Feasibility of Organizations - A Refinement of Chemical Organization Theory with Application to P Systems

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Abstract. In membrane computing, a relatively simple set of reaction rules usually implies a complex "constructive" dynamics, in which novel molecular species appear and present species vanish. Chemical organization theory (COT) is a new approach that deals with such systems by describing chemical computing as a transition between organizations, which are closed and self-maintaining sets of molecular species. In this paper we show that for the case of mass-action kinetics some organizations are not feasible in the space of concentrations and thus need not to be considered in the analysis. We present a theorem providing a criteria for an unfeasible organization. This is a refinement of organization theory making its statements more precise. In particular it follows for the design of a membrane computing system that in each compartment the desired resulting organization of a chemical computing process should be a feasible organization. Unfeasible organizations might be used as transient states in a decision process, because it is guaranteed that the system will never enter a stationary state within an unfeasible organization.

Key words: reaction networks, constructive dynamical systems, chemical organization theory, feasibility, evolution in P systems

1 Introduction

Inspired by Fontana and Buss [6], Dittrich and Speroni have developed a general definition of a chemical organization [4]. Compared to other network analysis approaches like elementary flux modes[13, 14], feedback loops[15], Petri nets [12] or deficiency [5], organization theory works on a very abstract level which allows for dealing with *constructive dynamical systems*. These systems allow for appearance and disappearance of qualitatively new variables beyond a quantitative change of a constant number of variables. They arise in *particle physics*, *chemical systems* or even in *social systems* [7] where communication can produce further, new communication. In those systems chemical organization theory can be applied for static [2, 3] and dynamic [11] analyses, description [9] or design of chemical programs [8] despite a huge number of species effecting huge non-simulatable systems or incomplete information.

Fixed points are important in the dynamical analysis of reaction systems [18]. Dittrich and Speroni have shown that every fixed point of a chemical reaction system corresponds to an organization (Theorem 1 in [4]). Given kinetic laws, there is not necessarily a fixed point for each organization. Thus, it is useful to rule out such *unfeasible* organizations. Assuming mass-action kinetics, in this paper we give a necessary and sufficient criterion for the feasibility of organizations. This criterion gives a refinement of the systems organizational structure allowing for a better description of its dynamical behavior.

Membrane computing or P systems [19, 20] also deal with the understanding of chemical reaction systems, but its focus is different. They are concerned with reaction systems distributed to several compartments. We show that in a P system membranes can effect the occurrence of organizations. In Section 2 the basic concepts of chemical organization theory are provided. In Section 3 it is introduced the feasibility of organizations in chemical organization theory, the necessary and sufficient conditions to decide if an organization is feasible for mass-action kinetics systems and it is discussed the relevance of feasibility in P systems. In Section 4 there are presented some illustrative examples showing the consequences of feasibility in chemical organization theory and the tight relation between organizations, feasibility and membranes in the dynamics of a chemical system. Finally we conclude the work with the indication of future work and open questions.

2 Chemical organization theory (COT)

This chapter provides the basics of chemical organization theory. In what follows let $\mathcal{M} = \{s_1, \ldots, s_m\}$ be a finite set of m *species* reacting with each other according to a finite set $\mathcal{R} = \{r_1, \ldots, r_n\}$ of n *reactions*. Together, the set of species and the set of reactions is called *reaction network*.

2.1 Preliminaries

Given a vector $\mathbf{k} \in \mathbb{R}^n_{>0}$ containing a strictly positive rate constant for each reaction, we can describe the dynamics of the species concentrations $\mathbf{x}$ by the ODE

$$\dot{\mathbf{x}} = \mathbf{N}\mathbf{v}(\mathbf{x}; \mathbf{k}), \tag{1}$$

where $\mathbf{N} \in \mathbb{N}^{m \times n}$ is the stoichiometric matrix and $(\mathbf{v}(\mathbf{x}; \mathbf{k}))_\mathbf{i} = \mathbf{k_i} * \prod_{\mathbf{j=1}}^{\mathbf{m}} \mathbf{x_j^{a_{ij}}}$ for $i = 1, \ldots, n$, is the *flux* according to mass-action kinetics. Here x_j denominates the concentration of the species s_j. We call ODE 1 a *chemical reaction system.*

The number $a_{ij} \in \mathbb{N}_{\geq 0}$ denominates the number of occurences of s_j in the support (reactants) of the i-th reaction. Together these numbers form a matrix

$\mathbf{A} \in \mathbb{N}^{n \times m}$. With the rate constants $\mathbf{k}$ on the diagonal of a diagonal matrix $\mathbf{K} \in \mathbb{N}^{n \times n}$ we can write

$$\mathbf{v}(\mathbf{x};\mathbf{k}) = \mathbf{K}\mathbf{x}^{\mathbf{A}}. \tag{2}$$

