Brusselator's pseudograph is depicted in Fig. 4, and Oregonator's pseudograph in Fig. 5.

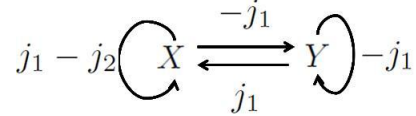


Fig. 4. Weighted directed pseudograph for Brusselator

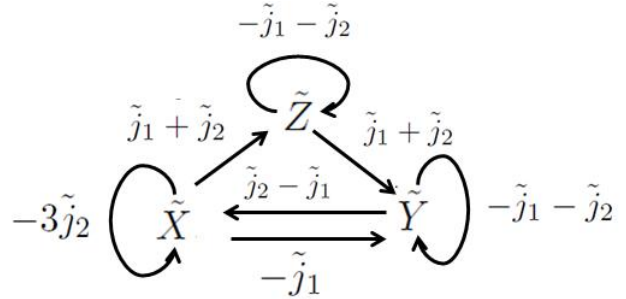


Fig. 5. Weighted directed pseudograph for Oregonator

Evidently the topology of the Brusselator's graph is embedded in the Oregonator's graph (see interaction between species $\{X, Y\}$ and $\{\tilde{X}, \tilde{Y}\}$), i. e. both graphs share that particular structure. But what happen with the weights? Is there a transformation from the weights in $Jac|_{Oreg}$ to $Jac^*|_{Oreg}$ whose linear combination of weights (entries) equals those in $Jac|_{Brus}$? The answer is yes.

$$Jac^*|_{Oreg} = T \cdot Jac|_{Oreg} \quad (17)$$

$$Jac^*|_{Oreg} \cdot (Jac|_{Oreg})^{-1} = T \quad (18)$$

Because $Jac|_{Oreg}$ is not singular, $(Jac|_{Oreg})^{-1}$ exist but T^{-1} does not have an inverse because the third row of zeroes in T .

$$T = \begin{bmatrix} \frac{\tilde{j}_2^2 - \tilde{j}_1^2 - \tilde{j}_1 \tilde{j}_2}{2\tilde{j}_2(\tilde{j}_2 - 2\tilde{j}_1)} & \frac{\tilde{j}_2^2 - 5\tilde{j}_1 \tilde{j}_2 + \tilde{j}_1^2}{2\tilde{j}_2(\tilde{j}_2 - 2\tilde{j}_1)} & \frac{\tilde{j}_2^2 - 5\tilde{j}_1 \tilde{j}_2 + \tilde{j}_1^2}{2\tilde{j}_2(\tilde{j}_2 - 2\tilde{j}_1)} \\ \frac{\tilde{j}_1(\tilde{j}_1 + 2\tilde{j}_2)}{2\tilde{j}_2(\tilde{j}_2 - 2\tilde{j}_1)} & \frac{\tilde{j}_1(4\tilde{j}_2 - \tilde{j}_1)}{2\tilde{j}_2(\tilde{j}_2 - 2\tilde{j}_1)} & \frac{\tilde{j}_1(4\tilde{j}_2 - \tilde{j}_1)}{2\tilde{j}_2(\tilde{j}_2 - 2\tilde{j}_1)} \\ 0 & 0 & 0 \end{bmatrix}$$

IV-B. Equality between graphs

We now wish to determine whether two graphs are "equal". The importance of knowing this equality lies in the fact that if a graph G_1 and G_2 are two equal graphs

which are models of two situations, then there is something basically similar about the two situations, in this case about both oscillatory mechanisms.

We refer to two equal graphs as *isomorphic graphs*. Let G_1 and G_2 be two graphs. By an *isomorphism* from G_1 to G_2 we mean a one-to-one mapping $f : V(G_1) \rightarrow V(G_2)$ from $V(G_1)$ onto $V(G_2)$ such that two vertices v_1 and v_2 are adjacent in G_1 if and only if the vertices $f(v_1)$ and $f(v_2)$ are adjacent in G_2 .

Before proceed, a graph concept that will help us to reveal in an easier way the isomorphism between Brusselator and Oregonator pseudographs, is the concept of *underlying graph*. The underlying graph of a directed graph G_D is the graph that results from removing all the designations of *head* and *tail* from the directed edges of G_D (Bondy and Murty, 1976). If there exist bidirected arcs in G_D it is a convention to represent them as a single edge in the underlying graph.

The underlying graphs of both oscillators looks like:

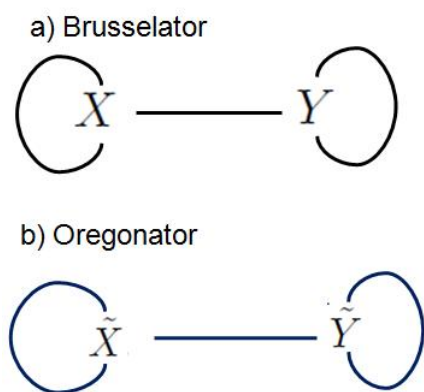


Fig. 6. Underlying graphs. a) Brusselator, b) Oregonator after transformation

Clearly from Fig. 6 both graphs are isomorphic. From a graph theoretic point of view, both mechanism are similar.

V. CONCLUSIONS

We have shown that through a transformation T of the Oregonator's Jacobian is possible to obtain the same linear combination of convex coordinates \tilde{j}_1, \tilde{j}_2 as in the Brusselator's Jacobian entries. Using this last Jacobian matrix as and adjacency matrix of a pseudograph and following some basic definitions and conventions from graph theory was possible to show that both underlying graphs are isomorphic, that is, even though in both mechanisms are present distinct chemical species reacting in different ways, these are equal from a graph theoretic point sense.

This result may shed some light on the relation both mechanisms could share from a dynamical point of view. In order to understand how the network structure and dynamic behavior are related between the Brusselator and Oregonator we conjecture that, under some assumptions, equation 1 can be expressed as a *dynamical network* (Wang

and Chen, 2003). The state equations of a network with M nodes are described by

$$\dot{x}_i = f(x_i) + c \sum_{j=1}^M a_{ij} \Gamma x_j, \quad i = 1, \dots, M \quad (19)$$

where $x_i = (x_{i1}, \dots, x_{in})^T \in \mathbb{R}^n$ are the state variables of node i , the constant $c > 0$ represents the coupling strength, and $\Gamma \in \mathbb{R}^{n \times n}$ is a constant $0 - 1$ matrix linking coupled variables. The coupling matrix $A = a_{i,j} \in \mathbb{R}^{M \times M}$ is called the Laplacian matrix, and encode the coupling configuration of the network; moreover, its diagonal elements are the negative degree of each node. On the other hand, meanwhile equation 1 stands for an isothermic batch reactor, the ODEs for a isothermic open reactor are (Gavalas, 1968)

$$\dot{x}_i = (1/\theta)f(x_i) + \sum_{j=1}^r n_{ij} v_j(k, x), \quad i = 1, \dots, s \quad (20)$$

where θ is the holding time of the reactor. At first glance, equation 20 resembles to 19, meanwhile equation 1 could be a special case when $f : \mathbb{R}_+^s \rightarrow \mathbb{0}$, $x \mapsto \mathbb{0}$. These ideas and the role of T on the Oregonator ODEs will be investigated in further studies.

VI. ACKNOWLEDGMENTS

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