Definition 1. *For a reaction $r_i \in \mathcal{R}$, the set supp$(r_i) \equiv \{s_j \in \mathcal{M} : \ a_{ij} > 0\}$ is the* ***support*** *of r_i.*

Definition 2. *Let $\mathcal{P}(\mathcal{M})$ be the power set of $\mathcal{M}$ and*

$$\phi : \mathbb{R}^m_{\geq 0} \rightarrow \mathcal{P}(\mathcal{M}), \ \mathbf{x} \mapsto \phi(\mathbf{x}) \equiv \{s \in \mathcal{M} : \ x_s > 0\}. \tag{3}$$

For a state $\mathbf{x} \in \mathbb{R}^m_{\geq 0}$, the set $\phi(\mathbf{x})$ is the ***abstraction*** *of $\mathbf{x}$. For a given set of species $S \subseteq \mathcal{M}$, a state $\mathbf{x} \in \mathbb{R}^m_{\geq 0}$ is an* ***instance*** *of S if and only if its abstraction equals S.*

2.2 Chemical organizations

The following definition is the core of chemical organization theory.

Definition 3. *A subset of species $S \subseteq \mathcal{M}$ is an* ***organization*** *if and only if*

1. *S is* ***closed****, i.e. none of the reactions with support within S produces a species which is not contained in S, and*
2. *S is* ***self-maintaining****, i.e. there is a flux vector $\mathbf{v} = (v_1, ..., v_n)$ with $\mathbf{N}\mathbf{v} \geq 0$ and*

$$v_i \begin{cases} > 0 \ \Leftrightarrow \ \mathit{supp}(r_i) \subseteq S, \\ = 0 \ \mathit{otherwise.} \end{cases}$$

The following Theorem from [4] relates fixed points to organizations.

Theorem 1. *If $\mathbf{x}$ is a fixed-point of the ODE 1, i.e. $\mathbf{N}\mathbf{v}(\mathbf{x};\mathbf{k}) \geq 0$, then the abstraction $\phi(\mathbf{x})$ is an organization.*

Proofs can be found in [4] and [11].

Remark 1. Since fixed points play a crucial role in the analysis of dynamical systems [18], Theorem 1 provides a link between the behavior of a chemical reaction system and its underlying set of reactions. This justifies the study of the systems dynamics by chemical organization theory. In particular, organizations appear in the long-term behavior of chemical reaction systems making the observation of organizations in such systems provable [11].

Remark 2. The converse of Theorem 1 does not hold in general, i.e., given a chemical reaction system, the underlying reaction network can exhibit an organization O for which there is no fixed point with abstraction equal to O. This *unfeasibility* is studied in the next chapter.

3 Feasibility

In this section we introduce and study the feasibility of an organization. In what follows assume that $O \equiv \mathcal{M}$ is an organization.

3.1 Definitions

We are going to introduce the notations required to state the main theorem.

Definition 4. *O is **feasible** with respect to $\mathbf{k}$ if and only if there is a vector of concentrations $\mathbf{x} \in \mathbb{R}^m_{>0}$ such that*

$$\mathbf{N}\mathbf{v}(\mathbf{x};\mathbf{k}) \geq \mathbf{0}. \tag{4}$$

*O is **feasible** if and only if it is feasible with respect to each $\mathbf{k} \in \mathbb{R}^n_{>0}$. Otherwise it is **unfeasible**.*

Now we define the image $Im(\mathbf{A})$ of the matrix $\mathbf{A}$ and the set $Ker^{\geq 0}_{\geq 0}(\mathbf{N})$ derived from the kernel of the matrix $\mathbf{N}$ by only allowing for vectors with all components strictly positive and fulfilling an inequality instead of the equality required for the definition of the kernel.

Definition 5. *We define*

$$Im(\mathbf{A}) \equiv \{\mathbf{y} : \mathbf{y} = \mathbf{A}\mathbf{x},\, \mathbf{x} \in \mathbb{R}^m\}, \tag{5}$$

$$Ker^{\geq 0}_{\geq 0}(\mathbf{N}) \equiv \{\mathbf{v} \in \mathbb{R}^n_{>0} :\; \mathbf{N}\mathbf{v} \geq \mathbf{0}\}. \tag{6}$$

Next we define the application of the logarithm function to vectors and sets of vectors.

Definition 6. *For a set U of vectors, a vector $\mathbf{u} = (\mathbf{u}_1, \mathbf{u}_2, ...) \in U$ and a number $\beta > 0$ we define*

$$log_\beta(\mathbf{u}) \equiv (log_\beta(\mathbf{u}_1), log_\beta(\mathbf{u}_2), \ldots)^T, \tag{7}$$

$$log_\beta(U) \equiv \{\mathbf{w} : \mathbf{w} = log_\beta(\mathbf{u}),\, \mathbf{u} \in U\}, \tag{8}$$

where superscript T denotes vector transposition.

Lastly, we define arithmetic operations over sets of vectors.

Definition 7. *For sets U, V of vectors we define*

$$U + V \equiv \{\mathbf{w} : \mathbf{w} = \mathbf{u} + \mathbf{v},\, \mathbf{u} \in U, \mathbf{v} \in V\}. \tag{9}$$

3.2 Theorem

Now we state the main theorem which gives a necessary and sufficient criterion for feasibility in mass-action kinetics.

Theorem 2. *O is feasible if and only if*

$$\mathbb{R}^n \setminus (log_\beta(Ker^{>0}_{\geq 0}(\mathbf{N})) - Im(\mathbf{A})) = \emptyset. \tag{10}$$

Proof. For any $\beta > 0$, O is feasible if and only if

$$\forall \mathbf{k} \in \mathbb{R}^n_{>0}\, \exists \mathbf{x} \in \mathbb{R}^m_{>0} : \mathbf{N}\mathbf{v}(\mathbf{x};\mathbf{k}) \geq \mathbf{0} \tag{11}$$

$$\overset{\text{Eq. 2}}{\Longleftrightarrow}$$

$$\forall \mathbf{k} \in \mathbb{R}^n_{>0}\, \exists \mathbf{x} \in \mathbb{R}^m_{>0}, \hat{\mathbf{v}} \in \mathbb{R}^n_{>0} : \mathbf{N}\hat{\mathbf{v}} \geq \mathbf{0} \wedge \hat{\mathbf{v}} = \mathbf{v}(\mathbf{x};\mathbf{k}) = \mathbf{K}\mathbf{x}^{\mathbf{A}} \tag{12}$$

$$\overset{\text{Def. 5}}{\Longleftrightarrow}$$

$$\forall \mathbf{k} \in \mathbb{R}^n_{>0}\, \exists \mathbf{x} \in \mathbb{R}^m_{>0}, \hat{\mathbf{v}} \in Ker^{>0}_{\geq 0}(\mathbf{N}) : \hat{\mathbf{v}} = \mathbf{K}\mathbf{x}^{\mathbf{A}} \tag{13}$$

$$\Leftrightarrow$$

$$\forall \mathbf{k} \in \mathbb{R}^n_{>0}\, \exists \mathbf{x} \in \mathbb{R}^m_{>0}, \hat{\mathbf{v}} \in Ker^{>0}_{\geq 0}(\mathbf{N}) : log_\beta(\hat{\mathbf{v}}) = log_\beta(\mathbf{k}) + \mathbf{A} * log_\beta(\mathbf{x}) \tag{14}$$

$$\Leftrightarrow$$

$$\forall \mathbf{k} \in \mathbb{R}^n_{>0}\, \exists \mathbf{x} \in \mathbb{R}^m_{>0}, \hat{\mathbf{v}} \in Ker^{>0}_{\geq 0}(\mathbf{N}) : log_\beta(\mathbf{k}) = log_\beta(\hat{\mathbf{v}}) - \mathbf{A} * log_\beta(\mathbf{x}) \tag{15}$$

$$\overset{\hat{\mathbf{k}} \equiv log_\beta(\mathbf{k})}{\Longleftrightarrow}$$

$$\forall \hat{\mathbf{k}} \in \mathbb{R}^n\, \exists \mathbf{x} \in \mathbb{R}^m_{>0}, \hat{\mathbf{v}} \in Ker^{>0}_{\geq 0}(\mathbf{N}) : \hat{\mathbf{k}} = log_\beta(\hat{\mathbf{v}}) - \mathbf{A} * log_\beta(\mathbf{x}) \tag{16}$$

$$\overset{\mathbf{y} \equiv \mathbf{A} * log_\beta(\mathbf{x})}{\Longleftrightarrow}$$

$$\forall \hat{\mathbf{k}} \in \mathbb{R}^n\, \exists \mathbf{y} \in Im(\mathbf{A}), \hat{\mathbf{v}} \in Ker^{>0}_{\geq 0}(\mathbf{N}) : \hat{\mathbf{k}} = log_\beta(\hat{\mathbf{v}}) - \mathbf{y} \tag{17}$$

$$\overset{\mathbf{w} \equiv log_\beta(\hat{\mathbf{v}})}{\Longleftrightarrow}$$

$$\forall \hat{\mathbf{k}} \in \mathbb{R}^n\, \exists \mathbf{y} \in Im(\mathbf{A}), \mathbf{w} \in log_\beta(Ker^{>0}_{\geq 0}(\mathbf{N})) : \hat{\mathbf{k}} = \mathbf{w} - \mathbf{y}, \tag{18}$$

$$\Leftrightarrow$$

$$\mathbb{R}^n \setminus (log_\beta(Ker^{>0}_{\geq 0}(\mathbf{N})) - Im(\mathbf{A})) = \emptyset. \tag{19}$$

Theorem 2 reveals how both the structure of the supports of the reactions (represented by $\mathbf{A}$) and the stoichiometric matrix $\mathbf{N}$ restrict the possible flux vectors. When the set of restrictions has a special structure the organization O is unfeasible. That means that there are rate constants such that there exist no species concentrations to build up a flux vector $\mathbf{v}$ which is in $Ker^{>0}_{\geq 0}(\mathbf{N})$.

Remark 3. The set $log_\beta(Ker^{>0}_{\geq 0}(\mathbf{N}))$ is not a linear vector space with respect to addition. This makes difficult the computational verification of Theorem 2 by methods from linear algebra.

As a consequence of Theorem 2 we get the following statement about the existence of fixed points.

Corollary 1. *If the set* $\mathbb{R}^n \setminus (log_\beta(Ker^{\geq 0}_{\geq 0}(\mathbf{N})) - Im(\mathbf{A}))$ *is not empty, then there are rate constants* $\mathbf{k}$ *such that the ODE 1 has no fixed point with abstraction equal* O*.*

Proof. We assume that the set $\mathbb{R}^n \setminus (log_\beta(Ker^{\geq 0}_{\geq 0}(\mathbf{N})) - Im(\mathbf{A}))$ is not empty. Then from Theorem 2 follows that O is unfeasible. Then there exists a vector of rate constants $\mathbf{k}$ such that O is not feasible with respect to this $\mathbf{k}$ (Definition 4). Also from Definition 4 follows that then for all vectors of concentrations $\mathbf{x} \in \mathbb{R}^m_{>0}$ the inequality

$$\mathbf{Nv}(\mathbf{x}; \mathbf{k}) \geq \mathbf{0} \tag{20}$$

does not hold. Particularly, $\mathbf{Nv}(\mathbf{x}; \mathbf{k}) \neq \mathbf{0}$ for all $\mathbf{x} \in \mathbb{R}^m_{>0}$, *i.e.*, there exists no fixed point with abstraction equal O for the ODE 1.

Remark 4. If the set $\mathbb{R}^n \setminus (log_\beta(Ker^{\geq 0}_{\geq 0}(\mathbf{N})) - Im(\mathbf{A}))$ is empty, there can also exist rate constants such that the ODE 1 has no fixed point with abstraction equal O. The reason is that $\mathbf{Nv}(\mathbf{x}; \mathbf{k}) \geq \mathbf{0}$ does not imply $\mathbf{Nv}(\mathbf{x}; \mathbf{k}) = \mathbf{0}$. And fixed points require strict equality.

3.3 Feasibility in P systems

Now we know that the set of species representing an unfeasible organization O is not probable to be observed in a single chemical reaction system which represents one compartment of a P system. We will show in the next section that membranes can compensate for this phenomenon (cf. Example 5): a membrane can provide several compartments each possibly containing different subsets of species (feasible organizations) such that there union is O. In this case, the unfeasibility of organization O can be attributed to an *incompatibility* of two smaller feasible organizations. I.e., whenever an unfeasible organization O can be written as union of feasible organizations, membranes can allow for the appearance of O even though it is unfeasible, because the membranes help to separate properly the incompatible organizations. Furthermore, we will show that, even when an exchange of molecules is permitted between the compartments, the unfeasible organization can be maintained in time. Thus, in a P system, membranes can allow for the appearance of those sets of species which - following the refinement of chemical organization theory stated in the previous sections - could not appear if there would not be a membrane. This implies that destruction of membranes can lead also to the opposite effect, destabilizing the equilibria process described above between unfeasible organizations (partially or totally) separated by the membranes.

4 Examples

In this section there are shown different aspects of the unfeasibility as well as its relation with P systems. In this section is used the notation of Theorem 2. The following two examples show straight consequences of Theorem 2:

Example 1 Let $\mathcal{M} = \{s_1, s_2\}$ and $\mathcal{R} = \{s_1 \to s_2, s_2 \to s_1\}$. We have

$$\mathbf{A} = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}, \quad \mathbf{N} = \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix}.$$

Note that

$$Im(\mathbf{A}) = \mathbb{R}^2, \quad Ker^{\geq 0}_{\geq 0}(\mathbf{N}) = \{(v_1, v_2) \in \mathbb{R}^2_{>0} : \ v_1 = v_2\}.$$

Then we have

$$\mathbb{R}^2 \setminus (log_\beta(Ker^{\geq 0}_{\geq 0}(\mathbf{N})) - Im(\mathbf{A})) = \emptyset.$$

Thus, $\mathcal{M}$ is feasible. We are going to verify this.
We have to solve the system

$$\mathbf{Nv(x)} = \mathbf{NKx^A} = \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix} \begin{pmatrix} k_1 x_1 \\ k_2 x_1 \end{pmatrix} \geq 0. \tag{21}$$

Where k_i and x_i are the rate constants of reaction r_i and the concentration of the molecule x_i for $i = 1, 2$, respectively. Then, $\mathbf{Nv(x)} \geq 0$ iff $x_1 = \frac{k_2}{k_1} x_1$. The later equation has solution for all strictly positive rate constants $\mathbf{k} = (k_1, k_2)$, thus we conclude $\mathcal{M}$ is feasible.

Example 2 Let $\mathcal{M} = \{s_1, s_2\}$ and $\mathcal{R} = \{s_1 + s_2 \to 2s_2, s_1 + s_2 \to 2s_1\}$. Then we have

$$\mathbf{A} = \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix}, \quad \mathbf{N} = \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix}.$$

Note that

$$Im(\mathbf{A}) = \{(v_1, v_2) \in \mathbb{R}^2 : \ v_1 = v_2\} = Ker^{\geq 0}_{\geq 0}(\mathbf{N}) \tag{22}$$

$$\Rightarrow$$

$$Im(\mathbf{A}) - log_\beta(Ker^{\geq 0}_{\geq 0}(\mathbf{N})) = \{(v_1, v_2) \in \mathbb{R}^2_{>0} : \ v_1 = v_2\} \tag{23}$$

$$\Rightarrow$$

$$\mathbb{R}^n \setminus (Im(\mathbf{A}) - log_\beta(Ker^{\geq 0}_{\geq 0}(\mathbf{N}))) \neq \emptyset. \tag{24}$$

Thus, for this example $\mathcal{M}$ is unfeasible. Now we are going to verify that $\mathcal{M}$ is not feasible with respect to all rate constants $\mathbf{k}$ for which $k_1 \neq k_2$. We have to solve the system

$$\mathbf{Nv(x)} = \mathbf{NKx^A} = \begin{pmatrix} -1 & 1 \\ 1 & -1 \end{pmatrix} \begin{pmatrix} k_1 x_1 x_2 \\ k_2 x_1 x_2 \end{pmatrix} \geq 0. \tag{25}$$

Where k_i and x_i are the rate constants of reaction r_i and the concentration of the molecules x_i for $i = 1, 2$, respectively. Then, $\mathbf{Nv(x)} \geq 0$ is solvable if and only if $k_1 x_1 x_2 = k_2 x_1 x_2$,*i.e.* $k_1 = k_2$. Thus, $\mathcal{M}$ is unfeasible, because $\mathcal{M}$ is not feasible with respect to any rate constant vector $\mathbf{k} \in \mathbb{R}^2_{\geq 0}$. $\mathcal{M}$ is feasible only with respect to rate constant vectors $\mathbf{k} = (k_1, k_2)$ which fulfills $k_1 = k_2$.

Remark 5. Note that in Examples 1 and 2 it is obtained the same stoichiometric matrix from the reactions which defines the system. But in Example 1 the organization $\{s_1, s_2\}$ is feasible and in Example 2 the organization $\{s_1, s_2\}$ is not feasible. Then we conclude that feasibility is a phenomena which is beyond the stoichiometric information.

Example 3 In this example it is shown a way to build unfeasible organizations. We will use a reaction network of four molecular species and four reactions, but the method we are going to exemplify could be done for any set of molecules and reactions. Let $\mathcal{M} = \{s_1, s_2, s_3, s_4\}$ and x_i the concentration of species s_i for $i = 1, ..., 4$. We are going to build $\mathcal{R}$ such that $\mathcal{M}$ would be an unfeasible organization. First we are going to choose $Ker^{>0}_{\geq 0}(\mathbf{N})$ such that $log_\beta(Ker^{>0}_{\geq 0}(\mathbf{N})) \underset{\neq}{\subseteq} \mathbb{R}^n$ (In other case $\mathcal{M}$ would be feasible without necessity of knowing $\bar{\mathbf{A}}$). For simplicity we choose

$$Ker^{>0}_{\geq 0}(\mathbf{N}) = \{(v, v, v, v) : \; v > 0\}.$$

Now we are going to choose the support of the reactions:

$$\begin{aligned} \mathbf{v}(\mathbf{x}) = (&k_1 x_1 x_2, \\ &k_2 x_1 x_3, \\ &k_3 x_3 x_4, \\ &k_4 x_4 x_2). \end{aligned} \tag{26}$$

Note there are two shared species between every triad of reactions, this would help to obtain the unfeasibility. As we already know $Ker^{>0}_{\geq 0}(\mathbf{N})$, we can choose some relation between the rate constants in order to obtain contradictory concentration equations for every vector in $Ker^{>0}_{\geq 0}(\mathbf{N})$ fulfilling mass-action kinetics (Equation 4). Note that to every flux vector which verifies the self-maintenance property of $\mathcal{M}$ has to hold that $k_1 x_1 x_2 = k_2 x_1 x_3 = k_3 x_3 x_4 = k_4 x_4 x_2$. We are going to prove that if $k_1 > k_2$ and $k_3 > k_4$ the organization is unfeasible with respect to $\mathbf{k}$. By the first and second reactions we have $k_1 x_1 x_2 = k_2 x_1 x_3$. As $k_1 > k_2$ we have

$$x_3 > x_2. \tag{27}$$

By third and fourth reaction we have $k_3 x_3 x_4 = k_4 x_4 x_2$. As $k_3 > k_4$ we have

$$x_2 > x_3. \tag{28}$$

We have a contradiction. Note that if we would choose $k_1 < k_2$ and $k_3 < k_4$ we would obtain also a contradiction. Now we just have to build up the stoichiometric matrix by choosing the produced species of each reaction, in order to keep $Ker^{>0}_{\geq 0}(\mathbf{N})$ as it was stated at the beginning of the example. Choosing the reactions:

$$\begin{aligned} s_1 + s_2 &\to 2s_1, \\ s_1 + s_3 &\to 2s_2, \\ s_3 + s_4 &\to 2s_3, \\ s_2 + s_4 &\to 2s_4, \end{aligned} \tag{29}$$

where species s_i has concentration x_i for $i = 1, ..., 4$, the network defined in (29) keeps $Ker^{\geq 0}_{\geq 0}(\mathbf{N})$ as it was stated at the beginning of this example, then the organization $\{s_1, s_2, s_3, s_4\}$ is unfeasible. Theorem 2 confirms this.

Remark 6. It is interesting that in Example 2 both reactions have the same support. Example 3 shows that even if all reactions have different supports, the organization can be unfeasible.

Remark 7. In Example 3, note that if we would have choosen $Ker^{\geq 0}_{\geq 0}(\mathbf{N}) = \{(v_1, v_2, v_3, v_4) : \ v_1 \geq v_2 \geq v_3 \geq v_4\}$ and the same support for the reactions, it would be obtained the same contradictions stated in Equations 27 and 28 when $k_1 > k_2$ and $k_3 > k_4$. In the opposite case, if we would have choosen $Ker^{\geq 0}_{\geq 0}(\mathbf{N}) = \{(v_1, v_2, v_3, v_4) : \ v_1 \leq v_2 \leq v_3 \leq v_4\}$ it would be obtained the contradictions when $k_1 < k_2$ and $k_3 < k_4$. In both cases mentioned above, the stoichiometric matrix which keeps $Ker^{\geq 0}_{\geq 0}(\mathbf{N})$ would look quite different to the stoichiometric matrix of Example 3.

Remark 8. The contradiction which we found between Equations 27 and 28 can be thought as a *game* where given $Ker^{\geq 0}_{\geq 0}(\mathbf{N})$, it has to be chosen the support of the reactions and the relation between rate constants to obtain a system of Equations $\mathbf{Nv} \geq 0$ with no solution.

The unfeasible organizations shown in the previous examples were composed by non-reactive organizations, this means any organization which is (strictly) contained in the unfeasible organization mentioned in every previous example verifies its self-maintenance by an empty flux vector.

Definition 8. *An organization is non-reactive if its self-maintainance is verified by an empty flux vector.*

From the point of view of combining organizations, what is shown in the previous examples is that combining non-reactive (trivially feasible) organizations it is possible to obtain an unfeasible organization. An interesting question is that if it is possible the emergence of an unfeasible organization from combining feasible and reactive organizations. The next example shows the positive answer to that question.

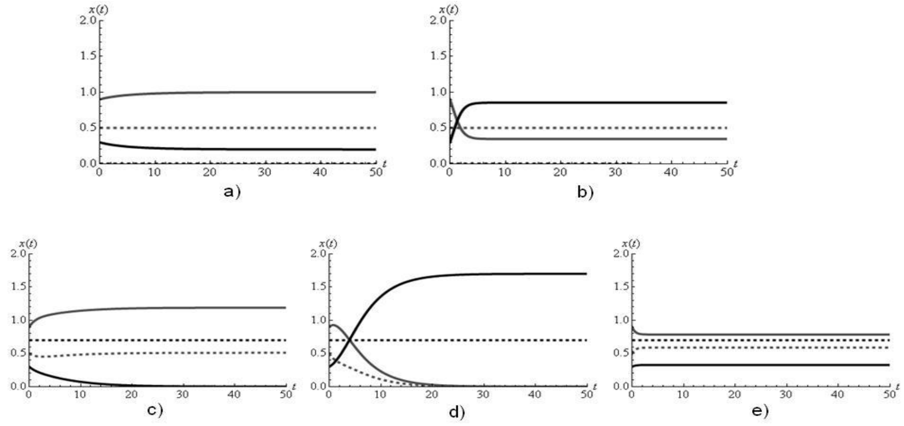
Example 4 In this example we are going to show that unfeasibility can be also generated by incompatibility between reactive organizations.

Let $O_8 = \{s_1, s_2, s_3\}$, $O_7 = \{s_1, s_2, s_4\}$, $\mathcal{M} = O_8 \cup O_7$ and $\mathcal{R} = \{r_1, r_2, r_3, r_4\}$, where

$$\begin{aligned} r_1 &= s_1 + s_3 \to 2s_3, \\ r_2 &= s_2 + s_3 \to s_1 + s_2, \\ r_3 &= s_s + s_4 \to 2s_4, \\ r_4 &= s_1 + s_4 \to s_1 + s_2. \end{aligned}$$

Let x_i the concentration of s_i and k_i the rate constants of r_i for $i = 1, ..., 4$. Note that O_8 and O_7 are both feasible (and reactive) organizations, but together they

form $\mathcal{M}$ which is an unfeasible organization. This is because under $k_1 < k_2$ and $k_3 > k_4$ (or $k_1 > k_2$ and $k_3 < k_4$) the flux vector which verifies the self maintainance of $\mathcal{M}$ has to hold $x_1 > x_2$ and $x_2 > x_1$ simultaneously[1].
For the results of simulations of this example see Figure 1 and Figure 2 (Left).



a) b)

c) d) e)

Fig. 1. Evolution of the concentrations in mass-action kinetics. The concentration of s_1, s_2, s_3, s_4 are grey, grey-dashed, black and black-dashed respectively. Figures **a**) and **b**) shows the evolution in time beggining from an instance of the organization O_8 for two different sets of rate constants. Thus, despite changing the rate constants, the evolution of O_8 in **a**) and **b**) is structurally the same, asymptotic convergence to a fixed point corresponding to O_8, i.e. all species are *persistent.* This is possible since O_8 is feasible. Beginning from O_7 we obtain the same behavior (not shown in the figures) because of its feasibility. Figures **c**),**d**),**e**) show the evolution of concentrations beginning from an instance of $\mathcal{M}$ for three different sets of rate constants, such that $\mathcal{M}$ is unfeasible with respect to the rate constants chosen for Figures **c**) and **d**) and feasible with respect to the rate constants chosen for **e**). The system asymptotically tends to the reactive organization O_7 (Figure **c**)), the non-reactive organization $O_5 \equiv \{s_3, s_4\}$ (Figure **d**)) or $\mathcal{M}$ (Figure **e**)). Non-persistence of $\mathcal{M}$ in cases **c**) and **d**) is predicted by the unfeasibility of $\mathcal{M}$. The situation is illustrated within the lattice of organizations in Figure 2 (Left).

Example 5 In this example we show how feasibility and membranes are complementary concepts to understand the asymptotic behaviour in biological systems.

We are going to define a P system of two membranes, one internal and the other external, such that there are an inner and an outer compartment. Both compartments have the same reaction rules (we are going to use the reactions of Example 4), and we are going to allow exchange of molecules through the

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[1] To verify this it is required to build $Ker^{\geq 0}_{\geq 0}(\mathbf{N})$ and check that under those rate constants no flux vector can follow mass-action kinetics and simultaneously verify the self-maintainance property.

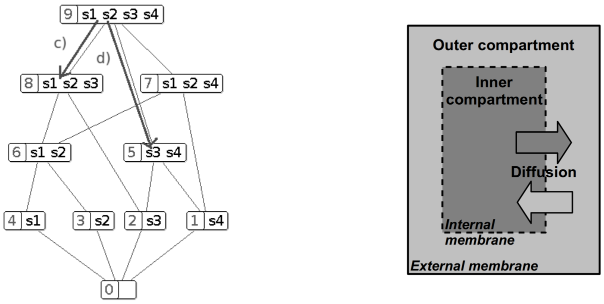

Fig. 2. Left: Lattice of organizations of Example 4. Each rectangle stands for an organization. There is a thin line between two organizations of different sizes iff the smaller organization is a subset of the bigger one and no other organization is between them. The arrows denote the (down-)movement in time from the unfeasible organization O_9 to the feasible organization O_8 (cf. Fig. 1 (c)), and to the non-reactive organization O_5 (cf. Fig. 1 (d)). **Right:** Diagram of the P system of Example 5. There are two compartments each surrounded by a membrane. The membranes allows exchange-diffusion of molecules between compartments. Within each compartment the reaction rules are the same. But due to different initial conditions, different rate constants (for the same set of reactions) in each compartment, the species concentrations can differ and different organizations can appear in each compartment.

internal membrane (from the inner to outer compartment and *vice versa*). See Figure 2 (Right) for an illustration.

We allow that reactions are fired with different rate constants in the inner and outer compartment (this assumption is theoretically plausible for example in charged membranes). This fact makes possible the *coexistence* of the two incompatible organizations O_7 and O_8 of Example 4 (one organization in each compartment), and thus when considering the P system as a whole, we have that the organization O_9 increases its rates-region of feasibility because of the exchange reactions . Furthermore, for some exchange rates the resulting behaviour is an asymptotic stability of O_9 in each compartment, but in an oscillatory regime (if the membrane is destroyed this equilibrium is broken). Finally, for certain exchange rates, the asymptotic behavior of a feasible and reactive organization is a non-reactive organization, this implies that the creation/destruction of membranes can also break the stability of feasible organizations. See Figure 3 for simlations showing these phenomena.

5 Conclusions

We have shown that, given a kinetic law of mass-action type, feasibility can be computed for each organization, i.e. whether it has a corresponding fixed point in the ODE (Eq. 1) or not. This complements the fixed point theorem (Theorem 1 in [4]) and refines the information organization theory can give about a systems dynamics. We presented an intuitive way to build unfeasible organiza-

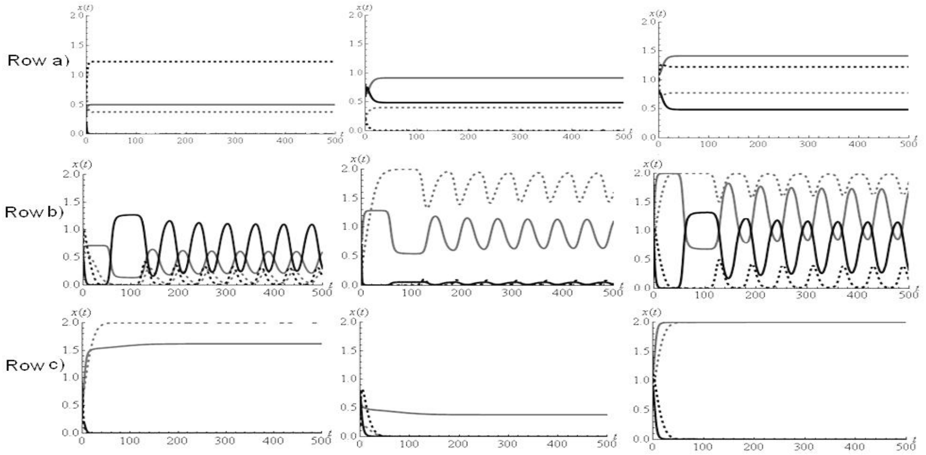

Fig. 3. In all plots the grey, grey-dashed, black, black-dashed curve represents the concentration of s_1, s_2, s_3, s_4 respectively. In rows **a)**, **b)** and **c)** the left plot shows the concentration of molecules in the inner compartment, the middle plot shows the concentration of the outer compartment and the right plot shows the sum of inner and outer concentrations (the total concentration in the P system considered as a whole). The plots in row **a)** shows the P system when the exchange rate constants are switched to zero (compartments do not interact each other). We see that the inner compartment tends to O_7 and outer compartment to O_8, and thus the P system considered as a whole tends to O_9. The plots in row **b)** show the same system as in row **a)**, but permitting exchange of molecules through the membranes. It is observed an oscillatory regime in which O_9 is maintained in both compartments, because the exchanged molecules support the long-term stability of the system. This oscillatory regime is not possible in a single membrane system. The plots in row **c)** shows again the same system as in **a)** but with different exchange-rate constants. This time the exchange reactions lead in asymptotic regime to the non-reactive organization O_6.

tions (cf. Example 3). We have shown that the unfeasibility can emerge from combining reactive as well as non-reactive feasible organizations. This means the phenomena of unfeasibility is potentially present in any reaction network. Thus, terms like feasibility or incompatibility of organizations can give rise to formalizations of various ecological-like phenomena in nature, e.g., competition, symbiosis, depredation, etc. (cf. Example 2, 4 and 5). We succesfully applied chemical organization theory to P systems: We have shown that in a P system creation and destruction of membranes allow for the occurrence of unfeasible organizations as well as destruction of feasible organizations, thus enriching the set of possible behaviors of a chemical reaction system.

The interface of COT and P systems provides a wide field for further research promising new analysis techniques for reaction networks. E.g., the concept of compatibility of organizations informally introduced in this paper could be further developed and applied to the above mentioned ecological-like concepts. Future work should also be concerned with the relation between different kinetic laws and feasibility of organizations. Furthermore it should be analyzed how complicated it is to determine feasibility automatically since methods from linear algebra do not suffice.

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